KUWAIT MEDICAL JOURNAL
KMJ
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KMJ
KUWAIT MEDICAL JOURNAL

The Official Journal of The Kuwait Medical Association

EDITORIAL

REVIEW ARTICLE

ORIGINAL ARTICLES

CASE REPORTS

KU ISSN 0023-5776

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Vol. 47 No. 3 SEPTEMBER 2015

KUWAIT MEDICAL JOURNAL

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IMEMR Current Contents (*Index Medicus* for the Eastern Mediterranean Region; available online at: www.emro.who.int/EMRJorList/online.aspx

PUBLISHER: The Kuwait Medical Journal (KU ISSN-0023-5776) is a quarterly publication of THE KUWAIT MEDICAL ASSOCIATION. Address: P.O. Box 1202, 13013 Safat, State of Kuwait; Telephone: 1881181 Fax: 25317972, 25333276. E-mail : kmj@kma.org.kw

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Kuwait Medical Journal (KMJ)

Published by the Kuwait Medical Association
Previously known as The Journal of the Kuwait Medical Association (Est. 1967)

EDITORIAL ADDRESS

P.O. Box: 1202, 13013-Safat, Kuwait
Telephone: (00-965) 1881181(Ext. 201) - Fax: (00-965) 25317972, 25333276
E-mail: kmj@kma.org.kw
Website: www.kma.org.kw/KMJ

KUWAIT MEDICAL JOURNAL (KMJ)
Instructions for Authors

INTRODUCTION

Formerly known as 'The Journal of the Kuwait Medical Association', the Kuwait Medical Journal (KMJ) was established in the year 1967. It is the official publication of the Kuwait Medical Association and published quarterly and regularly in March, June, September and December.

AIMS AND SCOPE

KMJ aims to publish peer-reviewed manuscripts of international interest. Submissions on clinical, scientific or laboratory investigations of relevance to medicine and health science come within the scope of its publication. **Original articles, case reports, brief communications, book reviews, insights and letters to the editor are all considered. Review articles are solicited.** Basic medical science articles are published under the section 'Experimental Medicine'.

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and References followed by (if relevant), Legends to figures, Tables, and Figures. Details of the section contents are explained below for further adherence.

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EXAMPLES

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Burrows B, Lebowitz MD. The β agonists dilemma (editorial). N Engl J Med 1992; 326:560-561.

Book

Roberts NK. The cardiac conducting system and His bundle electrogram. New York, Appleton-Century-Crofts, 1981; 49-56.

Book chapter

Philips SJ, Whisnam JP. Hypertension and stroke, In: Laragh JH, Bremner BM, editors. Hypertension: pathophysiology, diagnosis, and management. 2nd Ed. New York: Raven Press; 1995. p 465-478.

Weblinks

U.S. positions on selected issues at the third negotiating session of the Framework Convention on Tobacco Control. Washington, D.C.: Committee on Government Reform, 2002. (Accessed June 4, 2003, at http://www.house.gov/reform/min/inves. tobacco/ index_accord.htm.)

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The Kuwait Foundation for the Advancement of Sciences

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Editorial

Modern Medicine: a Trick Or a Trade?

Belle M Hegde
[1]The Journal of the Science of Healing Outcomes, State College, Pennsylvania, USA and Mangalore, India
[2]Manipal University, Manipal India
[3]The Middlesex Medical School, University of London, UK
[4]Northern Colorado University, USA

Kuwait Medical Journal 2015; 47 (3): 189 - 192

"Surgeons must be very careful
When they take the knife!
Underneath their fine incisions
Stirs the culprit-Life!"

Emily Dickinson (1830-1886) **

The British Medical Journal dated 2nd August 2002 had a very interesting editorial by the editor, Dr. Richard Smith himself. My letter to the editor in the same issue runs like this:

I have been saying this for a long time!

4 August 2002
Dear Richard,

Congratulations! You have hit the nail on its head in your editorial. Jonathan Swift was dead right. "Knowledge" wrote Karl Popper "advances not by repeating known facts, but by refuting false dogmas". One of the greatest dogmas in modern medicine is that drugs and surgical procedures only cure illnesses. It is the immune system that really heals. The latter needs to be assisted.

I teach my students that if anyone wants to preserve his/her health intact, he/she should avoid hospitals and doctors to the extent possible, but when one is ill, one needs to see a doctor without delay and be a partner in the management. Most of what we do today in modern medicine reminds me of what our ancestors did by branding for every major illness and bloodletting to cure, swearing by their efficacy. We are able to comfort most of the time, which our forefathers in medicine could not achieve. That is the progress we have achieved in the last century, though. Hippocrates could well be right when he said: "cure rarely, comfort mostly, but console always."

Modern medical claptrap, assisted by the drug industry and instrument manufacturers, has made doctors forget their greatest role in consoling every patient.

The false sense of faith in our scanners, scopes, and the powerful chemicals and the heroic surgical techniques (poor patient playing the hero's role, though), has made us forget our primary role of consoling the suffering patients who still have confidence in us. Most drugs harm the system in the long run; there are hardly any exceptions, although they do help when given for symptom relief for a short period of time. There are exceptions to every rule and it is the exceptions that prove the rule. While there is no pill for every ill, every pill has some ill following its use.

Time really is ripe for more openness in our work. We need very bold editors, indeed!

Yours,
bmhegde (copied from the eBMJ)

I know most of you won't believe this, but this is exactly what I have been writing for nearly four decades. Some of my colleagues and many in the industry have been very angry with me. Truth is always bitter but has to be exposed, sometime or the other, for the good of humanity at large. Doctors are being brainwashed from day one at the medical school[1]. The public, especially the so-called "literate class," is being systematically influenced through doctored articles in magazines and advertisements in print and electronic media. Medical profession would do well to remember the prophetic words of Jonathan

Address correspondence to:
Prof. B M Hegde, MD, FRCP, FRCPE, FRCPG, FRCPI, FACC, FAMS, "Manjunath", Pais Hills, Bejai, Mangalore 575004, India; Tel: +91 824 245 0450, E-mail: hegdebm@gmail.com, website: www.bmhegde.com
[1]Editor in Chief; [2]Cardiologist & Former Vice Chancellor (Retd), [3]Former Visiting Professor of Cardiology, [4]Affiliate Professor of Human Health

Swift, one of the most admired Irish authors:

"Satire is like a glass through which the observer could see everyone else's face but his own."

It is time that the medical world had a better look at its own face to mend things. I was amazed to read an article extolling the virtues of coronary angioplasty in the Sunday magazine section of one of the leading Indian newspapers, while the truth is that almost all the large prospective studies from 1978 to 2000 did not show this procedure in good light; the latter fact was left out in the narrative, knowingly or unknowingly, by the learned author! [2]

In an unprecedented move, The Times, London published an article on the 3rd August 2002, exposing the hazards of the "white coat hypertension", an entity where the hapless healthy person is labelled as hypertensive by the cursory check by the doctor on routine screening. If the individual is healthy, his blood pressure should go up marginally (in some studies even as much as 20 - 30 mm of Hg systolic) due to the sheer anxiety of seeing the doctor. This entity adds millions of healthy individuals to the label of hypertension. Almost all of them receive lifelong expensive medications to lower that pressure. Future predictions of epidemics are based on this kind of data! Interestingly, the latest JNC VIII, the body that gives BP guidelines opines that the normal BP for an adult could be up to 159/99 and if s/he is a diabetic, it could be 140/90[3]. In my book of hypertension written in 1993, I had proposed this level and critics were baying for my blood[4].

Doctors are made to believe that they are practising this kind of medicine in the long-term interest of their patients lest the latter should get life threatening complications decades later! Lay press calls hypertension the "silent killer" and creates more anxiety. This pushes up the BP of all hypochondriacs. The fact, however, is that after the first five years on drugs, the projected death rate in drug controlled hypertensives gradually goes up three times compared to their normotensive cousins[5]. I have even written a book on this enigma called "white-coat hypertension," but who cares? Patients are made to believe that they are protecting themselves against future dangers. Both are untrue, scientifically[6].

"We shall not cease from explorations
And the end of exploring
Will be to arrive where we started
And know the place for the first time."

T.S. Eliot

Identical logic, syllogism of Aristotle, is invading the field of human blood sugar measurements in healthy people. Drug companies are getting doctored data to show that high risk people (what does that mean?) would do well to take quite expensive medicine, glitazide, and rosiglitazone even when their sugar levels are within normal limits, to prevent the future onset of diabetes. The scientific data, however, shows that even diabetics, who have established disease without symptoms, do not do well on those drugs in the long run[7]. More than all that, the "leaders" in their specialties are taken around the country to give "educative" lectures in five star luxury hotels extolling the virtues of the system that they are yet to understand fully. This would soon create an epidemic of diabetes and hypertension helping the drug company business.[8]. Do epidemiologists cause epidemics?[9] The paradox is that the medical profession does not take enough care of the really sick severe hypertensives and diabetics, making life miserable for them. Audits have clearly shown inadequate management of severe hypertensives and diabetics - the class that could benefit most from drug therapy, by the profession in their enthusiasm to care for the healthy people. Resistant hypertension and resistant diabetes both have a large share of doctor responsibility, since drug compliance is very poor in both those classes of patients. A good doctor has a vital role in improving patient compliance, but that takes time and patience - the two traits not stressed in the present day medical education.

Future predictions in the dynamic human body never could prove correct. Doctors have been predicting the unpredictable for decades. The story repeats in the area of cancer and AIDS. While cancer has not been defeated even with all our publicity, a recent world congress of AIDS showed that all the expensive new drugs did not change either the mortality or morbidity scenario. On the contrary, these drugs encouraged youngsters to venture into dangerous life styles! This strategy helps the drug and instrument manufacturers. Most apparently healthy people, even before the age of sixty and certainly after that, take on an average, 4 - 6 pills per day. Their doctors believe that they are being very scientific and cover their skin against any future legal claims and the poor patient is made to believe that he/she is protecting himself against all future complications and death. Both the assumptions are far removed from the truth. Every single pill has ills following its use in the long run. Even an innocuous pill like paracetamol did kill 136 people in one year in a small country, the UK, due to liver damage. While drugs are needed to control symptoms on a short-term basis, long term use of any drug is fraught with danger. Emergency care is the only area where modern medicine and technology have really helped the sick and they are indispensable there.

This scenario has produced a new category of disease, not described in the past in any system of medicine, which I would like to call as doctor-thinks-you-have-a-disease syndrome. This new non-disease produces so much of social distress in, that the hapless victim suffers constant anxiety of incubating a disease. His family suffers psychologically and financially. The whole purpose of living-for life, liberty, and pursuit of happiness - as envisioned in the preamble to the American Constitution, written by Thomas Jefferson in 1772, is lost forever. It would be difficult to get an American who is not taking some drug or the other, all his/her life; if not anything else, at least a multivitamin. Even the latter has side effects. At times, they could even be fatal! Naturally, people worldwide will have to follow that, as America is our intellectual master these days.

This is the largest catchment area for drug companies and instrument manufacturers, who make trillions of dollars profit with this trick. It is more profitable to target the whole healthy population of this world to make money rather than aiming at the sick, as the latter number is very small compared to the healthy ones. Luckily, nearly 80% of the world population today has no touch with modern medicine! Screening healthy people could seriously damage their health. There are two exceptions. Heavy alcoholics and heavy smokers blunt their body messages of initial illnesses that they realize there is something amiss, only when it is too late. They could profit by regular screening. The latter two categories of people are not healthy individuals, anyway! Even mammography, with all its advertisements, has not been shown to be beneficial![10]

For a few people who could not get into this arena of regular check-ups because of poverty, another new disease awaits to rob them of their happiness. Happiness is man's only birth right! They are always anxious that they have not been properly evaluated to be kept constantly healthy. They live under the shadow of doubt. The constant anxiety could give rise to most chronic dangerous diseases. I would class this group under another new disease category, patient-thinks-he-has-a-disease syndrome. The reasons why these people do not get into the first net thrown by the drug and industry group could be economical. Poverty being the mother of all illnesses, they succumb to real disease sooner than later. Poor pay for their poverty with their lives, anyway.

In this whole game of the drug and technology mania, the key element in human health and disease is forgotten. It is the human mind. The seed of every single disease is first sown here. The seed then grows in the soil, *i.e*. the human body and its environment, getting help from tobacco smoke and alcohol, eventually to result in disease. Quantum physics in 2015 says that mind and body are but one. Matter is not made out of matter. Matter is made out of energy (mind). Final penetrance of the type of disease depends, of course, on the genetic predisposition. To cite an example, heavy alcoholics could either die of liver damage early on, or live to get a heart attack or sudden death due to heart muscle disease, depending on their genetic pattern. Similar is the story of tobacco smoke resulting in a heart attack, lung cancer, or emphysema based on the genetic background of the person. However, epigenetics now shows that the genetic predisposition is not as important as the environment, which mainly is the human mind! This, in essence, is the long and short of human illness. Any anxiety that upsets the happy human mind is the beginning of a disease. The medical profession's present preoccupation in creating more anxiety will result in higher morbidity and mortality. The earlier we understand this, the better for mankind.

** I could rewrite the poem by Emily Dickinson, incorporating the physicians as well, thus:

Physicians must be very careful
When they give a pill for every ill!
Deep inside their victim
Stirs the Culprit-life!

That said, I must provide some solid evidence to throw light on the darker side of the moon described above to make the narrative more authentic for a discerning reader! Here are some of the important landmark studies.

There are three important research papers giving us details as to how the drug industry runs the medical education in America and how they start brainwashing students from day one. All of them are in the most respected medical journals[11-13]. The futility of screening healthy individuals about which I have written above has been brought out very well in the editorial in BMJ[14].

Long term follow up of patients either advised bypass surgery by doctors or those who have had bypass surgery showed that in asymptomatic patients, the operation did not do any good. Worse still, only 16% of patients who underwent this operation did get some benefit and that was by way of pain relief. Angioplasty audit did not show any extra benefit in those patients who underwent the procedure compared to medical management[15]. In addition, this procedure almost always led to bypass surgery and the latter was more hazardous following angioplasty. There is now evidence to show that these results are even tampered with and doctored to show benefit![16]. There is a very significant study from Harvard that showed that the biggest culprit

to "catch" patients and frighten them is the routine use of angiogram in every one with chest pain[17]. Early bypass after a heart attack has been shown to be the biggest risk factor for strokes in the immediate future[18]. There is a plea for going slow on both these areas. Incidentally, doctors' mistakes and unnecessary interventions have resulted in 100,000 deaths in the USA in one year of study![19]. Compared to Canada, where fee-for-service does not obtain, the bypass rate in the USA was ten times more. However, at the end of one year, surprisingly, equal number of patients in the two groups was alive despite ten times more intervention in the USA!

Another area where India is trying to catch up with America is in the field of corporate hospitals, which are called for-profit-hospitals in the USA. In a recent issue of the Canadian Medical Association Journal, there has been a study on the role played by such hospitals, and the conclusions are better summed up in the words of the guest editor David Naylor. Patients treated in these hospitals had 2% increased risk of death. In Canada, it means 2200 extra deaths per year equal to total traffic deaths in that country or deaths due to colon cancer! "Does anyone still want to contract out patients to those hospitals?" asks Dr Naylor[20].

Paradoxically, many newer studies have shown that most, if not all, of the major killer diseases are not caused by anyone of the risk factors that the medical profession is trying to sell and correct with drugs and interventions[21]. Major risk factors are hatred, jealousy, pride, ego, anger, and destructive hostility. We do not seem to have woken up yet to manage these negative traits in society. We need to move in that direction. That is real patient care, *i.e*. caring for the patient and people at large. Simple life style changes and sensible diet with exercise would save millions of lives than all these interventions put together. Even intercessory prayer, in well-controlled study, has reduced death and disability in heart attack patients[22].

A strike by all the doctors in Israel recently, where they attended to all emergencies but avoided routine work and elective interventions for three months, death rate and disability fell down remarkably, only to go up to the usual level after doctors came back to work[22]. This speaks volumes in favour of what is written above. Let us hope that sanity will prevail.

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Review Article

Bariatric Surgery: Is It a Safe Treatment Modality?

Mohammad H Jama[1], Ali Aminian[2]
[1]Department of Surgery, Kuwait University, Kuwait
[2]Bariatric and Metabolic Institute, Cleveland Clinic, Cleveland, Ohio, USA

Kuwait Medical Journal 2015; 47 (3): 193 - 200

ABSTRACT

Introduction: Bariatric surgery is currently the most effective treatment for morbid obesity with proven benefits in terms of improvement of the quality of life, obesity related morbidity and obesity related mortality. Safety of bariatric surgery is widely documented in the literature. In this review, we discuss types of bariatric surgeries and their safety and complications.

Methods: A review of the current literature concerning bariatric surgery and its complications and safety was undertaken.

Conclusion: Bariatric surgery is very safe with safety profile comparable to commonly performed abdominal surgeries.

KEY WORDS: bariatric surgery, metabolic Surgery, obesity, weight loss, safety, gastric bypass, complication, morbidity, mortality

INTRODUCTION

Bariatric surgeries performance is increasing worldwide for several factors[1] . Bariatric surgery is the most and probably the only effective durable treatment for the severe obesity and does have positive effect on long term survival and quality of life of the obese individuals. The adoption of minimally invasive techniques in the field of bariatric surgery made it even more widely used[1-5]. Based on data of 2008, an estimated 350,000 bariatric procedures per year were performed worldwide, which correspond to the absolute growth rate of 135% since 2003[6]. Although these are impressive numbers, we are in fact treating only less than 2% of eligible patients surgically annually[6-8].

Obesity and diabetes are major underlying causes of death and disabilities in Kuwait. While recent high quality evidences including randomized controlled trials and long-term studies have shown the remarkable effects of bariatric surgery on type 2 diabetes with respect to glycemic control and cardiovascular risk factor modification, the safety profile of bariatric/ metabolic surgery has been a matter of concern among patients and physicians. Kuwait was the only country in the world with a ban on bariatric surgery in 2013, that lasted for 3 months[9]. It was a result of public and political pressure due to concerns over safety of bariatric surgery. In this review we will focus on the morbidity and mortality associated with different bariatric procedures in order to show its safety

WHO IS A SURGICAL CANDIDATE?

Surgical candidates are those with a body mass index (BMI) ≥40 kg/m^2, or those with a BMI ≥35 kg/m^2 with significant obesity-related co-morbidities[10]. An additional criteria should be met by surgical candidates including failed previous weight loss attempts, the patient's commitment to long-term follow-up and aftercare, and absence of ongoing substance abuse, or unstable psychiatric illness, and severe medical conditions making anesthesia or surgery very risky (Table 1)[1, 8]. Overall, medical, social, and psychological aspects of an individual patient should be considered to determine the eligibility for weight loss surgery. Table 2 summarizes potential contraindications of bariatric surgery[1, 8].

CLASSIFICATION OF BARIATRIC SURGERY

Traditionally, bariatric surgery has been classified as either restrictive, malabsorptive, or both (Table 3). Restrictive component reduces the volume of the gastric reservoir, and malabsorptive component reduces the absorptive surface of GI tract by changing nutrient flow. Commonly performed bariatric operations include laparoscopic adjustable gastric banding (LAGB), laparoscopic sleeve gastrectomy (LSG), Roux-en-Y gastric bypass (RYGB), bilio-pancreatic diversion (BPD), and the duodenal switch variant (BPD-DS) (Fig. 1)[1-6,11,12]. Laparoscopic gastric

Address correspondence to:
Mohammad H. Jamal, MD, Department of Surgery, Kuwait University, Kuwait. Email: Mohammad.jamal@mail.mcgill.ca

Table 1: Characteristics of candidates for bariatric surgery[1, 8]

Body mass index (BMI) > 40 kg/m^2; or BMI = 35 - 40 with significant obesity-related co-morbidities
Acceptable operative risk
Documented failed attempt on nonsurgical methods of weight-loss
Psychologically stable with realistic expectations

Table 2: Potential contraindications for bariatric surgery[a][1,8]

1. Severe medical disease that makes anesthesia or surgery prohibitively risky (American Society of Anesthesiologists class IV)
2. Mental incompetence that prevents the patient from understanding the procedure
3. Inability or unwillingness of the patient to change lifestyle postoperatively
4. Drug, alcohol, or other substance addiction[b]
5. Uncontrolled bulimia or other eating disorder
6. Psychologic instability
7. Nonambulatory status
8. Patient view of surgery as a "magic bullet"
9. Antagonistic family, unsupportive home environment
10. Noncompliant behavior

[a] These relative contraindications should be weighed against the potential benefits of surgery which may be the only treatment likely to yield significant weight loss and clinical improvement in the high-risk patient.
[b] Requirement of cessation of smoking varies among surgeons.

Table 3: Classification of Bariatric/Metabolic Procedures

Classification	Procedures
Restrictive	Adjustable gastric banding (AGB) Sleeve gastrectomy (SG) Gastric plication (GP) Vertical banded gastroplasty (VBG)[a]
Malabsorptive	Biliopancreatic diversion (BPD) Jejunoileal bypass (JIB)[a]
Combined restrictive and malabsorptive	Roux-en-Y gastric bypass (RYGB) BPD with duodenal switch (BPD-DS) Mini-gastric bypass (MGB) Single anastomosis duodeno-ileal bypass with sleeve gastrectomy (SADI-S)
Experimental metabolic operations[b]	Duodenal-jejunal bypass (DJB) Ileal interposition (IT)

[a] Now offered infrequently and of historic interest only.
[b] For use in experimental setting now.

plication (LGP), mini-gastric bypass (MGB), and single anastomosis duodeno-ileal bypass (SADI) have emerged as new procedures in the recent years and their long-term results have yet to be verified[13-15]. The significant long-term complications and suboptimal long-term results of the Jejunoileal bypass (JIB) and vertical banded gastroplasty (VBG) made them fall out of favor[8].

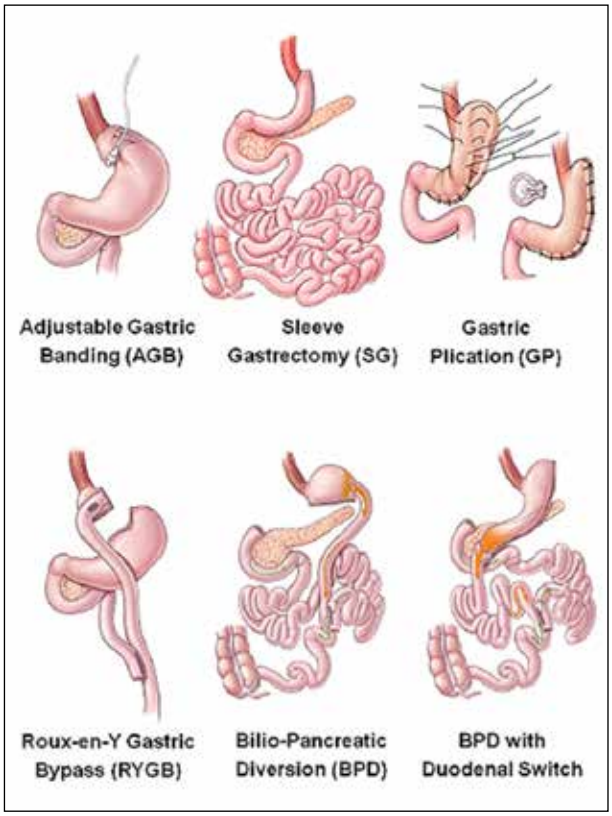

Fig. 1: Bariatric Operations Performed in Clinical Practice[1]

Open approach was utilized in the past for all bariatric surgeries, but now it's only reserved for some revisional cases and complex bariatric procedures.

Minimally invasive approach is utilized in the majority of bariatric procedures, as it has been shown to be associated with fewer postoperative complications than the open approach, most notably the risk of wound infection and incisional hernia[7, 16]. Robotic and single incision laparoscopic approaches are considered emerging platforms in the field of bariatric surgery with more studies required to ascertain their risks and potential benefits.

Not all bariatric procedures focus on weight loss as the single aim of surgery. The terms "metabolic surgery" or "diabetes surgery", are favored over "bariatric surgery" when the primary intention of surgical approach is to improve metabolic syndrome and diabetes. Several experimental procedures (*e.g.*, duodenal-jejunal bypass (DJB) and ileal interposition (IT)) aim to treat diabetes and not to reduce weight (Fig. 2). The clinical utility of these procedures need to be determined, but it is shown by limited clinical studies some promising anti-diabetic results[1-5, 17].

PREOPERATIVE ISSUES[1]

All patients are encouraged to attempt conservative approaches of weight loss with diet and exercise prior

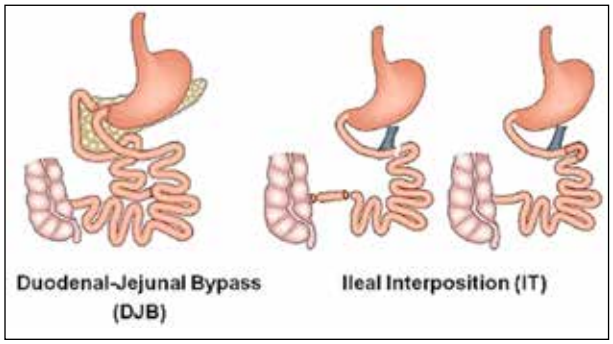

Fig. 2: Novel Experimental Metabolic Procedures[17]

to choosing bariatric surgery. In this way, the severely obese patients practice the life-style changes which are the key to long-term success after any bariatric operation. In order to reduce the size of the liver to expand the operative field, some surgeons instruct patients to follow a low calorie diet in the immediate preoperative period (*e.g.* 800 - 1200 calorie per day for 2 weeks prior to surgery. Moreover, this preoperative weight loss approach is shown by some studies to be associated with better outcomes[1-8].

Preoperative evaluation and optimization of bariatric surgical candidates requires multidisciplinary team approach. Before operation, careful nutritional, medical, and psychological assessments are essential steps in preparation of patients for surgery. Cardiac evaluation for patients over age 50 or those with known cardiovascular disease is necessary. Pulmonary evaluation is indicated for patients with asthma, hypoventilation syndrome, and pulmonary hypertension. In patients with symptoms suggestive of obstructive sleep apnea (OSA) including history of loud snoring, tiredness, and falling asleep easily during the day, a diagnostic sleep study is indicated. Once diagnosis of sleep apnea is confirmed, patients should use continuous positive airway pressure (CPAP) appliance. Use of CPAP in the immediate postoperative period is especially important to prevent episodes of hypoxia and cardiac arrhythmias. Prophylactic ursodiol in a daily dose of 600 mg for the first six months after the surgery has been shown to decrease the incidence of gallstone formation[18]. A preoperative screening Upper GI (UGI) endoscopy is indicated in patients with history of UGI diseases including gastroesophageal reflux disease (GERD) to rule out internal pathologies such as Barrett's esophagus. This evaluation is especially important for patients planning RYGB, where the distal stomach and duodenum will not be easily accessible after operation. Baseline routine blood tests, renal, liver, and thyroid function tests are indicated. Before surgery, a preoperative anesthesiology visit for assessment of air-way issues and co-morbid medical problems is also necessary for all patients undergoing bariatric surgery[8,19].

SURGICAL PROCEDURES[1]

a) Laparoscopic adjustable gastric banding

Considered a restrictive procedure, the LAGB is achieved by the placement of an inflatable silicone band just below the gastroesophageal junction, thus creating a small gastric pouch and a narrow stoma. The band is attached to a subcutaneous port that allows adjustment of tightness of the band. Saline is injected in to the port usually beginning one month after surgery. Frequent follow-up is essential after the LAGB to achieve the optimal band tightness for each patient. Overall, the LAGB is the most reversible and one of the safest and least invasive bariatric procedures. Most of postoperative complications are non-life-threatening events and overall mortality is about 0.1%[1,11,19-22].

b) Laparoscopic sleeve gastrectomy

The LSG is a restrictive procedure initially described as the first procedure in very high-risk super-obese patients who ultimately underwent BPD-DS or RYGB. After excellent weight loss results of LSG were reported, it rapidly gained popularity as a stand-alone bariatric operation. In this procedure, a linear cutting stapler is utilized to make a narrow gastric tube along the lesser curvature. The remaining 75% to 80% of the gastric body and fundus are removed. The LSG is a safe and relatively simple procedure and is associated with a reasonably low complication rate even in very high-risk patients[12,20-22].

c) Laparoscopic gastric plication

Laparoscopic gastric plication is performed by suturing the greater curvature of the stomach and invaginating it creating a tubular stomach replicating potentially the shape of the stomach after sleeve gastrectomy. Therefore, it is a low cost restrictive procedure that is potentially reversible on the short term, since it does not involve resection or anastomosis. The weight loss associated with LGP is less than that of LSG, but it is theoretically associated with lesser complications rate given that there is no gastric resection involved. A recent systematic review of the published literature on LGP found that the percentage of excess weight loss (%EWL) varied from 31.8% to 74.4% with follow-up from 6 months to 24 months and rate of major complications requiring reoperation ranged from 0% to15.4% (average 3.7%)[23]. We still need to clarify the durability of weight loss resulting from LGP, as no sufficient data exists.

d) Roux-en-Y gastric bypass

In laparoscopic RYGB, which is the most common approach, the jejunum is divided approximately 50 cm from the ligament of Treitz and the proximal end of jejunum is anastomosed to the distal part of jejunum at 150-cm below the site of transection (jejunojejunostomy). The resultant 150-cm Roux limb of proximal jejunum is brought up and anastomosed to the proximal gastric pouch of small size (15 - 30 ml). The effect of RYGB is more pronounced in terms of beneficial effects on weight and co-morbidities, especially type 2 diabetes and GERD[20-22, 24].

e) Billiopancreatic diversion and duodenal switch

In BPD, a horizontal partial gastrectomy (resection of the distal ½ to 2/3 of stomach) is performed. Then the terminal ileum is divided 250 cm proximal to the ileocecal valve. The distal end of that divided ileum (alimentary Roux limb) is anastomosed to the stomach (gastroileostomy). The proximal end of the ileum (biliopancreatic limb) is then anastomosed to the terminal ileum approximately 50 to 100 cm proximal to the ileocecal valve to create a small common channel. Prophylactic cholecystectomy is performed due to the high incidence of gallstone formation following the malabsorption of bile salts. High incidence of marginal ulcers at gastroileal anastomosis after BPD led to a modification in original technique. The modified procedure, BPD-DS, differs from the BPD only in the gastric portion of the operation. In the BPD-DS variant, instead of horizontal gastrectomy, a narrow sleeve gastrectomy is performed and pylorus is preserved. After division of duodenum, the Roux alimentary limb is anastomosed to the first portion of the duodenum after pylorus (duodenoileostomy) and distal duodenal end is closed. Again, a short common channel is created by connecting the biliopancreatic limb to the alimentary limb 50 to 100 cm from the ileocecal valve. Preservation of the pylorus significantly reduces the incidence of marginal ulcer and dumping syndrome[20-22, 24].

Both procedures provide excellent and durable weight loss (70 - 75% EWL, >15 years). In addition to weight loss, they are generally superior to other bariatric procedures for resolution of most of co-morbidities, but in the expense of technical difficulty, higher perioperative and late complications and nutritional deficiencies. Lifetime follow-up and nutritional supplements are essential to maintain good health[8,20,24].

COMPLICATIONS

Bariatric surgery is safe, with morbidity and mortality comparable to other common abdominal operations such as cholecystectomy, appendectomy, and hysterectomy. Post bariatric surgery complications can be divided to procedure-independent (table 4), which can occur after any type of weight loss surgery, or procedure-specific complications (Table 5) [12,21].

SAFETY ANALYSIS

The Longitudinal Assessment for Bariatric Surgery consortium performed a prospective multicenter observational study to evaluate the 30 day outcome in consecutive patients who underwent bariatric surgery in 10 centers in the US. Out of 4,610 patients undergoing RYGB or LAGB, the overall 30-day mortality was 0.3% with no mortality in any of the patients undergoing LAGB. Mortality rate following open and laparoscopic RYGB was 2.1% and 0.2%, respectively[25].

In a meta-analysis of mortality data, 85,048 patients were subjected to analysis in 3,061 studies and 478 treatment arms. Meta-analysis of 30-day total mortality was 0.28% and total mortality at >30 days to 2 years was 0.35%. Thirty day mortality rate of restrictive procedures (AGB and VBG) was 0.30%, RYGB 0.41%, and BPD and BPD-DS 0.76%. With the exception of BPD and BPD-DS, the meta-analysis

Table 4: Procedure-independent Complications of Bariatric Surgery[1]

Early Complications	Late Complications
Surgical site infection (superficial, deep)	Intractable nausea and vomiting, food intolerance, dehydration
Bleeding (GI, intraperitoneal)	Intestinal obstruction (due to adhesion, abdominal wall hernia)
Pulmonary complications (airway obstruction, atelectasis, pneumonia, pneumothorax, respiratory failure)	Incisional hernia
Deep vein thrombosis and pulmonary embolism	Weight loss failure
Nausea and vomiting, food intolerance, dehydration	Weight regain
Prolonged post-operative ileus	Nutritional deficiencies
Intestinal obstruction (due to intraluminal clot, adhesion, abdominal wall hernia)	Hypoglycemia
Cardiac arrhythmia (induced by hypoxia)	
Myocardial infarction	
Dehiscence and evisceration	
Rhabdomyolysis (due to pressure necrosis of the gluteal muscles), acute tubular necrosis	
Pancreatitis	
Sepsis and multiple organ failure	

Table 5: Procedure-specific Complications of Bariatric Surgery[1]

Procedure	Early Complications	Late Complications
LAGB	Gastroesophageal reflux Band misplacement Band slippage	Gastroesophageal reflux Pouch enlargement, esophageal dilation Gastric prolapsed Band slippage Mechanical port and tubing complications Band erosion into the stomach Necessity for multiple adjustments
LSG, LGCP	GI leak (generalized peritonitis, abscess, fistula formation) Gastric obstruction Gastroesophageal reflux	Gastroesophageal reflux Gastric dilation
RYGB	GI leak (generalized peritonitis, abscess, fistula formation) Acute distal gastric dilatation and rupture Roux limb obstruction	Stomal stenosis (at gastrojejunostomy) Marginal ulcer (at gastrojejunostomy) Dumping syndrome Internal hernia Staple line disruption and gastro-gastric fistula Stomal dilation Gallstone Nutritional deficiencies (Calcium, Iron, Vitamin D & B12)
BPD, BPD-DS	GI leak (generalized peritonitis, abscess, fistula formation) Roux limb obstruction	Diarrhea and flatulence Marginal ulcer (after BPD) Dumping syndrome (after BPD) Internal hernia Electrolyte abnormalities Liver failure Gallstone Renal stone High risk of nutritional deficiencies: Anemia Protein-calorie malnutrition Vitamin B12 deficiency Hypocalcemia, Osteoporosis Night blindness

showed a higher mortality for open than laparoscopic approach. Mortality rates had a downward trend over the years[26].

The total sixty day mortality of bariatric procedures was reported to be 0.25% based on an analysis of a national database containing details on 13,871 bariatric procedures. The type of surgical procedure significantly influenced mortality risk: 0.1% AGB, 0.15% VBG, 0.54% RYGB, 0.8% BPD. Pulmonary embolism represented the most common cause of death (38.2%), followed by cardiac failure 17.6%, and intestinal leak 17.6%. Open surgery and case load per center were among the major risk factors of mortality[27].

The US national average in-hospital mortality rates after aortic aneurysms (3.9%), coronary artery bypass grafting (3.5%), craniotomy (10.7%), esophageal resections (9.9%), hip replacement (0.3%), pancreatectomy (8.3%), and pediatric heart surgery (5.4%) all, with the exception of hip replacement, are >1%, exceeding that of the generally reported experience with bariatric surgery (<0.5%)[28].

Short-term safety analysis of bariatric/metabolic surgery in a cohort of diabetic patients using the American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) dataset was recently reported. Of the 66,678 diabetic patients included, 16,509 underwent laparoscopic RYGB. The mean operative time of laparoscopic RYGB and length of hospital stay were 138 min and 2.5 days, respectively. Serious events within 30-days after LRYGB included need for transfusion (1.22%), sepsis (0.81%), pneumonia (0.66%), deep vein thrombosis (0.36%), septic shock (0.30%), acute renal failure (0.22%), pulmonary embolism (0.22%), myocardial infarction (0.16%), and stroke (0.05%), which led to a mortality rate of 0.30%. The composite complication rate after laparoscopic RYGB was comparable to laparoscopic cholecystectomy and hysterectomy (Fig. 3). Mortality rate of LRYGB (0.30%) was comparable to total knee arthroplasty (Fig. 4). Gastric bypass patients had significantly better short-term outcomes in all examined variables compared to coronary artery bypass graft, infra-inguinal revascularization, and laparoscopic colectomy (Fig. 3 and 4). The study concluded that RYGB can be considered a safe procedure in diabetics with comparable short-term morbidity to common procedures such as cholecystectomy and appendectomy and mortality similar to knee arthroplasty. The mortality risk of RYGB is one-tenth that of cardiovascular surgery

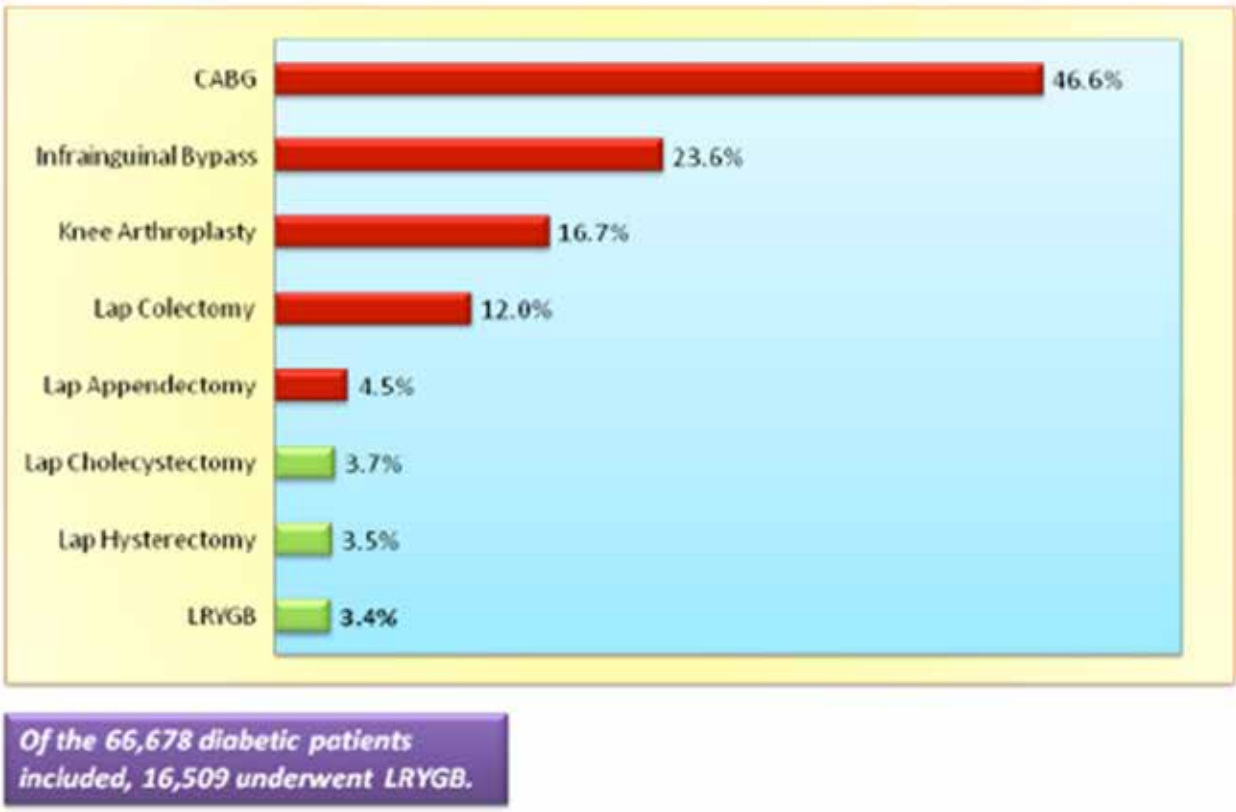

Fig. 3: US national data of postoperative composite complication rate (%) of 8 procedures in patients with Type 2 Diabetes[29]

and earlier intervention with bariatric/metabolic surgery to treat diabetes may eliminate the need for some later higher-risk procedures to treat diabetes complications[29].

In a study performed by our group, we looked at the highest risks patients undergoing bariatric surgery by using the Obesity Surgery Mortality Risk Score (OS-MRS). We strictly defined an extremely high-

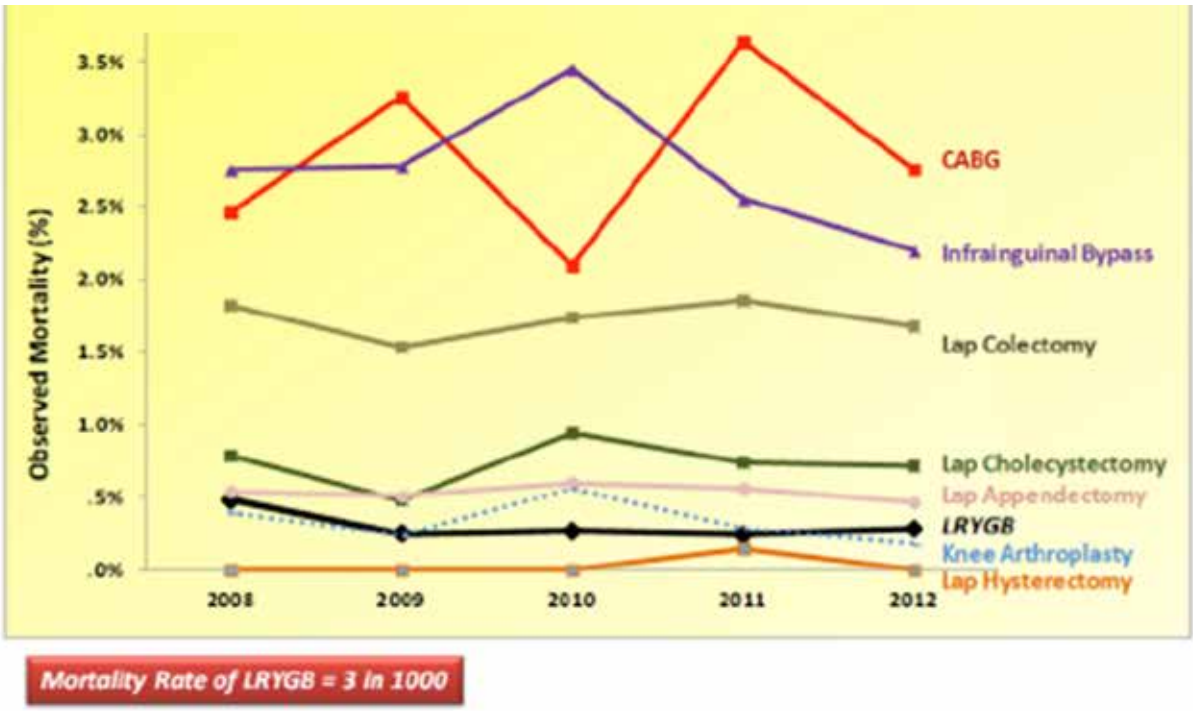

Fig. 4: Mortality rates (%) of 8 procedures in diabetics in the United States, 2008-2012[29]

risk group of patients by age at the time of surgery ≥ 65 years, BMI ≥ 50 kg/m^2, and presence of at least 2 of 6 cardiopulmonary or vascular comorbidities We identified 44 extremely high-risk patients who underwent laparoscopic Roux-en-Y gastric bypass (N = 23), adjustable gastric banding (N = 11), and sleeve gastrectomy (N = 10). Only thirteen (29.5%) 30-day postoperative complications occurred; with only six were major complications. Thirty-day postoperative re-admission, re-operation, and mortality rates were 15.9%, 2.3%, and zero, respectively. In a mean follow-up time of 24 months, late morbidity and mortality rates were 18.2% and 2.3%, respectively. Therefore, laparoscopic bariatric surgery in the extremely high-risk patients can be done safely with acceptable early and late morbidity and mortality rates. Advanced age, high BMI, and severe cardiopulmonary comorbidities should not exclude patients from consideration for bariatric surgery[30].

Summary

Safety and efficacy are two fundamental factors when a treatment modality is being evaluated in clinical practice. Currently, bariatric surgery is the most effective weight loss method and is associated with favorable metabolic outcomes and survival benefit among morbidly obese individuals[31-33].

Improvement in surgical techniques and perioperative management protocols has led to continuous improvement of the safety profile. Mortality of bariatric surgery has decreased substantially from 1.5 - 2% two decades ago to 0.1 - 0.3%. The reported complication rate of surgery based on several available large databases is about 2 - 4%[25,29,34]. Despite high quality data on safety and efficacy of bariatric and metabolic surgery that has led to incorporation of surgery in management guidelines for obesity and diabetes[35], many physicians and patients do not consider the option of surgery. One reason may be an incorrect perception of the risk-to-benefit ratio of medical and surgical approaches in obesity and diabetes management, *i.e.*, overestimation of benefit of medical approach and risk of surgical approach[29,36]. Nonetheless, the obesity epidemic we currently face caused a dramatic rise in the numbers of bariatric surgeries performed.

CONCLUSION

Safety of bariatric surgery can be enhanced, if performed in high volume centers, if high risks patients are identified properly preoperatively, and if the appropriate procedure is tailored to the right patient. A review and audit of national results should be undertaken periodically, to improve results and encourage research in the field.

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Original Article

The Accuracy of Tests Used to Predict Difficult Airway and a Comparison of Macintosh Laryngoscope to Video Laryngoscope for Intubation

Tarkan Mıngır[1], Dilek Kitapcıoglu[2], Namigar Turgut[2], Cengiz Yumru[3]
[1]Anesthesiology and Reanimation Clinic, Okmeydani Training and Research Hospital Istanbul, Turkey
[2]Acıbadem University, Istanbul, Turkey
[3]Anesthesiology and Reanimation Clinic, Gaziosmanpasa Taksim Training and Research Hospital Istanbul, Turkey

Kuwait Medical Journal 2015; 47 (3): 201 - 209

ABSTRACT

Objectives: To compare TruView EVO2 video laryngoscope (VL) and Macintosh laryngoscope (ML) as regards their success rates in difficult intubation, hemodynamic response and postoperative complications.
Design: Prospective study
Setting: Training and Research Hospital, Istanbul, Turkey
Subjects and Methods: A total of 60 cases were enrolled to the study. Group ML (N = 30) were intubated using ML and Group VL (N = 30) were intubated using TruView EVO2™ VL.
Main Outcomes Measures: Cormack-Lehane score was used to evaluate the visualization vocal cords and intubation difficulty. The time required for visualization of vocal cords, total intubation time, difficulty in intubation were also recorded.
Results: For all cases, having BMI > 30, Mallampati grade > 3, Cormack-Lehane score > 3, short neck, not being able to touch chin to chest, no mandibular protrusion, distance between incisor teeth < 3 cm and, thyromental distance < 7 cm corresponded to the difficult intubation cases of 46.15%. The time period of visualization of vocal cords was significantly longer in Group VL. Cormack-Lehane > 3 and difficult intubation rate was significantly higher in Group ML. The ratio of ones having Mallampati scores of III - IV and Cormack-Lehane scores of I - II was found 17% in Group ML, while the ratio was 30% for Group VL. In all cases, regarding patients having difficult intubation, the success rate of intubation was found as 79.3%.
Conclusion: High success rates of intubation were seen with both TruView EVO2™ VL and ML. Either ML or VL can be used in case of difficult intubations.

KEY WORDS: difficult airway, Mackintosh laryngoscope, video laryngoscope, vocal cord

INTRODUCTION

"Breathing is the most important sign of life for human beings, starting from the birth, in order to understand, if they are alive or not. During their life, spontaneous or artificially, easy or difficult but, breathing somehow and making them breathe is the fundamental''[1].

Intubation process during anesthesia administration has certain advantages such as maintaining an open airway at all time, respiratory and airway control, decreasing respiratory effort, dead-space and aspiration hazard, providing a surgical comfort by keeping away anesthetist and equipment from the area and, airway control during resuscitation. Nevertheless, laryngoscopy and endotracheal intubation cannot be performed easily in every case and intubation process cannot be successful always because of certain anatomical difficulties and existing systemic diseases (*e.g.*, ankylosing spondylitis, thyrocele *etc.*).

Due to the increase of plasma catecholamine concentration resulting from reflex sympathetic response from the larynx and trachea to mechanical stimulus, laryngoscopy and intubation may cause tachycardia, hypertension, arrhythmia and myocardial ischemia especially in patients with restricted cardiac reserve[2] .

Address correspondence to:
Namigar Turgut, Tepecik Yolu Taşlıçay Sok, No. 3 / 3, Etiler,Istanbul,Turkey. Tel: 00905333607659, E-mail: drnamigar@yahoo.com.tr, mavi.ilke@hotmail.com

In this study, our aim was to measure the predictability of difficult intubation and the accuracy of tests used for this purpose in patients with Mallampati scores of II-IV and posted for elective surgery. The secondary aim of the study was to compare TruView EVO2 video laryngoscope (VL)[3,4] with the commonly used Mackintosh laryngoscope (ML). The VL was developed, especially for difficult intubation cases but could also be used routinely even when no difficulty is anticipated. VL and the ML were compared from the point of view of success rates during difficult intubation, hemodynamic response to laryngoscopy and early-stage postoperative complications.

In cases where intubation was not successful with both the ML and VL, LMA-Fastrach™ was used as a rescue device for intubation.

SUBJECTS AND METHODS

This study was performed in H.M. Training and Research Hospital Anesthesiology and Reanimation Clinic operation rooms (OR), after approval from the Ethics Committee and consent from patients. A total of 60 cases aged between 25 to 82 years, classified as ASA I-II, posted for elective surgery, and having a Mallampati score II-IV along with other parameters indicating the possibility of difficult intubation were enrolled into the study.

Patients classified as ASA III and above risk group, those having history of allergy, uncontrolled respiratory, cardio-vascular and central nervous system disease, hemorrhagic diathesis or those who had undergone head and neck surgery, those taking medications affecting endocrine response and neuromuscular block and, un-cooperative patients were excluded from the study.

Using a computer program, the patients were randomly divided into two groups of 30 persons. Group ML (n = 30) patients were intubated using the ML while patients in Group VL (n = 30) were intubated using the VL.

During the preoperative physical examination, age, gender, length, weight, body mass index (BMI), thyromental distance (TMD), mouth opening or distance between upper and lower incisor teeth (inter-incisor gap or IIG), head and neck movements and their characteristics, the ability to protrude the lower incisor teeth in front of the upper incisor's ability to touch the chin to the chest and the Mallampati scores were recorded. For premedication, 0.5 mg alprazolam tablet was administered orally the night before the operation and 0.1 mg/kg midazolam was administered intramuscularly in the morning just before arriving in the OR. For preoperative standard monitoring, electrocardiogram (ECG) in lead II, non-invasive blood pressure (systolic, diastolic, and mean arterial pressure), and peripheral oxygen saturation (SpO_2) monitors were used in the OR.

Vascular access was secured by a 20 G intravenous cannula and isotonic fluid at the rate of 2 ml/kg/hr was infused as maintenance fluid requirement. For induction of anesthesia, 2 mg/kg propofol, 2 μg/kg fentanyl citrate and 0.60 mg/kg rocuronium bromide were administered. Then, after waiting for 120 seconds, endotracheal intubation was performend. In Group VL, the display unit of TruView™ EVO2 VL was prepared before the process and mounted on the device. The blade was placed in the mouth in midline and the vocal cords were visualized. Endotracheal intubation was performed by watching the images on the screen. The blade was then removed from the mouth. Cormack-Lehane scoring system was used for assessing the view of the vocal cords obtained during laryngoscopy. The scores were recorded as I-II-III-IV. The time from termination of ventilation with mask to visualization of vocal cords was considered as visualization time. The time from the point of vocal cord visualization to end tidal CO_2 value reading was considered as intubation time. The number of attempts for successful intubation were recorded (LMA-FASTRACH™ was used as a rescue device after a failed third attempt). Any complications during intubation (bleeding, tooth damage, *etc.*) were recorded. Operator-assessed subjective difficulty of the intubation and the success of intubation were also recorded.

Anesthesia maintenance was provided by 45% O_2, 55% NO_2 and, 1.5% sevoflurane. During endotracheal intubation, the endotracheal tube (ET) sizes used for female and male patients were 7.0 and 8.0 respectively in the ML group. In the VL group, size 7.0 ET was used for female and size 8.0 armoured ET was used for male patients. Cuffs were inflated to a pressure of 20 - 40 cm H_20 pressure.

Perioperative cardio-vascular and hemodynamic responses (for *e.g.*, heart rate (HR), mean arterial blood pressure (MAP), peripheral oxygen saturation (SpO_2) and, end tidal carbon dioxide ($ETCO_2$) were recorded at baseline, induction, right after the intubation and then at 5^{th}, 10^{th}, 20^{th}, 30^{th}, 40^{th}, 50^{th}, 60^{th} minutes during extubation, and postoperatively, at 5^{th}, 10^{th}, 15^{th}, 20^{th} minutes. At the end of the operation, a fresh gas flow (FGF) of 6 l/min of O_2, was maintained and the patient was administered a reversal agent (atropine and neostigmine). Patients were extubated when signs of complete recovery from neuro-muscular block and wakefulness (at least 8 ml/kg tidal volume with spontaneous respiration, ability to lift up the head and maintain this position for > 5 seconds, ability to generate an inspiratory negative force (> 40 cm H_2O),

able to squeeze hand, or lift arm), response time to obeying verbal commands, *i.e.,* from the moment of last anesthetic administration, to responding to simple verbal commands such as "open your eyes" or "squeeze your hand" given every minute, orientation to time and place, *i.e,* be able to say their names, birth dates and where they are and total duration of operation were recorded. During the early postoperative period, leading questions were asked and any difficulty in breathing, stridor, cough, nausea, vomiting, sore throat, hoarseness were recorded.

Statistical analysis

The data obtained was evaluated using SPSS 15.0 (Statistical Package for the Social Sciences) program. In data evaluation, crosstabs were utilized besides descriptive statistics (average, standard deviation). Independent two-sample t-test and Chi-Square test were used for comparing quantitative data. All of the study's findings were tested in 95% confidence interval (CI), and a p-value of < 0.05 was considered significant and bidirectional.

RESULTS

There was no significant difference between groups as regards age, gender, body mass index (BMI) and duration of surgery (p > 0.05, Table 1).

Table 1: Comparison of the demographics in groups

Characteristics	Group ML	Group VL
Female	21	27
Male	9	7
Age (mean ± SD) years	46.66 ± 13.93	48.37 ± 13.58
BMI (kg/m^2)	31.23 ± 6.74	30.43 ± 8.14
Duration of the operation (min)	114.76 ± 45.49	115.77 ± 44.07

ML (n = 30), ML= Macintosh laryngoscope group, VL = TruView EVO2™ Video laryngoscope group

There was no significant difference between groups from the point of view of Mallampati scores, TMD, IIG (< 3 cm), thick or thin neck and being able to touch chin to chest (p > 0.05, Table 2).

Table 2: Comparison of diagnostic findings in groups

Diagnostic findings	Group ML	Group VL	p-value
Mallampati Score	2.37 ± 0.61	2.53 ± 0.57	0.281
Cormack-Lehane	2.28 ± 1.07	2.10 ± 0.88	0.493
Thyromental distance (cm)	6.43 ± 1.07	6.33 ± 1.27	0.743
Incisor teeth distance < 3 cm	20	20	0.781
Short neck	18	26	0.020*
Thick neck	24	26	0.488
Thin neck	6	4	0.488
Long neck	12	4	0.020*
Is chin to chest possible?	20	18	0.592

*p < 0.05, ML = Macintosh laryngoscope group (n = 30)
VL = TruView EVO2™ Video laryngoscope group (n = 30)

Patients with a short neck were more in Group VL (p = 0.020) and those with long neck were more in Group ML. (p = 0.020, Table 2). The ratio of those having Mallampati scores of 3 - 4 and Cormack-Lehane scores of 1 - 2 was 17% in Group ML and 30% for Group VL. The number of intubation attempts, intubation complication, duration of intubation (in sec) and orientation time was not significantly different between groups (p > 0.05). The time taken for visualization of vocal cords (in sec) was significantly higher in Group VL (p = 0.009). Vocal cords could not be visualized in seven patients in Group ML. The number of unsuccessful visualization of vocal cords in Group ML was significantly more than Group VL (p < 0.05) (Table 3).

Table 3: Comparison of intubation parameters in groups

Intubation	Group ML	Group VL	p-value
The number of attempts	1.53 ± 1.01	1.33 ± 0.48	0.330
Visualization time of the vocal cords (sec)	17.00 ± 23.27	34.50 ± 23.23	0.009**
The time of intubation (sec.)	57.72 ± 81.25	72.87 ± 65.90	0.434
The time of orientation (min.)	131.86 ± 41.24	126.70 ± 43.84	0.643
Complication of intubation	5	4	0.718
Not visualizing vocal cord	7	0	0.005**

ML (n = 30), ML= Macintosh laryngoscope group VL (n = 30) = TruView EVO2™ Video laryngoscope group

Extubation time, response time to verbal commands (in min) and orientation time (in min) was not significantly different between the two groups (p > 0.05, Table 4).

Table 4: Comparison of extubation parameters in groups

Parameters	Group ML	Group VL	p-value
The time of intubation	122.72 ± 40.81	117.47 ± 44.05	0.636
Response time to verbal commands (min)	127.62 ± 40.72	123.13 ± 43.89	0.686
The time of orientation (min)	131.86 ± 41.24	126.70 ± 43.84	0.643

p > 0.05

Between groups, there was a significant difference in heart rate before operation and at postoperative 10^{th} and 15^{th} minutes (p < 0.05). In Group ML, heart rate was found significantly higher before operation and at postoperative 10^{th} and 15^{th} minutes (p = 0.027, p = 0.027, p = 0.027 respectively, Table 5).

MAP, SPO_2, $EtCO_2$ measurements were not significantly different between groups (p > 0.05, Table 6, 7 and 8). In case of Cormack-Lehane view > III, difficult intubation rate of Group ML was found

Table 5: Comparison of heart rate (HR) changes in the two groups

Heart Rate	Group ML		Group VL		p-value
	Average	SD	Average	SD	
Preoperative	84.60	14.81	73.97	20.96	0.027*
Induction	86.41	17.05	78.47	14.28	0.057
E.end	85.72	14.66	82.97	15.07	0.479
5th min.	80.90	11.73	78.30	15.08	0.464
10th min.	75.45	9.87	73.93	11.79	0.595
20th min.	75.55	12.61	72.70	10.53	0.349
30th min.	72.10	13.56	73.20	10.97	0.734
40th min.	70.26	12.48	71.97	10.85	0.583
50th min.	67.19	9.60	72.34	12.75	0.099
60th min.	66.15	15.70	72.07	12.93	0.132
Extubation	78.79	13.20	74.60	16.36	0.284
PO 5th min	79.17	11.95	74.03	16.83	0.183
PO 10th min	80.17	12.21	72.93	12.26	0.027*
PO 15th min	79.48	11.49	71.30	10.28	0.006**
PO 20th min	77.97	11.47	72.93	10.77	0.088

p > 0.05, *p < 0.05, **p < 0.01
ML (n = 30) = Macintosh laryngoscope group, VL (n = 30): TruView EVO2™ Video laryngoscope group, E. end = End of intubation, PO 5th min: postoperatively at 5th minute, PO 10th min: postoperatively at 10th minutes, PO 15th min = postoperatively at 15th minute, PO 20th min = postoperatively at 20th minute

Table 6: Comparison of mean arterial pressures (MAP) in groups

Arterial pressures	Group ML		Group VL		p-value
	Average	SD	Average	SD	
Preoperative	98.37	15.20	95.33	26.38	0.587
Induction	98.17	16.11	97.83	15.83	0.935
E. end	98.14	27.17	96.67	19.74	0.812
5th min	91.17	22.77	94.97	17.07	0.471
10th min	89.76	20.10	92.00	18.05	0.654
20th min	92.41	17.83	92.80	13.99	0.926
30th min	87.00	26.12	123.80	165.96	0.243
40th min	95.37	15.94	95.80	16.94	0.922
50th min	99.23	15.45	97.07	14.86	0.599
60th min	101.27	21.36	94.14	22.63	0.236
Extubation	100.07	20.91	97.97	18.19	0.682
PO 5th min	101.83	18.98	98.50	11.24	0.414
PO10th min	99.48	16.20	96.20	19.50	0.485
PO15th min	96.48	14.24	95.27	9.31	0.698
PO 20th min	93.38	15.01	95.37	11.53	0.570

p > 0.05, MAP = mean arterial pressure, SD = Standard deviation; ML (n = 30): Macintosh laryngoscope group, VL (n = 30) = TruView EVO2™ Video laryngoscope group, Preop: Preoperative, E. end = End of the intubation, PO 5th min = postoperatively at 5th minutes, PO 10th min = postoperatively at 10th minutes, PO15th min = postoperatively at 15th minutes, PO 20th min = postoperatively at 20th minutes

significantly higher than that of Group VL (Table 9). For the ratio of difficult intubation, there was not any statistical difference between Group ML and Group VL (47% and 50%, respectively) (p > 0.05). The ratio of difficult intubation in all the patients was 48%. The rate of successful intubation was 90 % in all 60 cases. Success rate of intubation ascended to 98.3% by using the LMA Fastrach. Failed intubation rate was found as 1.7 %. Three cases in each group could not be

Table 7: Comparison of oxygen saturations (SpO_2) in groups

Oxygen Saturations	Group ML		Group VL		p-value
	Average	SD	Average	SD	
Preoperative	97.60	2.80	97.97	2.03	0.563
Induction	99.03	1.40	98.80	1.58	0.550
E.end	99.38	1.12	99.47	0.86	0.737
5th min	99.48	1.18	99.50	0.90	0.950
10th min	99.24	1.24	99.43	0.94	0.505
20th min	99.21	1.24	99.37	1.22	0.619
30th min	96.24	16.62	99.30	1.15	0.319
40th min	99.22	1.15	99.43	1.10	0.484
50th min	99.23	1.11	99.34	1.08	0.700
60th min	95.85	17.54	99.28	1.19	0.298
Extubation	99.41	0.98	98.93	1.36	0.127
PO 5th min	98.79	3.24	98.33	3.26	0.590
PO 10th min	99.00	2.05	98.87	1.78	0.790
PO 15th min	99.17	1.47	99.27	1.26	0.792
PO 20th min	99.17	1.63	99.30	1.37	0.745

p > 0.05, MAP = mean arterial pressure, SD = Standard deviation; ML (n = 30): Macintosh laryngoscope group, VL (n = 30) = TruView EVO2™ Video laryngoscope group, Preop: Preoperative, E. end = End of the intubation, PO 5th min = postoperatively at 5th minutes, PO 10th min = postoperatively at 10th minutes, PO15th min = postoperatively at 15th minutes, PO 20th min = postoperatively at 20th minutes

Table 8: Comparison of end tidal carbon dioxide ($ETCO_2$) in groups

$EtCO_2$	Group ML		Group VL		p-value
	Average	SD	Average	SD	
Intubation	32.90	4.70	31.27	3.96	0.155
5th min	30.93	3.63	30.77	3.73	0.865
10th min	30.66	3.00	30.93	3.03	0.725
20th min	30.17	3.64	30.73	2.91	0.515
30th min	40.45	56.20	30.70	3.20	0.347
40th min	29.63	3.61	30.45	3.44	0.388
50th min	29.54	3.43	31.07	4.29	0.153
60th min	29.81	3.20	30.66	3.71	0.371

p-value > 0.05
ML (n = 30) = Macintosh laryngoscope group, VL (n = 30): TruView EVO2™ Video laryngoscope group, Average: Mean, SD: Standard deviation

Table 9: The ratios of difficult intubation (%)

Intubation	Group ML	Group VL	p-value
BMI (body mass index) > 30	61.54	46.67	0.431
Mallampati Score > 3	66.67	66.67	0.999
Cormack-Lehane Score > 3	100.00	66.67	0.038
Incisor teeth distance < 3cm	61.54	46.67	0.431
Thyromental distance < 7cm	50.00	46.15	0.781
Short neck	55.56	50.00	0.717
Thick neck	50.00	53.85	0.786
Thin neck	33.33	25.00	0.778
Long neck	33.33	50.00	0.551
Chin to chest possible	40.00	38.89	0.994
Chin to chest impossible	60.00	66.67	0.746
Mandibular protrusion	40.91	47.62	0.658
No Mandibular protrusion	62.50	55.56	0.772

intubated by the method used. Therefore, the rescue technique of LMA Fastrach was attempted. Five of the cases were intubated by Fastrach, whereas one case could not be intubated even by this method. In Group ML, success rate of intubation was 90% while failed intubation rate was 10%. Identically, for Group VL, success rate of intubation was 90% while failed intubation rate was 10%. In Fastrach method, success rate of intubation was 83%; whereas failed intubation rate was 17 %.

With respect to difficult intubation cases, success rate of intubation was 79.3%. Success rate of intubation in ML Group was 78.6 %, success rate of intubation in VL Group was 80% and, success rate of Fastrach intubation was 83.3%. In Group ML, the success rate of Fastrach was found as 66.6%. In Group ML, 33.3% of the patients could not be intubated. Success rate of Fastrach intubation in VL Group was found as 100%.

With respect to postoperative complications, there was no significant difference between groups ($p>0.05$). In total, 26 patients had postoperative complications in Group ML (sore throat in two patients; cough in seven patients; nausea in 11 patients; vomiting in five patients and, stridor in one patient), while 31 patients had postoperative complications in Group VL (sore throat in two patients; difficulty in breathing in one patient; cough in eight patients; nausea in nine patients; vomiting in eight patients and, stridor in three patient). The most frequent postoperative complication was nausea. Hoarseness was not at all seen (Table 10).

Table 10: Postoperative complications findings

Complications	Group ML	Group VL	p-value
Postoperative sore throat	2	2	0.972
Postoperative breathing difficulty	0	1	0.321
Postoperative hoarseness	0	0	-
Postoperative cough	7	8	0.824
Postoperative nausea	11	9	0.520
Postoperative vomiting	5	8	0.383
Postoperative stridor	1	3	0.317

$p < 0.05$, ML = Macintosh laryngoscope group, VL = TruView EVO2™ Video laryngoscope group

DISCUSSION

Tracheal intubation is required in many general anesthetics. Efforts for decreasing the inconvenience in difficult airway management have directed researchers to investigating alternative methods. The development presents importance of preoperative airway evaluation in patients. Not only Mallampati score, but all other tests for predicting difficult intubation (measurement of SMD, TMD, IIG *etc,*) when taken together will increase the accuracy of predicting a difficult airway during preoperative airway evaluation.

In this study, out of 60 cases, the difficult intubation rate was 48%; in Group ML the rate was

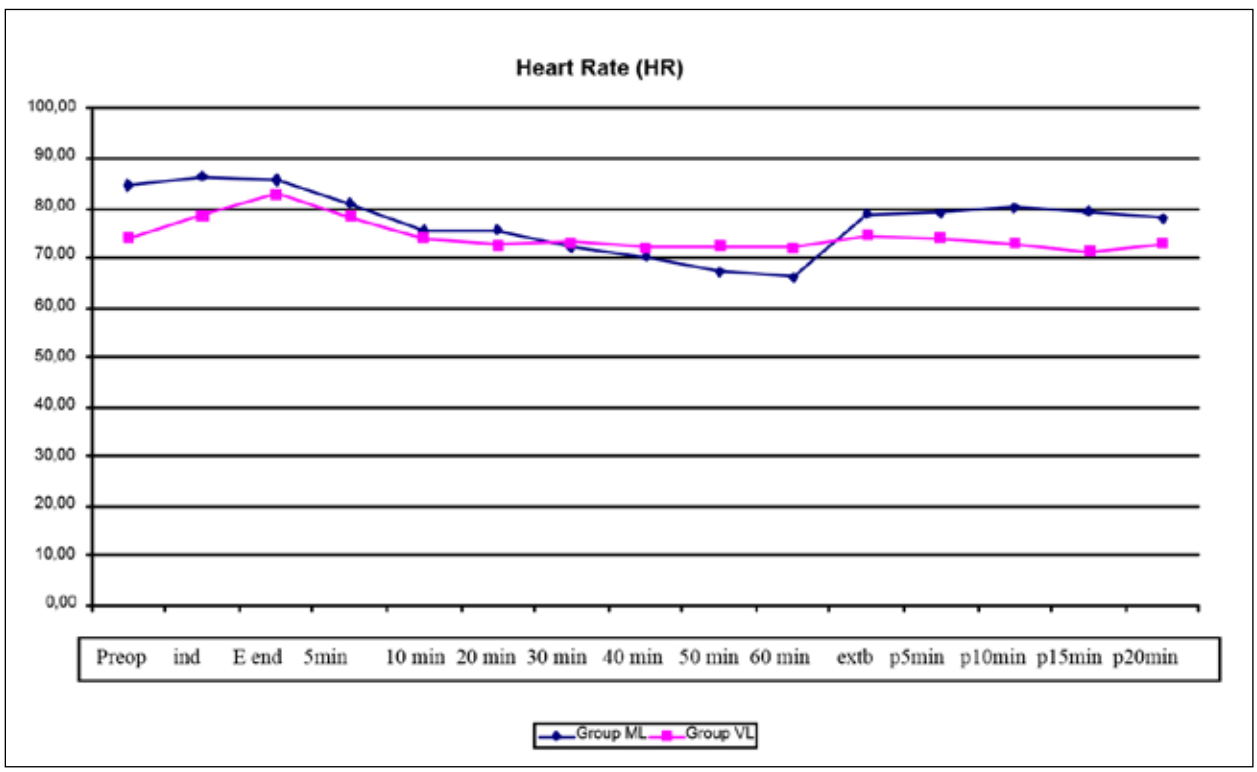

Fig. 1: Comparison of heart rates (HR) in two groups.

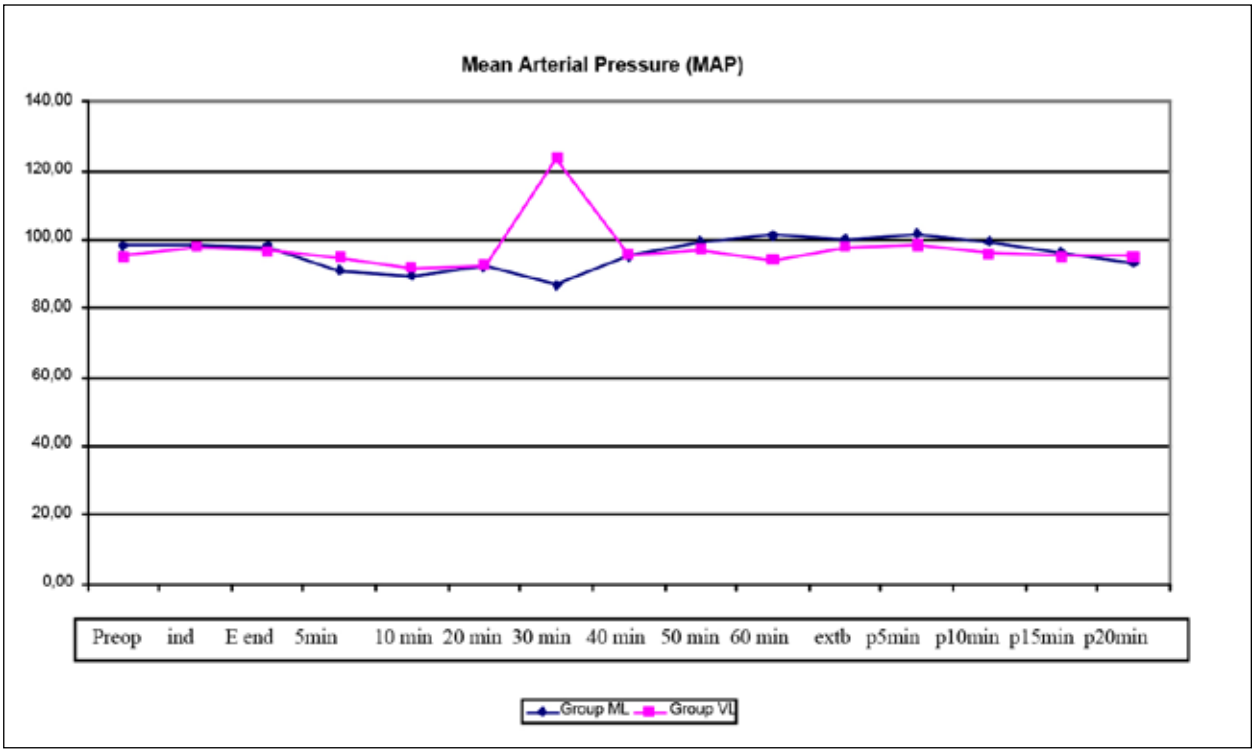

Fig. 2: Comparison of mean arterial pressures (MAP) in two groups

47%, while it was 50% in Group VL. Having BMI > 30, Mallampati > III, Cormack-Lehane > III, short and thick neck, chin-to-chest impossibility, no mandibular protrusion, IIG < 3 cm, TMD < 7cm matched with difficult intubation cases between 46.15% and 100%. Interestingly, in being able to touch chin-to-chest, thin neck and long neck cases, difficult intubation was 25 - 50%. Ishwar *et al*[5]. studied 50 patients whose Cormack-Lehane score was two and more and were predicted to have difficult intubation. In their study,

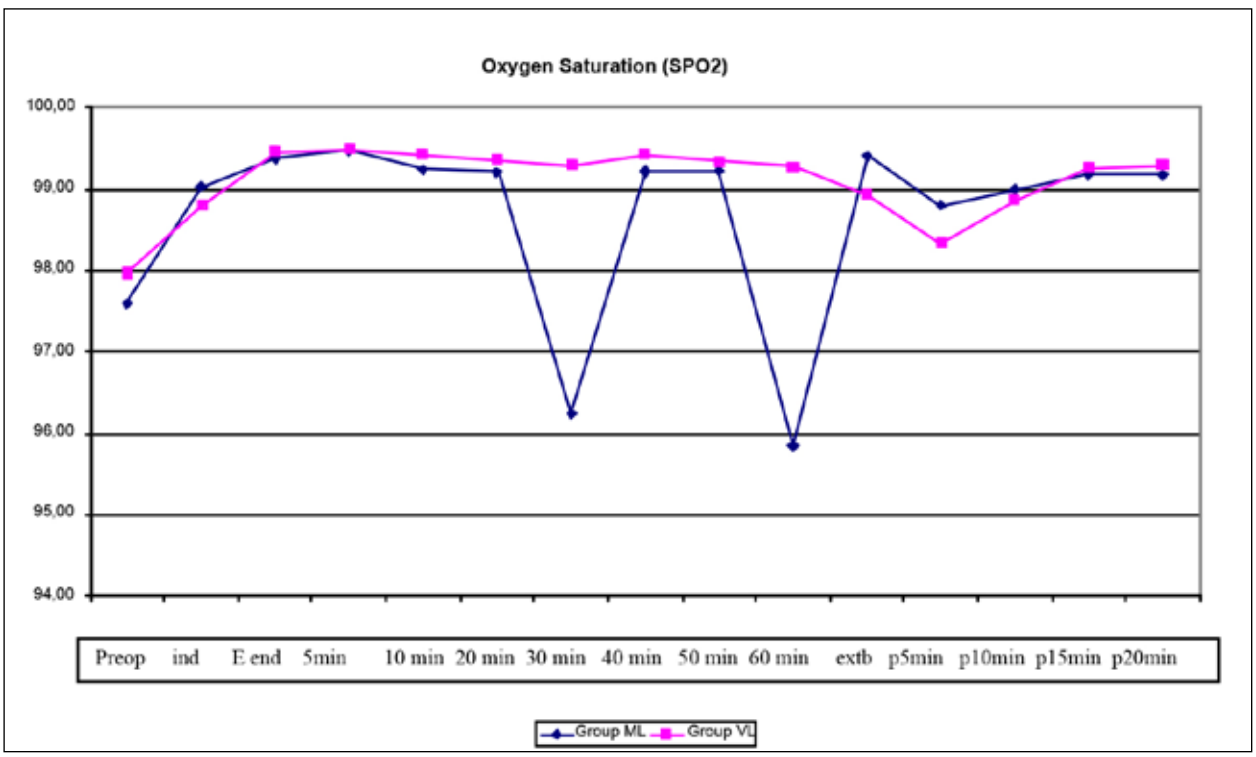

Fig. 3: Comparison of oxygen saturations (SPO_2) in two groups

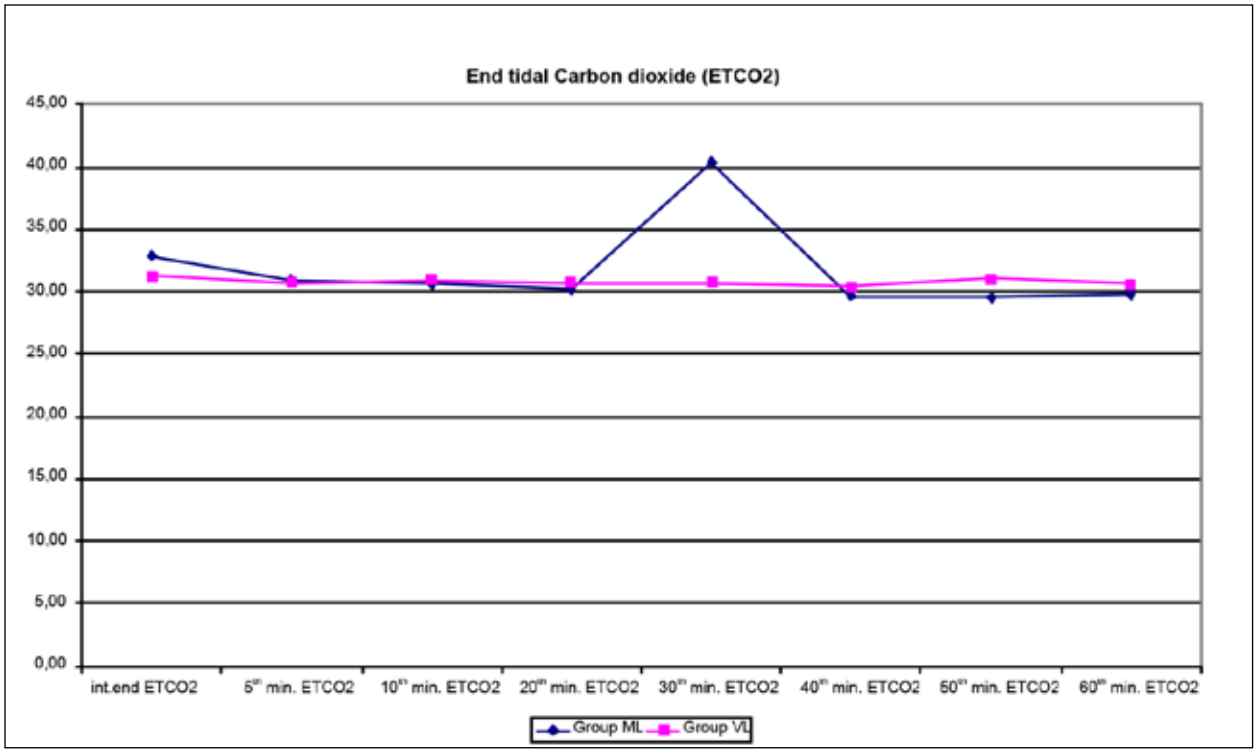

Fig. 4: Comparison of end tidal carbon dioxide ($ETCO_2$) in two groups

they compared TruView™ EVO2 VL and ML during intubation and reported intubation success rate as 88%. Also in their study, Cormack-Lehane score was four with ML while the score was converted to 1 - 2 with TruView™ EVO2 VL in five patients. In our study, the percentage of cases whose Mallampati scores were 3 - 4 and Cormack-Lehane scores 1 - 2 was 47%. Li *et al*[6] reported intubation success rates with ML and TruView™ EVO2 VL 100%. Raveendra *et al*[7] used TruView™ EVO2 VL in 50 patients in their study and reported their success rate as 94% in patients planned to have nasotracheal intubation.

Lili *et al*[8] used TruView™ EVO2 VL in their study, since they could not perform intubation by ML in patients with predicted difficult airway and they reported 100% success rate in all patients. In our study, intubation success rate in Group ML and Group VL was 90%. For Fastrach, which is a rescue method, intubation success rate was 98.3%.

In their study including 170 patients planned to have general anesthesia, Barak *et al*[9] compared Truview blade and Macintosh blade and determined intubation times as 62 sec and 51 sec respectively. In their study, Timanaykar *et al*[10] reported intubation times as 33.06 sec and 23.11 sec for Truview VL and ML respectively. Besides, they also examined the percentage of glottic opening in the same study and they found the values as 97.26% and 83.70%for TruView™ VL and ML respectively. They emphasized the difference as statistically significant. In their study, Li *et al*[6] determined that the intubation time lengthened with ML as compared to TruView™ EVO2 VL, as Cormack-Lehane glottic view score increases. From the point of intubation tube placement time, no statistically significant difference was found between groups in our study.

Hemodynamic response to intubation is higher in direct laryngoscopy. Although LMA Fastrach is a time-consuming operation, its superior hemodynamic stability makes it a suitable choice for patients unsuitable for tolerating the hemodynamic response to intubation[11]. Similarly, Joseph *et al*[12] used TruView™ EVO2 VL and ML for intubation in patients with cervical spine immobilization and showed that hemodynamic response was reduced. In another study, the percentage of glottic opening score with TruView™ EVO2 VL (98%) decreased to 77% with ML. Due to the 42 degree slope in blade, glottic view was obtained by applying approximate external force of 19.6 newton with TruView™ EVO2 VL while the pressure was 32.3 newton with ML in this study. Also, similar to our findings, less peak heart rate and systolic blood pressure values were obtained with TruView™ EVO2 VL[13].

Xue *et al*[14] found that hemodynamic responses to orotracheal intubation performed by GlideScope VL on direct laryngoscopy were similar. Joo *et al*[15] compared hemodynamic responses to "blind

intubation with ILMA", "fiber optic assisted intubation with ILMA" and, "endotracheal intubation with direct laryngoscopy" in 40 female patients. They also compared the effects on postoperative morbidities. In their study, they found that intubation success rates were equal in all three groups, MAP values were higher in "endotracheal intubation with direct laryngoscopy" group and there was reduced hemodynamic response to LMA Fastrach.

Postoperative sore throat and hoarseness were found in equal percentages for all three groups. They suggested that LMA Fastrach could be used as a primary airway for oxygenation and ventilation and that it could be an alternative to tracheal intubation with laryngoscopy. In comparing Truview blade and Macintosh blade, they found that soft palate injury and bleeding, dental avulsion, desaturation, postoperative sore throat, nausea and stridor were experienced more in direct laryngoscopy with Macintosh blades during intubation[9,11,16]. TruView EVO2™ VL provides a higher quality image of the vocal cords[9].

Inal *et al*[17] compared TruView EVO2™ VL and Miller laryngoscope in 50 pediatric patients and in their study, they found a correlation between preoperative Mallampati scores and intubation difficulty scales of the patients. TruView EVO2™ VL provided higher quality Cormack-Lehane glottic image scores than those of Miller laryngoscope. In scenarios of easy-moderate-difficult airway of 20 anesthesia simulation mannequins, while success rate of laryngoscopy was similar for intubations with ML Truevuew VO2 VL, GlideScope VL and Airtraq VL in scenarios of easy and moderate airway, Airtraq VL was found unique in providing high quality laryngeal image without tongue compression in difficult airway scenario where they made this type of airway with tongue edema in a mannequin[18].

On the contrary, an absolute need for stlyet for intubations with TruView EVO2™ VL maybe be considered a disadvantage. It was reported that TruView EVO2™ VL did not reduce incidence of intubation failure in patients with Cormack-Lehane grade 2 - 3[14]. In our study, although vocal cords were displayed in all the patients considered having difficult airway and planned to intubate with TruView EVO2™ VL, three patients in this group could not be intubated successfully. Because of solid structure of stylet in TruView EVO2 VL, the ETT could not be directed towards vocal cords displayed on the screen. Changing the solid structure of stlyet could improve the success of Truview EVO2 VL in patients with difficult airway. Since TruView EVO2 VL has an oxygen insufflation facility to keep secretions away from the optical lens, vocal cord image is sharper than that of ML.

CONCLUSION

In general anesthesia administration, airway should be evaluated comprehensively and assessment of different tests together will increase the predictability of difficult airway. In case of a difficult airway prediction, we should be prepared for difficult airway management and difficult intubation. TruView EVO2 VL and ML have high success rates of intubation and where difficult intubation is encountered, intubation could be attempted by both of these devices. Since difficult intubation may occur in cases with no predicted airway difficulty, alternative airway devices (such as VL, Fastrach *etc.*) should be used frequently during routine anesthesia so that the anesthesiologist's experience with these devices will be increased. An anesthetist using these alternative airway management devices easily will enhance the chances of successful airway management in difficult intubation cases.

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Original Article

Post-Tonsillectomy Hemorrhage: An Analysis of Incidence and Risk Factors in Kuwait

Bashaer Abdullah, Imtiaz M Qazi, Jamal M Al Harbi, Milind Gosavi, Zakir Hussain, Abdullah Al Shukry
Department of Otorhinolaryngology and Head & Neck Surgery
Zain and Al-Sabah Hospitals, Ministry of Health, Kuwait

Kuwait Medical Journal 2015; 47 (3): 210 - 214

ABSTRACT

Introduction: Post-Tonsillectomy Hemorrhage (PTH) remains one of the commonest complications associated with tonsillectomies. Its incidence and risk factors vary widely in literature.
Objective: To examine our local experience and assess the incidence of PTH in comparison to that in the literature and to identify factors that contribute in increasing the risk of PTH in our setup.
Design: Retrospective study
Setting: Al-Sabah and Zain Hospital, MoH, Kuwait
Methods: A retrospective chart review was conducted on 2,038 patients who underwent tonsillectomy with or without adenoidectomy during a 12-month period (January to December 2010) in Zain and Al Sabah hospitals. Details regarding the patients' age, gender, surgical technique, and level of the operating surgeon were recorded in order to assess any correlation.
Intervention: Tonsillectomy
Main Outcome Measure: Incidence of PTH
Results: Out of the 2,038 patients included in this study, a total of 98 patients (4.8%) developed PTH. Thirty-one patients (31.6%) who developed PTH were above the age of 26 years. Out of the 98 patients (4.8%) who developed PTH, 63 patients (64.3%) were male. 'Hot' dissection technique was associated with higher incidence of PTH (71 patients; 72.4%) in comparison to the 'cold' dissection (27 patients; 27.5%).
Conclusion: The incidence of PTH in our institution is 4.8%, which is comparable with that reported in the literature, ranging between 1.5% and 6.68%. Male patients, increasing age and 'Hot' dissection technique were all identified as risk factors for PTH in our setup.

KEYWORDS: complications, hemorrhage, risk factors, tonsillectomy, techniques

INTRODUCTION

Tonsillectomy, with or without adenoidectomy, remains the most common procedure performed in the field of otorhinolaryngology. Although it is usually considered a fairly safe procedure, tonsillectomy still has the potential to cause lethal complications[1]. Post-tonsillectomy hemorrhage (PTH) is considered to be one of the most common and most anticipated complications associated with this procedure[2]. PTH is classified as primary (occurring intra-operatively), reactionary (within 24 hours post-operatively), or secondary, which might occur any time more than 24 hours post-operatively[3]. Primary PTH is generally considered to be directly related to the surgical technique used and intra-operative control of bleeding. However, secondary PTH is thought to be due to a combination of factors and its direct causation is not fully understood[4]. Many studies have been undertaken to determine and identify the risk factors associated with PTH and many theories regarding these factors have been suggested in order to help reduce the overall incidence of PTH. Some studies suggest that increasing age is associated with an increased risk of PTH, while others suggest that PTH is mainly related to the intra-operative technique of surgery and hemostasis. Despite all differences, there seems to be an agreement that PTH is likely to be due to a combination of factors. Furthermore, there remains to be an agreement to disagree regarding which technique should be considered as 'ideal' in performing tonsillectomies.

With this background in mind, the present study was conducted to determine the incidence of PTH in

Address correspondence to:
Dr Bashaer Abdullah, Specialist, Department of Otolaryngology, Zain Hospital, Al Sabah area, Kuwait. Tel:+965-99750612, E-mail: bashaerabdullah@gmail.com

our institution, as well as to identify the risk factors associated with it and to compare our data with the data published in international literature.

SUBJECTS AND METHODS

A retrospective chart review of 2,038 patients who underwent tonsillectomy, with or without adenoidectomy, between January 1st and December 31st 2010 (12-month period) at the department of Otorhinolaryngology and Head and Neck surgery, Zain and Al-Sabah hospitals, Kuwait was undertaken. Zain and Al-Sabah hospital is an exclusively otorhinolaryngology and head and neck surgery tertiary care teaching hospital attached to the Ministry of Health, Kuwait. It is the main otorhinolaryngology center in the state of Kuwait which caters to approximately half of the population of the country (approximately 1.35 millions)[5]. All patients included in the present study underwent tonsillectomy, with or without adenoidectomy, for non-oncological indications. Patients who underwent tonsillectomy for suspicion of carcinoma were excluded from the study. Inpatient files and operative notes were thoroughly scanned and details regarding the patients' age, gender, days of hospital stay, surgical technique, level of the operating surgeon and the presence of peri and postoperative hemorrhage were recorded. A record was also made of patients who required surgical control of PTH as well as those who required only conservative management. It is also worth mentioning that none of the patients included in the present study had a known or suspicious history of a bleeding disorder based on history and clinical examination. Hence, coagulation screening was not performed routinely and only a complete blood count was done for all patients.

RESULTS

Patient Demographics

During the study period of 12 months (between 1st January – 31st December 2010), 2,038 patients were found to be eligible for inclusion in the study. The age of patients ranged from one to 43 years, with the majority of patients being between the ages of 1 - 5 years (n = 1073; 52.6%). Five-hundred and fifty-one patients (27.0%) were between six and 10 years of age, 149 patients (7.3%) were 11 to 15 years old, 66 patients (3.2%) were 16 to 20 years old, 60 patients (2.9%) were 21 to 25 years old. One hundred and thirty-nine patients (6.8%) were above 26 years of age (Fig. 1). 1,277 patients (62.7%) were male and 761 (37.3%) were female (Table 1). The majority of patients were discharged from the hospital on day one postoperatively (1,990 patients; 97.6%). Thirty-three patients (1.6%) were discharged from the hospital on day two postoperatively, six patients (0.3%) each were discharged on day three and day four respectively, whereas three patients (0.1%) were discharged on or after the 5th postoperative day (Table 2).

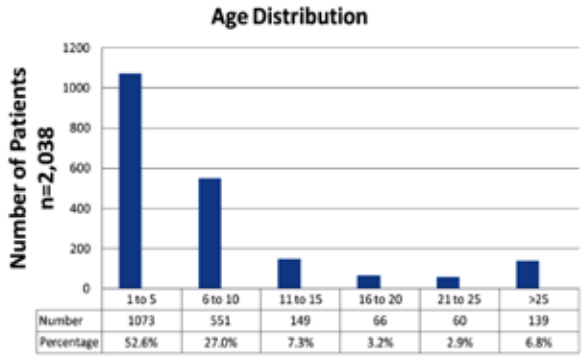

Fig. 1: Age distribution of all patients

Table 1: Distribution of patients according to gender

Gender	Number (n = 2,038)	Percentage
Male	1,277	62.7
Female	761	37.3

Table 2: Total days of hospital stay postoperatively

Hospital Stay	Number (n = 2,038)	Percentage
Day 1	1,990	97.6
Day 2	33	1.6
Day 3	6	0.3
Day 4	6	0.3
Day 5 and beyond	3	0.1

Operative Details

Details of the operation were reviewed, including the operative technique and the level of the operating surgeon (*i.e.*, resident, registrar, senior registrar or consultant). Operative techniques employed included 'cold' dissection (n = 680; 33.4%), 'hot' dissection (unipolar and bipolar) (n = 1,356; 66.5%) and coblation (n = 2; 0.1%). The majority of cases were operated by surgeons at registrar / senior registrar level (n = 1,748; 85.8%), followed by residents (n = 147; 7.2%) and consultants (n = 143; 7.0%).

Incidence of PTH

Out of a total number of 2,038 patients included in the study, 98 patients (4.8%) developed PTH. Most of these patients (31 patients; 31.6%) were above the age of 26 years, 21 patients (21.4%) were 1 - 5 years old, 17 patients (17.3%) were 6 - 10 years old, seven patients (7.1%) were 11 - 15 years old, 13 patients (13.3%) were 16 - 20 years old, and nine patients (9.2%) were of 21 - 25 years (Fig. 2). Out of the 98

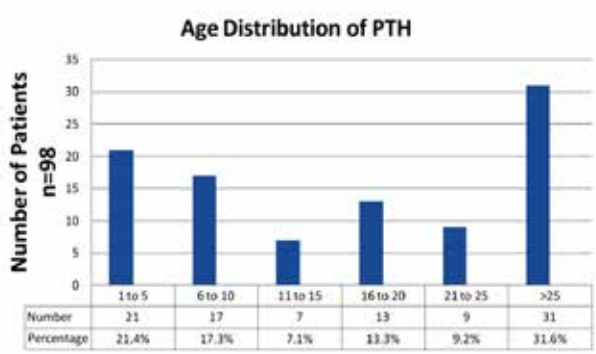

Fig. 2: Age distribution of patients who developed PTH

patients who developed PTH, 63 (64.3%) were male and 35 (35.7%) were female. Three patients (3.1%) had primary PTH (intra-operatively), 22 patients (22.4%) had reactionary PTH (within 24 hours of surgery), where as 73 patients (74.5%) had secondary PTH (> 24 hours postoperatively). Regarding the technique of surgery, 1,356 tonsillectomies were performed *via* 'hot' dissection; more specifically, 1,228 by unipolar electrodissection and 128 by bipolar electrodissection, and 680 tonsillectomies were performed *via* 'cold' dissection. PTH was noted in 71 patients (5.2%) out of those who underwent tonsillectomy *via* 'hot' dissection (69 patients (5.6%) by unipolar electrodissection and two patients (1.6%) by bipolar electrodissection). On the other hand, PTH was noted in 27 patients (4.0%) out of the total number of patients who underwent tonsillectomy *via* 'cold' dissection. Only two patients underwent tonsillectomy by coblation and no evidence of PTH was noted in them (Table 3).

Table 3: Incidence of PTH according to surgical technique

Technique	Number of PTH cases	Percentage
Cold	27	4.0
Unipolar	69	5.6
Bipolar	2	1.6
Coblation	0	0

DISCUSSION

The issue of PTH has been an area of extensive research over the last years. Despite all advances in technology and surgical techniques, PTH continues to be a prevalent and unforeseeable complication associated with this procedure[1,2,4,6,7]. Many guidelines have been published in an effort to identify risk factors and reduce the incidence of PTH[8-10].

Based on the results of our study, the rate of PTH was found to be 4.8%, occurring in 98 cases out of the total 2,038 patients, which is comparable to the rate in published literature. Although the reported incidence of PTH varies, the range has been reported to be between 1.5%[1] and 6.68%[2] in a recently published literature. Comparable results have been reported by other studies. In a study published in the Lancet by Lowe *et al*[11] which included 11,796 patients in England and Northern Ireland, the incidence of PTH and other complications arising up to the 28th day post-operatively were recorded. They reported that 389 patients (3.3%) of the total cohort size developed PTH. Out of the 389 patients, 59 patients (0.5%) had primary PTH, whereas the majority of patients (337 patients; 2.9%) developed secondary PTH. Similarly, in a retrospective study by Collison *et al*[12], the charts of 430 consecutive tonsillectomy patients were examined. All the tonsillectomies performed in this study were by one of two surgeons only, and both surgeons employed the same operative technique of tonsillectomy by 'cold' dissection. They reported that a total of 17 patients (4%) developed PTH, with the incidence of secondary PTH being reportedly higher than primary PTH. In a prospective study published in the American Academy of Otolaryngology and Head and Neck Surgery by Walker *et al*[13], data on children and adults was collected over a period of five years and included complications up to 28 days after surgery. The study included 1,133 patients who underwent tonsillectomy with or without adenoidectomy. They reported that PTH developed in 59 patients (5.2%) out of the total 1,133 patients, with the incidence being strongly correlated with increasing age.

In our study, the age of the patient also proved to be related to the increased risk of PTH. Out of the 98 patients (4.8%) who developed PTH, 31 (63%) were above the age of 26 years, implying that increasing age is directly proportional to the risk of PTH. In the National Prospective Tonsillectomy Audit (NPTA) [8], researchers of the Royal College of Surgeons of England acknowledged this relationship between increasing age and increased risk of PTH, with the incidence increasing from 1.9% in patients aged below five years to 4.9% in those above 15 years. Furthermore, in a retrospective study of 15,218 patients published in Germany, Windfuhr *et al*[1] reported a clear relation between increasing age and PTH. In their study, the risk of PTH for patients younger than four years was noted to be 1.27%. This increased gradually with increasing age to reach a maximum of 9.0% in patients older than 70 years. Similar findings have also been reported by other studies[14,15].

In addition to increasing age, the results of our study show a strong correlation between the patients' gender and the incidence of PTH. A total of 63 male patients (64.3%) developed PTH, in comparison to only 35 female patients (35.7%).

This finding is in conformity to that published in the literature, where the male gender was found to be a risk factor for PTH[1-4,6,7].

Despite the considerable number of tonsillectomies performed worldwide, differences still prevail regarding what surgical technique should be regarded as the 'ideal', and many surgeons often have a personal preference in the approach to this procedure[16]. Many surgical techniques have been adjusted and modified over the years, and many advances have been made to the surgical equipment available for performing the procedure. Common techniques include electrocautery dissection, also known as the 'hot' technique and the 'cold' dissection (using elevator and snare). Newer methods are also available but remain under investigation and these include the harmonic scalpel, ultrasonic dissector, and radiofrequency thermal ablation[17,18]. In our study, the 'hot' and 'cold' techniques were mainly employed. Out of the total 2,038 patients, 1,356 underwent tonsillectomy by 'hot' dissection and 680 underwent tonsillectomy by 'cold' dissection. Of the 1,356 patients who underwent 'hot' dissection, 71 patients (5.2%) developed PTH. On the other hand, of the 680 patients who underwent 'cold' dissection, 27 patients (4.0%) developed PTH, suggesting that the 'hot' technique is associated with a slightly higher risk of PTH in comparison with the 'cold' approach. These results are consistent with results from most studies. However, several other studies did not observe any association with the type of technique used. In a retrospective review of 495 patients, Ali *et al* observed that the incidence of PTH with hot techniques is at least double the rate of that associated with the traditional cold technique[2]. Similarly, the NPTA study[8] also found a 2.5 - 3.2 times greater risk for PTH with the use of diathermy compared with cold steel. They also advised surgeons who performed tonsillectomies using electrocautery to get adapted to an alternative technique in order to reduce the risk of peri and postoperative bleeding. On the contrary, in a recent retrospective study by Akin *et al*[19], no association was found between PTH and the type of surgical technique. Similar results were reported by Leinbach *et al*[20] who concluded, in their systematic review, that there were no meaningful differences when comparing the two techniques in terms of PTH. However, they observed that hot dissection was associated with more postoperative pain.

Furthermore, no association was found between the level of the operating surgeon and the incidence of PTH. The incidence of PTH was noted to be highest in tonsillectomies performed by middle grade surgeons (registrars / senior registrars, 45 cases; 46.0%). However, this group of surgeons also performed the highest number of procedures (1,748 out of the total of 2,038 procedures; 85.8%). Therefore, due to the unequal distribution of procedures, this result is deemed insignificant and no direct association should be implied.

CONCLUSION

Although advances in technology, in association with the production of newer and safer surgical instruments, have helped in reducing the overall incidence of complications related to tonsillectomy, PTH remains a major drawback that has the potential to be life threatening. Despite the frequency of this procedure, no level of experience can predict the occurrence of such complication and no substitute can be found for careful preoperative assessment, including a clear history and examination, and a cautious intraoperative attitude to ensure adequate hemostasis. Most importantly, patients should be clearly informed about the possible risks and complications associated with the procedure in order to allow them to make an informed decision regarding consent to surgery.

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Original Article

Knowledge, Attitudes and Practices among Urban Women of Riyadh, Saudi Arabia, Regarding Breast Cancer

Eyad Fawzi AlSaeed[1], Mutahir A Tunio[2], Yasser Bayoumi[3], Omar AlObeed[1], Ahmad Zubaidi[1], Farjah Alqahatani[1]
[1]Department of Radiation Oncology, King Khalid University Hospital, King Saud University, Riyadh, Saudi Arabia
[2]Department of Radiation Oncology, King Fahad Medical City, Riyadh, Saudi Arabia
[3]Department of Radiation Oncology, NCI Cairo, Egypt

Kuwait Medical Journal 2015; 47 (3): 215 - 220

ABSTRACT

Objectives: To determine the knowledge, attitudes and practices (KAP) of urban women in Riyadh regarding Breast Cancer (BC) and its available screening and treatment modalities
Design: Cross-sectional descriptive study
Setting: BC Awareness day campaigns conducted in Riyadh city from October 2010 to October 2013
Subjects: Six hundred females aged more than 18 years who responded to a well-structured questionnaire comprising of 37 questions.
Main Outcome Measures: The level of knowledge and awareness regarding the risk factors and prevention of BC, misconceptions, symptomatology including KAP, regarding self breast examination (SBE), mammography and treatment for BC
Results: Out of the 600 participants with a mean age of 31.9 years (± 10.49), 342 (57.0%) were married, and 215 (35.8%) were employed. The education level was considerably high; with 363 (60.5%) graduates. Late child bearing age (48.2%), positive family history (75%), increase in age (83.5%), and fatty diet (60.5%) were reported important risk factor for BC. A breast lump (70.8%), underarm lump (60.2%), breast pain (53.7%), change in nipple shape (58.7%) and nipple discharge (51.8%) were reported as the important symptoms for BC. About 348 (58.0%) had heard about SBE and 290 (48.3%) knew how to perform SBE. Nearly 433 (72.2%) believed that early detection for BC is possible with mammography and sound waves. Only 42 (7.0%) knew the treatment for BC. Majority of women 565 (94.2%) wanted more media awareness campaigns regarding the issue.
Conclusion: There is an immediate need for an aggressive campaign to increase awareness regarding BC in Saudi Arabia.

KEYWORDS: attitude, BC, knowledge, practices, Riyadh, Saudi Arabia

INTRODUCTION

Breast Cancer is the most frequent malignancy in women worldwide. It is the leading cause of female cancer related disability and mortality[1]. According to the World Health Organization (WHO), 1.4 million women are diagnosed with BC each year which accounts for 23% of all newly diagnosed malignancies[2].

According to the International Agency for Cancer Research and GLOBOCAN 2008, in the Gulf Cooperation Council (GCC) countries, BC in Saudi Arabia accounts for 26% of all newly diagnosed cancers in Saudi women, with an incidence of 21.6 per 100,000; however, it is not associated with a similar pattern of increased early detection and decreased mortality, as is the case in the developed world[3,4].

In Saudi Arabia, the BC is associated with significant mortality, as most cases present at young age and in an advanced stage, which may in part be attributed to lack of knowledge or awareness of the risk factors, early detection, screening and treatment for the BC[5]. Previously, similar community based studies from different regions in Saudi Arabia have reported the lack of knowledge about the common risk factors for BC, lack of understanding of the importance of breast self-examination (BSE) and mammography[6,7].

Our aim was to determine the level of knowledge or awareness regarding the risk factors and ways of prevention for BC, misconceptions, symptomatology including knowledge, attitudes and practices (KAP), regarding SBE, mammography and treatment for BC in women of urban Riyadh city.

Address correspondence to:
Dr. Mutahir A Tunio, MBBS, FCPS (Radiation Oncology), Assistant Consultant, Department of Radiation Oncology, King Fahad Medical City, Riyadh, Saudi Arabia Tel: +96612889999, Fax: +96612889999 E-mail: mkhairuddin@kfmc.med.sa

SUBJECTS AND METHODS

A cross-sectional descriptive study on females aged above 18 years was carried out in Riyadh (after approval from the institutional ethical review committee) with a well-structured questionnaire distributed among women during BC awareness day campaigns in 2010 to 2013.

Exclusion criteria

1. Women working in the health industry (doctors, nurses, pharmacists, medical students)
2. Known BC patients

The questionnaire was written in Arabic language and had 37 questions which were divided into the four components, namely, (a) Knowledge about BC risk factors and protective factors (15 items), (b) symptomatology and signs of BC (8 items), (c) BC prevention and screening tools (11 items) and (d) cure and treatment for BC (3 items). Each question was ranked separately and scored by knowledge, attitude and practice (KAP) component. Each correct answer was given a score of +1, while every incorrect answer resulted in a deduction of 0.5 from the cumulative score according to discrete probability function f(x) and probability density functions (Bayesian hierarchical approach)[8]. Answer identifying a lack of knowledge (don't know) was given no score. Hence,

Table. 1: Demographic characteristics of six hundred participants

Characteristics	Participants* n (%)
Age groups	
Below 30 years	120 (20.0)
31 - 40 years	210 (35.0)
41 - 50 years	161 (26.8)
Above 50 years	109 (18.2)
Education Status	
Uneducated	21 (3.5)
Primary	40 (6.7)
Matric /O level	40 (6.7)
Intermediate/ A level	91 (15.2)
Graduate	363(60.5)
Masters	40 (6.7)
Ph.D.	5 (0.83)
Occupation	
Students	182 (30.3)
Housewives	197 (32.8)
Employed	215 (35.8)
Retired	6 (1.0)
Marital status	
Single	223 (37.2)
Married	342 (57.0)
Widow	11 (1.83)
Divorced	24 (4.0)
Location	
Central Riyadh	598 (99.7)
Peripheral Riyadh	2 (0.33)

* Mean age: 31.9 years (Range 19 – 60 years); SD: 10.49
SD = standard deviation

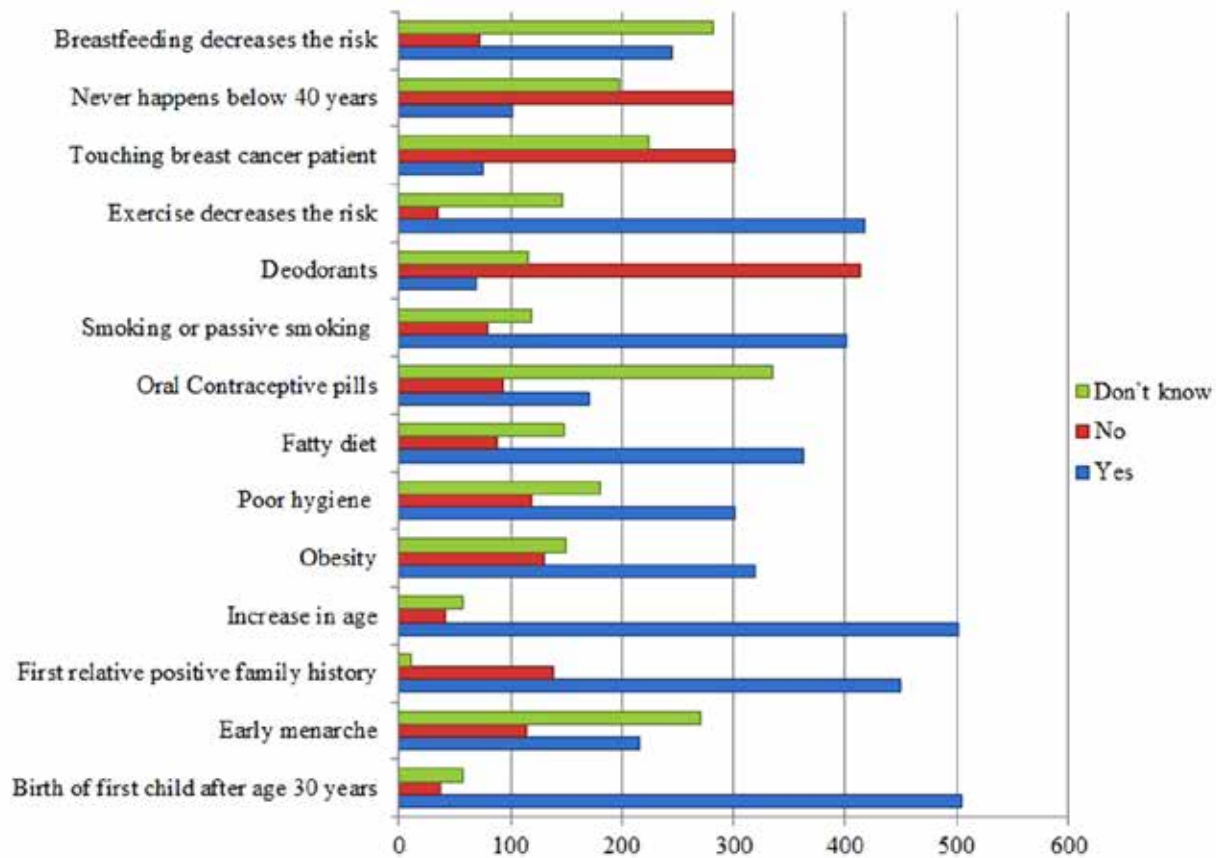

Fig. 1: Response to questions regarding knowledge about BC risk factors and protective factors

the scores ranged between -7.5 and +15 for knowledge regarding risk factors and protective factors, -4 and +8 for knowledge regarding symptomatology and signs, -5.5 and +11 for knowledge regarding the prevention and screening and -1.5 and +3 for treatment modalities.

The sample size was calculated using a confidence level of 95% and a 5% bound-on error and prevalence BC of 55.2%[9,10]. The required sample size came out to be 584. Assuming a refusal rate of 10%, 642 potential subjects were approached and the target achieved was 600 participants.

Statistical analysis

The data was analyzed using Statistical Package for Social Sciences (SPSS) version 17.0. Descriptive statistics were used to calculate mean and standard deviations for demographic characteristics. Frequencies and percentages were computed for categorical variables. Mean and corresponding 95% confidence interval for continuous variables was calculated and analysis of variance (ANOVA) was used to confirm significance values. A p-value of less than 0.05 was taken to be statistically significant. Binary multivariable logistic regression was used in ascertaining the independent risk factors about BC, and adjusting the confounding factors between variables.

RESULTS

The mean age was 31.9 years (range: 19 – 60 years) with standard deviation (SD) of 10.49.The demographic characteristics are shown in Table 1.

Knowledge of participants about prevention of BC is shown in Fig. 1. Knowledge of participants about symptomatology of BC is shown in Fig. 2. Common misconceptions were; (a) active or passive smoking causes BC (66.8%), (b) BC never happens in women below 40 years (17.0%) and (c) BC can happens after touching any BC patient (12.5%).

Knowledge of participants about BC prevention and detection is shown in Table 2. The main reasons for lack of attention to BSE and mammography were

Table 2: Knowledge of participants about BC prevention and detection

Sr. No.	Questions	Response	Participants n (%)
1	Do you know what SBE is?	Yes	348 (58.0)
		No	168 (28.0)
		Don't know	161 (26.8)
2	Is SBE important?	Yes	300 (50.0)
		No	190 (31.7)
		Don't know	110 (18.3)
3	Do you know how to do SBE?	Yes	290 (48.3)
		No	180 (30.0)
		Don't know	130 (21.7)
4	Are you doing SBE periodically?	Yes	79 (13.2)
		No	270 (45.0)
		sometimes	186 (31.0)
5	Do you encourage your relatives and friends to do SBE?	Yes	384 (64.0)
		No	99 (16.5)
		sometimes	116 (19.3)
6	What is right time for doing SBE?	Any time	62 (10.3)
		Don't know	193 (32.2)
		After end of menstrual cycle	321 (53.5)
		Before starting menstrual cycle	24 (4.0)
7	What do you think of doing medical tests from time to time?	Important	541 (90.2)
		Not important	14 (2.3)
		Fear of detection	19 (3.2)
		High costs	3 (0.50)
		Lack of time	18 (3.0)
8	What do you think of screening measures to combat BC?	Good	368 (61.3)
		Medium	203 (33.8)
		Worse	25 (4.2)
		Don't know	4 (0.67)
9	Does early detection of BC helps in cure?	Yes	522 (87.0)
		No	39 (6.50)
		Don't know	39 (6.50)
10	Are you aware of mammography?	Yes	508 (84.7)
		No	28 (4.7)
		Don't know	64 (10.7)
11	Do sound waves and mammogram help in early detection of BC	Yes	433 (72.2)
		No	6 (1.0)
		Don't know	161 (26.8)

SBE = Self breast examination

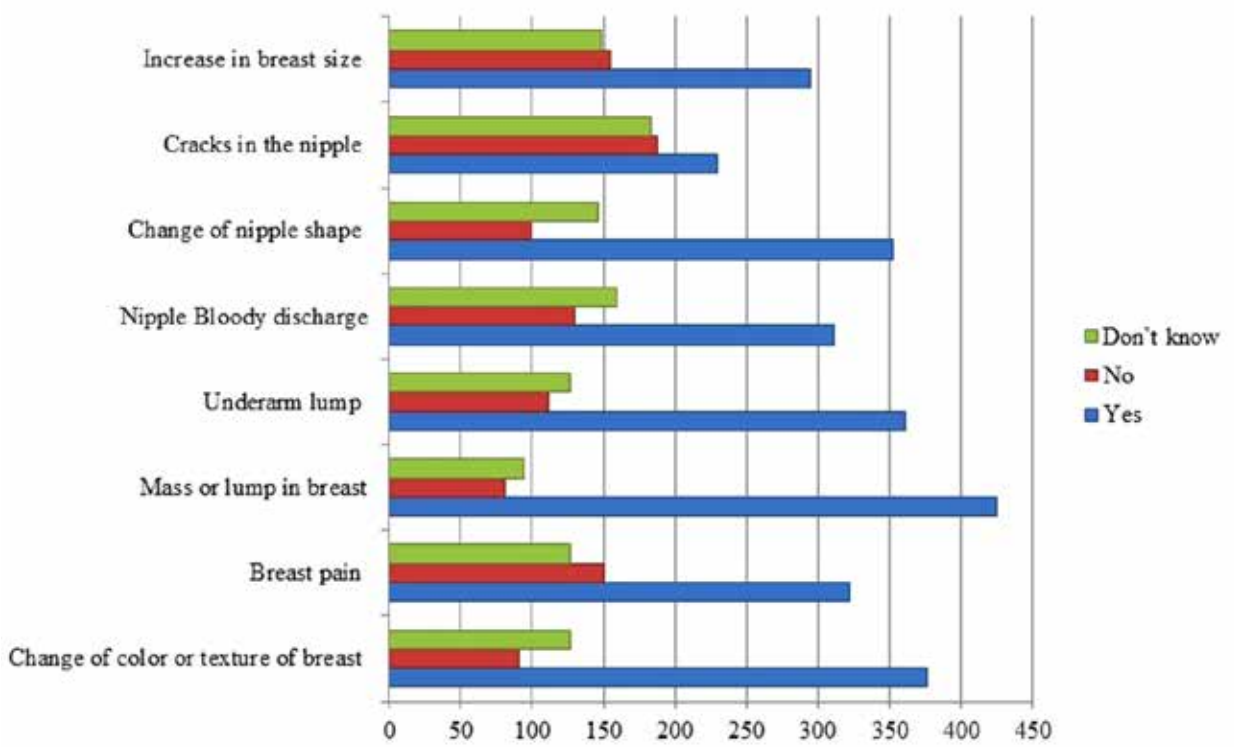

Fig. 2: Response to questions regarding signs and symptoms of BC

the hesitance among females' in discussing breast-related problems (21%) and the fear of finding a mass in their breasts (20%).

Among participants, responses to questions about cure, treatment modalities and need for more awareness are shown in Fig. 3.

Regarding the awareness of risk factors, the mean score for the overall knowledge of risk factors was 5.84 (SD: 3.52), mean scores for the overall knowledge of BC symptoms and signs, screening and treatment modalities were 4.02 (SD: 3.13), 3.94 (SD: 2.63) and 1.82 (SD: 1.59) respectively (Table 3).

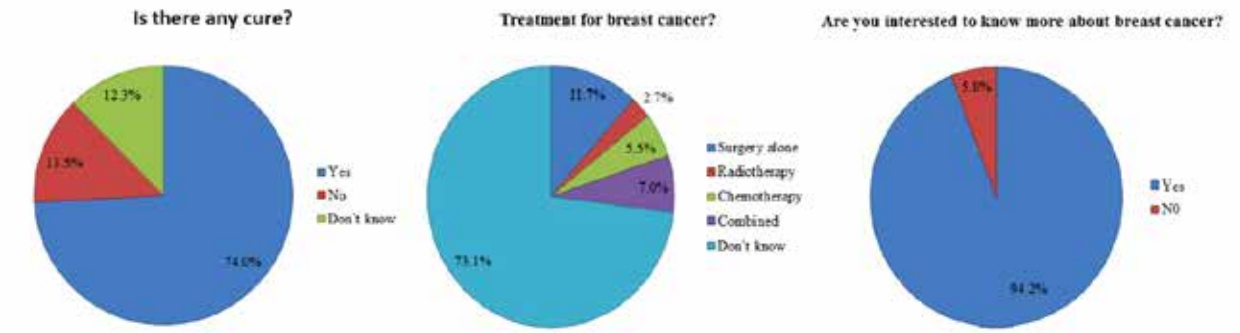

Fig. 3: Response about treatment and more need for education regarding BC

Table 3: Knowledge of participants about BC symptoms and signs

Sr. No.	Questions	Yes n (%)	No n (%)	Don't know n (%)
1	Does change of color or texture of breast indicate to BC?	376 (62.7)	91 (15.2)	127 (21.2)
2	Does breast pain indicate to BC?	322 (53.7)	150 (25.0)	127 (21.2)
3	Does presence of mass or lump indicate the BC?	425 (70.8)	81 (13.5)	94 (15.7)
4	Does underarm lump indicate to BC?	361 (60.2)	111 (18.5)	127 (21.2)
5	Do nipple secretions indicate BC?	311 (51.8)	130 (21.7)	159 (26.5)
6	Does the change of nipple shape indicate to BC?	352 (58.7)	100 (16.7)	146 (24.3)
7	Do cracks in the nipple indicate to BC?	230 (38.3)	187 (31.2)	183 (30.5)
8	Does increase breast size indicate to BC?	295 (49.2)	155 (25.8)	148 (24.7)

BC = Breast cancer

Table 4: Regression analysis of variables associated with high awareness in the study

Variable	p-value	OR (95% CI)
Risk factors and protection		
Age of 40 years and above (n = 270)	0.6	1.5 (0.9 - 2.5)
Education level of graduate and above (408)	0.01	2.4 (1.4 - 3.7)
Marital status (377)	0.8	1.7 (1.1 - 2.7)
Employed or retired (221)	0.02	2.3 (1.2 - 3.6)
Symptoms and signs		
Age of 40 years and above (283)	0.8	1.7 (1.0 - 2.8)
Education level of graduate and above (403)	0.02	2.5 (1.7 - 3.8)
Marital status (365)	0.6	1.4 (0.8 - 2.2)
Employed or retired (220)	0.04	2.0 (1.2 - 3.4)
Detection and Screening		
Age of 40 years and above (265)	0.06	1.7 (1.0 - 3.2)
Education level of graduate and above (395)	0.02	2.5 (1.5 - 3.6)
Marital status (377)	0.7	1.6 (1.0 - 2.4)
Employed or retired (250)	0.5	1.3 (1.1 - 2.4)
Treatment modalities		
Age of 40 years and above (276)	0.9	1.0 (0.5 - 2.5)
Education level of graduate and above (402)	0.01	2.6 (1.7 - 3.8)
Marital status (350)	0.7	1.6 (1.1 - 2.6)
Employed or retired (254)	0.3	1.2 (0.9 - 2.2)

OR = Odds Ratio, CI = confidence intervals, OCP = oral contraceptive pills

A multiple logistic regression was applied to high awareness group (mean scores > 4.5). In this group and it was noticed that that educational status, age above 40 years and employment were the main statistically significant variables associated with high awareness level (Table 4).

DISCUSSION

Many surveys regarding BC awareness and the screening modalities have been conducted in the different parts of Saudi Arabia[5-7,11,12]. Similar to our findings, other investigators have reported that Saudi women have limited information and knowledge of BC and this attributes to presentation of BC at advanced stages[13]. Further, similar to our findings, other investigators also endorsed the demographic characteristics (higher levels of education and age above 40 years) as significant determinants of knowledge about BC risk factors, prevention, adherence to SBE, early detection and knowledge about treatment options.

A study conducted in Dammam, Saudi Arabia, in 1991 by Ibrahim *et al*, demonstrated the education level was statistically associated with awareness; whereas age and family history were not. It did not investigate income levels as in our study[14]. Knowledge without its application is of no use. In our study, 58% of the population had heard about BSE, and nearly 48.3% of our total study population knew how to perform a BSE. The major reason for not performing a BSE identified by the participants in our study was a lack of knowledge or fear (41%) regarding the BSE. However, the percentage of women periodically performing BSE was found to be 13.2% which is comparable to yields of other national studies but far less than as compared to developed countries. In USA, two surveys carried on immigrants' women showed that 53.9% to 55% of the respondents regularly practiced BSE[15,16]. Interestingly, a studies conducted on Nigerian women found that about 87.7% of the respondents had heard of BSE and only 19.0% of them were performing this examination periodically. If we compare Nigerian results with our setting, a greater proportion of Nigerian women were performing the BSE[17, 18]. This difference can be explained by cultural and religious barriers in Saudi Arabia. However, majority of women in our study were willing for media campaigns for BC awareness as currently Saudi Arabia seems to be way behind in media based culturally sensitive campaigns. However, recently successful efforts (Pink Hijab Day and BC day) by Saudi Cancer Society, Zahra BC Association have been made to create awareness in Saudi Arabia without violating the cultural and religious values. However, there is room for more television based media campaigns or organizing frequent open BC forums to enhance the knowledge of Saudi women regarding BC.

The strong points of our study were; (a) reasonable sample size, (b) questionnaire was filled-up in the presence of volunteers who were provided by investigators, (c) we also investigated about participants' knowledge about cure and treatment as well. Limitations of our study were; (a) it was carried out on a segment of the population visiting hospitals or BC awareness campaigns which may be frequented by a specific subset of the overall population, (b) the respondents showed some degree of health seeking behavior (already had some knowledge about BC) by visiting these hospitals or campaigns and (c) we did not look into monthly incomes of participants.

CONCLUSION

Educational level, age above 40 years and employment status had significant association with knowledge and attitude. It seems that improvement of knowledge and practice of Saudi women and their awareness of BC risk factors and early detection and intervention are limited. There is an immediate need for an aggressive campaign to increase awareness regarding BC in Saudi Arabia.

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Original Article

Seroprevalence of Hepatitis B and C, and Human Immunodeficiency Viruses in Saudi Pregnant Women and Rates of Vertical Transmission

Hazem M Al-Mandeel[1], Manahel Alansary[1], Fatimah Algawahmed[1], Hind Al-Mojally[1], Khalid M Alfaleh[2], Lateefa O Aldakhil[1]
[1]Department of Obstetrics & Gynecology, College of Medicine, King Saud University, Riyadh, Saudi Arabia
[2]Department of Pediatrics, Division of Neonatology, College of Medicine, King Saud University, Riyadh, Saudi Arabia

Kuwait Medical Journal 2015; 47 (3): 221 - 224

ABSTRACT

Objectives: Information regarding the prevalence of hepatitis B (HBV), hepatitis C (HCV), and human immunodeficiency (HIV) viruses in Saudi pregnant women is either lacking or outdated. The aims of this study were to determine the current prevalence of these viruses among Saudi pregnant women and to estimate the rates of vertical transmission.
Design: Retrospective cross-sectional study
Setting: Antenatal clinic at a university hospital in Kingdom of Saudi Arabia (KSA)
Subjects: Three thousand two hundred and forty-six Saudi pregnant women seen in antenatal clinics between July, 2010 and June, 2011
Main Outcome Measures: Laboratory results of HBsAg, anti-HCV, and HIV antibodies in all subjects and vertical transmission rates to newborns of seropositive mothers
Results: The mean age was 31 years (± 6.5 years). HBsAg was detected in 1.08% out of the 3,242 tested women. Two babies (6.25%) out of the 32 live tested neonates were positive. Only two (0.07%) women out of 3,051 were positive for anti-HCV antibodies with no vertical transmission. 3119 (96.1%) women were tested for HIV antibodies and none were found to be positive.
Conclusion: The prevalence of HBsAg among Saudi pregnant women (1.08%) is lower than previously reported. However, antenatal testing for HBV is still warranted. Universal antenatal screening of HCV or HIV in Saudi Arabia may not be justifiable due to the very low prevalence of these viruses among pregnant women.

KEY WORDS: hepatitis B virus, hepatitis C virus, human immunodeficiency virus, seroprevalence, vertical transmission

INTRODUCTION

Chronic blood-borne viral infections such as hepatitis B virus (HBV), hepatitis C virus (HCV), and human immunodeficiency virus (HIV) can have a major impact on affected individuals and more so on newborns of pregnant women as a result of vertical transmission. Thus, testing for HBV and HIV in pregnancy is medically indicated to prevent vertical transmission[1-3].

Vertical transmission of HBV, for instance, is known to be the leading cause of infection transmission, and perinatal infection is associated with an extremely high rate of chronicity (up to 90%)[4]. In 1991, WHO recommended that HBV vaccine be part of national immunization programs of all countries in an attempt to reduce the prevalence of HBV. Saudi Arabia was one of 151 countries that followed such recommendation[5]. In addition, the American Congress of Obstetricians and Gynecologists endorsed routine screening for HBV in all pregnant women since 1992[6,7]. This practice was recommended to ensure that women receive optimal medical care as well as appropriate post-exposure prophylaxis is given to the newborn of seropositive mothers.

Prevalence of these aforementioned viruses among the antenatal population may be a reliable indicator of its prevalence in the general population. Nonetheless, the prevalence of HBV is variable based on the population tested. In Saudi Arabia, previous studies estimated that HBV prevalence averaged between 5% and 10% in the 1980's. In 2000, the rate dropped to 1.7% but this was among blood donors samples[8]. A study on

Address correspondence to:
Dr. Hazem Al-Mandeel, MBBS, MSc, FRCSC, Associate Professor & Consultant, Department of Obstetrics & Gynecology, P O Box 7805, King Saud University Medical City and College of Medicine, King Saud University, Riyadh 11472, Saudi Arabia. Tel: +966-11-467-0818, Fax: +966-11-467-9557, E-mail: halmandeel@ksu.edu.sa

the prevalence of HBV among Saudi pregnant women was published in 2005. The investigators found 2.46% seropositive rate among 2664 tested women[9].

On the other hand, antenatal screening for HCV and HIV have not been universally accepted for routine testing in all pregnant women. It is generally reserved for women in high-risk groups. Few countries, however, such as the Netherlands, Estonia and Czech Republic introduced routine universal antenatal screening of HIV for all pregnant women with opting-out policy[10 -11].

We expect that the prevalence of HBV among Saudi pregnant women will even be lower than previously reported mainly due to the strict implementation of HBV vaccinations among all children born in Saudi Arabia. As for HCV and HIV seroprevalence in Saudi pregnant women, there is no published data but it's expected that they are very low.

Currently, the department of Obstetrics and Gynecology in a university public hospital in Riyadh city in Saudi Arabia has introduced routine antenatal testing of HCV and HIV for all women following their pregnancy at this hospital along with HBV testing.

The aims of this study were to determine the prevalence of hepatitis B virus, hepatitis C virus, and HIV in Saudi pregnant women attending antenatal clinics in a university hospital in Saudi Arabia and to determine the transmission rates of those viruses to the newborns of seropositive women. Such information will update and provide data that can lead to some recommendation about antenatal screening for those three viruses based on the results, which can help decision makers in the health ministry to consider testing for HIV and HCV as part of routine testing for all pregnant women in Saudi Arabia.

MATERIAL AND METHODS

A cross-sectional study of all pregnant women attending antenatal clinics of a university hospital in Riyadh city between July 1, 2010 and June 30, 2011 was conducted. No consent from the included subjects was needed because the data was retrieved from hospital health information system and patient's identity was not declared. The Institutional Review Board (IRB) approved the study prior to commencing data collection based on no consent form. Laboratory data for HBV, HCV, and HIV tests of eligible women were retrieved. Women with invalid file numbers or those who did not have the test done were excluded from analysis. Screening tests for the aforementioned viruses, Hepatitis B surface antigen (HBsAg), Hepatitis e Antigen (HBeAg), anti-HCV antibodies, and HIV-1 antibodies was requested during the first antenatal visit. Enzyme Immunoassay (EIA) test was used to determine the presence of HBsAg and HBeAg; anti-HCV antibodies and HIV-1 antibodies were assessed by the same method (EIA and confirmatory test was done by polymerase chain reaction or PCR). Results of these tests were obtained from the Laboratory Access System and were recorded in a standardized data collection form.

Data with regard to the newborns of seropositive mothers were collected from their medical charts. Data regarding postnatal testing of newborns and any prophylactic treatment were collected as well.

Statistical Analysis

Our sample was chosen by convenience. Continuous data is presented as mean and standard deviation if centrally distributed. Skewed data were presented as median and interquartile range. Seroprevelance data were presented as numbers and percentages. Data was analyzed by using PASW Statistics™ program, version 18. Prevalence for each infection was calculated with confidence intervals based on the Poisson distribution for HBsAg, anti-HCV, and HIV antibodies.

RESULTS

The mean age of included women was 31 years (± 6.5), and ranged from 16 to 53 years. Almost all women (99.9%) out of this cohort were tested for Hepatitis B virus antigens and 35 women were found to be positive (1.08%; 95% C.I: 0.72% – 1.44%). Among these seropositive women, 32 women delivered in the same hospital and all their live newborns were tested for HBsAg. Only two newborns were delivered vaginally, out of the 32 tested neonates (6.25%) were found to be positive and their mothers were found to be the only women with positive HBeAg. All live newborns of infected mothers were given immunoglobulin therapy and vaccination at birth.

Regarding HCV testing, two women (0.07%, 95% CI: 0.02% - 0.12%) out of the 3,051 tested subjects were positive for anti-HCV antibodies; both babies were born at this hospital and the test for HCV antibodies was negative up to 12 months of age. None of the tested mothers for HIV (3,119) was positive in this cohort.

DISCUSSION

Hepatitis B and C infections are leading causes of chronic liver disease worldwide. Saudi Arabia was considered one of the endemic areas for those viruses in the 1980's prior to the introduction of several strategies to reduce the transmission of such viruses. Since then, information on the epidemiology of HBV and HCV was accumulated over the last two decades and it showed a marked decline (more than 50%) during the studied period[8]. This decline in prevalence was more significant in HBV (1.7% from 4.7%) compared to HCV (0.28% from 0.58%)[8]. For HIV type 1, the joint United Nations Program on HIV / AIDS reported a projected prevalence of 0.3% in Saudi Arabia[12].

This study is the first study that assessed the prevalence of HCV and HIV along with HBV in obstetrics population in Saudi Arabia. We had the opportunity to check the results of universal antenatal screening for all above-mentioned viruses. The percentage of tested women for each virus was variable but quite high in general; HBV was tested in 99.9% of the total sample, while HIV was tested in 96.1% and HCV in 94%.

Among 3242 Saudi pregnant women, HBsAg was found in 1.08% women. This may indicate a further decrease in the prevalence of HBV in pregnant women compared to previously reported 2.44% seroprevalence rate among 2664 pregnant Saudi women[13]. Such decrease could be due to sampling techniques or more likely due to true change in the prevalence of HBV among women of reproductive age in Saudi Arabia. The prevalence of HBV was similar to that in neighboring countries within relatively similar populations like for instance a study done in Oman, Qatar, and the United Arab Emirates (UAE). The investigators found that out of a total of 1710 enrolled women between the ages of 15 - 45 years (only 1694 had serological results available), HBsAg was positive in 7.1% in Oman, 1% in Qatar, and 1.5% in the UAE. Thus, the prevalence in Qatar and the UAE are quite similar to Saudi Arabia while Oman shows seven-fold higher prevalence rate[14].

The transmission rate of HBV to newborns of infected mothers was estimated to be 6.25% in this study. Worldwide, perinatal transmission of HBV is an important route of infection. Studies have shown vertical transmission rates of HBsAg between 10% and 85%[15]. But El-Magrahe *et al* reported the lowest vertical transmissions of 0.9% only[16]. A study done in India which investigated the seroprevalence of HBV in pregnant women showed that vertical transmission was only in women who had vaginal delivery and none among those who delivered by elective cesarean section[17]. This finding was similar to that in our study where all positive babies were delivered by the vaginal route. This may add to the evidence that elective cesarean section may protect babies from vertical transmission[18].

Regarding hepatitis C, the seropositive rate for anti-HCV antibodies was 0.07% out of the 3,051 women who had the test done. Again, in this study the prevalence is much lower (0.07%) than a previously reported prevalence of HCV in pregnant women in Saudi Arabia (0.7%) by Shobokshi *et al*[19]. However, the seroprevalence of HCV among children in Saudi Arabia in two different studies published over 10 years ago was ranging from 0.04% to 0.1%[20, 21]. Abdel-Moneim *et al* reported the most recent estimation of HCV infection among Saudi population for the period between 2008 and 2011. They found HCV seroprevalence of 7.3% among 15,323 Saudi individuals[22]. Their population included many older subjects above the reproductive age group, which can explain the possible high prevalence of HCV in their study.

As for the neonatal vertical transmission in our sample, none was positive within the twelve-month time frame.

HIV was not detected in our sample, corroborating low prevalence noted in Saudi population. This may be, however, due to sampling error but the scattered reports on HIV-1 prevalence in Saudi Arabia support that HIV prevalence is low in low-risk groups. For example, studies on blood donors in Saudi Arabia showed HIV prevalence as low as 0.006%[23]. In another low risk group, 926 pregnant women in Makkah City were negative for HIV-1 antibodies on antenatal screening[24]. These studies may indicate the extremely low prevalence of HIV-1 in low risk populations in Saudi Arabia. A recent study on the prevalence of HBV, HCV, and HIV in 500 infertile couples attending a tertiary care facility in Saudi Arabia reported similar findings like in our study[25]. The overall prevalence of HBV in the population studied was 1.8%. For females only, HBV prevalence was 1.5%, and for males it was 2.1%. Overall HCV prevalence in this group was 0.5%. All females were negative for HCV, while males had a prevalence of 1.1%. All males and females were negative for HIV.

CONCLUSION

The prevalence of HBsAg among Saudi pregnant women (1.08%) in a tertiary care hospital is lower than the previously reported figure. However, antenatal testing for HBV is still paramount important due to the available preventive measure to minimize vertical transmission. On the other hand, universal antenatal screening of HCV or HIV in Saudi Arabia may not be justified at this point of time due to the very low prevalence of both infections.

Limitations of the study

This study has relatively small sample size in relation to disease prevalence and not all subjects in the cohort were included in the final analysis. Also, the lack of data on any risk factors or other demographics has limited its conclusion.

ACKNOWLEDGEMENTS

We would like to acknowledge the support we received from the Deanship of Scientific Research at King Saud University for funding this project through Research Group Project # RGB-VPP-241.

Conflict of interest: None to disclose

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Original Article

Diffuse Sclerosing Variant Papillary Thyroid Carcinoma: Clinicopathological and Treatment Outcome Analysis of 44 Cases

Khalid Hussain AL-Qahtani[1], Mushabbab Al Asiri[2], Mutahir A Tunio[3], Naji J Aljohani[4], Yasser Bayoumi[5], Wafa AlShakwer[6]
[1]Department of Otolaryngology-Head & Neck Surgery, College of Medicine; Advanced Head & Neck Oncology, College of Medicine, King Saud University, Riyadh, Saudi Arabia
[2]Department of Radiation Oncology, Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia
[3]Department of Radiation Oncology, King Fahad Medical City, Riyadh, Saudi Arabia
[4]Department of Endocrinology and thyroid Oncology, King Fahad Medical City, Riyadh, Saudi Arabia
[5]Department of Radiation Oncology, NCI, Cairo University, Cairo, Egypt
[6]Department of Histopathology, Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia

Kuwait Medical Journal 2015; 47 (3): 225 - 230

ABSTRACT

Objectives: Aim was to evaluate clinicopathological and treatment outcomes of diffuse sclerosing variant papillary thyroid carcinoma (DSV-PTC).
Design: Retrospective study
Setting: Two major tertiary care hospitals of Riyadh, Saudi Arabia
Material: Medical records of 1192 patients with confirmed papillary thyroid cancers (PTC), who were treated or followed up during the period of July 2000 and December 2012 were reviewed.
Main outcome measure: To evaluate the clinicopathologic features and treatment outcomes of patients with DSV-PTC and perform comparative analysis of DSV-PTC with classic-variant PTC (CV-PTC).
Results: A total of 44 cases (3.7%) of DSV-PTC were identified. DSV-PTC patients were younger than their CV-PTC ($p = 0.001$). The mean tumor size was larger in DSV-PTC as compared to CV-PTC ($p < 0.0001$). Advanced pathologic tumor (pT) stage and positive lymph nodes were more often present in DSV-PTC than in CV-PTC ($p < 0.0001$ and $p < 0.0001$ respectively). Median follow-up was 8.05 years (range: 1.62-11.4). Ten-year disease-specific survival (DSS) rates were lower in DSV-PTC (74.4%) than in CV-PTC (89.4%); $p = 0.001$.
Conclusion: DSV-PTC is more aggressive variant as compared to CV-PTC, and is associated with inferior DSS rates. An aggressive surgical approach followed by radioiodine therapy is warranted for these patients.

KEY WORDS: Papillary thyroid cancer, diffuse sclerosing variant, clinicopathologic features, treatment outcomes

INTRODUCTION

The incidence of differentiated thyroid cancers (DTC) especially papillary thyroid cancers (PTC) is increasing exponentially over the past years throughout the world with a wide geographic variation[1]. In the Kingdom of Saudi Arabia, PTC has become the second most common malignancy behind only breast cancer, accounting for more than 10% of all cancers among women[2]. Classical variant of PTC (CV-PTC) is the most predominant variant. This variant has an excellent outlook and prognosis. However, some other variants (follicular, macropapillary and encapsulated) also show a fairly good prognosis as CV-PTC, while some of variants appear to have a decidedly worse prognosis (tall cell and diffuse sclerosing) [3].

Diffuse sclerosing variant of PTC (DSV-PTC) is morphologically characterized by extensive squamous metaplasia, scattered microscopic tumor islands, diffuse fibrosis, calcification, abundant lymphocytic aggregation and innumerable psammoma bodies[4]. Compared to CV-PTC, the DSV-PTC is associated with greater incidence of cervical lymph node involvement and greater incidence of

Address correspondence to:
*Dr. Mutahar Ali Khairuddin Tunio, **MBBS, FCPS**, Assistant Consultant, Radiation Oncology Comprehensive Cancer Center, King Fahad Medical City, Riyadh, Saudi Arabia. Tel: +96612889999, Fax: +96612889999 Email: drmutahirtonio@hotmail.com, Ext:1050, Pager:5922*

distant metastases[5]. However, the probability of disease-specific survival (DSS) and overall survival (OS) after thyroidectomy, adjuvant modalities (radioiodine-131 therapy and neck irradiation) is not well characterized, because of rarity of this variant.

In the present study, we aimed to evaluate the clinicopathologic features and treatment outcomes including DSS in a large series of 44 patients with DSV-PTC and to compare them with a larger group of 532 patients with the CV-PTC; those were evaluated in the same period.

MATERIALS AND METHODS

After formal approval from the institutional ethical committee, medical records of 1192 patients with confirmed papillary thyroid cancers (PTC), who were treated or followed up in two major tertiary care hospitals of Riyadh, Saudi Arabia, during the period of July 2000 and December 2012 were reviewed retrospectively using computer based departmental database system. Patients with DSV-PTC were retrieved in following manner:

Demographic, clinicopathological and radiological variables

Demographic and clinical data including age at the diagnosis, gender, and symptomatology were reviewed. Different histopathological parameters, including the location of tumor, tumor size, multifocality, extrathyroidal extension (ETE), lymphovascular space invasion (LVSI), surgical margin status, and cervical lymph node status, distant metastasis at time of diagnosis and background thyroid tissue were also recorded. Patterns of different immunohistochemical panel including cytokeratin (CK) AE1/AE3, CK19, thyroid transcription factor-1 (TTF-1), thyroglobulin, S-100, and Ki-67 were noted down. Data from different imaging modalities, including ultrasonography, whole body I-131 scintigraphy (WBS), computed tomography (CT) scan of neck and chest, flourodeoxyglucose positron emission tomography (FDG-PET) was collected. Postoperative thyroid function tests (TFTs) and thyroglobulin (TG) levels were also reviewed. Data regarding different treatment modalities, including the type of surgery, neck dissection types, adjuvant radioactive iodine 131 (I-131), its dose regimens in millicurie (mCi) and the details of neck irradiation details (if given) were also recorded.

Statistical analysis

The primary endpoint was the disease specific survival (DSS). Secondary points were; the frequency of DSV-PTC, local recurrence free survival (LRFS), distant metastasis free survival (DMFS) and overall survival (OS). Comparison of DSV-PTC was

Table 1: Patients' characteristics

Variables	SCV- Papillary n (%)	Classic- Papillary n (%)	p-value
Total patients	44/576 (7.6)	532/576 (92.4)	< 0.0001
Age (years)			
≤ 45 years	38 (86.4)	345 (64.8)	
≥ 45 years	6 (13.6)	50 (35.2)	0.001
Gender			
Female	39 (88.6)	452 (84.9)	
Male	5 (11.4)	80 (15.1)	0.05
Type of surgery			
Near or total thyroidectomy	44 (100)	437 (82.1)	0.84
Lobectomy	-	95 (17.9)	
Lymph node surgery			
Central neck dissection	23 (52.3)	174 (32.7)	
Lateral neck dissection	11 (25.0)	102 (19.2)	0.05
Sampling	5 (11.4)	133 (20.8)	
None	5 (11.4)	123 (23.1)	
Mean size (cm)	4.5 (1-9.8) ± 2.1	2.7 (0.1-7) ± 1.9	< 0.0001
≤ 2 cm	4 (9.1)	408 (76.7)	
≥ 2 cm	40 (90.9)	124 (23.3)	
Location (dominant mass)			
Right lobe	18 (40.9)	171 (32.2)	
Left lobe	11 (25.0)	176 (37.8)	0.09
Isthmus	5 (11.4)	64 (12.4)	
Bilateral	10 (22.7)	121 (22.7)	
Multifocal			
Yes	12 (27.3)	239 (44.9)	< 0.0001
No	32 (72.7)	293 (55.1)	
ETE			
Yes	29 (65.9)	191 (35.9)	< 0.0001
No	15 (34.1)	341 (64.1)	
LVSI			
Yes	31 (70.5)	148 (27.8)	< 0.0001
No	13 (29.5)	384 (72.2)	
Surgical margins			
Positive	14 (31.8)	184 (34.6)	0.83
Negative	30 (68.2)	348 (65.4)	
Lymph node metastasis			
Yes	34 (77.3)	255 (47.9)	< 0.0001
N1a	31 (91.2)	165 (64.7)	
\N1b	3 (8.8)	90 (35.3)	
N0	10 (22.7)	277 (52.1)	
Background thyroid tissue			
Normal	19 (43.2)	253 (47.6)	
Multi-nodular goiter	6 (13.6)	122 (22.9)	
Lymphocytic thyroiditis	12 (27.3)	42 (7.9)	
Hashimotos' thyroiditis	7 (15.9)	115 (21.6)	0.04
Distant Metastasis at presentation	6 (13.6)	24 (4.5)	< 0.0001
pT staging			
T1	1 (2.2)	157 (29.5)	
T2	12 (27.3)	165 (31.0)	
T3	29 (65.9)	191 (35.9)	< 0.0001
T4	2 (4.5)	19 (3.6)	
Mean postoperative TG (ng/ml)	2.44 (0.1-42890)	2.39 (0.1-34550)	0.62
I-131 dose			
30 mCi	-	54 (10.2)	
100 mCi	4 (9.1)	199 (37.4)	
150-200 mCi	40 (90.9)	279 (52.4)	< 0.0001
RT to Neck	1 (2.2)	13 (2.4)	0.73

*Mean age in SCV-PTC 34.5 years (18-54); SD ± 8.63 and mean age in CV-PTC 43.2 (8-71); SD ± 12.3

I-131 = radioactive iodine 131, N= number, SD = standard deviation, ETE= extra-thyroidal extension, LVSI = lymphovascular space invasion, pT= primary tumor, TG= thyroglobulin, mCi= millicurie, RT= radiation therapy

performed with CV-PTC those were evaluated in the same period.

Local recurrence was defined as, clinically or radiologically detectable recurrences in the thyroid bed or in cervical lymph nodes, and distant metastasis was defined as, clinically or radiologically detectable disease outside the neck. The DSS was defined as, the duration between the completion of treatment date and the date of documented disease reappearance/ relapse, death from cancer and/or last follow-up (censored). The OS was defined as, the duration between the completion of treatment date and the date of patient death or last follow-up (censored). Chi-square test, Student's t test, or Fisher exact tests were used to determine the differences in various clinical variables. Multivariate logistic regression was done using Cox proportional hazards modeling. Probabilities of LRFS, DMFS, DSS and OS were shown with the Kaplan-Meier method and the comparisons for various survival curves were performed using log rank. All statistical analyses were performed using the computer program SPSS version 16.0.

RESULTS

Among the 1192 PTC patients in our departmental database, 44 (3.7%) patients were found to have DSV-PTC, while 532 patients (44.6%) had CV-PTC. The study cohort was predominantly consisted of female gender (85.3%). The female to male ratio was slightly higher in DSV-PTC (7.6) as compared to CV-PTC (5.6) with $p = 0.05$. The majority of patients had near or total thyroidectomy (n = 481, 83.5%); only 95 (17.9%) patients underwent lobectomy. All DSV-PTC patients (100%) underwent near or total thyroidectomy. Prophylactic central neck dissection (pCND) was performed in 23 in DSV-PTC cases (52.3%) and 174 CV-PTC cases (32.7%) $p = 0.05$. Positive lymph nodes were more often present in DSV-PTC (77.3%) than in their counterpart ($p < 0.0001$). The mean tumor size was 4.5 cm in DSV-PTC while mean tumor size was 2.7 cm in CV-PTC ($p < 0.0001$). Advanced pathologic tumor (pT) stage and distant metastasis at time of diagnosis was higher in DSV-PTC as compared to CV-PTC ($p < 0.0001$, $p < 0.0001$ respectively). Other clinicopathological features are described in Table 1.

Table 2: Disease specific survival according to different prognostic factors

Variables	DSV - PTC				CV - PTC			
	5 year DSS (%)	p-value	10 year DSS (%)	p-value	5 year DSS (%)	p-value	10 year DSS (%)	p-value
Age								
≤ 45 years	93.9		81.8		97.6		95.1	
≥ 45 years	85.7	0.061	57.1	0.037	94.5	0.72	84.4	0.06
Gender								
Female	93.8		71.3		96.6		91.5	
Male	96.8	0.76	80.4	0.065	96.8	0.81	95.3	0.73
Multifocal								
Yes	90.2		64.3		95.2		90.9	
No	96.7	0.72	82.9	0.001	90.0	0.72	88.3	0.60
Lymph node surgery								
Neck dissection								
Yes	96.8		81.8		97.6		95.1	
No	83.3	0.90	57.0	0.001	94.5	0.90	91.7	0.08
Lymph node status								
N0	96.0		71.8		97.6		80.1	
N1	83.3	0.001	53.8	0.001	94.5	0.67	91.7	0.04
Surgical margins								
Positive	96.6		80.4		86.3		84.0	
Negative	96.8	0.60	85.3	0.091	93.2	0.64	87.9	0.60
ETE								
Yes	92.9		57.1		94.5		80.1	
No	96.2	0.63	80.4	0.001	97.6	0.90	90.2	0.01
LVSI								
Yes	92.3		58.5		94.5		80.1	
No	96.3	0.82	80.9	0.001	97.6	0.71	95.3	0.01
Mean postoperative TG								
≤ 2 ng/ml	96.6		83.4		93.2		91.7	
>2 ng/ml	89.5	0.93	85.5	0.95	87.9	0.63	80.1	0.04

DSV-PTC = Diffuse sclerosing variant of papillary thyroid cancer, CV = classical variant, yr = year, DSS = disease specific survival, SD = standard deviation, ETE = extra-thyroidal extension, LVSI = lymphovascular space invasion, TG = thyroglobulin

Table 3: Univariate and multivariate Model of various prognostic factors for disease specific survival in whole cohort

Variable	All patients			
	Univariate analysis		Multivariate analysis	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Age				
≤ 45 years	1.04 (0.7 - 1.3)		1.06 (0.8 - 1.3)	
≥ 45 years	1.34 (1.0 - 2.0)	0.6	1.25 (1.0 - 1.9)	0.6
Gender				
Female	1.07 (0.9 - 1.4)		1.05 (0.7 - 1.3)	
Male	1.05 (0.7 - 1.3)	0.6	1.40 (1.2 - 1.6)	0.05
Lymph node surgery /Neck dissection				
Yes	1.30 (1.1 - 1.7)		2.00 (1.6 - 2.4)	
No	2.70 (1.6 - 4.5)	< 0.0001	2.82 (2.4 - 4.6)	< 0.0001
Histopathologic variants				
Classical	1.05 (0.7 - 1.2)		1.20 (0.8 - 1.6)	
Diffuse Sclerosing	2.80 (1.6 - 3.9)	< 0.0001	2.70 (1.5 - 3.4)	< 0.0001
Multifocal				
Yes	1.93 (1.2 - 2.2)		1.44 (0.9 - 1.7)	
No	1.00 (1.0 - 1.2)	0.9	1.07 (0.9 - 1.3)	0.82
Surgical margins				
Positive	1.10 (0.9 - 1.4)		1.20 (0.8 - 1.6)	
Negative	1.07 (0.9 - 1.4)	0.7	1.17 (0.6 - 1.2)	0.68
ETE				
Yes	4.2 (3.5 - 5.1)		3.31 (1.7 - 4.2)	
No	1.05 (0.7 - 1.1)	< 0.0001	1.17 (0.9 - 1.4)	< 0.0001
LVSI				
Yes	2.3 (1.7 - 2.9)		1.91 (1.7 - 2.8)	
No	1.2 (0.9 - 1.3)	0.02	1.05 (0.9 - 1.4)	0.03
Lymph nodes				
Positive	4.75 (3.7 - 7.8)		3.84 (3.4 - 6.9)	
Negative	1.17 (0.9 - 1.4)	< 0.0001	1.01 (0.8 - 1.4)	< 0.0001

I-131 = radioactive iodine 131, RR = relative risk, CI = confidence interval, ETE = extra-thyroidal extension, LVSI = lymphovascular space invasion

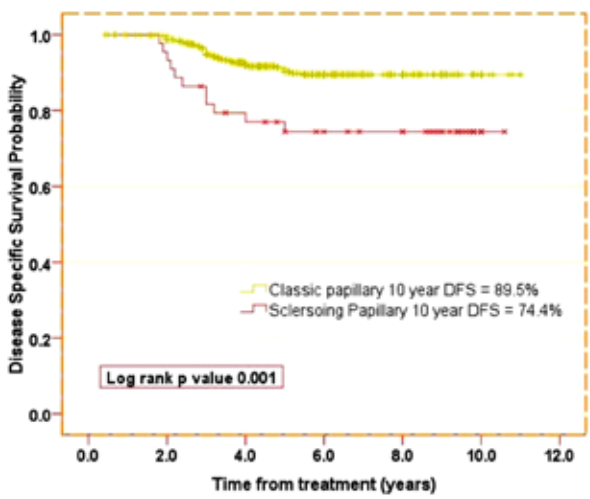

Fig 1: Kaplan-Meier curves of disease specific survival (DSS) according to classical and diffuse sclerosing variants of papillary thyroid cancer

Locoregional recurrences, distant metastasis, overall survival and disease specific survival rates

A median follow-up period was 8.05 years (range: 1.62-11.4). For the whole cohort (CV-PTC and DSV-PTC), the 10 year LRFS, DMFS and OS rates were 91.7%, 91.0% and 98.6% respectively and the 10 years DSS rates were 81.95%.

A total of 32 local recurrences (5.56%) were observed; 7/44 (15.9%) in DSV-PTC patients and 25/532 (6.77%) in CV-PTC patients (*p <0.0001*). The pattern of local recurrences was: 12/32 patients (37.5%) had disease in thyroid bed only (DSV-PTC; 3 patients, CV-PTC; 9 patients) and 20/32 (62.5%) developed cervical lymphadenopathy (DSV-PTC; 9 patients, CV-PTC; 11 patients). Combined locoregional and distant metastasis were seen in 5/44 (11.4%) DSV-PTC patients and 13/532 (3.2%) in CV-PTC patients. The isolated locoregional recurrences were salvaged by surgery (lateral neck dissection

for 10 patients, and completion thyroidectomy for 4 patients) followed by I-131 ablation (12 patients). Distant metastasis were seen in 5/44 (11.4%) in DSV-PTC patients and 26/532 (4.9%) in CV-PTC patients (*p <0.0001*). All DSV-PTC had metastases in the lungs. All distant metastases were salvaged by I-131 ablation and palliative irradiation for bony lesions (three CV-PTC patients). In DSV-PTC patients, time to initial local recurrence was 1.8 years and time to initial distant metastasis was 2.0 years. The 10 year DSS rates were 89.5% vs. 74.4% in CV-PTC and DSV-PTC patients respectively (*p = 0.001*) Fig. 1. The 5 and 10 year DSS rates in CV-PTC and DSV-PTC patients according to different variables are summarized in Table 2. No transformation to squamous cell carcinoma or death was reported in our series of DSV-PTC patients.

Prognostic Factors

The results of Cox regression Model using univariate and multivariate analysis for DSS to predict important prognostic factors are shown in Table 3. Important prognostic factors found were; sclerosing variant (*p < 0.0001*), lymph node dissection (*p < 0.0001*), ETE (*p < 0.0001*), LVSI (*p = 0.03*) and nodal status (*p < 0.0001*).

DISCUSSION

DSV-PTC is rare aggressive variant, and according to several reports, the prevalence of DSV-PTC of all papillary carcinomas has been reported to be 0.3% to 5.3%[6]. In this large series of DSV-PTC patients, we were able to determine overall ten years DSS rates of 74.4% after aggressive treatment by near or total thyroidectomy followed by I-131 therapy in the majority of cases in our cohort. These results are in consistent with similar reported data[3,5,7,8,9]. However, one series found that the prognosis of DSV-PTC was similar to CV-PTC[10]. The poor outcome in our series can be justified by (a) larger tumors (mean: 4.5 cm Vs. 3.6 cm); (b) predominant elderly population (mean: 34.5 years vs. 29 years) and (c) few patients received external beam irradiation (1 Vs. 4) in our cohort. However, in our series no cancer related death was reported, in contrary to studies by Thompson LD, *et al* (4.5%), Koo JS, *et al* (3.6%) and Lam AK, *Lo CY* (6.7%).[3,8,10]

Malignant transformation of squamous metaplasia to squamous cell carcinomas (SCC) of thyroid, albeit very rare have been reported in few DSV-PTC case reports and series[11]. Thompson LD, *et al* have reported one (4.5%) squamous cell carcinoma in a series of 22 DSV-PTC patients[3]. In our series, although no case of DSV-PTC transformed SCC was observed, but to differentiate DSV-PTC transformed SCC from primary SCC of thyroid needs extensive work up. Primary SCC lacks psammoma bodies, extensive lymphocytic thyroiditis, the presence of characteristic PTC and appears at older age[12,13]. Although not reported in our series, another rare entity that shall be differentiated from DSV-PTC is the primary mucoepidermoid carcinoma (MEC) and sclerosing mucoepidermoid carcinoma with eosinophilia (SMECE) of the thyroid. MEC consists of nests of epidermoid or even squamous appearance and mucin-containing cysts and in MECE, there is extensive fibrosis with eosinophilic leukocytes enriched stroma with background of chronic lymphocytic thyroiditis and extensive fibrosis[14,15]. Similar to DSV-PTC, MEC and MECE are TTF-1 and P-cadherin immunoreactive, however MEC and MECE lacks extensive lymphovascular space invasion (LVSI), psammoma bodies, and extensive cervical lymph node metastasis as compared to DSV-PTC[16].

In our series, none of DSV-PTC patient had history of radiation exposure, as related literature has suggested possible epidemiologic link between radiation exposure and the development of DSV-PTC[4,17].

Lymph node involvement was the most significant independent risk factor for recurrence in our cohort of DSV-PTC patients. Failure of I-131 therapy to minimize the risk of locoregional recurrence in lymph node positive DSV-PTC is an indicator of underlying tumor burden in neck and this supports the hypothesis of extensive prophylactic central and lateral neck dissection during thyroidectomy in such patients[10]. However, there is potential increased risk of hypoparathyroidism associated with central neck dissection.

Strengths of our study are; (a) according to our knowledge, this is the largest series of DSV-PTC to date and (b) comparative analysis was performed with CV-PTC. However, limitations of our study were (a) it was retrospective, and (b) potential selection bias could not be ruled out.

CONCLUSION

DSV-PTC is rare variant and we should be familiar with the clinicopathological features and treatment outcomes of this variant. Long terms outcomes can be achieved by aggressive surgical approaches (neck dissection) and adjuvant modalities (I131 therapy and neck irradiation).

ACKNOWLEDGMENT

Conflict of interests: Authors have no potential conflict of interest. No any grant or funds have been received for this case report. A formal consent was taken for the publication from Institutional Ethical review committee.

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Original Article

Impact of Weekend Admission on the Outcome of Patients with Acute Gastro-Esophageal Variceal Hemorrhage

Hamad Hadi Al-Qahatani[1], Muhammad Ibrar Hussain[2], Mohammed Khurshid Alam[3], Reem Al-Salamah[4], Malak Al-Zahrani[1], Huda Saddig I Al-Maghrabi[5]

[1]Department of Surgery, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia (KSA)

[2]Department of Surgery, College of Medicine, Taibah University, Al-Madinah Al-Munawarah, KSA

[3]Department of Surgery, Al Maarefa College of Medicine, Riyadh, KSA

[4]General Surgery, College of Medicine, Al-Qassim University, KSA

[5]General Surgery, King Faisal Specialist Hospital & Research Center, Riyadh, KSA

Kuwait Medical Journal 2015; 47 (3): 231 - 235

ABSTRACT

Objectives: To evaluate the impact of weekend admission on the outcome of patients with acute variceal hemorrhage (AVH)

Design: Retrospective study

Setting: Department of Surgery, College of Medicine, King Saud University, KSA

Main Outcome Measures: AVH, weekend admission and clinical outcome

Subjects: Nine hundred and thirty-seven admitted during the period 1st January 2005 to 31st July 2013 and documented to have AVH. The selected patients were divided into two groups based on the admission day (weekday or weekend admission). The data regarding patients characteristics and outcome in both the groups were retrieved from medical records and compared by using c2 test / Fisher's exact and student T- test.

Results: Weekday admissions included 685 patients, while the weekend group comprised of 252 patients. The demographic, clinical and laboratory characteristics of patients admitted with AVH in both the groups were comparable. Statistically, there was no significant difference in the need for blood transfusion (46% versus 48%, p = 0.5868), and surgical intervention (5.4 % versus 4.7 %; p = 0.6595) between the groups. There was a little, but statistically significant delay in endoscopic intervention in the weekend group (7.56 ± 7.8 hours versus 9 ± 2.32; p = < 0.0001). However, this delay did not lead to adverse outcome for patients (mortality rate 6.8% versus 5.25%; p = 0.389).

Conclusions: The weekend admissions were not associated with increased mortality in patients with AVH. Moreover, the length of hospital stay, need for blood transfusion, and rate of surgical intervention were similar in weekdays and weekend admissions.

KEY WORDS: endoscopy, gastro-esophageal variceal, upper gastrointestinal hemorrhage, mortality, weekend effect

INTRODUCTION

Upper gastrointestinal hemorrhage (UGIH) remains a major indication for emergency hospital admission[1]. Although, many episodes of hemorrhage are self-limiting, yet associated with significant morbidity and mortality (5 to 10%)[2]. Acute non-variceal hemorrhage (ANVH) accounts for a majority of UGIH, followed by acute variceal hemorrhage (AVH) secondary to portal hypertension. The management of these patients requires a multidisciplinary approach which includes prompt resuscitation, triage to appropriate level of care, medical and supportive management, risk stratification, and access to early endoscopy. The outcome depends upon the patient's factors, course of primary disease, associated co-morbid conditions, expertise of the treating team, and level of the facilities available at the presenting hospital[3,4]. Over the past two decades, substantial evidence in medical literature has demonstrated an association between weekend admission and increased mortality for various medical and surgical emergencies, termed as "weekend effect"[5,6]. This effect has been attributed to reduced hospital staffing, delay in the invasive procedure and treatment on weekends[5-9]. The adverse outcome of patients with UGIH, admitted on

Address correspondence to:

Dr. Hamad Hadi Al-Qahatani, MBBS, MD (Hon), CABS, FRCSI, Associate Professor & Consultant General and Hepatobiliary Surgeon, Department of Surgery, College of Medicine, King Saud University, Riyadh, Kingdom of Saudi Arabia. Tel: 00966-554412324 (mob), Fax: 00966-2074787, E-mail: hamad_qah@hotmail.com

weekend has also been observed in some reports,[3,10,11] while others failed to demonstrate this effect[12-14]. The majority of these studies focused on patients with ANVH, and only few studies addressed this issue in patients with AVH. Therefore, the objectives of this study were to evaluate the impact of weekend admission on the outcome of patients with AVH in terms of mortality, hospital stay, need for blood transfusion and surgery.

SUBJECTS AND METHODS

This retrospective cohort study was conducted in the department of surgery, King Saud Medical City; Riyadh, Kingdom of Saudi Arabia. It included all the patients with symptoms of UGIH, (hematemesis or melena or both) who were admitted through the emergency department (ED) to hematemesis and melena unit (HMU) between 1st January 2005 to 31st July 2013. Patients, who were managed by conservative treatment, had not undergone esophagogastroduodenoscopy (EGD) or who found to have non-variceal source of bleeding on EGD were excluded from the study. The selected patients were divided into two groups based on the admission day (weekday or weekend admission). Weekend admission was defined as from Wednesday at 16:00 hrs to Friday at midnight and others were those of weekday admissions.

It is the policy in our institution that general surgical (GS) team, lead by board certified senior registrar or consultant surgeon, is responsible for care of all the patients with gastrointestinal bleeding (GIB). General surgeons assess these patients, resuscitate them, request appropriate investigations and involve the gastroenterologist to perform EGD at appropriate stage of the management. After EGD, these patients are admitted in HMU under the care of general surgeons. However, hepatologists and gastroenterologists closely follow up these patients as a part of multidisciplinary team.

This HMU is well equipped with critical care monitoring devices and fully trained nursing staff. The endoscopy services are available around the clock during the weekdays and weekend, covered by two gastroenterologists (one senior registrar and one consultant gastroenterologist) with all the tools needed for management of UGIH. The routine management of all patients with portal hypertension related UGIH includes : 1) Intravenous infusion of

Table 1: Characteristics of weekday and weekend admission of patients with AVH

Characteristics	Weekday Admissions	Weekend Admissions	p-value
Age (years)	57 ± 9.3 (range 37 - 77)	56 ± 8.8 (range 36 - 78)	0.1391
Gender			0.188
Male	77	81	
Female	23	19	
Presenting symptoms			
Hematemesis	28	26	0.5387
Melena	60	63	0.4011
MH	12	11	0.6678
Presenting vital signs/Hemoglobin (Hgb)			
SBP (mean ± SD)	118.7 ± 28.6	117.5 ± 45.7	0.6325
HR (mean ± SD)	86.3 ± 21.3	87.6 ± 17.6	0.3867
Hgb (mean ± SD)	9.3 ± 3.5	9.1 ± 6.7	0.5539
Liver related variables :			
1) Cirrhotic liver	82	84	0.4650
2) Non-cirrhotic liver	18	16	0.4650
3) Hepatic decomposition	55.6	53.5	0.5674
4) Hepatic encephalopathy	17	18.2	0.6708
5) Ascites	33.4	31.1	0.5024
6) Hepatorenal syndrome	3.3	4.5	0.4156
7) Spontaneous bacterial Peritonitis	1.4	1.3	0.9056
8) Coagulopathy	33	31.5	0.6623
9) Hepatocellular carcinoma	2.2	1.9	0.7702
Child-Pugh score			
A	32	34	0.5652
B	57	59	0.5818
C	11	9	0.3554
Comorbid conditions (n)			
0	11.8	10.5	0.5705
1	32	31	0.7697
2	28	27	0.7606
≥3	28.2	31.5	0.3311

The data for comparisons between the two groups are presented as proportion (%) unless otherwise specified.
Abbreviations: SD: standard deviation; SBP: systolic blood pressure (mmHg); HR: heart rate (beats/min); MH: melena and hematemesis. AVH: acute variceal hemorrhage, Hgb: hemoglobin

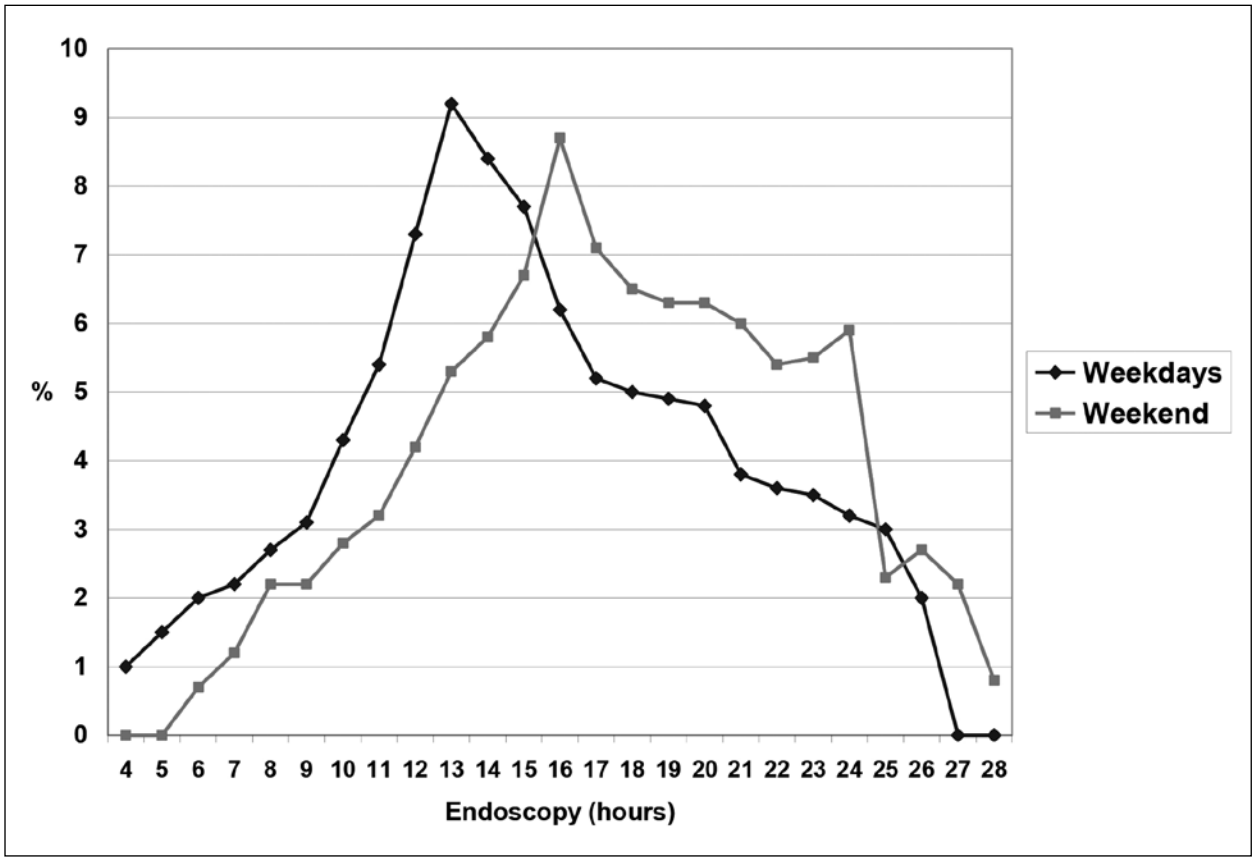

Fig.1: Difference in endoscopic timing between weekday and weekend admissions

octreotide, 2) intravenous proton pump inhibitors, 3) Intravenous Ceftriaxone, 4) Oral lactulose, 5) Rectal wash, 6) Nil orally, 7) Intravenous infusion of low sodium containing fluids, 8) Blood testes: complete blood count, renal profile, serum electrolytes, liver function test, coagulation profile, hepatitis screening, and bilharziasis titer when indicated, 9) Ultrasound abdomen and computed tomography when indicated and 10) Second therapeutic endoscopy within one week from the first endoscopy.

Medical records of all these patients were reviewed after the approval of local research and ethical committee of the King Saud Medical City. The data regarding demography, time of admission, presenting symptoms, vital signs and hemoglobin concentration on presentation, coagulation parameters and the need for international normalized ratio (INR) reversal prior to endoscopy, blood transfusion, endoscopic therapy, re-endoscopy, re-bleeding, experience of the gastroenterologist, surgical intervention, length of hospital stay (LOS) and in-patient hospital mortality was collected. The main outcome measures studied were in-patient's mortality, LOS, need of blood transfusion and surgery.

Statistical analysis: Statistical analysis was performed by using Statistical Package for the Social Sciences (SPSS) version 19 software (SPSS Inc. Chicago, IL, USA). Data for dichotomous variables and nominal variables are expressed as percentages and were compared by a c2 test or Fisher's exact test. Means of numerical or continuous variables were compared by student T- test. The P-value of <0.05 was considered as statistically significant.

RESULTS

A total of, 937 patients were admitted with a diagnosis of AVH during the study period. Their mean age was 57 ± 9.5 years (range 36 - 78 years) and men outnumbered women; 761 to 176. All the patients were subjected to EGD within 28 hours of presentation to ED and documented to have AVH. Six hundred and eighty-five patients were admitted during the weekday while the weekend admissions comprised of 252 patients. The demographic features, clinical and laboratory characteristics of patients admitted with AVH both on weekends and weekdays were comparable (Table 1).

A significant number of patients received blood transfusion with no difference between the groups. (46% weekday versus 48% weekend group, P = 0.5868). EGD was performed within 24 hours in 95% and 92 % of the patients in weekday and weekend admissions respectively; however, it was performed within 28

hours in all patients of both the groups. Endoscopic therapy (band ligation or sclerotherapy) was performed with similar proportion in both groups (88% weekday versus 91 % weekend, P = 0.1709). The percentage of patients, who required repeat EGD was significantly higher in weekend admissions (7% Vs. 14 %; P = 0.0035). Obscured bleeding was the probable cause in most of these cases. Moreover, most of the primary interventions were performed by the clinical fellows/ senior registrars.

The proportion of patients who re-bleed after first endoscopy, (8% weekday versus 7% weekend; P = 0.6012), required balloon tamponade (6% weekday versus 5.11% weekend; P = 0.5914) and surgical intervention (5.4 % versus 4.7 %; P = 0.6595) was almost similar in both the groups. There was a small, but statistically significant differences (7.56 ± 7.8 hours versus 9 ± 2.32; P = <0.0001) in the timing of endoscopy between the two groups (Fig. 1). This delay was due to correction of coagulopathy before intervention, not because of the non availability of endoscopist. However, this delay did not affect the outcome of the patients. The in-hospital mortality was slightly higher in weekend admissions (6.8% weekday versus 5.25% weekend admissions), but it was not statistically significant (P = 0.389). Similarly the length of hospital stay in both the groups was 8 ± 6 and 8 ± 9 days, respectively (P = 0.999).

DISCUSSION

Patients with AVH secondary to portal hypertension require complex management (initiation of early resuscitation, specific medical therapy and supportive therapy to manage the complications of portal hypertension) with multidisciplinary team approach. [3,4] We examined the impact of weekend admissions on the outcome of patients with AVH and found no difference in the mortality of these patients admitted on weekdays or weekends. Our results are in accordance with the published series[5,12-14]. Bell CM and Redelmeier DA [5] failed to demonstrate any weekend effect on the mortality of their patients with unspecified UGIH. Myer RP and colleagues [13] concluded that weekend effect did not apply to their patients hospitalized with AVH. Nevertheless, the delay encountered in the endoscopic intervention didn't contribute to the increased mortality. Similarly, Jairath V et al [14] found to have no difference in the mortality for weekend versus weekday presentation despite the fact that patients were more critically ill and had greater delay to EGD at weekends.

However, contrary evidence also exists in the medical literature describing the adverse outcome of patients admitted on weekends with UGIH [3,10,11]. Dorn SD *et al*[10] have observed increased mortality, longer hospital stay, overall higher medical expenditures, and long waiting time for EGD for weekend admission in patients with UGIH. They have related their adverse outcome with fewer and less experienced medical staffing, increase work load and suboptimum quality of care provided to these patients on weekends. In addition, admission of relatively sicker patients on weekends could be the probable reason of the increased mortality. [10]

Two other trials [2,11] from the United States of America (USA) have demonstrated an increased mortality (10 - 13%) and delayed endoscopy in patients with UGIH admitted at weekends compared to weekdays. The difference of higher mortality in their studies can be explained by their patient's selection and multi institutional study design. They included all the patients admitted both from clinics and ED in their weekday group. The outcome of both groups could vary, because majority of the patients presented in ED were critically ill and hemodynamically unstable at presentation. Eventually, their outcome was expected to be the worst compared to weekday admissions. Secondly, there was a great variation in delivery of health care system across USA. [14] Hence, the quality of resuscitation, availability of endoscopic therapy and general medical care of these complicated patients might be different from place to place, which affected the outcome of these patients. But our study included only the patients admitted through ED in a specialized unit (HMU) of a single tertiary care hospital.

Early endoscopic intervention within 24 hours has proved to reduce the LOS, overall cost of treatment, need of surgery, blood transfusion, and the mortality of those patients with UGIH. [12,15-17] We have observed a statistically significant delay in endoscopic intervention during weekends compared to weekday's admission, but all these patients underwent EGD within 28 hours of admission. Therefore, this delay was not long enough to increase the mortality of these patients. These findings are in agreement with some other studies. [11,13]

Some authors suggested that weekend admissions comprised of critically sick patients who had advanced primary liver disease[10,14]. Hence, they needed more blood transfusions for resuscitation. Our findings are contrary to them, because the blood transfusion requirement and need of surgical intervention in our groups were similar. We think, prompt resuscitation, and stabilization of the patients with fluids and drug therapy are of utmost importance prior to endoscopy in patients with AVH. Delay in the endoscopic intervention on weekends may contribute to longer hospital stay and higher hospitalization costs.[3,10,13] Length of hospital stay was almost the same in our groups.

Our study is limited by its retrospective study design, which is usually associated with selection bias. We tried to remove the selection bias by including all the consecutive patients admitted through ED and divided them into two groups based on the admission day, irrespective of their demographic, clinical and laboratory characteristics. Secondly, it was a single institutional study conducted in a specialized unit of a teaching hospital. Therefore, the results of this study can't be applied over a whole population. We recommend conducting a multi-centric country based study to determine the weekend effect on the outcome of patients with UGIH. That will help to know about the standard of care, and availability of endoscopic facilities in both teaching and non-teaching hospitals. Thirdly, our analysis of patient's outcome was limited to in-patient mortality. Further studies are required to evaluate an association between weekend admissions and increased mortality in patients with AVH over the long term follow up.

CONCLUSIONS

The weekend's admission was not found to be associated with increased mortality of the patients with AVH. Moreover, the length of hospital stay, need of blood transfusion and rate of surgical intervention were similar on weekdays as well as weekend's admissions.

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Case Report

Renal Disease in Bodybuilders

Ahmad Ramadan[1], Kamel El-Reshaid[2], John Patrick Madda[3]
[1]Department of Medicine, Al-Amiri Hospital, Kuwait
[2]Department of Medicine, Faculty of Medicine, Kuwait University
[3]Department of Histopathology, Al-Amiri Hospital, Kuwait

Kuwait Medical Journal 2015; 47 (3): 236 - 239

ABSTRACT

We report our experience with the development of focal segmental glomerulosclerosis (FSGS) in two adult bodybuilders who had consumed high protein diet, anabolic steroids and growth hormone for years in their attempt to gain more muscular appearance. The first patient presented with severe renal failure (serum creatinine 700 umol/l) and kidney biopsy showed advanced FSGS. The second had moderate renal disease (serum creatinine 170 umol/l) and hypercalcemia (3.8 mmol/l) due to his high intake of milk instead of water to promote more protein intake. His kidney biopsy showed early FSGS with diffuse interstitial fibrosis associated with extensive calcium deposition in the tubules. Both patients were instructed to avoid such attitude and were treated conservatively. However, the first patient required kidney transplantation four months later. The second one improved gradually, over the past two months, with decrease of serum creatinine to 96 umol/l. He is currently on telmisartan 40 mg daily to decrease his glomerular pressure. In conclusion, athletes and bodybuilders should consider the risks involved with the use of high protein diet, anabolic steroids and growth hormone alone or in combination to avoid the development of serious renal disease such as FSGS.

KEY WORDS: anabolic steroids, bodybuilders, focal segmental glomerulosclerosis

INTRODUCTION

Many athletes use high protein diet and pharmacological doses of anabolic steroids and growth hormone to enhance their physique and improve their achievements. The anabolic steroids are banned drugs for their serious side effects on the immune system, blood, sterility, atherosclerosis, blood pressure, lipid, heart, liver, immune system and mood[1]. The renal complications of such practice are emerging yet remain rare[2,3]. In this case report, we present two adult bodybuilders who presented with advanced and moderate renal failure subsequent to consumption of such diet and drugs for years.

CASE REPORTS

Case 1

A 41-year-old Philipino man presented to our renal unit with progressive lower limbs edema and shortness of breath over the past few weeks. He denied fever, chest or abdominal pain, skin rash and joint pains. The patient was a coach for body building and he had used for years, high protein diet (20 - 30 g/kg/day), multiple anabolic steroids and growth hormone for > 20 years. The patient had muscle aches and laboratory tests six months ago showed serum creatinine at 135 umol/l and albumin at 34 g/l. Otherwise, he did not have significant medical illness, surgery, and allergy. On his initial physical examination, the patient was conscious and oriented. He did not have pain yet was in distress due to shortness of breath. Blood pressure was 150/90 mmHg and temperature was normal. He was very muscular with a body weight of 89 kg and height 1.82 meters. He did not have lymphadenopathy or goiter. However, he had jugular venous distension and edema. Systemic examination did not show abnormality except for bilateral basal crepitations. Laboratory investigations showed normal peripheral leucocytic and platelets counts. Hemoglobin was 110 g/l with normal MCV. ESR was 20 mm/h. Serum

Address correspondence to:
Dr. Kamel El-Reshaid, MBBCH, Am B Med, Am B Nephrology, FRCP (Ed), Professor, Dept. of Medicine, Faculty of Medicine, Kuwait University, P O Box 24923, 13110 Safat, Kuwait. Tel: 99896110 (Dr. Ahmad Ramadan), Fax: (965) 5318454, E-mail: ahmzaad@yahoo.com, hotmail.com

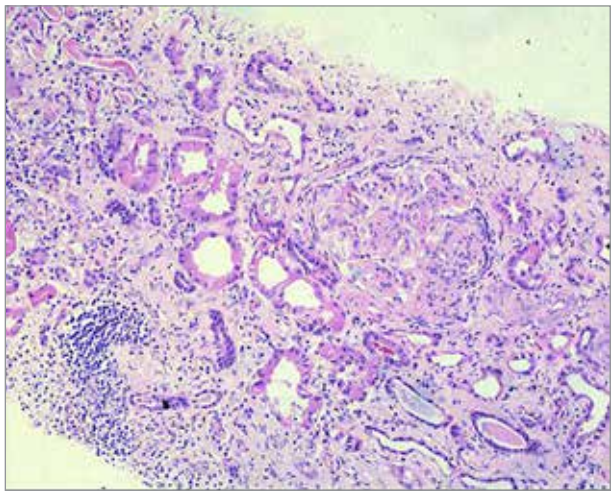

Fig. 1: Photomicrograph of kidney biopsy of the first patient showing global sclerosis of 80% of the glomeruli. The remaining glomeruli show segmental sclerosis. There is mild mesangial cell proliferation, interstitial infiltration by lymphocytes, plasma cells and few neutrophils around the global sclerosis glomeruli. (H&E, original magnification x 200)

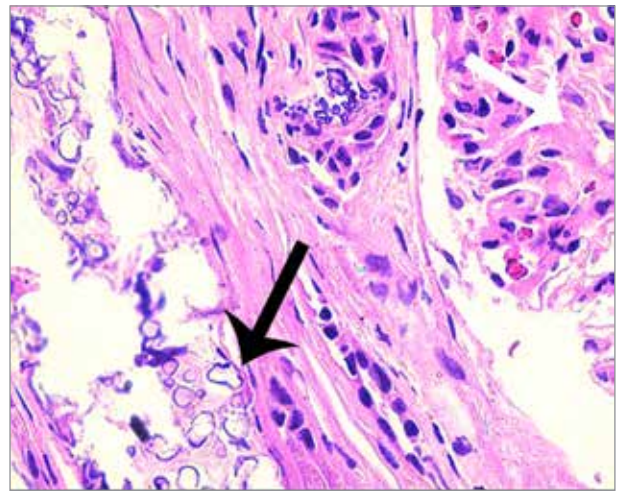

Fig. 2: Photomicrograph of the kidney biopsy of the second patient showing a glomerulous with mesangial sclerosis (white arrowhead) next to tubules containing calcium deposits (black arrowheads) which had extended into the interstitium. (H&E, original magnification x 400)

glucose was normal. Serum urea and creatinine were elevated at 40 mol/l and 700 umol/l, respectively. Serum electrolytes were normal except for phosphate at 2.5 mmol/l. Liver functions were normal except for albumin at 27 g/l. Serum CPK was 250 iu and serum cholesterol 6 mmol/l. His TSH was normal. Urine routine and microscopy showed 3+ protein with 25 RBCs / HPF and yet no pyuria. Serum complements (C3 & C4) and protein electrophoresis was normal. The ANA, anti-ds DNA, ANCA, RA, hepatitis B surface antigen (HBsAg) and anti-HCV antibodies were negative. Twenty four hour urine showed protein excretion at 6 g/day. Stool testing for ova, parasites and occult blood was normal. Chest X-ray and ECG were also normal. Abdominal and pelvic ultrasound was normal except for echogenic cortex of both kidneys. Percutaneous kidney biopsy showed a total of 11 glomeruli, out of which nine had global sclerosis (Fig. 1). The remaining ones showed focal and segmental glomerulosclerosis. There was mild diffuse interstitial infiltrate of lymphocytes and plasma cells. Blood vessels showed mild medial hypertrophy. Immunoflourescent stains were negative. The patient was instructed to have low protein diet and avoid the use of anabolic steroids and GH. Four months later, he received successful kidney transplant and since then, is well.

Case 2

A 36-year-old Iraqi man was referred to our renal unit for high serum creatinine (170 umol/l). His main complaint was bilateral loin pain and lower limbs edema for six months. He denied fever, skin rash and joint pains. The patient was a body builder and had used, for years, high protein diet (30 - 50 g/kg/day) and had used milk up to 10 liters/day instead of water. He had used testosterone injections up to 250 mg/day intramuscularly in addition to growth hormone on an average of 100 mg/day. He was a heavy cigarette smoker. He did not have any other significant medical illness, surgery, and allergy. On his initial physical examination, the patient was conscious and oriented. He looked very muscular without pain or shortness of breath. Blood pressure was 120/80 mmHg and temperature was normal. He was very muscular with a body weight of 76 kg and height of 1.78 meters. He did not have jugular venous distension, lymphadenopathy or goiter. However, he had pallor and bilateral lower limbs oedema. Systemic examination did not show any abnormality. Laboratory investigations showed normal peripheral leucocytic and platelets counts. Hemoglobin was 129 g/l with normal MCV. ESR was 20 mm/h. Serum sugar was normal. Serum urea and creatinine were elevated at 11 mmol/l and 170 umol/l, respectively. Serum electrolytes were normal except for phosphate at 2.8 mmol/l and corrected calcium at 3.8 mmol/l. Liver functions were normal except for albumin at 34 g/l. Serum CPK was 970 iu. Serum cholesterol was 5.2 mmol/l. TSH and parathyroid hormones were normal. Urine routine and microscopy did not show pyuria. Yet he had proteinuria 3 +, 12 - 15 RBCs/HPF and excess calcium oxalate. Serum complements (C3 & C4) and protein electrophoresis was normal. ANA, anti-ds DNA, ANCA, RA, HBsAg, anti-HCV and anti-HIV antibodies were negative. A twenty-four hour urine

sample showed protein excretion at 6 g/day. Stool testing for ova, parasites and occult blood was normal. Chest X-ray and ECG were normal. Abdominal and pelvic ultrasound was normal except for echogenic cortex of both kidneys with two non-obstructing calculi at the lower pole of the right kidney which were confirmed by plain KUB. Initial management included intravenous normal saline to correct his hypercalcemia. Serum calcium dropped to 2.6 mmol/l yet, without significant change in his kidney function. A percutaneous kidney biopsy showed a total of 13 glomeruli with variable mesangial matrix increase and yet, without cellular proliferation. Only one glomerulus showed segmental sclerosis. There was marked interstitial fibrosis with tubular atrophy. Most tubules contained calcium crystals (Fig. 2). The blood vessels were normal. Immunoflourescent stains were negative. The final diagnosis was FSGS with interstitial fibrosis associated with excessive calcium deposition in the tubules. The patient was instructed to have low protein diet and avoid dairy products, the use of anabolic steroids and GH. He received telmisartan (micardis) 40 mg daily to protect his kidney by decreasing glomerular pressure. Two months later, his blood pressure was normal and he did not have edema or muscular pains. Serum urea and creatinine had dropped to 6 mmol/l and 97 umol/l, respectively. His serum calcium remained 2.4 mmol/l.

DISCUSSION

FSGS is produced by many mechanisms[4]. In our patients (2 cases), lack of florid nephrotic state and IgM deposition are against a primary immunological disease. Moreover, the normal kidney size indicates lack of previous significant kidney injury leading to progressive hyperfilteration due to compensatory hypertrophy of the remaining glomeruli. Lastly, the patients did not have a family history of similar glomerulopathy, diabetes, congenital cyanotic heart disease, morbid obesity, familial dysautonomia, acromegaly, infections, IV drug abuse or HIV infection. The only relevant insult in their past medical history was the use of high protein diet, pharmacological doses of anabolic steroids and growth hormone. The high protein "myth" has been floating around for generations. Historically, it can be traced to *Milo* of Crotona in the sixth century B.C. He was a famous Greek athlete who was considered to be one of the strongest men in ancient Greece. He had won wrestling victories in five Olympic games as well as in other sacred festivals.

The optimal protein requirement for adults hardly exceeds 0.8 g/kg/day as recommended by the US food and nutrition agency[5]. Our patients had consumed 30 - 50 g/kg/day. High protein intake increases the renal blood flow and glomerular filtration rate in an attempt to excrete the nitrogenous by-products of its catabolism. Such chronic hyperfilteration may be a factor or may accelerate the development of FSGS[6]. The use of androgenic anabolic steroids (AASs) to promote wound healing in World War II and those in concentration camps is well documented. However, abuse of such drugs in sports started in 1940 and especially during the cold war between the west and east. Their emerging systemic side effects on the heart, liver and mood led to its ban in Olympic games in 1976. Interestingly, the direct toxic effect of such banned drugs on the glomeruli has been clearly documented and has been shown to be mediated *via* specific testosterone receptors in the glomeruli[7,8]. Moreover, the usual dose of replacement therapy of testosterone hardly exceeds 250 mg IM every three weeks. As has been shown, our patients had consumed pharmacological doses of such drug reaching up to 100 times the usual therapeutic one and for years. The last insult came with addition of GH to their regimen. Interestingly, the drug had limited success in treatment of short stature children and yet is being promoted as body building agent. Experimental reports in mice have shown its renal toxicity and induction of glomerulosclerosis through increase in renal blood flow and GFR[9]. Moreover, it has been shown that its target site was specifically on the glomerular podocyte[10]. In fact, a case report on an FSGS patient with acromegaly who had failed all therapeutic drug regimens improved after treatment with trans-sphenoidal microsurgery of the adenoma[11]. The deleterious effects of other factors such as hypercalcemia in our patient who used milk instead of water to promote his protein intake should not be underestimated as well as the effect of episodic severe elevations of blood pressure associated with weight lifting. Moreover, these patients are liable to use less water, diuretics, laxatives and non-steroidal anti-inflammatory drugs for pain. The latter combinations are harmful to the kidney, though not documented in our patients.

CONCLUSION

The idea of burning fat and feeding the muscle should not be on the expense of serious renal disease such as FSGS. Athletes and bodybuilders should not dismiss these facts as an "anti-anabolic steroid propaganda" and should consider the risks involved before losing their career and even their life with such banned practice.

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Case Report

Wilson's Disease Masked by Glucose-6-phosphate Dehydrogenase Deficiency – A Case Report

Medhat M S Abdelshahid, Maged Y Z Youssef, Ahmed Alqallaf
Department of Internal Medicine, Mubarak Al-Kabeer Hospital

Kuwait Medical Journal 2015; 47 (3): 240 - 243

ABSTRACT

Wilson's disease usually presents with hepatic or neurological manifestations. Hemolysis is an unusual presentation. We describe a case of a young man who had multiple attacks of hemolysis, diagnosed as glucose-6-phosphate dehydrogenase (G-6-P D) deficiency, and followed many years later by hepatic manifestations eventually diagnosed as Wilson's disease.

KEYWORDS: hemolytic anemia, hepatic dysfunction

INTRODUCTION

Clinical presentation of Wilson's disease can vary widely. Hepatic dysfunction tends to affect younger individuals while neuropsychiatric manifestations are more common among older patients. Unusually, hemolysis can be the only presenting symptom[1]. The diagnosis of Wilson's disease can be difficult in this situation. The exact mechanism of hemolysis in Wilson's disease is uncertain. It can be due to oxidative damage of the red cell membrane. Inhibition of antioxidant enzymes including Glucose-6-phosphate dehydrogenase and glutathione reductase may also be involved[2]. The presence of G-6-P D deficiency poses a special challenge for a clinician. Recurrent hemolysis, in this case, can be a part of the disease process. On the other hand, it can delay the diagnosis of the disease, if the physician is not alert to the possibility of this diagnosis in a case of Coombs-negative Hemolytic anemia.

CASE PRESENTATION

A 42-year-old Iranian gentleman, married with three children, presented to our hospital with a history of increasing tiredness, easy fatigue and deepening jaundice and deterioration of level of consciousness. He gave a history of previous recurrent attacks of jaundice with multiple hospital admissions in Iran diagnosed as G-6-P D deficiency. He had multiple blood transfusions and was advised to receive desferral injections to decrease iron overload. He was otherwise well with no history of diabetes or hypertension. He was a lifetime non-smoker and denied any history of alcohol intake or drug abuse. Family history was positive for G-6-P D deficiency.

On examination, he was drowsy but oriented to time and place. There was hyperpigmentation of the skin and mild flapping tremors. Temperature was 37.5 ºC; blood pressure was 110/70 mm/Hg. There was no edema of lower limbs. Abdominal examination showed moderate hepatosplenomegaly and positive shifting dullness. Chest and cardiac examination was unremarkable and neurological examination showed no lateralization or signs of meningeal irritation.

Investigations

Laboratory data included hemoglobin of 89 g/L, white cell count of 6.6 x 10^9 /L, platelets of 80 x 10^9 /L, reticulocytic count of 3.28%, peripheral smear showed normocytic normochromic anemia with anisopoikilocytosis, pencil cells and target cells. Coomb's test was negative. INR was 1.8 and APTT was 43 seconds (ref up to 39).Glucose, urea and electrolytes were within reference range. Other investigations showed total bilirubin of 120 mcmol/L, direct bilirubin of 40 mcmol/L, aspartate aminotransaminase of 98 IU/L (ref up to 50), alanine aminotrasaminase of 210 IU/L (ref up to 60) alkaline phosphatase of 67 IU/L (ref, 30 - 110), and albumin of 30 g/L (ref, 35 - 50).

Address correspondence to:
Medhat M S Abdelshahid, Department of Internal Medicine, Mubarak Al-Kabeer Hospital, Kuwait, Mobile no :(965)51197991; email: mabdel_shahid@yahoo.com

Hepatitis panel testing and auto-immune liver antibodies were negative, and other miscellaneous measurements included iron of 51 mcmol/L (ref, 8 - 35), transferrin saturation 99.6% (ref, 10 - 50%), ferritin of 1035 ng/ml (ref 22 - 322), ceruloplasmin of 0.09 g/L (ref, 0.2 - 0.6), urinary copper of 3.2 mcmol/24 hours(ref up to 0.6). G-6-P D level was 26 (ref 118 - 999).

Ultrasound examination of abdomen showed mild hepatic enlargement with coarse echotexture, moderate splenomegaly and moderate ascites. Slit lamp examination of both corneas was normal. Based on clinical and biochemical findings, a diagnosis of Wilson's disease was made with a Leipzig score of 5.

During hospitalization, he was treated for hepatic encephalopathy. After his condition was stabilized and liver function tests and INR improved, transjugular liver biopsy was done and showed picture highly suggestive of Wilson's disease with moderate iron deposition in keeping with hemosiderosis (Fig. 1, 2). Hepatic concentration of copper could not be assessed because of lack of its unavailability in our hospital. He was treated with D-penicillamine, zinc and pyridoxine in addition to iron chelating therapy. Follow up of the liver function tests and coagulation profile after treatment revealed a steady improvement but remained elevated after discharge.

Given the young age of the patient, together with the fact that he presented with acute liver failure and the persistence of elevated liver enzymes after treatment, he was counseled regarding liver transplantation and he chose to go back to his country (Iran) where liver transplant was arranged for him. Prior to that, another liver biopsy was performed and at that time, hepatic copper concentration was high. After recovery, he came back to Kuwait. He was on immunosuppressive therapy. On follow up in medical outpatient clinic, six months after transplantation and three months later, he was asymptomatic and liver function tests and ceruplasmin level became normal. His anemia also improved and G-6-P D level was normal.

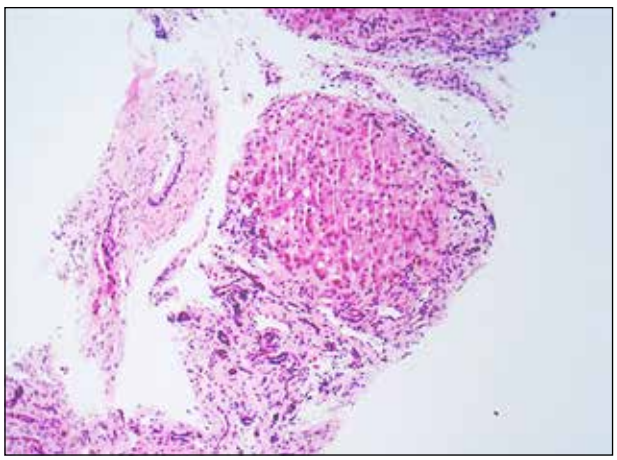

Fig. 1: Low power view of liver tissue shows fibrosis with micro-regenerative nodules, mild steatosis, and bile ductular proliferation. Some brown pigment also noted within hepatocytes.

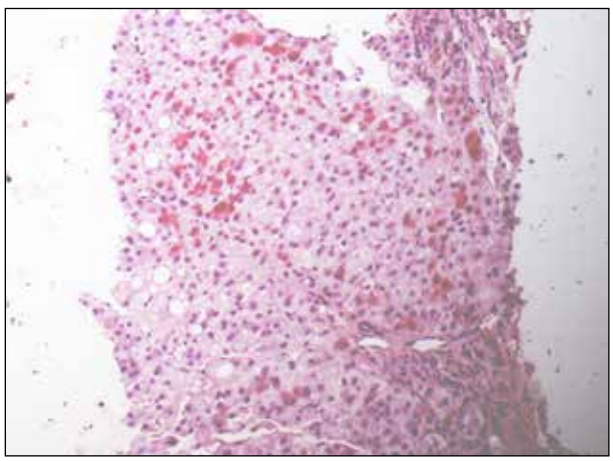

Fig. 2: Orcein stains some hepatocytes in keeping with copper-related proteien deposits

DISCUSSION

Wilson's disease is an inherited disorder in which defective biliary excretion of copper leads to its accumulation particularly in liver and brain[3]. Wilson's disease is due to mutation of ATP7B gene on chromosome 13[4]. Clinical presentation can vary widely, but the most common presentations are liver disease and neuropsychiatric disorders. Kayser-Fleischer ring is present in 95% of patients with neurological symptoms and over half of those without neurological symptoms.

Coombs-negative hemolytic anemia is an uncommon complication of this disease (5 - 20%). Marked hemolysis is commonly associated with severe liver disease. However, hemolysis can be the only initial symptom of the disease. In one series, hemolysis was a presenting feature in 12% of cases, either as a single acute episode, or recurrently[1]. Some patients presenting with neurologic symptoms report previous transient episodes of jaundice, probably due to hemolysis[5].

Self-limiting episodes of hemolytic anemia have been diagnosed, often retrospectively, as being the first manifestation of Wilson's disease, antedating symptoms of liver or neurologic disease by months to years[6]. The exact mechanism of hemolysis in Wilson's disease is uncertain. Excessive inorganic copper in circulation may cause oxidative damage of the red cell membrane. The action of antioxidant enzymes including Glucose-6-phosphate dehydrogenase and glutathione reductase may also be inhibited[2]. The erythrocyte enzyme activity was studied in some cases at times of hemolytic episodes, in which decrease in G-6-PD was reported[7, 8].

Table 1: Scoring system developed at the 8th International Meeting on Wilson's disease, Leipzig 2001[10].

Typical clinical symptoms and sign	Score	Other tests	Score
KF rings		Liver copper (in the absence of cholestasis)	
Present	2	>5 x ULN (>4 μmol/g)	2
Absent	0	0.8 - 4 μmol/g	1
Neurologic symptoms**		Normal (<0.8 μmol/g)	-1
Severe	2	Rhodanine-positive granules*	1
Mild	1	Urinary copper (in the absence of acute hepatitis)	
Absent	0	Normal	0
Serum ceruloplasmin		1 - 2 x ULN	1
Normal (>0.2 g/L)	0	>2 x ULN	2
0.1 - 0.2 g/L	1	Normal, but >5x ULN after D-penicillamine	2
<0.1 g/L	2	Mutation analysis	
Coombs-negative hemolytic anemia		On both chromosomes detected	4
Present	1	On 1 chromosome detected	1
Absent	0	No mutations detected	0

Total Score Evaluation: 4 or more = Diagnosis established; 3 = Diagnosis possible, more tests needed; 2 or less = Diagnosis very unlikely
*If no quantitative liver copper available. **or typical abnormalities at brain magnetic resonance imaging. KF, Kayser–Fleischer; ULN, upper limit of normal

The diagnosis can be established by the presence of Kayser-Fleischer ring with low serum ceruplasmin. When Kayser-Fleischer ring is not present (this is common with hepatic manifestation of the disease), a combination of tests may be needed[9]. A diagnostic score based on available tests was proposed by the Working Party at the 8th International Meeting on Wilson's disease, Leipzig 2001[10] (table 1). The Wilson's disease scoring system provides a good diagnostic accuracy[11]. A diagnostic algorithm is shown in Fig. 3.

A number of drugs are available for the treatment of Wilson's disease. Chelating agents have been the cornerstones in treatment for decades. D-penicillamine promotes the urinary excretion of copper. It may also act by inducing metallothionein[12]. In patients with symptomatic liver disease, recovery of synthetic liver function and recovery in clinical signs occur typically during the first 2-6 months [10]. Trientine is an alternative chelating agent. Its potency in comparison to D- penicillamine is controversial[13].

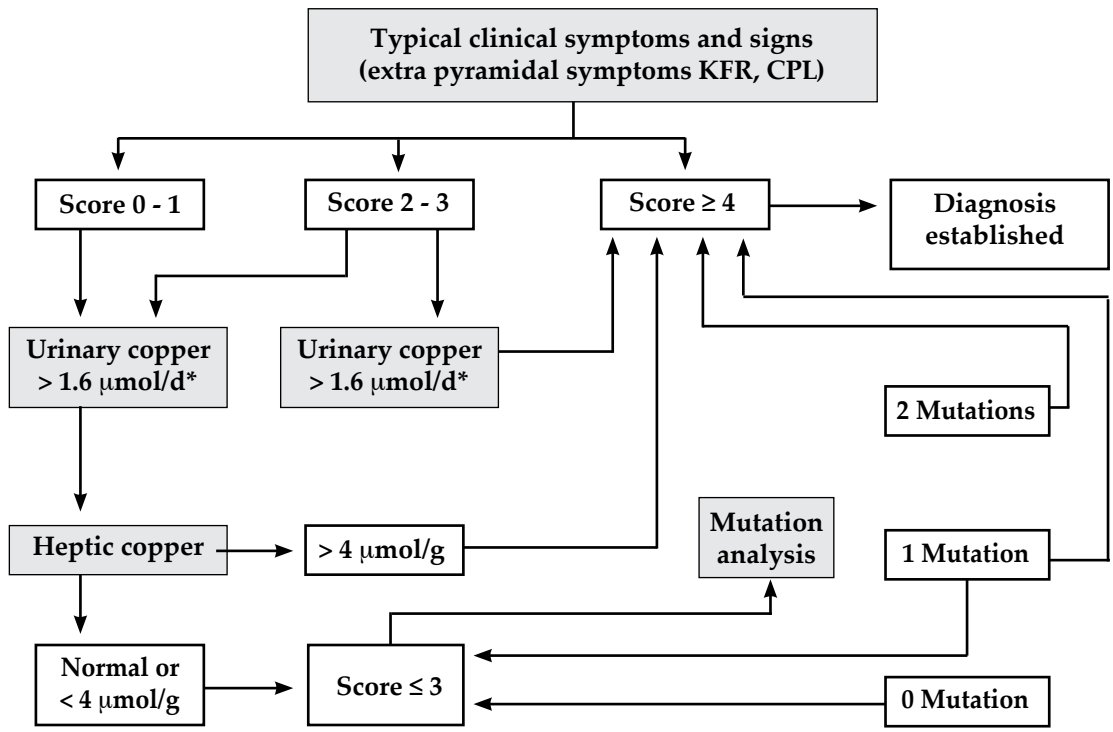

Fig. 3: Diagnostic algorithms for Wilson's disease based on Leipzig score[10].

* In children, the cut off can be lowered to 0.64 μml/d

Adverse effects due to D-penicillamine resolve when it is substituted for trientine. Zinc was first used to treat Wilson's disease in the early 1960s. It interferes with the uptake of copper from the gastrointestinal tract. Zinc induces enterocyte metallothionein, an endogenous chelator of metals. Zinc appears to be equally effective as D- penicillamine but better tolerated[14].

Liver transplantation is frequently necessary for patients presenting with acute liver failure and is indicated for all patients with decompensated cirrhosis due to Wilson's disease not responsive to treatment. The median survival after orthotopic liver transplantation in one study was 2.5 years. Survival at one year was 79%[15]. Living related donor transplantation (where the donor is an obligate heterozygote) gives excellent results[16].

CONCLUSION

The association between hemolytic anemia and Wilson's disease can easily be missed by clinicians. We emphasize the importance of checking liver functions tests in young patient with coomb's negative hemolytic anemia. Recurrent hemolysis, as in G-6-P D deficiency, may mask the picture of Wilson's disease. A high index of suspicion is needed in such cases.

ACKNOWLEDGEMENT

The authors are grateful to Dr Maamoun Al Aynati and Dr Mohammad Al-Kandari from hisopathology department, Mubarak Al-Kabeer Hospital for their valuable contributions in this work.

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Case Report

Pancreatic Tuberculosis: An Elusive Challenge

Hashim S Khayat[1], Mohammed H Saeed Al-Hijaji[1], Rasha S Shamoon[2]
[1]Department of Surgery, Basrah General Hospital, Basrah, Iraq
[2]Department of Pathology, Basrah General Hospital, Basrah, Iraq

Kuwait Medical Journal 2015; 47 (3): 244 - 247

ABSTRACT

Pancreatic tuberculosis is a rare entity which needs a high index of suspicion. We report four cases of pancreatic tuberculosis that presented to us as pancreatic malignancy with obstructive jaundice.

KEY WORDS: atypical presentation, diagnosis, pancreas, tuberculosis

INTRODUCTION

Tuberculosis (TB) of pancreas is a rare health problem in the world, with incidence of pancreatic involvement in miliary TB autopsy cases ranging from 2.1 to 4.7%[1]. Pancreatic TB typically affects adults with equal sex distribution and has a wide spectrum of presentation characteristics such as abdominal pain, fever, night sweats, anorexia, weight loss, malaise, back pain, jaundice, acute or chronic pancreatitis, portal vein compression, gastrointestinal bleeding, diabetes mellitus, obstructive jaundice and pancreatic mass mimicking pancreatic malignancy[2-4].

CASE REPORT

A sixty-eight-year-old retired male presented with upper abdominal pain, predominately central, vague in character with no related nor aggravating and relieving factors mentioned.

This pain was associated with dyspepsia, itching, poor appetite, clay colored stool and tea colored urine. No other significant manifestations were mentioned.

On examination, the patient looked ill with thin built, pallor and jaundice. Vital signs and chest examination were normal. Abdominal examination revealed a palpable gall bladder.

Work-Up Study

- Complete blood picture was normal apart from mild anemia (Hb level of 9.8 g/l
- Blood sugar, blood urea and serum creatinine were normal
- Coagulation profile showed an INR of 2.0
- Liver function tests revealed evidence of obstructive jaundice
- Renal function tests and serum protein levels were normal
- ESR was 30 mm/hr
- Abdominal ultrasound showed a hypoechoic irregular outline mass of 4 × 5 cm in the head of pancreas displacing nearby vessels (Fig. 1).
- Abdominal CT-scan with contrast showed mass in the uncinate processs of pancreas, measuring 5 × 5 cm of 44 HU with enhancement after IV contrast of 65 HU causing displacement of splenic vessels
- FNAC was not done due to technical difficulties

Surgical exploration

- Mass in the head of pancreas with dilated common bile duct
- Few lymph nodes in adjacent region, few taken for histopathological exam
- Palliative bilio-enteric bypass done
- One subhepatic drain left before closure in layers

Postoperatively, the patient improved gradually and jaundice decreased and he was discharged home on the 6th day.

Histopathological result revealed caseating granulomatous inflammation and presence of *Mycobacterium tuberculosis* complex on acid fast smear (Fig. 2 - 5). Anti-TB course was instituted resulting in complete cure. Other cases are summarized in Table 1.

Address correspondence to:
Dr Mohammed H. Saeed Al-Hijaji, MRCS (Ed), MRCS (Glasg), Specialty Registrar, Department of General Surgery, Basrah College of Medicine, Basrah, Iraq.Tel: 00964 – 7801125890, E-mail: mhs7855@yahoo.com

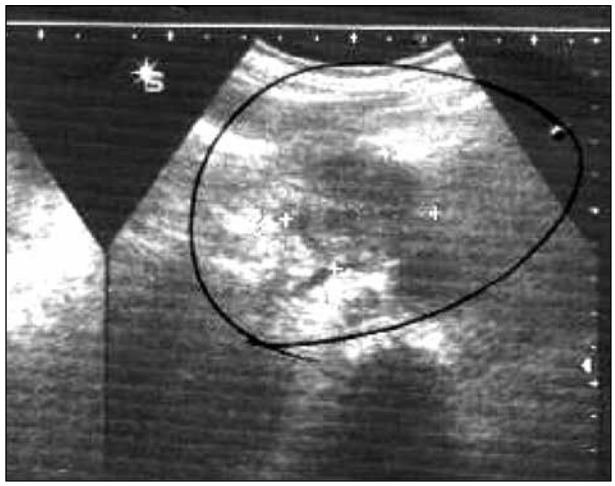

Fig. 1: Abdominal ultrasound showing hypoechoic irregular mass in the pancreatic region displacing nearby vessels

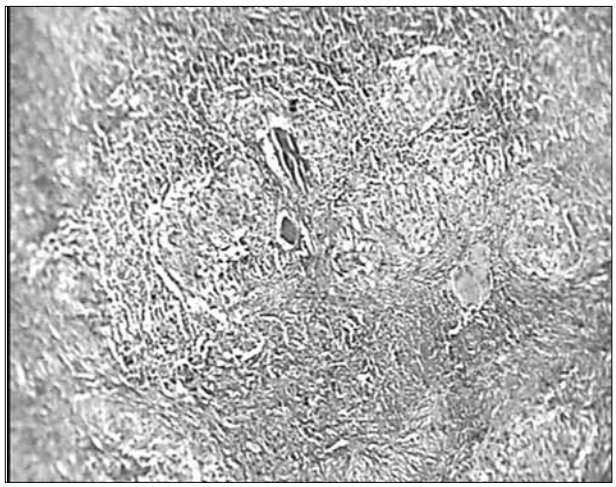

Fig. 2: Histopathological section showing granulomatous lesion

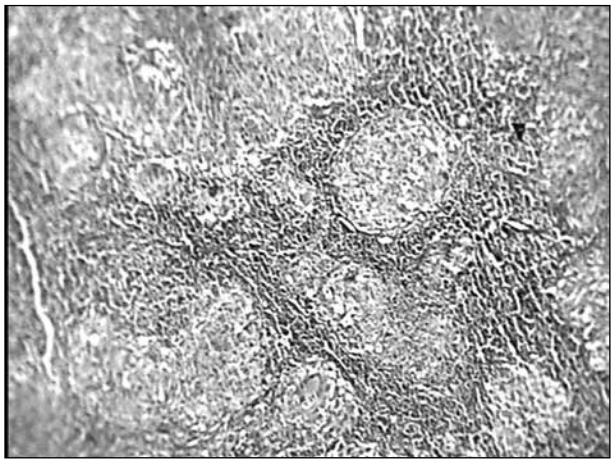

Fig. 3: Histopathological section showing caseating lesion

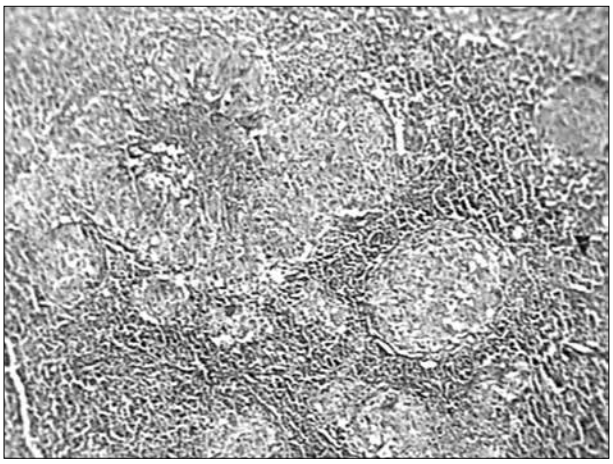

Fig. 4: Histopathological section showed multiple follicles of lymph nodes with a granuloma

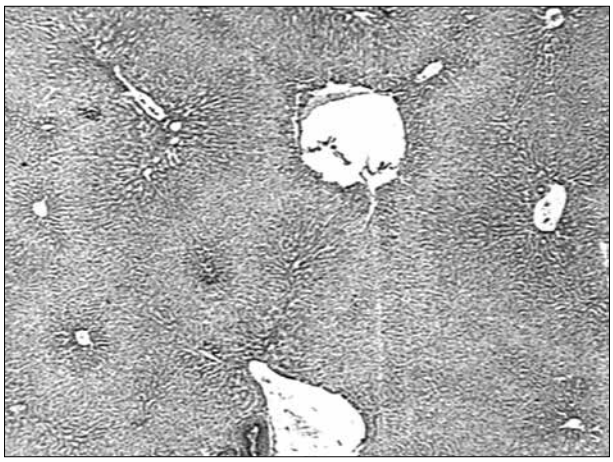

Fig. 5: Microscopic section showing follicles with suspicious lesions

DISCUSSION

Tuberculosis was a killer in the last decades because of the absence of effective prophylactic or therapeutic measures, in addition to poor socio- economic state. Its prevalence and resurgence during the last few years could be due to migration of people from other parts of the world, where there is a high prevalence of the disease and also might be attributable to increased immune suppressed states due to wide range use of immune suppressants, increased aged population as well as immune compromised diseases like AIDS.

The pathogenesis of pancreatic tuberculosis remains speculative which may include miliary, hematogenous[5] or direct spread from contiguous lymph nodes affected by tuberculosis[6-7]. Reactivation of a tubercular focus within the pancreatic tissue which is induced by alcoholism, pancreatitis, steroid therapy, or surgery also has been proposed[6]. Pancreatic involvement with *Mycobactrium tuberculosis* can have four clinical presentations: pancreatic mass mimicking carcinoma[8], pancreatitis[9], obstructive jaundice[10] and gastrointestinal bleeding[11].

CT scans and EUS - FNA of pancreatic lesions are the most common adopted modalities in further evaluation of suspected pancreatic lesions.

Table 1: A summary of cases of pancreatic tuberculosis

Sex/ age	Presentation	Surgery	Histopathological diagnosis	Anti-TB treatment	Response
M/68	Abdominal pain	Laparotomy/Biopsy	+	+	Complete recovery
F/57	Abdominal mass	Laparotomy/Biopsy	+	+	Complete recovery
M/28	Obstructive Jaundice	Laparotomy/Biopsy	+	+	Complete recovery
F/64	Tired patient with epigastric pain and abdominal mass	Laparotomy/Biopsy	+	+	Died on 4th postoperative day

This misdiagnosis of pancreatic carcinoma is not uncommon and over 90% of proven isolated pancreatic TB cases were only diagnosed at laparotomy[4]. A recent search of the literature revealed that there are only less than 50 reported cases of pancreatic TB mimicking pancreatic carcinoma. EUS and FNA evaluation permits cytologic biopsy of the pancreatic mass. Apart from cytological assessment in differentiating between benign and malignant masses, EUS has also other potential applications in the evaluation of pancreatic lesions. Sensitivities and specificities of EUS - FNA in diagnosing pancreatic lesions is reported to be as high as 90 and 100%, respectively[12-14].

According to Brusko *et al*[15], pancreatitis and pancreatic carcinoma are the differential diagnoses with similar imaging features. Pattern of enhancement of the mass lesion, pancreatic ductal dilatation, intra-parenchymal, ductal or mass calcification, and portal venous thrombosis can differentiate these conditions from tuberculous involvement of the pancreas.

A recent diagnostic test is the polymerase chain reaction (PCR) based assay, which has high specificity and is capable of detecting *Mycobacterium tuberculosis* DNA in resected specimens[8].

Response to multi-drug anti-TB chemotherapy (12 months) is predictable and complete[15]. Follow up is important to assess response as well as to exclude coexistent TB and malignancy especially, in endemic areas.

Clinical dilemma

1. Overlooking diagnostic entity is probably due to rarity, its stigmata and isolated pulmonary tuberculosis cases
2. Resurgence of clinical health problem in developed and developing countries primarily due to increased immune compromised people
3. Mimicking pancreatic pathology of inflammatory or oncologic process
4. Curability of illness has made it necessary to diagnose pancreatic TB as early as possible, as it can be cured by medical therapy and unnecessary operations can be avoided
5. Literature dearth on pancreatic TB, as it is mostly published occasionally as case report

Reference point

1. Local expertise of health professionals like surgeons, radiologists and pathologist is needed to judge the medical evidence and / or plan medical strategy for suspicious lesions. This could require the surgeons to get histopathological evaluation and be prudent to avoid surgery to allow for further diagnostic assessment so as to obviate morbidity and mortality of surgery.
2. Local evidence regarding the prevalence of tuberculosis in the country is important

Recommendations

1. Clinical awareness is the master of prevention
2. Accurate review of patient's medical and health profile
3. Improvement of intraoperative orientation of health professionals

CONCLUSION

Clinical awareness of pancreatic TB is so important as it may masquerade as pancreatic malignancy. It is a potentially reversible and treatable infection and carries excellent prognosis if diagnosed early and treated properly.

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Case Report

Congenital Insensitivity to Pain with Talar Avascular Necrosis and Neuropathic Arthropathy of the Ankle Joint

Mohamed Zaki Zaki Hatata
Department of Pediatric Orthopedics, Al Razi Hospital, MoH, Kuwait

Kuwait Medical Journal 2015; 47 (3): 248 - 250

ABSTRACT

Congenital insensitivity to pain with anhydrosis (CIPA), is a very rare genetic disorder characterized by recurrent episodes of unexplained fever, inability to feel pain and temperature, generalized anhydrosis, self-mutilating injuries and mental retardation. We present a case of a 8-year-old boy with these criteria who presented with gross right ankle swelling, collapse and avascular necrosis of the talus that was treated conservatively with non-weight-bearing cast.

KEY WORDS: anhydrosis, insensitivity, pain, talus

INTRODUCTION

Congenital insensitivity to pain with anhydrosis (CIPA) is a very rare autosomal recessive disorder; it is also known as hereditary sensory and autonomic neuropathy (HSAN) type four. CIPA is characterized by inability to feel pain and temperature. This often leads to repeated injuries sometimes unintentional or self-mutilating (*e.g.,* biting the tongue, lips or fingers).

Normally, sweating helps cool the body. However, in CIPA patients there is generalized anhydrosis often causing recurrent attacks of hyperpyrexia and seizures. They also develop characteristic emotional behavior and many affected individual have mental retardation. The touch and pressure sensations are preserved[1].

CIPA is caused by mutation of the NTRK1 gene. This gene is responsible for encoding the receptor tyrosine kinase (TrKA) for nerve growth factor (NGF) which is critical for the formation of autonomic neurons and the small sensory neurons in the dorsal root ganglia[2,3].

On skin biopsy, in CIPA, the sweat gland appears to be normal, but an ultrastructural study of skin biopsies revealed non-innervation of the eccrine sweat gland which affect the ability of the individual to sweat[4].

CASE REPORT

A 8-year-old boy was referred to the outpatient department because of gross right ankle swelling. He was a single child out of a consanguineous marriage between healthy parents of Iranian origin with no family history of a similar disease. The child was born after full term normal pregnancy *via* a normal vaginal delivery. His birth weight was 2.6 kg. The parents gave history of recurrent attacks of unexplained fever, insensitivity to pin prick and previous fractures.

The child was averagely built and his skin was dry. There was a healed ulcer over the lower lip and tongue, a healing ulcer over the base of the first metacarpal of the right hand (Fig. 1), and multiple healed scars of self-mutilating injuries over the areas of the lower left forearm ,wrist and left hand (Fig. 2).

A local examination showed gross right ankle swelling with mild hot skin and scars of previous healed heel ulcer. A plain X-ray showed recently healed fracture with exuberant callus over the first metatarsal bone (Fig. 3), and sclerosis of the dome of the talus with subchondral fracture and collapse of the articular surface (Fig. 4, 5). A real time ultrasound showed significant right ankle joint effusion. A magnetic resonance image (MRI) showed right ankle joint effusion, subchondral talar dome fracture and low signaled non-enhanced sclerosis of the posterior half of the talus (consistent with avascular necrosis) (Fig. 6).

His white cell count was 8.6 x 10^9/l with a normal differential count. His hemoglobin (Hb) was 12.3 g/dl, C reactive protein (CRP) was 19 mg/l, erythrocytic sedimentation rate (ESR) was 45 mm/hr, blood culture was negative and the tests for sickling and brucella agglutination were negative.

Address correspondence to:
Dr. Mohamed Zaki Zaki Hatata, FRCS (Glasgow), PO Box 5102, Hawalli -32082, Kuwait. Tel. +965 97194179, E-Mail: mzhatata@hotmail.com, Mohamed_hatata70@yahoo.com

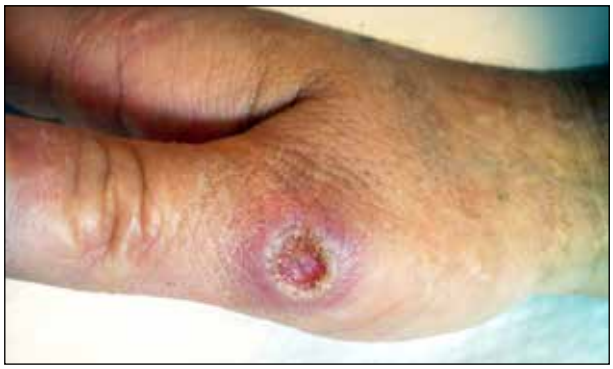

Fig. 1: Ulcer over base of the Rt. thumb

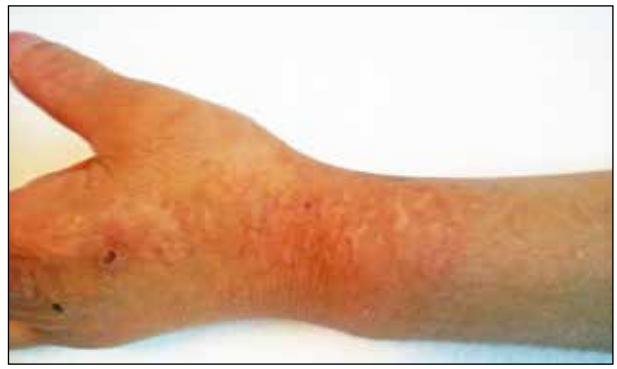

Fig. 2: Healed scars of self mutilating injuries of the wrist and forearm

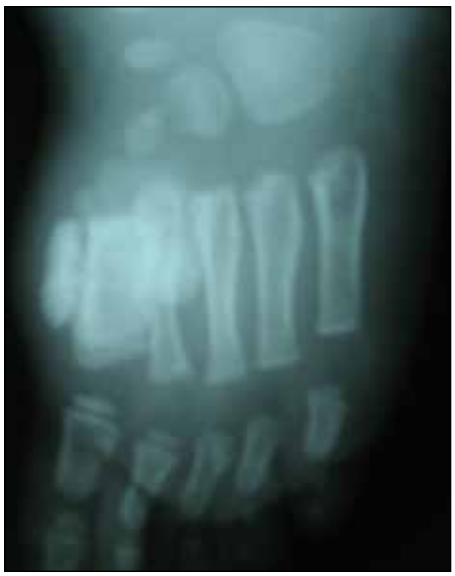

Fig .3: Exuberant callus formation of 1st metatarsal fracture

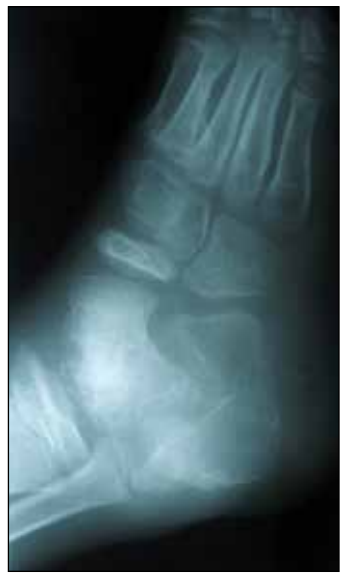

Fig. 4: Sclerosis of the talar body and irregularity of the talar dome

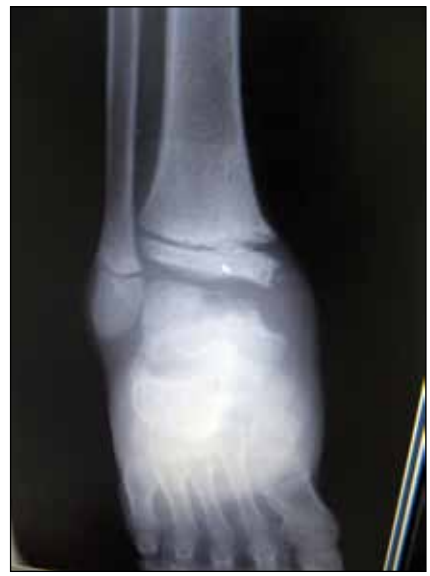

Fig. 5: Right ankle AP view showing subchondral fracture and collapse of the articular surface

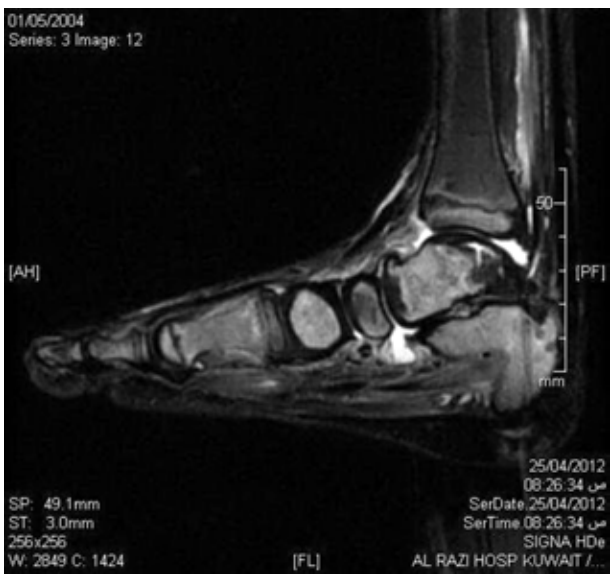

Fig. 6: Right ankle MRI showing joint effusion and avascular necrosis of the talus

The MRI of the brain was normal. The nerve conduction study (peroneal and posterior tibial) of both lower limbs was normal but the blink response of left and right supraorbital nerve was absent, sympathetic skin response to acoustic and electric stimuli in both upper and lower limbs were absent.

Psychiatric evaluation showed delay in motor, speech and play skills. His learning abilities were less than other peers. Wechsler intelligence scale for children (WISC) was performed and the result showed a total IQ: 61, verbal IQ: 58 and performance IQ: 69.

The patient was treated conservatively with non-steroidal anti-inflammatory drugs (NSAIDs), kept non-weight-bearing cast (protective splint) for nine weeks while he was an inpatient followed by POP cast after discharge" to reduce ankle swelling. Although, residual ankle swelling persisted after conservative treatment, the patient was kept in a protective weight bearing brace.

DISCUSSION

CIPA is a very rare hereditary disorder. It more likely occurs in homogeneous society. Dyck[5] recognized five types of hereditary sensory and autonomic neuropathies (HSAN). CIPA correspond to the fourth of the five types.

It is caused by lack of maturation of small myelinated and unmyelinated fibers of the peripheral nerves which convey sensation of pain and temperature[6]. Rafel *et al*[7] studied the cutaneous branch of the radial nerve by electron microscopy and they found complete absence of small myelinated (delta) and unmyelinated (C) fibers. Other studies confirm the same ultrastructure findings[8,9]. CIPA is caused by mutation in the NTRK1 gene which is responsible for encoding the receptor tyrosine kinase TrKA for nerve growth factor (NGF). It is a neurotrophic factor essential for survival and maintenance of sensory and sympathetic neurons. It is also an inflammatory mediator associated with pain and itching. NGF-TrKA system is essential for establishment of a neural network. NGF dependent neurons play a crucial role in the emotional experience, and cognitive and mental activity[10,11].

The sweat gland on skin biopsy in CIPA appeared to be normal but the ultrastructural studies of skin biopsies revealed non-innervation of the eccrine sweat glands which is the main reason of anhydrosis observed in these patients[4].

The clinical presentation could be classified according to Bar *et al*[12] into a) multiple infections, b) fractures, growth disturbances and avascular necrosis and c) Charcot arthropathies and dislocations.

Infection may be recurrent and destructive. Complications in wound healing and fracture treatment are also reported[13]. Most patients are mentally retarded with IQs varying from 41 to 78, the majority being in the range of 60s[7].

In our patient, diagnosis of CIPA was made on the basis of clinical features of insensitivity to pain and temperature, frequent hyperpyrexia and anhydrosis, scars of self mutilating injuries and frequent ulceration, multiple previous fractures that healed with exuberant callus formation (Fig. 3), absent sympathetic skin response to acoustic and electric stimuli of both upper and lower limbs associated with absent blink response of the left and right supra-orbital nerves. Delay in motor, speech, play skills and abnormal WISC are similar to the findings of Rosemberg *et al*[8].

CONCLUSION

Congenital insensitivity to pain with anhydrosis (CIPA) is characterized by absence of protective sensations that keep the body safe from injurious agents and prevents self-mutilation. CIPA patients require a team of multidisciplinary physician including dentist and educated parents. Absence of protective sensation from the joint leads to a continuous process of joint destruction. The treatment of this disorder consists of immobilization of the affected joint (brace or period of non-weight bearing cast), relief of pressure from weight-bearing areas and a weight relieving cast.

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Case Report

Complete Ureteral Avulsion during Ureteroscopy: A Case Report

Wadah Ceifo, Adel Al-Tawheed, Maher Gawish
Urology Unit, Department of Surgery, Al-Jahra-Hospital, Ministry of Health Kuwait

Kuwait Medical Journal 2015; 47 (3): 251 - 253

ABSTRACT

Ureteroscopy is a worldwide diagnostic and therapeutic procedure. This technique has some known complications, but proper ureteroscope handling is the cornerstone to prevent the catastrophic events such as ureteral avulsion. In this case report, we aim to review the cause and management of ureteral avulsion during ureteroscopy and presents recommendations to minimize the incidence of such serious consequence in the current practice.

KEYWORDS: injury, ureteral avulsion, ureteroscopy

INTRODUCTION

The urologists had considered uretero-renoscopy as a device to inspect and treat upper urinary tract pathology since the first attempt in 1912 by Hugh Hampton Young, and its clinical introduction in 1980 by Pérez-Castro and Martínez-Piñeiro[1,2]. However, improper use of this excellent surgical tool is prone to result in complications including false passage, bleeding, ureteral perforation, stricture and ureteral avulsion which is the most serious one[3].

CASE REPORT

A 48-year-old, married, Asian male presented to us with recurrent attacks of left flank pain since three months. Pain was colicky in nature and radiating to genitalia. There was no history of hematuria or change in bowel habits. There was no history suggestive of any other system involvement. Examination was unremarkable. On investigation, he was found to have an impacted left upper ureteric stone 1.2 cm in size causing moderate hydronephrosis and renal function impairment (serum creatinine 181 mmol/l).

An ureteroscopic removal of the impacted stone was planned. The ureteroscopy was performed under general anesthesia. On preliminary left retrograde study there were multiple ureteral kinks below the impacted upper ureteric stone. After balloon dilatation of the intra-mural part of the ureter and then with gentle manipulation by ureteroscope, the stone was fragmented by Holmium: YAG laser with extraction of multiple fragments using Nitinol Dormia basket. At the end of the procedure, an attempt was made to bypass the site of stone impaction to inspect the renal pelvis. However, the progress of the uretreoscope was arrested at this site. Another safety guide wire was introduced, but an attempt at extraction of ureteroscope produced ureteral avulsion, whereby about 20 cm of the ureter was brought out over the ureteroscope (Fig. 1, 2). As the injury was recognized immediately and the patient was stable, a repair was done based on standard open surgical techniques. The bladder was found to be of adequate capacity (400 ml). Therefore, an extended spiral bladder flap was fashioned (length: 12 cm, width: 4 cm) accompanied by a psoas hitch and an end to end anastomosis with remaining upper ureteral stump (length: 4 cm) was performed over a double J stent (8 Fr/26 cm, Fig. 3). The stent was removed eight weeks later. Convalescence was uneventful and renal function tests returned to normal. An intravenous urogram one year after the procedure showed an almost normal collecting system with excellent renal function (Fig. 4).

DISCUSSION

One of the complications of ureteroscopy is damage to the ureter in varying degrees, complete avulsion being the more serious one, but fortunately rare[4]. Although an infrequent event in the endoscopic management of ureteral calculi (0.2 - 1%)[5], with only few cases reported in the literature, ureteral

Adress correspondence to:
Dr. Wadah Ceifo, Urology Unit, Department of Surgery, Al-Jahra Hospital, Tel: 00965 97390065, Fax: 24569431, E-mail: wceifo@gmail.com

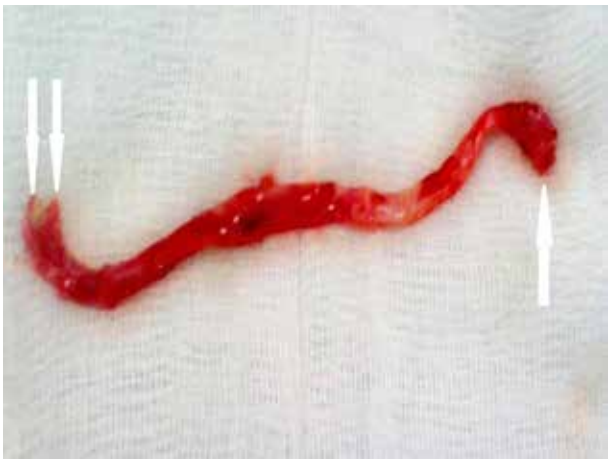

Fig. 1: Long ureteral defect: (↑) proximal ureteral end, (↓↓) distal ureteral end

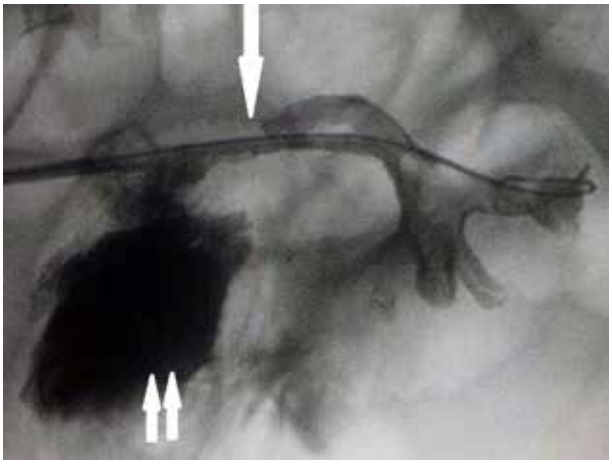

Fig. 2: Left retrograde ureteropyelography: (↓) complete ureteral avulsion, (↑↑) retroperitoneal extravasation of contrast medium

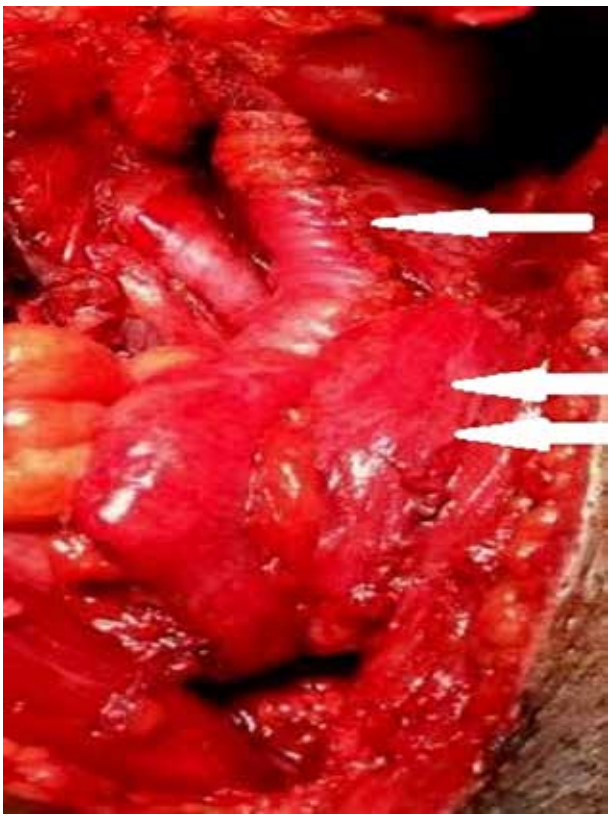

Fig. 3: (←) Extended Boari flap, raised from the mobilized left bladder dome and tubularized with continuous suturing. (⇄) Psoas hitch

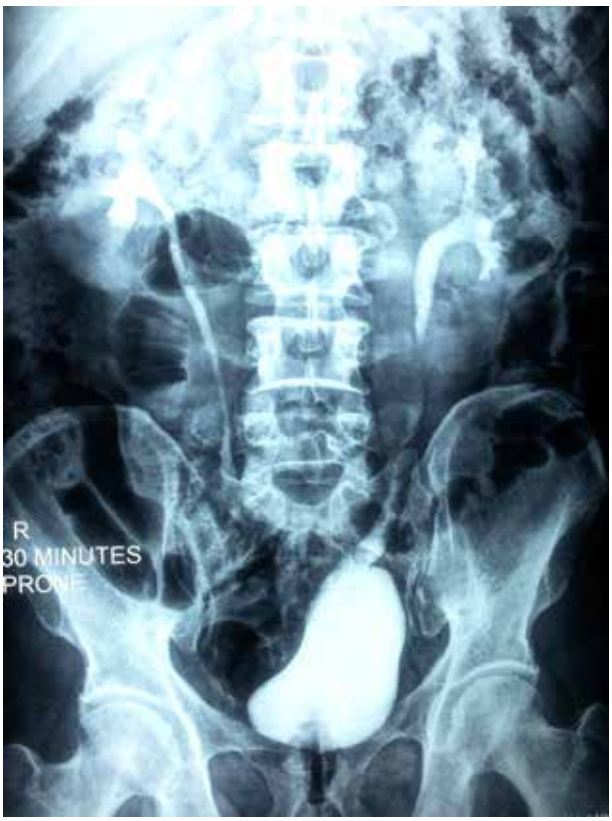

Fig. 4: Late intravenous pyelography: patency of the ureter without evidence of dilatation, 12 months postoperatively

avulsion should always be taken into account when performing such procedures. The incidence in the series by Alapont *et al* was only 0.11%[6].

Among the potential factors involved in the pathogenesis of ureteral avulsion, the presence of an anomalous ureter, either due to a diseased area (as in our case) or due to previous endourologic manipulations, is an important antecedent in the majority of cases[7]. Furthermore, the use of multiple-wire baskets for ureteral stones retrieval have also been implicated, and particularly with regard to the size of the stone (larger than 1 cm), and the distance the stone has to cross before exiting through the ureteral meatus[8].

Proper ureteroscopic handling is the key to prevent this catastrophic complication and extreme gentleness is required during the procedure. Adherence to some basic rules such as dilatation of intramural part of

ureter, if not able to accommodate the ureteroscope freely, doing retrograde study during the procedure, the mandatory placement of a safety guide wire, use of small ureteroscope or flexible one, extreme care during basket usage and during insertion of ureteroscope into diseased ureter, especially, if there are multiple severe kinks, and limiting ureteroscopy times are some ground rules to prevent major complications of ureteroscopy[9]. For an upper third ureteric calculus treatment options include *in situ* ESWL, pushing the stone into renal pelvis followed by ESWL or in case the calculus is really big, consider ureterolithotomy (open or laparoscopic).

Repair of complete ureteral avulsion following endoscopic surgery is a challenging task and treatment should be individualized. It varies according to the compromised ureteral segment (length and location) and functional status of the renal unit[10]. In cases of largely devitalized tissue or compromise of a large ureteric segment, extreme measures are necessary, such as renal auto-transplantation or ileal interposition, the latter replacing a segment or the entire ureter[11-13]. Both procedures are highly complex and have their own inherent risks. The patient must be counseled appropriately. Boari flap is a versatile technique in the repair of severe ureteral defects, and may eliminate the need for a possible ileal ureteric replacement[14,15].

In the present case, the avulsion occurred because of continued force applied to introduce the ureteroscope into the non-healthy upper ureteral segment due to stone impaction. We did repair with extended spiral bladder flap combined with psoas hitch as the patient was of short stature and capacious urinary bladder. Using the above mentioned technique, we could bridge the long ureteral defect without any major consequence.

CONCLUSION

While performing ureteroscopy, we should always keep in mind the possibility of serious complications, including ureteral avulsion. The use of an utmost careful technique and cautious handling of the instrument is the cornerstone to minimize the risk of untoward events. Repair of such complications is a challenging task which should be tailored according to the individual situation. An extended spiral bladder flap technique is still a valuable solution in the repair of long ureteral defects.

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Case Report

Repair of Complex Left Main Bronchial Rupture

Abdullah M Almulaifi*, Hassan Jamal Eddine**, Adel K Ayed**
*Department of Surgery , Jaber Al Ahmad Armed Force Hospital, Kuwait
**Department of Cardiothoracic Surgery, Chest Hospital, Kuwait

Kuwait Medical Journal 2015; 47 (3): 254 - 256

ABSTRACT

Complex left main bronchial rupture at or near the carina is extremely rare. This injury is frequently missed. The treatment requires surgical and anesthetic teams highly experienced with such complex injuries. We report the case of a 49-year-old man involved in a motor vehicle accident with a complex left main bronchus injury. He was successfully managed with primary repair.

KEY WORDS: complex bronchial rupture, pneumothorax, thoracotomy

INTRODUCTION

Post-traumatic complex bronchial injuries are rare but life threatening. 25 - 60%[1] of these cases can be missed at the early stage. The signs and symptoms may vary based on the location and severity of the injury. Bronchoscopy is the most effective method to diagnose and locate such injuries[2]. Maintaining oxygenation and ventilation remains a challenge especially in the presence of lung contusion. The surgical approach to repair is of utmost importance. We report a case of complex left main bronchus rupture, which was managed successfully. The objective of this case report is to describe the technique of airway management, and method of repair.

CASE REPORT

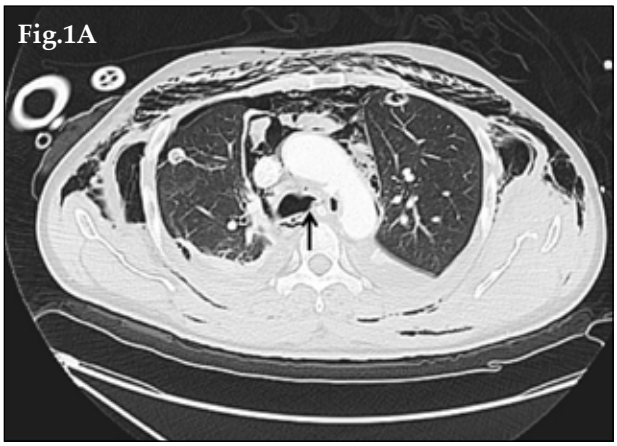
A 49-year-old man involved in motor vehicle accident was brought to the emergency department with respiratory distress and massive subcutaneous emphysema. He was tachycardic, on oxygen, with a saturation level of 88%.

He was intubated urgently. Bilateral chest tubes were inserted. Chest radiography showed right-sided pneumothorax, mediastinal and subcutaneous emphysema. Multiple upper ribs fractures were noted bilaterally. An urgent CT showed bilateral lung contusion, pneumomediastinum, and bronchial rupture (Fig. 1).

Fiberoptic bronchoscopy confirmed complete disruption of the left main bronchus at its origin. A double lumen endotracheal tube was not readily available. Under bronchoscopy guidance an endotracheal tube was advanced into the right main bronchus proximal to the right upper lobe. The ruptured bronchus was accessed through a left thoracotomy at the fourth intercostal space. The rupture was noted to be spiral, the membranous rupture extending to the carina posteriorly in conjunction with left main transverse bronchial rupture. During manipulation, the patient desaturated and an endotracheal tube was inserted into the distal end of the left main bronchus crossing the area of rupture. The left lung was manually ventilated with bag mask valve system. At the same time the right endotracheal tube was advanced distally with minimal cuff inflation to avoid narrowing of the tube, and minimize the herniation. Ventilation was maintained with two separate systems.

The aortic arch was mobilized and elevated to facilitate the repair of the posterior carina, which was done using interrupted suture of 4 - 0 polyglactin 910 (vicryl) (Fig. 2). The anastomosis was reinforced with a pleural flap. The patient was kept on ventilator for four days. After extubation, the patient required bronchoscopy to remove a mucus plug. At bronchoscopy we noticed left vocal cord paralysis.

Address correspondence to:
Abdullah M Almulaifi, Department of Surgery, Jaber Al Ahmad Armed Force Hospital, Kuwait, Tel: +965 66669922, E-mail: almulaifi@yahoo.com



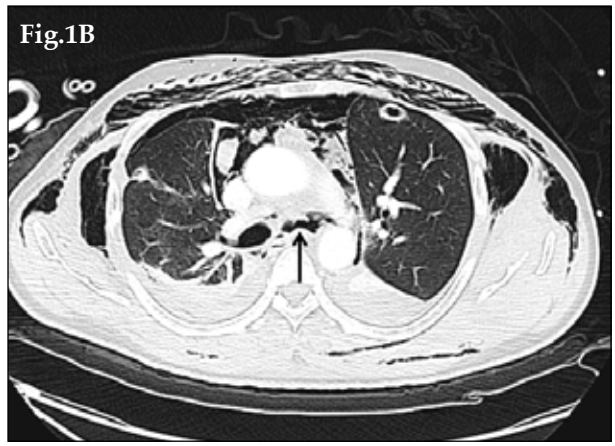


Fig 1: (A) Axial CT image just above the carina showing irregularity of the left trachea wall with posterior linear discontinuity (arrow) **(B)** Showing left main bronchus wall irregularity, disfigurement & wall discontinuity (arrow). Images show pneumomediastinum, bilateral hemopneumothorax with underlying posterior lung consolidations, bilateral chest tubes & chest wall surgical emphysema.

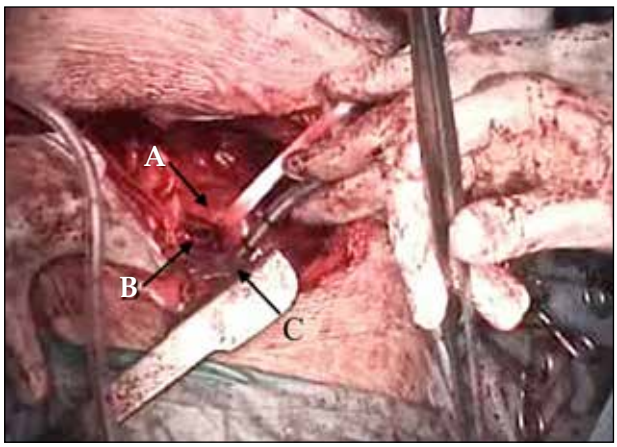


Fig 2: (A) Aortic arch after mobilization**; (B)** Proximal left main bronchus after repair; (**C)** Distal end of left main bronchus with endobronchial tube

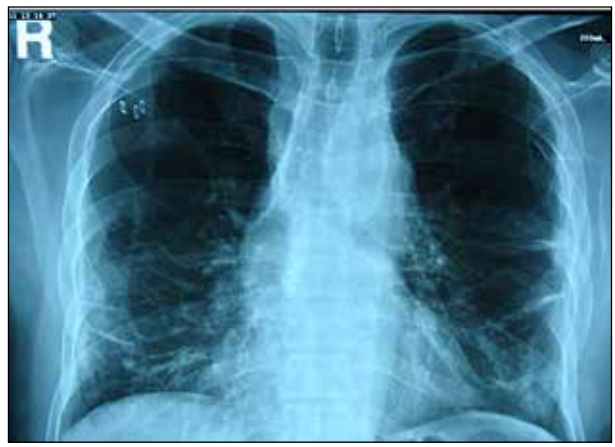


Fig 3: Follow up chest X-ray PA view showing the left main bronchus which has regained its normal shape

The suture line was intact. Chest radiography after two months showed full expansion of the left lung (Fig. 3).

DISCUSSION

Tracheobronchial rupture can occur at any level. More than 80% of injuries occurs within 2 - 5 cm from the carina[3]. 32% of all tracheobronchial rupture occurs at the left main bronchus[1]. Traumatic rupture of the airway may be transverse, longitudinal, multiple, or complex[4].

The proximal end of the left main bronchus is not covered by the pleura. Injuries in this area do not tear the pleura, and a massive mediastinal and subcutaneous emphysema will develop in association with a right-sided pneumothorax.

Taskineu *et al*[5] described a surrounding layer of peribronchial tissue on left side that protects the left main bronchus and allows for ventilation even in the setting of bronchial rupture. When rupture is incomplete, the missed injury results in recurrent atelectasis, infection and bronchiectasis. With complete bronchial rupture, the distal end fills with mucus and the lung collapses. Infection does not occur and the parenchyma of the lung remains undamaged. Clinical signs and symptoms are nonspecific and depend on the location and extent of the rupture. The lack of findings, leads to delayed diagnosis in 25% to 68% of the cases[1,2].

The most common clinical symptoms and signs are dyspnea, mediastinal and subcutaneous emphysema, and persistent pneumothorax despite satisfactory placement of thoracostomy tube[2-4].

Radiography is the initial screening test. The fallen lung sign and interruption of a radiolucent lumen are highly specific for complete bronchial transection[2-5]. Early bronchoscopy is the procedure of choice for diagnosis and airway management[2]. Double lumen endotracheal tube is the best choice for bronchial isolation in the setting of bronchial rupture.

However, it can worsen the existing injury at the carina or the proximal bronchus because of its large size and rigidity[6].

The left main bronchial injury repair is difficult to manage because it is encircled by the aorta. Right thoracotomy is recommended for right bronchial injuries and for proximal left main bronchus[4]. Left thoracotomy is recommended for all injuries in the left main bronchus[2]. In the presence of bilateral lung contusion, left thoracotomy is indicated even for proximal left main bronchial rupture at or near the carina. This can be achieved by aortic arch elevation to facilitate the repair. If ventilation proves inadequate, separate endobronchial tube crossing the defect and connected to another ventilation system is indicated.

Immediate and meticulous repair anastomosis should be carried out with a 4/0 polyglactin 910 (vicryl) interrupted sutures wrapped with pleura.

CONCLUSION

Repair of complex left main bronchial rupture at or near the carina can be achieved in most difficult situations with aortic arch elevation and double lung ventilation intraoperatively, avoiding cardiopulmonary bypass and its complications whenever possible.

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Case Report

Irreducible Dislocation of the Hallucal Interphalangeal Joint: A Rare Case Report and Literature Review

Khaled Ahmed Hamdy, Mohamed Hesham Almosalamy, Ahmed Hussein Mekky
Department of Orthopedic Surgery, Al-Adan Hospital, Kuwait

Kuwait Medical Journal 2015; 47 (3): 257 - 260

ABSTRACT

A 47-year-old male presented to emergency department with dislocation of hallucal interphalangeal joint of the left great toe. A trial of closed reduction under local anesthesia was attempted but failed. An emergency open reduction of the irreducible dislocation of hallucal interphalangeal joint was done with stabilization by K-wire. We report this unusual case of rare injury and review the relevant literature.

KEYWORDS: dislocation, hallux, sesamoid

INTRODUCTION

Toe dislocation is an uncommon disorder. Most reported cases are of dislocation of the metatarsophalangeal joint of the great toe owing to its greater mobility and longer lever arm [1].

Irreducible dislocation of the hallucal interphalangeal joint is a rare disorder. In the past six decades, only 41 cases have been reported in the literature [2].

The interphalangeal sesamoid of the phalanx is only present in approximately 13% of the population[3]. According to Miki *et al*, dislocation of the hallucal interphalangeal joint can be classified into two types based on radiographic and clinical findings. In the first type, the plantar plate is ruptured from one or both of its phalangeal attachment and is trapped within the joint. In the second type the distal phalanx lies dorsal to proximal phalanx, locking the joint in hyperextension [4].

We report a case of irreducible dislocation of hallucal interphalangeal joint after a fall down the stairs.

CASE REPORT

A 47-year-old male presented to the emergency department with painful swelling of left great toe following a fall down the stairs. The mechanism of injury described was one of hyperextension, with axial loading. Examination revealed a tender and swollen left hallux with distal phalanx in slight extension. Passive movements of the interphalangeal joint were painful. There was no wound on the hallux. Radiographs revealed a dorsal dislocation of hallucal interphalangeal joint and an interposed small sesamoid bone. The distal phalanx was subluxated dorsally and medially (Fig. 1). No fracture had been identified. After local anesthesia an attempt at closed reduction was undertaken, but was unsuccessful. An emergency open reduction was performed for irreducible dislocation of the interphalangeal joint. A dorsal inverted L-shaped incision was given with the transverse limb at the joint and the longitudinal limb placed dorsolaterally. Arthrotomy revealed the volar plate with its sesamoid bone over the proximal phalangeal head. The interposed structure was moved in the plantar direction while the distal phalanx was under traction. After relocation of the volar plate, the joint was stable, with full range of motion. Neither reconstruction of volar plate nor excision of the sesamoid was needed. An axial Kirschner wire (K-wire) was then fashioned to provide stability for the volar plate during healing (Fig. 2). The postoperative radiographs revealed satisfactory reduction of the joint and sesamoid bone. The joint was immobilized with a splint with strict elevation of the limb for five days and then partial weight bearing with crutches was allowed. The wire was removed after four weeks. The patient returned to normal activity without any kind of functional disability.

Address correspondence to:

Dr. Khaled Ahmed Hamdy, MD, Department of Orthopedic Surgery, Al-Adan Hospital, Kuwait. 437, Block 2, Abu Halifa, Kuwait. Tel: 00965 99497981 (M), 00965 23712029 (R), E-mail khaledortho@gmail.com

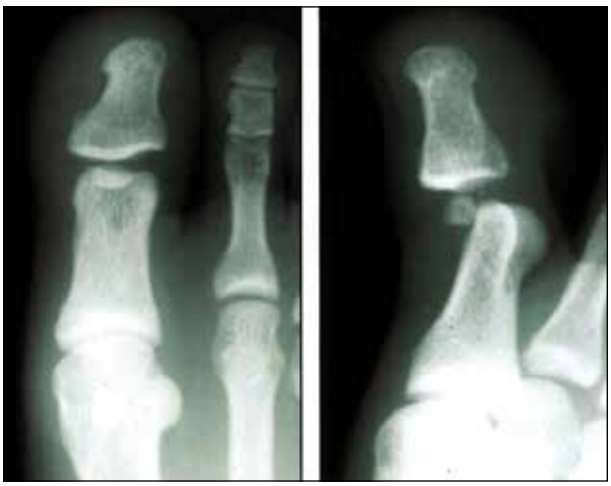

Fig. 1: (a) Anterior-posterior radiograph showing a widened hallucal interphalangeal joint space. The hallucal interphalangeal sesamoid is evident; and (b) lateral radiograph showing a dorsally dislocated interphalangeal joint with hyperextension deformity. The sesamoid is seen to override the proximal phalanx head.

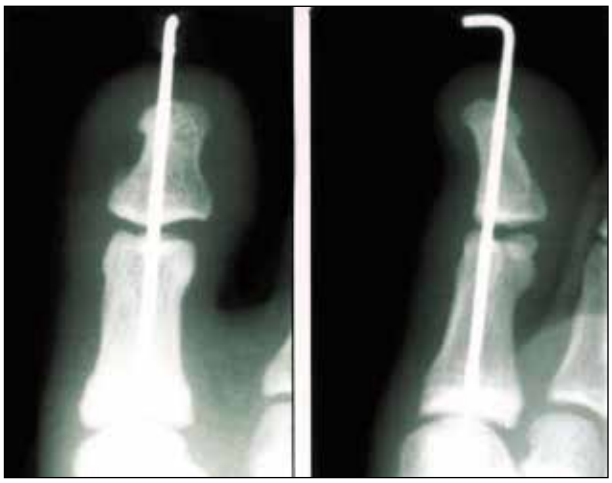

Fig. 2: (a) Anterior-posterior radiograph showing the reduced interphalangeal joint fixed with K-wire; and (b) oblique radiograph showing the reduced sesamoid bone

DISCUSSION

The interposition of the sesamoid bone with dislocation of the interphalangeal joint of the great toe is a rare disorder and may even remain neglected[5]. Sorene and Regev reported a case of traumatic complex dislocation of the interphalangeal joint of the hallux with intra-articular entrapment of two sesamoid bones. Intra-articular entrapment of the sesamoid may result in irreducible dislocation of the interphalangeal joint of great toe [6].

The sesamoid bone

Few osseous structures have received as little attention from anatomists and surgeons as the hallucal interphalangeal sesamoid bone (os sesamoidium interphalange hallux). The name 'sesamum' was first used for this bone by Galen in approximately AD 180 due to its resemblance to a sesame seed (*Sesamum indicum*) [7].

Since then, the limited attention probably reflects difficulty in recognition of the sesamoid and uncertainty of its nature. There is still controversy regarding whether it is a rudimentary structure, an accessory ossicle, or a pressure-induced reactive bone formation. Its size varies from 0.05 cm to 1 cm [7].

The sesamoid bone is known, however, to be associated with several clinical pathologies, ranging from relatively minor painful hyperkeratotic plantar lesion to irreducible interphalangael dislocation [4].

Miki *et al* described anatomical details of the irreducible dislocations of hallucal interphalangeal joint. There are two types of irreducible dislocations

Fig. 3: Anatomical specimens of the hallux (a) Normal anatomy of the hallux is demonstrated: the sesamoid is partly embedded within the volar plate. The major facet is articulating with the condyles of the proximal phalanx. The minor articulating facet is in contact with the base of the distal phalanx. Loose connective tissue intervenes between the volar plate and the flexor hallucis longus tendon; (b) Miki type 1 dislocation: the toe is slightly elongated with a widened joint space. There is gross alignment and the sesamoid is within the joint; and (c) Miki type 2 dislocation: the sesamoid is located over the proximal phalangeal head. The joint is hyperextended and a skin depression is noted [14].

depending on the position of the displaced volar plate including the sesamoid. In type I dislocations, sesamoid is entrapped in the joint. In type II dislocations, sesamoid is located over the proximal phalangeal head (Fig. 3) [4].

The dorsal surface, with two facets, is predominantly cartilaginous and articulates largely with the head of the proximal phalanx. The non-articulating part is osseous and firmly embedded within the plantar capsule of the interphalangeal joint, commonly termed the volar plate. Loose connective tissue spans the space between the volar plate and the flexor hallucis longus tendon proper. The bone is found in 57% of embryological specimens as a well-defined osseous structure, allowing it to be classified as an accessory ossicle within an otherwise normal foot [4]. The hallucal interphalangeal sesamoid can be identified radiographically with a frequency varying from 4.3 to 93% according to the penetration and focus of the film. Bilateral occurrence has been reported in 94% of cases, and in up to 95.5% in a study based on macroscopic examination of over 144 cadaveric feet [8].

Dislocation: Biomechanical considerations

The mechanism of dislocation of the hallucal interphalangeal joint is known to be a combination of axial loading with hypertensive force [9]. This is supported both by patient recall and by occasional lacerations seen over the plantar surface, suggesting a significant hyperextension force acting on the plantar skin at the time of injury [4, 10].

The stability of the hallucal interphalangeal joint appears dependent on the volar plate, joint capsule, collateral ligaments, and the tendons of extensor and flexor hallucis longus acting together to prevent the joint from hyperextension of more than 20°. The collateral ligaments not only confer side-to-side stability but also limit the amount of hyperextension. When these ligaments and the joint capsule are cut, further extension is possible up to the end-point limited by the volar plate. A cadaveric study performed by Miki *et al* [4] demonstrated that when the volar plate is detached from either the proximal or distal phalanx, dislocation of the interphalangeal joint becomes possible. However, the volar plate still cannot be invaginated into the joint. It is only when the attachment to both phalanges is disrupted that this can occur, as seen in reported case. As the interposed sesamoid effectively 'tightens' the intact collateral ligaments, close reduction becomes very difficult, if not impossible [11, 12]. Difficulty can be encountered during close reduction due to the 'tightened' collateral ligaments and problems handling the short and swollen distal phalanx. Only a handful of successful cases have been reported [11].

This should not preclude a trial of close reduction prior to operative treatment. Percutaneous reduction of an incarcerated interphalangeal joint sesamoid is an alternative to open surgery. The procedure is based on the anatomical understanding that the sesamoid-plantar plate complex displaces and reduces together as a unit. Percutaneous reduction is only possible in patients with radiographically apparent sesamoids, as intraoperative fluoroscopy is necessary to visualize engagement of the sesamoid by the reduction implement and confirm a satisfactory reduction after the maneuver. The K-wire is used as a joystick to lever the sesamoid away from the head of the proximal phalanx and into the joint and then to push it plantarward. This technique can be complicated by laceration of the extensor hallucis longus tendon and sesamoid fracture. Also, this technique cannot be done, if the sesamoid is not visible radiographically (in up to 44% of ambulatory patients) in chronic dislocations, when it is no longer possible to distract the joint space enough to allow passage of the sesamoid through it and in open dislocations [13].

Surgical approaches including plantar, medial, dorsal, and dorsal or dorsal-lateral with extensor tendon division approaches have been described. Although the medial approach is favoured by Japanese surgeons, none of the surgical options is clearly superior. Extensor tendon division offers better exposure than required and may result in greater surgical trauma. After reduction, it is not an uncommon practice to remove the offending volar plate. In general, the literature discourages repair of the dislocated volar plate in view of its inherent stability after reduction. Repair of both the origin and insertion of the minute volar plate is technically demanding. Moreover, repair of the volar plate necessitates use of a plantar approach, which is frequently complicated by a hyperkeratotic scar over the weight-bearing area [14].

CONCLUSION

Dislocation of interphalangeal joint of big toe is a rare disorder. Trial of closed reduction should be attempted first but if it fails, an emergency open reduction is advised. Most cases of dislocation of the hallucal interphalangeal joint require open reduction, with dorsal approach. The consensus view is that after reduction, the volar plate need not be repaired. The mode of immobilization to be followed is a matter of discussion. Regardless of the method of treatment adopted, the prognosis appears excellent in most, if not all, cases.

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Selected Abstracts of Articles Published Elsewhere by Authors in Kuwait

Kuwait Medical Journal 2015; 47 (3): 261 - 263

Gender Influence in EBV Antibody Response in Multiple Sclerosis Patients from Kuwait

Al-Temaimi R[1], Alroughani R[2], Jacob S[3], Al-Mulla F[3]
[1]Human Genetics Unit, Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait. Electronic address: rabeah@hsc.edu.kw
[2]Division of Neurology, Department of Medicine, Amiri Hospital, Kuwait, Kuwait; Neurology Clinic, Department of Medicine, Dasman Diabetes Institute, Kuwait
[3]Molecular Pathology Unit, Department of Pathology, Faculty of Medicine, Kuwait University, Kuwait

J Neuroimmunol 2015; 285:57-61. doi: 10.1016/j.jneuroim.2015.05.021. Epub 2015 May 21

Background: Epstein-Barr virus (EBV) infection is implicated with multiple sclerosis (MS) risk, exacerbation, and progression. The HLA-DRB1*1501 haplotype is a strong MS risk factor consistently documented in MS populations. There are no studies of EBV infections and HLA-DRB1*1501 haplotype associating with MS from Kuwait where MS prevalence has increased significantly.
Objectives: To determine the association of EBV infection with MS incidence, and to investigate HLA-DRB1*1501 as a potential genetic risk factor for MS in Kuwait.
Methods: This is a case-control study involving 141 MS patients and 40 healthy controls. Antibody titers against EBV antigens' viral capsid antigen (VCA) and Epstein-Barr nuclear antigen 1 (EBNA1) were measured using enzyme-linked immunosorbent assays. HLA-DRB1*1501 haplotype assessment was done using rs3135005 TaqMan genotyping assay.
Results: Antibody titers against EBV were significantly elevated in MS patients compared to healthy controls (anti-EBNA1, $p = 0.008$; anti-VCA, $p = 0.028$). MS males had higher antibody titers to EBNA1 than healthy male controls ($p = 0.005$) and female MS patients ($p = 0.03$). HLA-DRB1*1501 haplotype genotypes failed to generate a risk association with MS or EBV antibody titers ($p = 0.6$).
Conclusion: An increased immune response to EBV infection is associated with MS incidence influenced by the type of antigen and sex. HLA-DRB1*1501 haplotype is not associated with MS risk in our Kuwaiti MS cohort.

Metallothionein, Oxidative Stress and Trace Metals in Gills and Liver of Demersal and Pelagic Fish Species from Kuwaits' Marine Area

Beg MU[1], Al-Jandal N[2], Al-Subiai S[2], Karam Q[2], Husain S[2], Butt SA[2], Ali A[2], Al-Hasan E[2], Al-Dufaileej S[2], Al-Husaini M[2]
[1]Environmental Pollution and Climate Program, Environment and Life Sciences Research Centre, Kuwait Institute for Scientific Research, P.O. Box 24885, Safat 13109, Kuwait. Electronic address: mbeg@kisr.edu.kw
[2]Environmental Pollution and Climate Program, Environment and Life Sciences Research Centre, Kuwait Institute for Scientific Research, P.O. Box 24885, Safat 13109, Kuwait

Mar Pollut Bull 2015 Jul 28. pii: S0025-326X(15)00491-9. doi: 10.1016/j.marpolbul.2015.07.058. [Epub ahead of print]

Two fish species yellowfin seabream (Acanthopagrus latus) and tonguesole (Cynoglossus arel) were collected from two locations in Kuwait's territorial waters in non-reproductive periods and used as bio-indicator organism for the assessment of metals in the marine environment. Species variation in fish was observed; seabream contained high metal content and metallothionein in liver

and gill tissues compared to tonguesole, especially from Kuwait Bay area. Oxidative injury was registered in the gills of both species, but in tonguesole liver was also involved. Consequently, antioxidant enzyme catalase was elevated in tonguesole enabling bottom dwelling fish to combat oxidative assault. The study provided information about the current status of metals in marine sediment and levels of metals accumulated in representative species along with oxidative damage in exposed tissues and the range of biomarker protein metallothionein and enzymes of antioxidant defence mechanism enhancing our understanding about the biological response to the existing marine environment in Kuwait.

Historic and Contemporary Contamination in the Marine Environment of Kuwait: An Overview

Al-Sarawi HA[1], Jha AN[2], Al-Sarawi MA[3], Lyons BP[4]
[1]Kuwait Environment Public Authority, P.O. Box 24395, Safat 13104, Kuwait; School of Biological Sciences, Plymouth University, Drake Circus, Plymouth PL4 8AA, UK. Electronic address: h.alsarawi@gmail.com
[2]School of Biological Sciences, Plymouth University, Drake Circus, Plymouth PL4 8AA, UK.
[3]Department of Earth & Environmental Sciences, Kuwait University, Faculty of Science, P.O. Box 5969, Safat 13060, Kuwait
[4]Centre for Environment, Fisheries and Aquaculture Science (Cefas), Weymouth Laboratory, Barrack Road, Weymouth, Dorset DT4 8UB, UK

Mar Pollut Bull 2015 Jul 27. pii: S0025-326X(15)00472-5. doi: 10.1016/j.marpolbul.2015.07.052. [Epub ahead of print]

The rapid expansion of industry, along with previous pollution events linked to conflicts in the region, have led to a variety of contaminants being inadvertently or deliberately discharged into Kuwait's marine environment. These include polycyclic aromatic hydrocarbons (PAHs) and trace metals, from the petrochemical industry, and contaminated brine from the region's desalination industries. The present paper has reviewed over 60 studies that have reported the levels of contaminants, including PAHs, metals and polychlorinated biphenyls (PCBs) present in seawater, sediment and representative marine organisms. Most of the reviewed literature confirmed that while Kuwait's marine environment has been subjected to a wide array of pollution events, the actual levels of contamination remains relatively low. However, sediment contamination hotspots associated with point sources of industrial contamination, such as originating from the Shuaiba industrial area, do exist at a number of locations around the coast.

Patterns of Suicide in Kuwait: A Retrospective Descriptive Study from 2003 - 2009

Al-Waheeb S[1], Al-Kandary N
[1]Faculty of Medicine, Kuwait University, 72, 71661, Shamiyah, Kuwait. salah.w@hsc.edu.kw
[2]General Department of Criminal Evidence, Ministry of Interior, Farwaniyah, Kuwait
E-mail: pathgirl.n@gmail.com

BMC Public Health 2015; 15:527. doi: 10.1186/s12889-015-1862-7

Background: Prior to the invasion of Kuwait by Iraq in 1990, suicides were almost unheard of in Kuwait. However, there has been a notable increase in the referrals of suicide cases to the forensic authorities since then. A review of suicide cases was performed to investigate the demographics of this phenomenon and the suicide modalities used and to uncover issues that can be addressed by the region's government.

Methods: The sole source of data was the general department of criminal evidence (GDCE), where cases are referred by police authorities and by hospital investigators from the entire country. All cases signed out by forensic investigators as "suicide" during the time period 2003-2009 were retrieved. A full review of the data from the case files was made. This included demographic data, scene examination, radiographic investigations, autopsies with histo-pathological examination findings and toxicological screening results in each case.
Results: A total of 347 cases were retrieved and studied. Hanging was found to be the most common suicide modality used by subjects (60 %). Non-citizens constituted 87 % of cases, and no significant difference was found between married and single subjects or between Muslims and non-Muslims. Regions that were more populated with an expatriate labour force had the highest suicide prevalence.
Conclusion: The government of Kuwait needs to investigate the dire conditions in which some expatriates live and to improve their situation. More control over the dispensing of certain medications needs to be enforced. Finally, strict firearm control could help reduce the suicide rates in Kuwait.

Clinical and Molecular Characteristics of Non-Transfusion-Dependent Thalassemia in Kuwait

Adekile AD[1], Azab AF, Al-Sharida SI, Al-Nafisi BA, Akbulut N, Marouf RA, Mustafa NY
[1]Department of Pediatrics, Faculty of Medicine, Kuwait University , Jabriya , Kuwait

Hemoglobin 2015 Jun 15:1-7. [Epub ahead of print]

Although not regularly transfused, patients with non-transfusion-dependent thalassemia (NTDT) are prone to iron overload and its complications. Their molecular, phenotypical and laboratory characteristics vary in different populations and there is a need to document local prevailing patterns. We have reviewed the records of our patients with NTDT in Kuwait and documented their clinical and molecular characteristics in addition to iron status [serum ferritin and liver magnetic resonance imaging (MRI) T2*], management and complications. There were 41 patients, made up of 20 with β-thalassemia intermedia (β-TI), 18 with Hb H (β4) disease and three with Hb E (HBB: c.79G > A)-β-thalassemia (Hb E-β-thal); their ages ranged from 3 to 36 years (mean 12.5 ± 7.7). While 18 (43.9%) had been transfused at least once, only three (7.3%) had been transfused on multiple occasions. Three patients had serum ferritin >500 ng/mL; while four of 38 had mild or moderate liver iron overload. Seven (35.0%) of the β-TI patients were managed with hydroxyurea (HU) with good response. Other complications included five patients with gallstones and one each of hypothyroidism and moyamoya. The most common mutations among the β-TI patients were IVS-II-1 (G > A) and IVS-I-6 (T > C), while among the Hb H patients, the Saudi α2-globin gene polyadenylation (polyA) (AATAAA > AATAAG) mutation was responsible for all cases either as homozygotes (61.1%) or compound heterozygotes with the α-thal-2 ($-\alpha^{3.7}$) allele (33.3%). Although the pattern of NTDT in Kuwaiti patients is generally mild, there is a need to follow them to adulthood as the complications are cumulative and more prevalent in this group.

Forthcoming Conferences and Meetings

Compiled and edited by
Babichan K Chandy

Kuwait Medical Journal 2015; 47 (3): 264 - 276

15th European Society for **Biomedical Research on Alcoholism** Congress
Sep 13 - 16, 2015
Spain / Valencia
Contact: Technical Secretariat, Viajes El Corte Inglés, S.A.
Phone: 011-34-963-107-189; Fax: 011-34-963-411-046
Email: esbra2015@viajeseci.es

17th Congress of the European Society for **Organ Transplantation**
Sep 13 - 16, 2015
Belgium / Brussels
Contact: Congress Administrative Secretariat, Aim Group International Vienna
Phone: 011-43-1-402-7755; Fax: 011-43-1-402-7731
Email: esot2015@aimgroup.eu

2015 International Society for **Hemodialysis** Congress
Sep 13 - 16, 2015
Malaysia / Kuala Lumpur
Contact: Shu Shan, Conference Secretariat, Console Communications Sdn Bhd
Phone: 011-603-2162-0566; Fax: 011-603-2161-6560
Email: ishd2015@console.com.my

2015 World **STI & HIV** Congress
Sep 13 - 16, 2015
Australia / Brisbane
Contact: Conference Secretariat
Phone: 011-61-2-8204-0770; Fax: 011-61-2-8204-0779
Email: info@worldsti2015.com

11th North East International **Flap** Course
Sep 14 - 17, 2015
United Kingdom / Newcastle Upon Tyne
Contact: Secretary to Mr Matt Erdmann, North East Flap Course
Phone: 011-44-19-1333-6989; Fax: 011-44-19-1333-2337
Email: matt.erdmann@cddft.nhs.uk

4th International Conference on **Nephrology & Therapeutics**
Sep 14 - 16, 2015
United States / Maryland / Baltimore
Contact: James Crawler, OMICS International
Phone: 650-268-9744
Email: jamescrawler123@gmail.com

Basic Practical Skills in **Obstetrics & Gynaecology**
Sep 14 - 15, 2015
United Kingdom / London
Contact: Royal College of Obstetricians & Gynaecologists
Phone: 011-44-20-7092-1670; Fax: 011-44-20-7723-0575

International Conference on Targeting **Diabetes & Novel Therapeutics**
Sep 14 - 16, 2015
United States / Nevada / Las Vegas
Contact: Hailey Watson, Event Manager, OMICS International
Phone: 650-268-9744; Fax: 650-618-1414
Email: diabeticmedications@omicsgroup.com

Medical Ethics
Sep 14 - 18, 2015
United Kingdom / London
Contact: Centre for Continuing Professional Development, Imperial College London
Phone: 011-44-20-7594-6881; Fax: 011-44-20-7594-6883
Email: cpd@imperial.ac.uk

MRI of the Joints
Sep 14 - 18, 2015
France / Paris
Contact: Walter Rijsselaere, Erasmus Course on Magnetic Resonance Imaging
Phone: 011-32-2-477-5322; Fax: 011-32-2-477-5362
Email: walter.rijsselaere@uzbrussel.be

1st International Conference on **Paediatric Acquired Brain Injury**
Sep 16 - 18, 2015
United Kingdom / Liverpool
Contact: Colleen LoGrande,International Brain Injury Association
Fax: 703-960-6603
Email: clogrande@internationalbrain.org

2015 Faculty of **Child & Adolescent Psychiatry** Annual Conference
Sep 16 - 18, 2015
United Kingdom / Brighton
Contact: *Royal* College of Psychiatrists
Phone: 011-44-20-3701-2604
Email: csimms@rcpsych.ac.uk

Advanced **Airway Workshop**
Sep 16, 2015
United Kingdom / London
Contact: Meetings and Events, Royal College of Anaesthetists
Phone: 011-44-20-7092-1670; Fax: 011-44-20-7092-1730
Email: events@rcoa.ac.uk

12th Meeting of the Asian Society for **Neuro-Oncology**
Sep 17 - 20, 2015
Philippines / Manila
Contact: Secretariat, BM Events
Phone: 011-63-91-7855-2011
Email: bmevents8@gmail.com

15th **EURETINA** Congress
Sep 17 - 20, 2015
France / Nice
Contact: Agenda Communications & Conference Services Ltd
Phone: 011-353-1-210-0092; Fax: 011-353-1-209-1112
Email: euretina@euretina.org

16th **Scleroderma Society of Canada** (SSC) Annual Conference
Sep 17 - 19, 2015
Canada / Ontario / Hamilton, Ontario
Contact: SSC
Phone: 866-279-0632
Email: info@scleroderma.ca

22nd World Congress on Controversies in **Obstetrics, Gynecology & Infertility**
Sep 17 - 20, 2015
Hungary / Budapest
Contact: Ilana, Rabinoff-Sofer, CongressMed Ltd
Phone: 011-972-73-706-6954
Email: cogi@congressmed.com

30th International **Papillomavirus** Conference & Clinical & Public Health Workshops
Sep 17 - 21, 2015
Portugal / Lisbon
Contact: Charlotte Boskila, APM, Kenes International
Phone: 011-41-22-908-0488
Fax: 011-41-22-906-9140
Email: hpv2015@kenes.com

44th International Society for **Experimental Hematology** (ISEH) Annual Scientific Meeting
Sep 17 - 19, 2015
Japan / Kyoto
Phone: 312-321-5114
Fax: 312-673-6923
Email: info@iseh.org

2015 Hydrocephalus: 7th Meeting of International Society of **Hydrocephalus & Cerebrospinal Fluid Disorders**
Sep 18 - 21, 2015
Canada / Alberta / Banff
Contact: Linda Shorting, Cumming School of Medicine, University of Calgary
Phone: 403-220-4251
Email: shorting@ucalgary.ca

Challenges in **Pediatric Hematology & Oncology**: 2nd International / 9th National Congress of Iranian Society of Pediatric Hematology & Oncology (IPHOS)
Sep 18 - 20, 2015
Iran / Tehran
Contact: Gholamreza Bahoush, Scientific Secretary of the Congress, IPHOS
Phone: 011-98-21-6691-2679; Fax: 011-98-21-6691-2679
Email: Info@iphos.ir

Neonatology -The Sick Newborn
Sep 18 - 30, 2015
United States / South Carolina / Kiawah Island
Contact: Continuing Medical Education, Georgia Regents University
Phone: 706-721-2329; Fax: 706-721-4642
Email: coned@gru.edu

Tuscany Medical Conference
Sep 18 - 25, 2015
Italy / Pisa
Contact: Martin Kuba, Conference Manager, Zdravotnicky vzdelavaci institut
Phone: 011-42-412-384-013
Email: marketing@dentalcare.cz

Hands-On Interventional **Pain Management Cadaver** Course
Sep 19 - 20, 2015
United States / Illinois / Chicago
Contact: Society for Pain Practice Management
Phone: 913-327-5999

Benign **Abdominal Surgery**
Sep 21 - 22, 2015
United Kingdom / London
Contact: Royal College of Obstetricians & Gynaecologists
Phone: 011-44-20-7772-6200; Fax: 011-44-20-7723-0575

Preceptorship Course in **Metastatic Colorectal Cancer** Management
Sep 21 - 24, 2015
France / Paris
Contact: Denise Rizzitelli, Congress Coordinator, Meridiano Congress International
Phone: 011-39-6-8859-5210; Fax: 011-39-6-8859-5234
Email: denise.rizzitelli@meridiano.it

Royal College of **Anaesthetists** (RCA) CPD Days
Sep 21 - 22, 2015
United Kingdom / London
Contact: *Meetings* and Events, RCA
Phone: 011-44-20-7092-1670; Fax: 011-44-20-7092-1730
Email: events@rcoa.ac.uk

2015 International Union against **Sexually Transmitted Infections** (IUSTI) Europe Conference
Sep 22 - 24, 2015
Spain / Barcelona
Contact: Dr Janet Wilson, Secretary General, IUSTI
Email: secretary@iusti.org

2015 International Society for **Hip Arthroscopy** (ISHA) Annual Scientific Meeting
Sep 24 - 26, 2015
United Kingdom / Cambridge
Contact: Secretariat, ISHA
Email: secretary@isha.net

2015 **Pediatric Orthopaedic Trauma** Summit
Sep 24 - 25, 2015
United States / Minnesota / St. Paul
Contact: Susan Gordon, Office of Continuing Professional Development, University of Minnesota Medical School
Phone: 612-626-7600
Email: cme@umn.edu

Carbapenemases in Enterobacteriaceae: Challenges & Preparedness
Sep 24 - 26, 2015
Italy / Verona
Contact: European Society of Clinical Microbiology & Infectious Diseases
Phone: 011-41-61-508-0153; Fax: 011-41-61-508-0151
Email: info@escmid.org

Medical CBT: Ten-Minute **Cognitive Behaviour Therapy** Techniques for Real Doctors
Sep 24 - 25, 2015
Canada / British Columbia / Vancouver
Contact: Greg Dubord, MD, CME Director, CBT Canada
Phone: 877-466-8228
Email: registrar@cbt.ca

Assessment & Management of **Acute Hand Injuries**
Sep 25, 2015
United Kingdom / Derby
Contact: Stefania Wigelsworth, Postgraduate Administrator, Pulvertaft Hand Centre
Phone: 011-44-13-3278-7490
Email: stefania.wigelsworth@nhs.net

4th International Conference & Exhibition on **Immunology**
Sep 28 - 30, 2015
United States / Texas / Houston
Contact: Valentina Diaz, Event Manager, OMICS Group
Phone: 650-268-9744; Fax: 650-618-1414
Email: immunology@conferenceseries.net

Advanced Therapeutic Endoscopy Live Porcine Model Hands-on **EMR & ESD** Workshop
Sep 28 - 29, 2015
Netherlands / Rotterdam
Contact: Destination Services Europe GmbH
Phone: 011-49-202-870-2991; Fax: 011-49-202-257-2291
Email: eage@d-s-europe.com

Complex **Abdominal Wall Repair** Cadaveric Master Class
Sep 28, 2015
United Kingdom / Newcastle
Contact: Covidien
Phone: email to http://www.covidien.eu/herniacare

Intrapartum **Fetal Surveillance**
Sep 28, 2015
United Kingdom / London
Contact: Royal College of Obstetricians & Gynaecologists
Phone: 011-44-20-7772-6200
Fax: 011-44-20-7723-0575

World Congress on Interventional Therapies for **Type 2 Diabetes** / 2nd Diabetes Surgery Summit
Sep 28 - 30, 2015
United Kingdom / London
Contact: Ilana Eliav, Mr., Kenes International
Phone: 011-41-22-906-9178
Email: wcitt2d@kenes.com

28th International Course on **Therapeutic Endoscopy**
Oct 1, 2015
Canada / Ontario / Toronto
Contact: Charlene Reilly, Therapeutic Endoscopy Group, St. Michael's Hospital
Phone: 416-864-5329; Fax: 416-864-5803
Email: therendo@interlog.com

2nd International Conference on **Repair, Regeneration & Reconstruction**
Oct 1 - 3, 2015
United Kingdom / London
Contact: Institute of Surgery and Innovation
Phone: 011-44-87-1288-5135
Email: info@icr3.org

36th Annual Meeting of the International Society for **Dermatologic Surgery**
Oct 1 - 4, 2015
South Korea / Seoul
Contact: Congress Secretariat, Kokonex Ltd.
Phone: 011-82-2-3476-7700; Fax: 011-82-2-3476-8800
Email: isds2015@koconex.com

Cardiology Update
Oct 1, 2015
United Kingdom / London
Contact: Conferences Team, Royal College of Physicians of London
Phone: 011-44-20-3075-2389; Fax: 011-44-20-7487-5218
Email: conferences@rcplondon.ac.uk

Menopause Special Skills Module
Oct 1 - 2, 2015
United Kingdom / Leeds
Contact: Kate Ellis, British Menopause Society
Phone: 011-44-16-2889-0199; Fax: 011-44-16-2847-4042
Email: kate@thebms.org.uk

State of the Art: **Kidney & Pancreas** Transplantation
Oct 1, 2015
United States / Michigan / Ann Arbor
Contact: Stacy Brand, Office of Continuous Professional Development, Univ. of Michigan
Phone: 734-615-0832
Email: slipson@umich.edu

2015 International Society for **Prosthetics & Orthotics** (ISPO) Canada Symposium
Oct 2 - 3, 2015
Canada / Ontario / Toronto
Contact: Peter Kyberd, ISPO Canada Secretariat, ISPO Canada
Phone: 506-458-7025
Email: ispocanada@gmail.com

8th Annual Royal Marsden **Breast Cancer** Meeting: Hot Topics in Breast Cancer
Oct 2, 2015
United Kingdom / London
Contact: Education and Conference Centre, The Royal Marsden NHS Foundation Trust
Phone: 011-44-20-7808-2921
Fax: 011-44-20-7808-2334
Email: conferencecentre@rmh.nhs.uk

Advances in **Cancer Immunotherapy**™-Nashville, TN
Oct 2, 2015
United States / Tennessee / Nashville
Contact: Society for Immunotherapy of Cancer
Phone: 414-271-2456; Fax: 414-276-3349
Email: info@sitcancer.org

Advances in **Thoracic Surgical Oncology**
Oct 2 - 3, 2015
United States / New York / New York
Contact: Continuing Medical Education, Memorial Sloan Kettering Cancer Center
Phone: 646-227-2025; Fax: 212-557-0773
Email: brodheap@mskcc.org

15th International **Nutrition & Diagnostics** Conference
Oct 5 - 8, 2015
Czech Republic / Prague
Contact: Citlalli Garnica Ortiz, Radanal, Ltd.
Phone: 011-420-469-779-899
Email: info@indc.cz

17th International Society of **Addiction Medicine** (ISAM) Congress
Oct 5 - 8, 2015
United Kingdom / Dundee
Contact: ISAM Congress Team, ISAM Dundee
Phone: 011-44-14-1357-2235
Fax: 011-44-14-1357-5307
Email: contact@isamdundee2015.com

2015 International **Cancer Imaging** Society (ICIS) Meeting & 15th Annual Teaching Course
Oct 5 - 7, 2015
United Kingdom / London
Contact: Louise Mustoe, ICIS
Phone: 011-44-20-7036-8805
Email: louise.mustoe@cancerimagingsociety.org.uk

4th International Conference & Exhibition on **Surgery**
Oct 5 - 7, 2015
United Arab Emirates / Dubai
Contact: Isabella Jones, Program Manager, OMICS International
Phone: 888-843-8169
Fax: 650-618-1414
Email: surgery@conferenceseries.net

Basic Practical Skills in **Obstetrics & Gynaecology**
Oct 5 - 6, 2015
United Kingdom / London
Contact: Royal College of Obstetricians & Gynaecologists
Phone: 011-44-20-7772-6200; Fax: 011-44-20-7723-0575

2015 **Influenza Vaccines** for the World
Oct 6 - 9, 2015
Portugal / Algarve
Contact: Caroline Sumner, Events Director, Meetings Management
Phone: 011-44-14-8342-7770
Fax: 011-44-14-8342-8516
Email: csumner@meetingsmgmt.u-net.com

MS Academia: **Multiple Sclerosis** Advanced Course
Oct 6, 2015
Spain / Barcelona
Contact: Sara Guglielmini, Congress Coordinator, Meridiano Congress International
Phone: 011-39-6-8859-5211; Fax: 011-39-6-8859-5234
Email: sara.guglielmini@meridiano.it

Stroke: Modern Management
Oct 6, 2015
United Kingdom / London
Contact: Conferences Team, Royal College of Physicians of London
Phone: 011-44-20-3075-2389; Fax: 011-44-20-7487-5218
Email: conferences@rcplondon.ac.uk

2015 International Society for **Pediatric & Adult Diabetes** / Australasian Pediatric Endocrine Group Joint Annual Conference
Oct 7 - 10, 2015
Australia / Brisbane
Contact: Conference Secretariat, K.I.T. Group GmbH
Phone: 011-49-30-2460-3210; Fax: 011-49-30-2460-3200
Email: ispad-apeg@kit-group.org

2015 **Preceptorship in Metastatic Colorectal** Cancer
Oct 7 - 9, 2015
United Kingdom / Liverpool
Contact: David H. Slangen, Congress Coordinator, Meridiano Congress International
Phone: 011-39-6-8859-5250; Fax: 011-39-6-8859-5234
Email: david.slangen@meridiano.it

2015 **Transplant Immunosuppression**
Oct 7 - 10, 2015
United States / Minnesota / Minneapolis
Contact: Office of Continuing Professional Development, University of Minnesota Medical School
Phone: 612-626-7600
Email: cme@umn.edu

Sports Medicine for the primary care physician & fall update in family medicine
Oct 7 - 9, 2015
United States / Michigan / Ann Arbor
Contact: Kristen Taylor, Office of Continuous Professional Development, University of Michigan
Phone: 517-664-9086
Email: ktaylor@mafp.com

Cardiovascular with **CT Correlation MRI**
Oct 8 - 9, 2015
Italy / Rome
Contact: Walter Rijsselaere, Erasmus Course on Magnetic Resonance Imaging
Phone: 011-32-2-477-5322; Fax: 011-32-2-477-5362
Email: walter.rijsselaere@uzbrussel.be

Peritoneal Surface Malignancy
Oct 8 - 9, 2015
United Kingdom / Manchester
Contact: Ana Galan, Education Coordinator, European Society of Surgical Oncology
Phone: 011-32-2-775-0243
Email: ana.galan@essoweb.org

2015 **Quality Breast Imaging** Update
Oct 9 - 11, 2015
India / Mumbai
Contact: International Institute for Continuing Medical Education
Phone: 205-467-0290
Email: IICMEMAIL@gmail.com

7th Trends in **Medical Mycology**
Oct 9 - 12, 2015
Portugal / Lisbon
Contact: Pepijn Klerkx, Mr., Congress Care
Phone: 011-31-73-690-1415
Fax: 011-31-73-690-1417
Email: p.klerkx@congresscare.com

Kidney and Prostate Cancer
Oct 9, 2015
United Kingdom / London
Contact: Education and Conference Centre, The Royal Marsden NHS Foundation Trust
Phone: 011-44-20-7808-2921; Fax: 011-44-20-7808-2334
Email: conferencecentre@rmh.nhs.uk

11th International Congress on **Coronary Artery Disease**
Oct 11 - 13, 2015
Italy / Florence
Contact: APM, Kenes International
Phone: 011-41-22-908-0488; Fax: 011-41-22-906-9140
Email: calendar@kenes.com

25th World Congress on **Ultrasound in Obstetrics & Gynecology**
Oct 11 - 14, 2015
Canada / Quebec / Montreal
Contact: Congress Secretariat, International Society of Ultrasound in Obstetrics & Gynecology
Phone: 011-44-20-7471-9955; Fax: 011-44-20-7471-9959
Email: congress@isuog.org

2015 **Transcatheter Cardiovascular Therapeutics**
Oct 12 - 16, 2015
United States / California / San Francisco
Contact: Cardiovascular Research Foundation
Phone: 646-434-4500
Email: info@crf.org

2015 International **Psychhogeriatric** Association (IPA) Annual Congress
Oct 13 - 16, 2015
Germany / Berlin
Contact: IPA Secretariat, IPA
Email: ipa-info@ipa-online.org

15 Minute **CBT** for Use in Clinical Teams: a Five Areas Approach
Oct 15, 2015
United Kingdom / London
Contact: Royal College of Psychiatrists
Phone: 011-44-20-3701-2622 / 2611; Fax: 011-44-20-3701-2761
Email: rbrake@rcpsych.ac.uk

International Symposium - **Obstetric Anesthesia** - Effect on Mother & Newborn
Oct 15 - 17, 2015
Hungary / Budapest
Contact: Erna Sari, Conference Secretary, Akadémiai Kiadó / AKCongress
Phone: 011-36-1-464-8224
Email: obstanest@akcongress.com

Molecular Oncology for the Clinical Oncologist: Defining the Actionable Genome
Oct 16 - 17, 2015
United States / New York / New York
Contact: Continuing Medical Education, Memorial Sloan Kettering Cancer Center
Phone: 646-227-2025; Fax: 212-557-0773
Email: brodheap@mskcc.org

10th Asia / Oceania Congress of **Gerontology & Geriatrics**
Oct 19 - 22, 2015
Thailand / Chiangmai
Contact: Tanawan Pipatpratuang, APM, Kenes Asia
Phone: 011-662-748-7881; Fax: 011-662-748-7880
Email: info@iaggchiangmai2015.com

Chronic Pain Management for the Family Physician
Oct 19, 2015
United States / Alberta / Calgary
Contact: Sylvia Vespa, Cumming School of Medicine, University of Calgary
Phone: 403-909-9095
Email: sylvia.vespa@albertahealthservices.ca

Medical **CBT**: Ten-Minute Techniques for Real Doctors (cognitive behavior therapy)
Oct 19 - 30, 2015
Spain / Barcelona
Contact: Greg Dubord, MD, CME Director, CBT Canada
Phone: 877-466-8228
Email: registrar@cbt.ca

17th International Workshop on **Co-Morbidities & Adverse Drug Reactions in HIV**
Oct 21 - 24, 2015
Spain / Barcelona
Contact: Organising Secretariat, International Medical Press
Phone: 011-44-20-7398-0700; Fax: 011-44-20-7398-0701
Email: comorbidities@nucleuscentral.com

2015 World Conference on **Regenerative Medicine**
Oct 21 - 23, 2015
Germany / Leipzig
Contact: Conference Office, event lab. GmbH
Phone: 011-49-341-2405-9650; Fax: 011-49-341-2405-9651
Email: info@wcrm-leipzig.com

2015 International Conference on **Residency Education**
Oct 22 - 24, 2015
Canada / British Columbia / Vancouver
Contact: Event Management and Hospitality Services, Royal College of Physicians and Surgeons of Canada
Phone: 800-668-3740 ext. 176 or 613-260-4176 ext. 176; Fax: 613-730-8252
Email: icre@royalcollege.ca

3rd International Congress on Controversies in **Stem Cell Transplantation & Cellular Therapies**
Oct 22 - 24, 2015
Germany / Berlin
Contact: Natalie Ross, Congress Secretariat, Comtecmed
Phone: 011-97-2-3566-6166; Fax: 011-97-2-3566-6177
Email: costem@comtecmed.com

5th **Spine Deformity Solutions**: A Hands-on Course
Oct 22 - 24, 2015
Turkey / Istanbul
Contact: Ann Shay, Meetings Manager, Scoliosis Research Society
Phone: 414-289-9107; Fax: 414-276-3349
Email: ashay@srs.org

Basic Arthroscopy Cadaveric Course
Oct 22, 2015
United Kingdom / Newcastle Upon Tyne
Contact: Lorraine Waugh, Newcastle Upon Tyne Surgical Training Centre
Phone: 011-44-19-1223-1264; Fax: 011-44-19-1223-7248
Email: lorraine.waugh@nuth.nhs.uk

World Congress on Controversies in **Breast Cancer**
Oct 22 - 24, 2015
Australia / Melbourne
Contact: Ilana, Rabinoff-Sofer, CongressMed Ltd
Phone: 011-972-73-06-6954
Email: cobra@congressmed.com

World Summit on **Pediatric: Probiotics, Functional & Baby Food** Edition
Oct 22 - 25, 2015
Bulgaria / Sofia
Contact: Angelo Raganato, Dr., WHISPER - Pediatrics
Phone: 011-39-33-9411-5588
Email: info@wsp-congress.com

3rd **Anti-aging Medicine** European Congress
Oct 23 - 24, 2015
France / Paris
Contact: EuroMediCom
Phone: 011-33-1-5683-7800; Fax: 011-33-1-5683-7805

2015 **Acute & General Medicine** for the Physician
Oct 26 - 28, 2015
United Kingdom / London
Contact: Conferences Team, Royal College of Physicians of London
Phone: 011-44-20-3075-2389; Fax: 011-44-20-7487-5218
Email: conferences@rcplondon.ac.uk

4th International Conference & Exhibition on **Orthopedics & Rheumatology**
Oct 26 - 28, 2015
United States / Maryland / Baltimore
Contact: Kane Maxwell, Mr., OMICS Group Inc.
Phone: 800-216-6499 (USA & Canada) or 650-268-9744
Email: orthopedics.conference@omicsonline.us

Advanced Module: **Congenital Surgery**
Oct 26 - 30, 2015
United Kingdom / Windsor (UK)
Contact: European Association for Cardio-Thoracic Surgery
Phone: 011-44-17-5383-2166
Fax: 011-44-17-5362-0407

Intensive Course in **Transcranial Magnetic Stimulation**
Oct 26 - 30, 2015
United States / Massachusetts / Boston
Contact: Department of Continuing Education, Harvard Medical School
Phone: 617-384-8600; Fax: 617-384-8686
Email: hms-cme@hms.harvard.edu

19th **Human Antibodies & Hybridomas** Conference
Oct 28 - 30, 2015
Switzerland / Lausanne
Contact: Caroline Sumner, Events Director, Meetings Management
Phone: 011-44-14-8342-7770
Fax: 011-44-14-8342-8516
Email: csumner@meetingsmgmt.u-net.com

2015 Bio MicroWorld: 6th International Conference on **Environmental, Industrial & Applied Microbiology**
Oct 28 - 30, 2015
Spain / Barcelona
Contact: Aurora Solano, Formatex Research Center
Phone: 011-34-924-258-615; Fax: 011-34-924-263-053
Email: conference@biomicroworld2015.org

Endoscopy in Reproductive Medicine
Oct 28 - 30, 2015
Belgium / Leuven
Contact: Organising Secretariat, ESHRE Central Office
Phone: 011-32-2-269-0969; Fax: 011-32-2-269-5600
Email: info@eshre.eu

2015 Hot Topic Conference: **Obesity & Pregnancy**
Oct 29 - 30, 2015
United Kingdom / London
Contact: World Obesity Federation
Phone: 011-44-20-7685-2580
Fax: 011-44-20-7685-2581
Email: hottopics@worldobesity.org

2015 Hands-On **Transvaginal Pelvic Ultrasound Imaging & Doppler**
Oct 30, 2015
United States / Texas / Dallas
Contact: Amy Donaldson, Registrar, Keith Mauney & Associates Ultrasound Training Institutes
Phone: 800-845-3484 or 972-353-3200; Fax: 817-577-4250
Email: info@kmaultrasound.com

2015 **Orthopaedic** Symposium
Oct 30, 2015
United Kingdom / Edinburgh
Contact: Claire Forrest, Royal College of Surgeons of Edinburgh
Phone: 011-44-13-1527-3436
Email: C.Forrest@rcsed.ac.uk

22nd World Congress of **Neurology**
Oct 31 - Nov 5, 2015
Chile / Santiago
Contact: Rene Chait, APM, Kenes International
Phone: 011-41-22-908-0488; Fax: 011-41-22-906-9140
Email: wcn@kenes.com

7th World Congress of the World Sleep Federation: **World Sleep** 2015
Oct 31 - Nov 3, 2015
Turkey / Istanbul
Contact: Organizing Secretariat, Congrex Switzerland Ltd
Phone: 011-41-61-686-7777; Fax: 011-41-61-686-7788
Email: worldsleep@congrex-switzerland.com

3rd International Conference on **Hematology & Blood Disorders**
Nov 2 - 4, 2015
United States / Georgia / Atlanta
Contact: Alisha, Summer, OMICS Group. Inc
Phone: 888-843-8169
Email: hematology@conferenceseries.net

Molecular Diagnostics, Genomics & Epigenetics in Clinical Oncology
Nov 2 - 4, 2015
Italy / Rome
Contact: Rita De Martini, Organising Secretariat, European School of Oncology
Phone: 011-39-2-8546-4527
Email: rdemartini@eso.net

Preceptorship Course in **Metastatic Colorectal Cancer Management**
Nov 2 - 5, 2015
France / Paris
Contact: Denise Rizzitelli, Congress Coordinator, Meridiano Congress International
Phone: 011-39-6-8859-5210; Fax: 011-39-6-8859-5234
Email: denise.rizzitelli@meridiano.it

10th International Congress of **Laparoscopic Colorectal Surgery:** Navigating New Advances
Nov 5 - 7, 2015
Singapore / Singapore
Contact: Conference Secretariat, Globewerks International
Email: anna@globewerks.com

12th Congress of Arab Association of **Urology**
Nov 5 - 7, 2015
United Arab Emirates / Dubai
Contact: Neha Choudhary, Marketing Executive, MCI Middle East
Phone: 011-971-4-311-6300
Email: neha.choudhary@mci-group.com

2nd Congress on Controversies in **Thrombosis & Hemostasis**
Nov 5 - 7, 2015
Spain / Barcelona
Contact: Ilana Rabinoff-Sofer, CongressMed Ltd
Phone: 011-972-73-706-6954
Email: cith@congressmed.com

3rd Advanced **Breast Cancer** International Consensus Conference
Nov 5 - 7, 2015
Portugal / Lisbon
Contact: European School of Oncology
Phone: 011-39-2-854-6451; Fax: 011-39-2-8546-4545
Email: eso@eso.net

Surgical Complications of the **Foot & Ankle** Course
Nov 5 - 7, 2015
United States / Florida / Tampa
Contact: American Orthopaedic Foot & Ankle Society
Phone: 800-235-4855 or 847-698-4654 (outside US)

14th International **Kidney Cancer** Symposium
Nov 6 - 7, 2015
United States / Florida / Miami
Contact: Kidney Cancer Association
Email: outreachregistration@niu.edu

2nd **Breast Cancer** Update Course Part I
Nov 7 - 8, 2015
Portugal / Lisbon
Contact: Francesca Marangoni, Organising Secretariat, European School of Oncology
Phone: 011-39-2-8546-4525; Fax: 011-39-2-8546-4545
Email: fmarangoni@eso.net

Introduction to **Abdominal & Primary Care** Ultrasound
Nov 9 - 11, 2015
United States / Florida / St. Pete Beach
Contact: Gulfcoast Ultrasound Institute, Inc.
Phone: 727-363-4500
Fax: 727-363-0811

Joint Injections
Nov 12, 2015
United Kingdom / London
Contact: Beds and Herts Faculty, Royal College of General Practitioners Conferences
Phone: 011-44-15-8240-4085 / 8
Email: bedsandherts@rcgp.org.uk

Laparoscopic Gynae-Oncology Course
Nov 12 - 13, 2015
United Kingdom / Newcastle Upon Tyne
Contact: Professional Education Department, Ethicon
Email: profed@its.jnj.com

7th Annual Royal Marsden **Head & Neck** Conference
Nov 13, 2015
United Kingdom / London
Contact: Education and Conference Centre, The Royal Marsden NHS Foundation Trust
Phone: 011-44-20-7808-2921; Fax: 011-44-20-7808-2334
Email: conferencecentre@rmh.nhs.uk

Falk Workshop on **Gastrointestinal GVHD**
Nov 13 - 14, 2015
Germany / Regensburg
Contact: Berit Wolff, Congress Division, Falk Foundation e.V.
Phone: 011-49-761-151-4125; Fax: 011-49-761-151-4359
Email: symposia@falkfoundation.de

10th World Congress of the International Academy of **Cosmetic Dermatology**
Nov 14 - 16, 2015
Brazil / Rio de Janeiro
Contact: Executive Secretariat, MCI Group
Phone: 011-55-21-2286-2846
Email: contato@iacdRio2015.com.br

Ophthalmic Regional Block Hands-on Workshop
Nov 14 - 15, 2015
United States / Florida / Orlando
Contact: Coleen Hilliard, Meeting Coordinator, Northwest Anesthesia Seminars
Phone: 509-547-7065; Fax: 509-547-1265
Email: coleen@nwas.com

Breast Aesthetics & Reconstruction
Nov 16 - 17, 2015
United Kingdom / NEWCASTLE UPON TYNE
Contact: James Greene, Mentor
Email: jgreene4@its.jnj.com

Hands-On **Carotid & Peripheral Vascular Imaging**, Including Vascular Access
Nov 16 - 19, 2015
United States / Texas / Dallas
Contact: Amy Donaldson, Registrar, Keith Mauney & Associates Ultrasound Training Institutes
Phone: 800-845-3484 or 972-353-3200; Fax: 817-577-4250
Email: info@kmaultrasound.com

2015 Faculty of **Perinatal Psychiatry** Annual Conference
Nov 17, 2015
United Kingdom / London
Contact: Royal College of Psychiatrists
Phone: 011-44-20-3701-2618; Fax: 011-44-20-3701-2761
Email: calc@rcpsych.ac.uk

8th BIT World Congress of **Regenerative Medicine & Stem Cell**-China
Nov 18 - 20, 2015
China / Shanghai
Contact: Ms. Laura, Staff, BIT Congress Inc.
Phone: 011-86-411-8479-9609 ext. 801; Fax: 011-86-411-8479-5469
Email: laura@bitconferences.com

9th World Congress of the World Society for **Pediatric Infectious Diseases**
Nov 18 - 21, 2015
Brazil / Rio de Janeiro
Contact: Dina Davis, APM, Kenes International
Phone: 011-41-22-908-0488; Fax: 011-41-22-906-9140
Email: calendar@kenes.com

Preceptorship Course in **Head & Neck Cancer** Management
Nov 18 - 20, 2015
Japan / Kashiwa
Contact: EXCEMED
Email: info@excemed.org

2015 **Dilemmas & Debates** in Colorectal Surgery
Nov 19 - 21, 2015
United Kingdom / London
Contact: Mr Charles Everard, Conference Administrator, ISUCRS & KVL
Phone: 011-44-20-3299-5159; Fax: 011-44-20-3299-5158
Email: charles.everard@kcl.ac.uk

36th International Society of **Dermatopathology** (ISDP) Symposium
Nov 19 - 21, 2015
India / New Delhi
Contact: Dr. M Ramam, Professor, ISDP
Phone: 011-91-2-659-3217
Email: mramam@hotmail.com

3rd **ASEAN Sleep** Congress: Challenges in Sleep Medicine
Nov 20 - 22, 2015
Singapore / Singapore
Contact: Secretariat, SGH Postgraduate Medical Institute
Phone: 011-65-6321-4071; Fax: 011-65-6223-9789
Email: asc2015@sgh.com.sg

5th World Congress on Controversies to Consensus in **Diabetes, Obesity & Hypertension**
Nov 20 - 22, 2015
Turkey / Istanbul
Contact: Natalie Ross, Congress Secretariat, Comtecmed
Email: codhy@codhy.com

Dimensions in **Heart & Vascular Care**
Nov 20, 2015
United States / Pennsylvania / Philadelphia
Contact: Continuing Education Office, Penn State Hershey
Phone: 800-243-1455
Email: ContinuingEd@hmc.psu.edu

Microbiology for Diagnosis of **Infectious Diseases:** ABC & XYZ
Nov 20 – 22, 2015
China / Beijing
Contact: European Society of Clinical Microbiology & Infectious Diseases
Phone: 011-41-61-508-0153; Fax: 011-41-61-508-0151
Email: info@escmid.org

16th New Frontiers in **Interventional Cardiology** (NFIC)
Nov 25 - 28, 2015
Poland / Krakow
Contact: NFIC
Phone: 011-48-88-208-5575
Email: registration@nfic.pl

Medical Record Keeping for **Physicians**
Nov 25, 2015
Canada / British Columbia / Vancouver
Contact: College of Physicians & Surgeons of British Columbia
Phone: 604-733-7758 extension 2629

5th Annual BIT World Congress of **Endobolism**
Nov 26 - 28, 2015
Taiwan / Kaohsiung
Contact: Ms. Berry Han, BIT Congress Inc.
Phone: 011-86-411-8479-9609 ext. 829; Fax: 011-86-411-8479-9629
Email: berry@bitlifesciences.com

Head & Neck Preceptorship: Focus on Comprehensive Management
Nov 26 - 27, 2015
France / Nice
Contact: Titty Alvino, Congress Coordinator, Meridiano Congress International
Phone: 011-39-6-8859-5310; Fax: 011-39-6-8859-5234
Email: titty.alvino@meridiano.it

Neuromuscular Disorders & Long-Term Respiratory Support
Nov 30, 2015
United Kingdom / London
Contact: Conferences Team, Royal College of Physicians of London
Phone: 011-44-20-3075-2389; Fax: 011-44-20-7487-5218
Email: conferences@rcplondon.ac.uk

2015 International **Dementia with Lewy Bodies** Conference
Dec 1 - 5, 2015
United States / Florida / Fort Lauderdale
Contact: Mayo School of Continuous Professional Development
Phone: 800-323-2688
Email: cme@mayo.edu

Diagnostic & Operative Hysteroscopy
Dec 1 - 3, 2015
United Kingdom / London
Contact: Royal College of Obstetricians & Gynaecologists
Phone: 011-44-20-7772-6200; Fax: 011-44-20-7723-0575

Chest Wall Diseases
Dec 2 - 4, 2015
United Kingdom / Windsor (UK)
Contact: European Association for Cardio-Thoracic Surgery
Phone: 011-44-17-5383-2166; Fax: 011-44-17-5362-0407

Recent Advances in **Anaesthesia, Critical Care & Pain Management**
Dec 2 - 4, 2015
United Kingdom / Birmingham, UK
Contact: Meetings and Events, Royal College of Anaesthetists
Phone: 011-44-20-7092-1670; Fax: 011-44-20-7092-1730
Email: events@rcoa.ac.uk

2015 New England College of **Occupational & Environmental Medicine** (NECOEM) Conference
Dec 3 - 4, 2015
United States /Massachusetts / Boston
Contact: Dianne Plantamura, Executive Director, NECOEM
Phone: 978-373-5597; Fax: 978-373-5597
Email: necoem@comcast.net

20th Congress of the **Asian Pacific Society of Respirology**
Dec 3 - 6, 2015
Malaysia / Kuala Lumpur
Contact: Reliance Conventions & Events, Conference Secretariat
Phone: 011-60-1-2302-9898
Fax: 011-60-3-2730-9972 / 73
Email: apsr2015@relianceconventions.com

Laser **Prostate Cadaveric** Course
Dec 3 - 4, 2015
United Kingdom / Newcastle Upon Tyne
Contact: Lorraine Waugh, Newcastle Upon Tyne Surg. Training Centre
Phone: 011-44-19-1223-1264; Fax: 011-44-19-1223-7248
Email: lorraine.waugh@nuth.nhs.uk

Medical Management of **HIV/AIDS & Hepatitis**
Dec 3 - 5, 2015
United States / California / San Francisco
Contact: Office of Continuing Medical Education, UCSF
Phone: 415-476-4251; Fax: 415-476-0318
Email: info@ocme.ucsf.edu

2015 International Research Conference on **Health & Medical Sciences**
Dec 4 - 5, 2015
Albania / Tirana
Contact: Silvia Rossi, MCMScience
Email: conference@mcmscience.org

2015 **Heart and Stroke** Clinical Update
Dec 4 - 5, 2015
Ontario / Toronto
Contact: Heart and Stroke Foundation
Phone: 613-569-4361; Fax: 613-569-3278

International Conference on **Ovarian Cancer**
Dec 4 - 5, 2015
United States / New York / New York
Contact: CME, Memorial Sloan Kettering Cancer Center
Phone: 646-227-2025; Fax: 212-557-0773
Email: brodheap@mskcc.org

3rd International **Osteoporosis** Foundation Middle East & Africa Osteoporosis Meeting
Dec 5 - 7, 2015
United Arab Emirates / Abu Dhabi
Contact: Majd Zeitoun, IOF Regional Coordinator, Prime- Inspiring Meetings
Phone: 011-971-55-780-1010
Email: iofhousing@primemena.com

Introduction to **Adult Echocardiography**
Dec 7 - 11, 2015
United States / Florida / St. Pete Beach
Contact: Gulfcoast Ultrasound Institute, Inc.
Phone: 727-363-4500; Fax: 727-363-0811

Thoracic Surgery: Part II
Dec 7 - 11, 2015
Canada / Nova Scotia / Windsor Other Specialties
Contact: European Association for Cardio-Thoracic Surgery
Phone: 011-44-17-5383-2166; Fax: 011-44-17-5362-0407

2015 Middle East-Asia **Allergy Asthma Immunology** Congress
Dec 10 - 12, 2015
United Arab Emirates / Dubai
Contact: Neha Choudhary, Marketing Executive, MCI Middle East
Phone: 011-971-4-311-6300
Email: neha.choudhary@mci-group.com

2015 **Pelvic Anatomy & Gynecologic Surgery** Symposium (PAGS)
Dec 10 - 12, 2015
United States / Nevada / Las Vegas
Contact: Kim Kirchner, Registration Coordinator, Global Academy for Medical Education
Phone: 502-574-9023; Fax: 502-589-3602
Email: kkirchner@hqtrs.com

Musculoskeletal Ultrasound
Dec 11 - 13, 2015
Belgium / Brussels
Contact: Medipoint
Phone: 011-32-1520-2255; Fax: 011-32-1520-0192
Email: courseregistration@hitachi-medical-systems.com

Internal Derangements of Joints: Advanced & Intensive MR Imaging Course
Dec 11 - 14, 2015
China / Hong Kong
Contact: International Institute for Continuing Medical Education
Phone: 205-467-0290
Email: Iicmemail@Gmail.Com

Preceptorship Course on **Head & Neck Cancer** Management
Dec 14 - 16, 2015
Italy / Milan
Contact: Debora Urbinelli, Meridiano Congress International
Email: Debora.Urbinelli@Meridiano.It

2015 Hands-On **Carotid & Peripheral Vascular Imaging**, Including Vascular Access
Dec 14 - 17, 2015
United States / Texas / Dallas
Contact: Amy Donaldson, Registrar, Keith Mauney & Associates Ultrasound Training Institutes
Phone: 800-845-3484 or 972-353-3200; Fax: 817-577-4250
Email: Info@Kmaultrasound.Com

10th International Conference on **Healthcare & Biological** Research
Dec 17 - 18, 2015
Thailand / Bangkok
Contact: Prof. Davis Lazarus, Prof., Global R & D Services
Phone: 011-91-94-6283-2013
Email: Info@Ichbrthailand.Com

64th **Neurological Society** of India (NSI) Annual Conference
Dec 17 - 20, 2015
India / Hyderabad
Contact: Conference Secretariat, Cim Global
Phone: 011-91-80-2608-0700
Fax: 011-91-80-2608-0702
Email: Info@Nsicon2015.Com

1st Annual Bit World Congress of **Digestive Diseases**
Dec 18 - 20, 2015
China / Nanjing
Contact: Mandy Han, Program Coordinator, Bit Congress, Inc.
Phone: 011-86-411-8479-9609 Ext. 804
Fax: 011-86-411-8479-9609
Email: Mandy@Bitcongress.Com

9th International Conference on **Healthcare & Life** Science Research
Dec 27 - 28, 2015
Malaysia / Kuala Lumpur
Contact: Prof. Davis Lazarus, Prof., Global Research & Development Services
Phone: 011-91-94-6283-2013
Email: Info@Malaysiaichlsr.Com

49th Annual Conference of **Urological Society** of India
Jan 7 - 10, 2016
India / Hyderabad
Contact: Conference Manager, Kuoni Destination Management
Phone: 011-91-98-4844-0272
Email: Thirupathi.Atkapuram@In.Kuoni.Com

7th International Course on **Ophthalmic & Oculoplastic Reconstruction & Trauma** Surgery
Jan 13 - 15, 2016
Austria / Vienna
Contact: Helmut Weissmann, Advanced Ophthalmic Trainings
Phone: 011-43-2243-20898
Fax: 011-43-2243-20898 ext. 15
Email: office@ophthalmictrainings.com

6th Emirates **Otorhinolaryngology, Audiology** & Communication Disorders Congress
Jan 13 - 15, 2016
United Arab Emirates / Dubai
Contact: Nadia Ansari, Marketing Executive, Mci Middle East
Phone: 011-971-4-311-6300
Fax: 011-971-4-311-6301
Email: Nadia.Ansari@Mci-Group.Com

7th International Course On **Ophthalmic & Oculoplastic Reconstruction & Trauma Surgery**
Jan 13 - 15, 2016
Austria / Vienna
Contact: Helmut Weissmann, Advanced Ophthalmic Trainings
Phone: 011-43-2243-20898; Fax: 011-43-2243-20898 Ext. 15
Email: Office@Ophthalmictrainings.Com

2016 World Congress on **Recurrent Pregnancy Loss**
Jan 14 - 17, 2016
France / Cannes
Contact: Secretariat, Paragon Group
Phone: 011-41-22-533-0948; Fax: 011-41-22-580-2953
Email: Secretariat@Wcrpl.Com

1st Middle Eastern Conference for **Stereotactic & Functional Neurosurgery**
Jan 16 - 18, 2016
United Arab Emirates / Dubai
Contact:
Phone: 011-971-4-457-7966
Email: Info@mfsns.Org

11th International Conference on **Healthcare & Biological** Research
Jan 17 - 18, 2016
United Arab Emirates / Dubai
Contact: Prof. Davis Lazarus, Prof., Global Research & Development Services
Phone: 011-91-94-6283-2013
Email: Info@Ichbrdubai.Com

2016 **Tutorials in Diagnostic Radiology** Course
Jan 17 - 21, 2016
United States / Hawaii / Maui
Contact: Mayo School of Continuous Professional Development
Phone: 800-323-2688
Email: cme@mayo.edu

18th International Conference on **Dialysis:** Advances in Kidney Disease
Jan 20 - 22, 2016
United States / Florida / Miami
Contact: Ingrid Adelsberger, Renal Research Institute
Phone: 212-331-1700; Fax: 212-331-1774
Email: iadelsberger@rriny.com

2016 Progress & Controversies on **Gynecologic Oncology** Conference
Jan 22 - 23, 2016
Spain / Barcelona
Contact: Prime Oncology, Prime Oncology
Phone: 011-31-70-306-7190; Fax: 011-31-70-331-8335
Email: Gyncongress2016@Primeoncology.Org

2016 **Traumatic Brain Injury** Conference
Jan 29, 2016
Canada / Ontario / Toronto
Contact: Conference Services, University Health Network
Phone: 416-597-3422 Ext. 3448
Email: Conferences@Uhn.Ca

6th Advanced Course In **Knee Surgery**
Jan 31 - Feb 5, 2016
France / Val D'isère
Contact: Congress Centre Henri Oreiller
Phone: 011-33-4-7906-2123
Fax: 011-33-4-7906-1904
Email: Kneecourse@Valdisere-Congres.Com

Malignant Melanoma & Beyond: An introduction to Targeted Treatments & Cancer Immunotherapy
Feb 2, 2016
United Kingdom / London
Contact: Education and Conference Centre, The Royal Marsden NHS Foundation Trust
Phone: 011-44-20-7808-2334; Fax: 011-44-20-7808-2334
Email: conferencecentre@rmh.nhs.uk

2016 Advanced Technologies & Treatments for **Diabetes**
Feb 3 - 6, 2016
Italy / Milan e
Contact: Miron Abramson, Kenes International
Phone: 011-41-22-906-9178

3rd International 4 Corners of **Cardiology** Meeting
Feb 5 - 6, 2016
Australia / Melbourne
Contact: Meeting Manager, Arinex
Phone: 011-61-3-9417-0888; Fax: 011-61-3-9417-0899
Email: 4ccardiology@Arinex.Com.Au

1st Biennial Congress of The World Association for **Infect. Dis. & Immunological Disorders**
Feb 18 - 20, 2016
Italy / Milan
Contact: Organizing Secretariat, Aim Group International
Phone: 011-39-2-566-011; Fax: 011-39-2-7004-8578
Email: Waidid2016@Aimgroup.Eu
Email: eberkovitz@kenes.com

Recent Advances in **Anaesthesia**, Critical Care & Pain Management
Feb 3 - 5, 2016
United Kingdom / London
Contact: Meetings and Events, Royal College of Anaesthetists
Phone: 011-44-20-7092-1670; Fax: 011-44-20-7092-1730
Email: events@rcoa.ac.uk

4th **Systemic Sclerosis** World Congress
Feb 18 - 20, 2016
Portugal / Lisbon
Contact: Organizing Secretariat, Aim Group International
Phone: 011-39-55-233881; Fax: 011-39-55-248-0246
Email: Ssc2016@Aimgroup.Eu

2016 Multidisciplinary **Head & Neck Cancer** Symposium
Feb 18 - 20, 2016
United States / Arizona / Scottsdale
Contact: Christina Cleveland, Meetings Manager, American Society for Radiation Oncology
Phone: 703-839-7388

6th International Workshop on **HIV & Women**
Feb 20 - 21, 2016
United States / Massachusetts / Boston
Contact: Virology Education B.V.
Phone: 011-31-30-230-7140; Fax: 011-31-30-230-7148
Email: Info@Virology-Education.Com

Ultrasound Workshop
Feb 23, 2016
United Kingdom / London
Contact: Meetings and Events, Royal College of Anaesthetists
Phone: 011-44-20-7092-1670; Fax: 011-44-20-7092-1730
Email: events@rcoa.ac.uk

74th All India **Ophthalmological Society** Annual Conference
Feb 25 - 28, 2016
India / Kolkata
Contact: Ophthalmological Society Of West Bengal
Phone: 011-91-33-2237-1679
Email: Aioc2016kolkata@Gmail.Com

Airway Workshop
Feb 25, 2016
United Kingdom / London
Contact: Meetings and Events, Royal College of Anaesthetists
Phone: 011-44-20-7092-1670; Fax: 011-44-20-7092-1730
Email: Events@Rcoa.Ac.Uk

4th International Congress on **Cardiac Problems in Pregnancy**
Feb 27 - Mar 1, 2016
United States / Nevada / Las Vegas
Contact: Congress Secretariat, Paragon
Phone: 412-253-3094
Email: secretariat@cppcongress.com

32nd International **Seating Symposium**
Mar 1 - 4, 2016
Canada / British Columbia / Vancouver
Contact: Stephanie Lai, UBC Interprofessional Continuing Education
Phone: 604-822-2801
Email: marketing.ipce@ubc.ca

11th World Congress on **Brain Injury**
Mar 2 - 5, 2016
Netherlands / Den Hague
Contact: Secretariat, MCC Association Mgt.
Phone: 703-960-6500; Fax: 703-960-6603
Email: congress@internationalbrain.org

17th International Congress on **Infectious Diseases**
Mar 2 - 5, 2016
India / Hyderabad
Contact: International Society for Infectious Diseases
Phone: 617-277-0551; Fax: 617-278-9113
Email: info@isid.org

4th International Conference on **Prehypertension, Hypertension & Cardio Metabolic Syndrome**
Mar 3 - 6, 2016
Italy / Venice
Contact: Gail Tito, Conference Secretariat, Paragon Group
Phone: 011-41-22-533-0948
Email: secretariat@prehypertension.org

WHO-Facts Sheet

1. HIV/AIDS
2. Food Safety
3. Tuberculosis
4. Ebola Virus Disease
5. Disability and Health

Compiled and edited by
Babichan K Chandy

Kuwait Medical Journal 2015, 47 (3): 277 - 288

1. HIV/AIDS

Overview

The human immunodeficiency virus (HIV) is a retrovirus that infects cells of the immune system, destroying or impairing their function. As the infection progresses, the immune system becomes weaker, and the person becomes more susceptible to infections. The most advanced stage of HIV infection is acquired immunodeficiency syndrome (AIDS). It can take 10-15 years for an HIV-infected person to develop AIDS; antiretroviral drugs can slow down the process even further.

HIV is transmitted through unprotected sexual intercourse (anal or vaginal), transfusion of contaminated blood, sharing of contaminated needles, and between a mother and her infant during pregnancy, childbirth and breastfeeding.

KEY FACTS

- HIV continues to be a major global public health issue, having claimed more than 34 million lives so far. In 2014, 1.2 [1.0 – 1.5] million people died from HIV-related causes globally.
- There were approximately 36.9 [34.3 – 41.4] million people living with HIV at the end of 2014 with 2.0 [1.9 – 2.2] million people becoming newly infected with HIV in 2014 globally.
- Sub-Saharan Africa is the most affected region, with 25.8 [24.0 – 28.7] million people living with HIV in 2014. Also sub-Saharan Africa accounts for almost 70% of the global total of new HIV infections.
- HIV infection is often diagnosed through rapid diagnostic tests (RDTs), which detect the presence or absence of HIV antibodies. Most often these tests provide same day test results; essential for same day diagnosis and early treatment and care.
- There is no cure for HIV infection. However, effective treatment with antiretroviral (ARV) drugs can control the virus so that people with HIV can enjoy healthy and productive lives.
- It is estimated that currently, only 51% of people with HIV know their status. In 2014, approximately 150 million children and adults in 129 low- and middle-income countries received HIV testing services.
- In 2014, 14.9 million people living with HIV were receiving antiretroviral therapy (ART) globally, of which 13.5 million were receiving ART in low- and middle-income countries. The 14.9 million people on ART represent 40% [37 – 45%] of people living with HIV globally

HIV targets the immune system and weakens people's defence systems against infections and some types of cancer. As the virus destroys and impairs the function of immune cells, infected individuals gradually become immunodeficient. Immune function is typically measured by CD4 cell count. Immunodeficiency results in increased susceptibility to a wide range of infections and diseases that people with healthy immune systems can fight off.

The most advanced stage of HIV infection is Acquired Immunodeficiency Syndrome (AIDS), which can take from two to 15 years to develop depending on the individual. AIDS is defined by the development of certain cancers, infections, or other severe clinical manifestations.

Address correspondence to:
Office of the Spokesperson, WHO, Geneva. Tel.: (+41 22) 791 2599; Fax (+41 22) 791 4858; Email: inf@who.int; Web site: http://www.who.int/

Signs and symptoms

The symptoms of HIV vary depending on the stage of infection. Though people living with HIV tend to be most infectious in the first few months, many are unaware of their status until later stages. The first few weeks after initial infection, individuals may experience no symptoms or an influenza-like illness including fever, headache, rash or sore throat.

As the infection progressively weakens the immune system, an individual can develop other signs and symptoms, such as swollen lymph nodes, weight loss, fever, diarrhoea and cough. Without treatment, they could also develop severe illnesses such as tuberculosis, cryptococcal meningitis, and cancers such as lymphomas and Kaposi's sarcoma, among others.

Transmission

HIV can be transmitted *via* the exchange of a variety of body fluids from infected individuals, such as blood, breast milk, semen and vaginal secretions. Individuals cannot become infected through ordinary day-to-day contact such as kissing, hugging, shaking hands, or sharing personal objects, food or water.

Risk factors

Behaviours and conditions that put individuals at greater risk of contracting HIV include:

- having unprotected anal or vaginal sex;
- having another sexually transmitted infection such as syphilis, herpes, chlamydia, gonorrhoea, and bacterial vaginosis;
- sharing contaminated needles, syringes and other injecting equipment and drug solutions when injecting drugs;
- receiving unsafe injections, blood transfusions, medical procedures that involve unsterile cutting or piercing; and
- experiencing accidental needle stick injuries, including among health workers.

Diagnosis

Serological tests, such as RDTs or enzyme immunoassays (EIAs), detect the presence or absence of antibodies to HIV-1/2 and/or HIV p24 antigen. When such tests are used within a testing strategy according to a validated testing algorithm, HIV infection can be detected with great accuracy. It is important to note that serological tests detect antibodies produced by an individual as part of their immune system to fight off foreign pathogens, rather than direct detection of HIV itself.

Most individuals develop antibodies to HIV-1/2 within 28 days and therefore antibodies may not be detectable early after infection, the so-called window period. This early period of infection represents the time of greatest infectivity; however HIV transmission can occur during all stages of the infection.

It is best practice to also retest all people initially diagnosed as HIV-positive before they enrol in care and/or treatment to rule out any potential testing or reporting error.

HIV testing services

HIV testing should be voluntary and the right to decline testing should be recognized. Mandatory or coerced testing by a health-care provider, authority or by a partner or family member is not acceptable as it undermines good public health practice and infringes on human rights.

Some countries have introduced, or are considering, self-testing as an additional option. HIV self-testing is a process whereby a person who wants to know his or her HIV status collects a specimen, performs a test and interprets the test results in private. HIV self-testing does not provide a definitive diagnosis; instead, it is an initial test which requires further testing by a health worker using a national validated testing algorithm.

All HIV testing services must include the 5 C's recommended by WHO: informed Consent, Confidentiality, Counselling, Correct test results and Connection (linkage to care, treatment and other services).

Prevention

Individuals can reduce the risk of HIV infection by limiting exposure to risk factors. Key approaches for HIV prevention, which are often used in combination, include:

1. **Male and female condom use:** Correct and consistent use of male and female condoms during vaginal or anal penetration can protect against the spread of sexually transmitted infections, including HIV. Evidence shows that male latex condoms have an 85% or greater protective effect against HIV and other sexually transmitted infections (STIs).

2. **Testing and counselling for HIV and STIs:** Testing for HIV and other STIs is strongly advised for all people exposed to any of the risk factors. This way people learn of their own infection status and access necessary prevention and treatment services without delay. WHO also recommends offering testing for partners or couples.
   Tuberculosis (TB) is the most common presenting illness among people with HIV. It is fatal, if undetected or untreated, and is the leading cause of death among people with HIV- responsible for roughly one out of every 4 HIV-associated deaths.

Early detection of TB and prompt linkage to TB treatment and ART can prevent these deaths. It is strongly advised that HIV testing services integrate screening for TB and that all individuals diagnosed with HIV and active TB urgently use ART.

3. **Voluntary medical male circumcision**: Medical male circumcision, when safely provided by well-trained health professionals, reduces the risk of heterosexually acquired HIV infection in men by approximately 60%. This is a key intervention in generalized epidemic settings with high HIV prevalence and low male circumcision rates.

4. Antiretroviral (ART) use for prevention

4.1 ART as prevention

A 2011 trial has confirmed if an HIV-positive person adheres to an effective ART regimen, the risk of transmitting the virus to their uninfected sexual partner can be reduced by 96%. For couples in which one partner is HIV-positive and the other HIV-negative, WHO recommend offering ART for the HIV-positive partner regardless of her/his CD4 count.

4.2 Pre-exposure prophylaxis (PrEP) for HIV-negative partner

Oral PrEP of HIV is the daily use of ARV drugs by HIV-uninfected people to block the acquisition of HIV. More than 10 randomized controlled studies have demonstrated the effectiveness of PrEP in reducing HIV transmission among a range of populations including serodiscordant heterosexual couples (where one partner is infected and the other is not), men who have sex with men, transgender women, high-risk heterosexual couples, and people who inject drugs.

In July 2014, WHO released "Consolidated guidelines on HIV prevention, diagnosis, treatment and care for key populations" which recommended PrEP as an additional HIV prevention choice within a comprehensive HIV prevention package for men who have sex with men.

4.3 Post-exposure prophylaxis for HIV (PEP)

Post-exposure prophylaxis (PEP) is the use of ARV drugs within 72 hours of exposure to HIV in order to prevent infection. PEP includes counselling, first aid care, HIV testing, and administering of a 28-day course of ARV drugs with follow-up care.

Updated WHO guidelines issued in December 2014 recommend PEP use for both occupational and non-occupational exposures and for adults and children. The new recommendations provide simpler regimens using ARVs already being used in treatment. The implementation of the new guidelines will enable easier prescribing, better adherence and increased completion rates of PEP to prevent HIV in people who have been accidentally exposed to HIV such as health workers or through unprotected sexual exposures or sexual assault.

5. Harm reduction for injecting drug users

People who inject drugs can take precautions against becoming infected with HIV by using sterile injecting equipment, including needles and syringes, for each injection. A comprehensive package of interventions for HIV prevention and treatment includes:

- needle and syringe programmes;
- opioid substitution therapy for people dependent on opioids and other evidence based drug dependence treatment;
- HIV testing and counselling;
- HIV treatment and care;
- access to condoms; and
- management of STIs, tuberculosis and viral hepatitis.

6. Elimination of mother-to-child transmission of HIV (eMTCT)

The transmission of HIV from an HIV-positive mother to her child during pregnancy, labour, delivery or breastfeeding is called vertical or mother-to-child transmission (MTCT). In the absence of any interventions during these stages, rates of HIV transmission from mother-to-child can be between 15 - 45%. MTCT can be nearly fully prevented, if both the mother and the child are provided with ARV drugs throughout the stages when infection could occur.

WHO recommends options for prevention of MTCT (PMTCT), which includes providing ARVs to mothers and infants during pregnancy, labour and the post-natal period, and offering life-long treatment to HIV-positive pregnant women regardless of their CD4 count.

In 2014, 73% [68 – 79%] of the estimated 1.5 [1.3 - 1.6] million pregnant women living with HIV globally received effective antiretroviral drugs to avoid transmission to their children.

Treatment

HIV can be suppressed by combination ART consisting of 3 or more ARV drugs. ART does not cure HIV infection but controls viral replication within a person's body and allows an individual's immune system to strengthen and regain the capacity to fight off infections.

Approximately 14.9 million people living with HIV were receiving ART at the end of 2014 globally. About 823,000 of those were children.

In 2014, there was a large increase in number of people on ART – 1.9 million-- in a single year.

WHO recommends initiating ART when their CD4 cell counts falls to 500 cells/mm^3 or less. ART regardless of CD4 count is recommended for all people living with HIV in serodiscordant couples, pregnant and breastfeeding women living with HIV, people with TB and HIV, and people co-infected with HIV and hepatitis B infection with severe chronic liver disease. Likewise, ART is recommended for all children living with HIV who are younger than 5 years-old.

2. FOOD SAFETY

Overview

Access to sufficient safe food is a basic requirement for human health. Ensuring food safety and security in a highly globalized world presents increasingly difficult, and often under-appreciated challenges, for governments, commercial organizations and individuals alike[1,2].

The risks of unsafe food are substantial, but can be difficult to quantify. Diarrhoeal diseases – both foodborne and waterborne – kill an estimated two million people annually, including many children in developing countries. Food contaminants, such as harmful parasites, bacteria, viruses, prions, chemical or radioactive substances, cause more than 200 diseases – ranging from infectious diseases to cancers.

KEY FACTS

- Access to sufficient amounts of safe and nutritious food is key to sustaining life and promoting good health.
- Unsafe food containing harmful bacteria, viruses, parasites or chemical substances, causes more than 200 diseases - ranging from diarrhoea to cancers.
- Foodborne and waterborne diarrhoeal diseases kill an estimated 2 million people annually, including many children.
- Food safety, nutrition and food security are inextricably linked. Unsafe food creates a vicious cycle of disease and malnutrition, particularly affecting infants, young children, elderly and the sick.
- Foodborne diseases impede socioeconomic development by straining health care systems, and harming national economies, tourism and trade.
- Food supply chains now cross multiple national borders. Good collaboration between governments, producers and consumers helps ensure food safety.

Major foodborne illnesses and causes

Foodborne illnesses are usually infectious or toxic in nature and caused by bacteria, viruses, parasites or chemical substances entering the body through contaminated food or water.

Foodborne pathogens can cause severe diarrhoea or debilitating infections including meningitis. Chemical contamination can lead to acute poisoning or long-term diseases, such as cancer. Foodborne diseases may lead to long-lasting disability and death. Examples of unsafe food include uncooked foods of animal origin, fruits and vegetables contaminated with faeces, and raw shellfish containing marine biotoxins.

Bacteria

- *Salmonella, Campylobacter, and Enterohaemorrhagic Escherichia coli* are among the most common foodborne pathogens that affect millions of people annually – sometimes with severe and fatal outcomes. Symptoms are fever, headache, nausea, vomiting, abdominal pain and diarrhoea. Examples of foods involved in outbreaks of salmonellosis are eggs, poultry and other products of animal origin. Foodborne cases with *Campylobacter* are mainly caused by raw milk, raw or undercooked poultry and drinking water. *Enterohaemorrhagic Escherichia coli* is associated with unpasteurized milk, undercooked meat and fresh fruits and vegetables.
- *Listeria* infection leads to unplanned abortions in pregnant women or death of newborn babies. Although disease occurrence is relatively low, listeria's severe and sometimes fatal health consequences, particularly among infants, children and the elderly, count them among the most serious foodborne infections. Listeria is found in unpasteurised dairy products and various ready-to-eat foods and can grow at refrigeration temperatures.
- *Vibrio cholerae* infects people through contaminated water or food. Symptoms include abdominal pain, vomiting and profuse watery diarrhoea, which may lead to severe dehydration and possibly death. Rice, vegetables, millet gruel and various types of seafood have been implicated in cholera outbreaks.

Antimicrobials, such as antibiotics, are essential to treat infections caused by bacteria. However, their overuse and misuse in veterinary and human medicine has been linked to the emergence and spread of resistant bacteria, rendering the treatment of infectious diseases ineffective in animals and humans. Resistant bacteria enter the food chain through the animals (*e.g. Salmonella* through chickens).

Antimicrobial resistance is one of the main threats to modern medicine.

Viruses

Norovirus infections are characterized by nausea, explosive vomiting, watery diarrhoea and abdominal pain. Hepatitis A virus can cause long-lasting liver disease and spreads typically through raw or undercooked seafood or contaminated raw produce. Infected food handlers are often the source of food contamination.

Parasites

Some parasites, such as fish-borne trematodes, are only transmitted through food. Others, for example *Echinococcus spp*, may infect people through food or direct contact with animals. Other parasites, such as *Ascaris, Cryptosporidium, Entamoeba histolytica* **or** *Giardia*, enter the food chain *via* water or soil and can contaminate fresh produce.

Prions

Prions, infectious agents composed of protein, are unique in that they are associated with specific forms of neurodegenerative disease. Bovine spongiform encephalopathy (BSE, or "mad cow disease") is a prion disease in cattle, associated with the variant Creutzfeldt-Jakob Disease (vCJD) in humans. Consuming bovine products containing specified risk material, *e.g.* brain tissue, is the most likely route of transmission of the prion agent to humans.

Chemicals

Of most concern for health are naturally occurring toxins and environmental pollutants.

- Naturally occurring toxins include mycotoxins, marine biotoxins, cyanogenic glycosides and toxins occurring in poisonous mushrooms. Staple foods like corn or cereals can contain high levels of mycotoxins, such as aflatoxin and ochratoxin. A long-term exposure can affect the immune system and normal development, or cause cancer.
- Persistent organic pollutants (POPs) are compounds that accumulate in the environment and human body. Known examples are dioxins and polychlorinated biphenyls (PCBs), which are unwanted byproducts of industrial processes and waste incineration. They are found worldwide in the environment and accumulate in animal food chains. Dioxins are highly toxic and can cause reproductive and developmental problems, damage the immune system, interfere with hormones and cause cancer.
- Heavy metals such as lead, cadmium and mercury cause neurological and kidney damage. Contamination by heavy metal in food occurs mainly through pollution of air, water and soil.

The evolving world and food safety

Safe food supplies support national economies, trade and tourism, contribute to food and nutrition security, and underpin sustainable development.

Urbanization and changes in consumer habits, including travel, have increased the number of people buying and eating food prepared in public places. Globalization has triggered growing consumer demand for a wider variety of foods, resulting in an increasingly complex and longer global food chain.

As the world's population grows, the intensification and industrialization of agriculture and animal production to meet increasing demand for food creates both opportunities and challenges for food safety. Climate change is also predicted to impact food safety, where temperature changes modify food safety risks associated with food production, storage and distribution.

These challenges put greater responsibility on food producers and handlers to ensure food safety. Local incidents can quickly evolve into international emergencies due to the speed and range of product distribution. Serious foodborne disease outbreaks have occurred on every continent in the past decade, often amplified by globalized trade.

Examples include the contamination of infant formula with melamine in 2008 (affecting 300,000 infants and young children, 6 of whom died, in China alone), and the 2011 Enterohaemorrhagic *Escherichia* ***coli*** outbreak in Germany linked to contaminated fenugreek sprouts, where cases were reported in 8 countries in Europe and North America, leading to 53 deaths. The 2011 *E.coli* outbreak in Germany caused US$ 1.3 billion in losses for farmers and industries and US$ 236 million in emergency aid payments to 22 European Union Member States.

Food safety: a public health priority

Unsafe food poses global health threats, endangering everyone. Infants, young children, pregnant women, the elderly and those with an underlying illness are particularly vulnerable.

Foodborne and waterborne diarrhoeal disease kill an estimated 2 million people annually, including many children and particularly in developing countries. Unsafe food creates a vicious cycle of diarrhoea and malnutrition, threatening the nutritional status of the most vulnerable. Where food supplies are insecure, people tend to shift to less healthy diets and consume more "unsafe foods" – in which chemical, microbiological and other hazards pose health risks.

Governments should make food safety a public health priority, as they play a pivotal role in developing policies and regulatory frameworks, establishing and implementing effective food safety systems that ensure that food producers and suppliers along the whole food chain operate responsibly and supply safe food to consumers.

Food can become contaminated at any point of production and distribution, and the primary responsibility lies with food producers. Yet a large proportion of foodborne disease incidents are caused by foods improperly prepared or mishandled at home, in food service establishments or markets. Not all food handlers and consumers understand the roles they must play, such as adopting basic hygienic practices when buying, selling and preparing food to protect their health and that of the wider community.

Everyone can contribute to making food safe. Here are some examples of effective actions:

Policy-makers can

- build and maintain adequate food systems and infrastructures (*e.g.* laboratories) to respond to and manage food safety risks along the entire food chain, including during emergencies;
- foster multi-sectoral collaboration among public health, animal health, agriculture and other sectors for better communication and joint action;
- integrate food safety into broader food policies and programmes (*e.g.* nutrition and food security);
- think globally and act locally to ensure the food produce domestically be safe internationally.

Food handlers and consumers can:

- know the food they use (read labels on food package, make an informed choice, become familiar with common food hazards);
- handle and prepare food safely, practicing the WHO Five Keys to Safer Food at home, or when selling at restaurants or at local markets;
- grow fruits and vegetables using the WHO Five Keys to Growing Safer Fruits and Vegetables to decrease microbial contamination.

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3. TUBERCULOSIS

Overview

Tuberculosis (TB) is caused by bacteria (*Mycobacterium tuberculosis*) that most often affect the lungs. Tuberculosis is curable and preventable. It is spread from person to person through the air. When people with lung TB cough, sneeze or spit, they propel the TB germs into the air. A person needs to inhale only a few of these germs to become infected.

About one-third of the world's population has latent TB, which means people have been infected by TB bacteria but are not (yet) ill with the disease and cannot transmit the disease. People infected with TB bacteria have a lifetime risk of falling ill with TB of 10%. However persons with compromised immune systems, such as people living with HIV, malnutrition or diabetes, or people who use tobacco have a much higher risk of falling ill.

When a person develops active TB (disease), the symptoms (cough, fever, night sweats, weight loss etc.) may be mild for many months. This can lead to delays in seeking care, and results in transmission of the bacteria to others. People ill with TB can infect up to 10 - 15 other people through close contact over the course of a year. Without proper treatment up to two thirds of people ill with TB will die.

KEY FACTS

- Tuberculosis (TB) is second only to HIV/AIDS as the greatest killer worldwide due to a single infectious agent.
- In 2013, 9 million people fell ill with TB and 1.5 million died from the disease.
- Over 95% of TB deaths occur in low- and middle-income countries, and it is among the top five causes of death for women aged 15 to 44.
- In 2013, an estimated 550,000 children became ill with TB and 80,000 HIV-negative children died of TB.
- TB is a leading killer of HIV-positive people causing one fourth of all HIV-related deaths.
- Globally in 2013, an estimated 480,000 people developed multidrug resistant TB (MDR-TB).
- The estimated number of people falling ill with TB each year is declining, although very slowly, which means that the world is on track to achieve the Millennium Development Goal to reverse the spread of TB by 2015.
- The TB death rate dropped 45% between 1990 and 2013.
- An estimated 37 million lives were saved through TB diagnosis and treatment between 2000 and 2013.

Who is most at risk?

Tuberculosis mostly affects young adults, in their most productive years. However, all age groups are at risk. Over 95% of cases and deaths are in developing countries.

People who are infected with HIV are 26 to 31 times more likely to become sick with TB (see TB and HIV section). Risk of active TB is also greater in persons suffering from other conditions that impair the immune system. Over half a million children (0-14 years) fell ill with TB, and 80,000 HIV-negative children died from the disease in 2013.

Tobacco use greatly increases the risk of TB disease and death. More than 20% of TB cases worldwide are attributable to smoking.

Global impact of TB

TB occurs in every part of the world. In 2013, the largest number of new TB cases occurred in the South-East Asia and Western Pacific Regions, accounting for 56% of new cases globally. However, Africa carried the greatest proportion of new cases per population with 280 cases per 100,000 population in 2013.

In 2013, about 80% of reported TB cases occurred in 22 countries. Some countries are experiencing a major decline in cases, while in others the numbers are dropping very slowly. Brazil and China for example, are among the 22 countries that showed a sustained decline in TB cases over the past 20 years. In the last decade, the TB prevalence in Cambodia fell by almost 50%.

Symptoms and diagnosis

Common symptoms of active lung TB are cough with sputum and blood at times, chest pains, weakness, weight loss, fever and night sweats.

Many countries still rely on a long-used method called sputum smear microscopy to diagnose TB. Trained laboratory technicians look at sputum samples under a microscope to see if TB bacteria are present. With three such tests, diagnosis can be made within a day, but this test does not detect numerous cases of less infectious forms of TB.

Diagnosing MDR-TB (see Multidrug-resistant TB section below) and HIV-associated TB can be more complex. A new two-hour test that has proven highly effective in diagnosing TB and the presence of drug resistance is now being rolled-out in many countries.

Tuberculosis is particularly difficult to diagnose in children.

Treatment

TB is a treatable and curable disease. Active, drug-sensitive TB disease is treated with a standard six-month course of four antimicrobial drugs that are provided with information, supervision and support to the patient by a health worker or trained volunteer. Without such supervision and support, treatment adherence can be difficult and the disease can spread. The vast majority of TB cases can be cured when medicines are provided and taken properly.

Between 2000 and 2013, an estimated 37 million lives were saved through TB diagnosis and treatment.

TB and HIV

At least one-third of people living with HIV worldwide in 2013 were infected with TB bacteria, although they did not become ill with active TB. People living with HIV are 26 to 31 times more likely to develop active TB disease than people without HIV.

HIV and TB form a lethal combination, each speeding the other's progress. In 2013 about 360,000 people died of HIV-associated TB. Approximately 25% of deaths among HIV-positive people are due to TB. In 2013, there were an estimated 1.1 million new cases of TB amongst people who were HIV-positive, 78% of whom were living in Africa.

WHO recommends a 12-component approach of collaborative TB-HIV activities, including actions for prevention and treatment of infection and disease, to reduce deaths.

Multidrug-resistant TB

Standard anti-TB drugs have been used for decades, and resistance to the medicines is widespread. Disease strains that are resistant to a single anti-TB drug have been documented in every country surveyed.

Multidrug-resistant tuberculosis (MDR-TB) is a form of TB caused by bacteria that do not respond to, at least, isoniazid and rifampicin, the two most powerful, first-line (or standard) anti-TB drugs.

The primary cause of MDR-TB is inappropriate treatment. Inappropriate or incorrect use of anti-TB drugs, or use of poor quality medicines, can all cause drug resistance.

Disease caused by resistant bacteria fails to respond to conventional, first-line treatment. MDR-TB is treatable and curable by using second-line drugs. However, second-line treatment options are limited and recommended medicines are not always available. The extensive chemotherapy required (up to two years of treatment) is more costly and can produce severe adverse drug reactions in patients.

In some cases, more severe drug resistance can develop. Extensively drug-resistant TB, XDR-TB, is a form of multi-drug resistant tuberculosis that responds to even fewer available medicines, including the most effective second-line anti-TB drugs.

About 480,000 people developed MDR-TB in the world in 2013. More than half of these cases were in India, China and the Russian Federation. It is estimated that about 9.0% of MDR-TB cases had XDR-TB.

WHO response

WHO pursues six core functions in addressing TB.

- Provide global leadership on matters critical to TB.
- Develop evidence-based policies, strategies and standards for TB prevention, care and control, and monitor their implementation.
- Provide technical support to Member States, catalyze change, and build sustainable capacity.
- Monitor the global TB situation, and measure progress in TB care, control, and financing.
- Shape the TB research agenda and stimulate the production, translation and dissemination of valuable knowledge.
- Facilitate and engage in partnerships for TB action.
- The WHO's Stop TB Strategy, which is recommended for implementation by all countries and partners, aims to dramatically reduce TB by public and private actions at national and local levels such as :
- pursue high-quality DOTS expansion and enhancement. DOTS is a five-point package to:
    - secure political commitment, with adequate and sustained financing
    - ensure early case detection, and diagnosis through quality-assured bacteriology
    - provide standardized treatment with supervision and patient support
    - ensure effective drug supply and management and
    - monitor and evaluate performance and impact;
- address TB-HIV, MDR-TB, and the needs of poor and vulnerable populations;
- contribute to health system strengthening based on primary health care;
- engage all care providers;
- empower people with TB, and communities through partnership;
- enable and promote research.

4. EBOLA VIRUS DISEASE

Overview

Ebola virus disease (EVD), formerly known as *Ebola* haemorrhagic fever, is a severe, often fatal illness in humans. The *virus* is transmitted to people from wild animals and spreads in the human population through human-to-human transmission. The average EVD case fatality rate is around 50%.

The Ebola virus causes an acute, serious illness which is often fatal, if untreated. EVD first appeared in 1976 in 2 simultaneous outbreaks, one in Nzara, Sudan, and the other in Yambuku, Democratic Republic of Congo. The latter occurred in a village near the Ebola River, from which the disease takes its name.

The current outbreak in West Africa, (first cases notified in March 2014), is the largest and most complex Ebola outbreak since the Ebola virus was first discovered in 1976. There have been more cases and deaths in this outbreak than all others combined. It has also spread between countries starting in Guinea then spreading across land borders to Sierra Leone and Liberia, by air (1 traveller) to Nigeria and USA (1 traveller), and by land to Senegal (1 traveller) and Mali (2 travellers).

KEY FACTS

- Ebola virus disease (EVD), formerly known as Ebola haemorrhagic fever, is a severe, often fatal illness in humans.
- The virus is transmitted to people from wild animals and spreads in the human population through human-to-human transmission.
- The average EVD case fatality rate is around 50%. Case fatality rates have varied from 25% to 90% in past outbreaks.
- The first EVD outbreaks occurred in remote villages in Central Africa, near tropical rainforests, but the most recent outbreak in West Africa has involved major urban as well as rural areas.
- Community engagement is key to successfully controlling outbreaks. Good outbreak control relies on applying a package of interventions, namely case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilisation.
- Early supportive care with rehydration, symptomatic treatment improves survival. There is as yet no licensed treatment proven to neutralise the virus but a range of blood, immunological and drug therapies are under development.
- There are currently no licensed Ebola vaccines but two potential candidates are undergoing evaluation.

The most severely affected countries, Guinea, Liberia and Sierra Leone, have very weak health systems, lack human and infrastructural resources, and have only recently emerged from long periods of conflict and instability. The virus family *Filoviridae* includes three genera: *Cuevavirus, Marburgvirus,* and *Ebolavirus.* There are five species that have been identified: Zaire, Bundibugyo, Sudan, Reston and

Taï Forest. The first three, Bundibugyo ebolavirus, Zaire ebolavirus, and Sudan ebolavirus have been associated with large outbreaks in Africa. The virus causing the 2014 West African outbreak belongs to the Zaire species.

Transmission

It is thought that fruit bats of the Pteropodidae family are natural *Ebola virus* hosts. *Ebola* is introduced into the human population through close contact with the blood, secretions, organs or other bodily fluids of infected animals such as chimpanzees, gorillas, fruit bats, monkeys, forest antelope and porcupines found ill or dead or in the rainforest.

Ebola then spreads through human-to-human transmission *via* direct contact (through broken skin or mucous membranes) with the blood, secretions, organs or other bodily fluids of infected people, and with surfaces and materials (*e.g.*, bedding, clothing) contaminated with these fluids.

Health-care workers have frequently been infected while treating patients with suspected or confirmed EVD. This has occurred through close contact with patients when infection control precautions are not strictly practiced.

Burial ceremonies in which mourners have direct contact with the body of the deceased person can also play a role in the transmission of *Ebola*.

People remain infectious as long as their blood contains the virus.

No formal evidence exists of sexual transmission, but sexual transmission from convalescent patients cannot be ruled out. There is evidence that live *Ebola virus* can be isolated in seminal fluids of convalescent men for 82 days after onset of symptoms. Evidence is not available yet beyond 82 days. There is no evidence of live *Ebola virus* in vaginal secretions.

Symptoms of Ebola virus disease

The incubation period, that is, the time interval from infection with the virus to onset of symptoms is 2 to 21 days. Humans are not infectious until they develop symptoms. First symptoms are the sudden onset of fever fatigue, muscle pain, headache and sore throat. This is followed by vomiting, diarrhoea, rash, symptoms of impaired kidney and liver function, and in some cases, both internal and external bleeding (*e.g.*, oozing from the gums, blood in the stools). Laboratory findings include low white blood cell and platelet counts and elevated liver enzymes.

Diagnosis

It can be difficult to distinguish EVD from other infectious diseases such as malaria, typhoid fever and meningitis. Confirmation that symptoms are caused by *Ebola virus* infection are made using the following investigations:

- antibody-capture enzyme-linked immunosorbent assay (ELISA)
- antigen-capture detection tests
- serum neutralization test
- reverse transcriptase polymerase chain reaction (RT-PCR) assay
- electron microscopy
- virus isolation by cell culture.

Samples from patients are an extreme biohazard risk; laboratory testing on non-inactivated samples should be conducted under maximum biological containment conditions.

Treatment and vaccines

Supportive care-rehydration with oral or intravenous fluids- and treatment of specific symptoms, improves survival. There is as yet no proven treatment available for EVD. However, a range of potential treatments including blood products, immune therapies and drug therapies are currently being evaluated. No licensed vaccines are available yet, but two potential vaccines are undergoing human safety testing.

Prevention and control

Good outbreak control relies on applying a package of interventions, namely case management, surveillance and contact tracing, a good laboratory service, safe burials and social mobilisation. Community engagement is key to successfully controlling outbreaks. Raising awareness of risk factors for Ebola infection and protective measures that individuals can take is an effective way to reduce human transmission. Risk reduction messaging should focus on several factors:

- Reducing the risk of wildlife-to-human transmission from contact with infected fruit bats or monkeys/apes and the consumption of their raw meat. Animals should be handled with gloves and other appropriate protective clothing. Animal products (blood and meat) should be thoroughly cooked before consumption.
- Reducing the risk of human-to-human transmission from direct or close contact with people with Ebola symptoms, particularly with their bodily fluids. Gloves and appropriate personal protective equipment should be worn when taking care of ill patients at home. Regular hand washing is required after visiting patients in hospital, as well as after taking care of patients at home.

- Reducing the risk of possible sexual transmission, because the risk of sexual transmission cannot be ruled out, men and women who have recovered from *Ebola* should abstain from all types of sex (including anal- and oral sex) for at least three months after onset of symptoms. If sexual abstinence is not possible, male or female condom use is recommended. Contact with body fluids should be avoided and washing with soap and water is recommended. WHO does not recommend isolation of male or female convalescent patients whose blood has been tested negative for Ebola virus.
- Outbreak containment measures, including prompt and safe burial of the dead, identifying people who may have been in contact with someone infected with *Ebola* and monitoring their health for 21 days, the importance of separating the healthy from the sick to prevent further spread, and the importance of good hygiene and maintaining a clean environment.

Controlling infection in health-care settings

Health-care workers should always take standard precautions when caring for patients, regardless of their presumed diagnosis. These include basic hand hygiene, respiratory hygiene, use of personal protective equipment (to block splashes or other contact with infected materials), safe injection practices and safe burial practices.

Health-care workers caring for patients with suspected or confirmed *Ebola virus* should apply extra infection control measures to prevent contact with the patient's blood and body fluids and contaminated surfaces or materials such as clothing and bedding. When in close contact (within 1 metre) of patients with EBV, health-care workers should wear face protection (a face shield or a medical mask and goggles), a clean, non-sterile long-sleeved gown, and gloves (sterile gloves for some procedures).

Laboratory workers are also at risk. Samples taken from humans and animals for investigation of Ebola infection should be handled by trained staff and processed in suitably equipped laboratories.

WHO response

WHO aims to prevent *Ebola* outbreaks by maintaining surveillance for *Ebola* virus disease and supporting at-risk countries to developed preparedness plans. The document provides overall guidance for control of *Ebola* and Marburg virus outbreaks:

- *Ebola* and Marburg virus disease epidemics: preparedness, alert, control, and evaluation
- When an outbreak is detected WHO responds by supporting surveillance, community engagement, case management, laboratory services, contact tracing, infection control, logistical support and training and assistance with safe burial practices.
- WHO has developed detailed advice on *Ebola* infection prevention and control:
- Infection prevention and control guidance for care of patients with suspected or confirmed Filovirus haemorrhagic fever in health-care settings, with focus on *Ebola*
- Table: Chronology of previous *Ebola virus* disease outbreaks xls, 34kb
- Sexual transmission of the *Ebola Virus* : evidence and knowledge gaps

5. DISABILITY AND HEALTH

Overview

The International Classification of Functioning, Disability and Health (ICF) defines disability as an umbrella term for impairments, activity limitations and participation restrictions. Disability is the interaction between individuals with a health condition (*e.g,* cerebral palsy, Down syndrome and depression) and personal and environmental factors (*e.g,* negative attitudes, inaccessible transportation and public buildings, and limited social supports).

KEY FACTS

- Over a billion people, about 15% of the world's population, have some form of disability.
- Between 110 million and 190 million adults have significant difficulties in functioning.
- Rates of disability are increasing due to population ageing and increases in chronic health conditions, among other causes.
- People with disabilities have less access to health care services and therefore, experience unmet health care needs.

Disability and health

Over a billion people are estimated to live with some form of disability. This corresponds to about 15% of the world's population. Between 110 million (2.2%) and 190 million (3.8%) people 15 years and older have significant difficulties in functioning. Furthermore, the rates of disability are increasing in part due to ageing populations and an increase in chronic health conditions.

Disability is extremely diverse. While some health conditions associated with disability result in poor health and extensive health care needs, others do not. However all people with disabilities have the same

general health care needs as everyone else, and therefore need access to mainstream health care services. Article 25 of the UN Convention on the Rights of Persons with Disabilities (CRPD) reinforces the right of persons with disabilities to attain the highest standard of health care, without discrimination.

Unmet needs for health care

People with disabilities report seeking more health care than people without disabilities and have greater unmet needs. For example, a recent survey of people with serious mental disorders, showed that between 35% and 50% of people in developed countries, and between 76% and 85% in developing countries, received no treatment in the year prior to the study.

Health promotion and prevention activities seldom target people with disabilities. For example women with disabilities receive less screening for breast and cervical cancer than women without disabilities. People with intellectual impairments and diabetes are less likely to have their weight checked. Adolescents and adults with disabilities are more likely to be excluded from sex education programmes.

How are the lives of people with disabilities affected?

People with disabilities are particularly vulnerable to deficiencies in health care services. Depending on the group and setting, persons with disabilities may experience greater vulnerability to secondary conditions, co-morbid conditions, age-related conditions, engaging in health risk behaviors and higher rates of premature death.

Secondary conditions

Secondary conditions occur in addition to (and are related to) a primary health condition, and are both predictable and therefore preventable. Examples include pressure ulcers, urinary tract infections, osteoporosis and pain.

Co-morbid conditions

Co-morbid conditions occur in addition to (and are unrelated to) a primary health condition associated with disability. For example the prevalence of diabetes in people with schizophrenia is around 15% compared to a rate of 2-3% for the general population.

Age-related conditions

The ageing process for some groups of people with disabilities begins earlier than usual. For example some people with developmental disabilities show signs of premature ageing in their 40s and 50s.

Engaging in health risk behaviours

Some studies have indicated that people with disabilities have higher rates of risky behaviours such as smoking, poor diet and physical inactivity.

Higher rates of premature death

Mortality rates for people with disabilities vary depending on the health condition. However an investigation in the United Kingdom found that people with mental health disorders and intellectual impairments had a lower life expectancy.

Barriers to health care

People with disabilities encounter a range of barriers when they attempt to access health care including the following:

Prohibitive costs: Affordability of health services and transportation are two main reasons why people with disabilities do not receive needed health care in low-income countries, 32 - 33% of non-disabled people are unable to afford health care compared to 51 - 53% of people with disabilities.

Limited availability of services: The lack of appropriate services for people with disabilities is a significant barrier to health care. For example, research in Uttar Pradesh and Tamil Nadu states of India found that after the cost, the lack of services in the area was the second most significant barrier to using health facilities.

Physical barriers: Uneven access to buildings (hospitals, health centres), inaccessible medical equipment, poor signage, narrow doorways, internal steps, inadequate bathroom facilities, and inaccessible parking areas create barriers to health care facilities. For example, women with mobility difficulties are often unable to access breast and cervical cancer screening because examination tables are not height-adjustable and mammography equipment only accommodates women who are able to stand.

Inadequate skills and knowledge of health workers: People with disabilities were more than twice as likely to report finding health care provider skills inadequate to meet their needs, four times more likely to report being treated badly and nearly three times more likely to report being denied care.

Addressing barriers to health care

Governments can improve health outcomes for people with disabilities by improving access to quality, affordable health care services, which make the best use of available resources. As several factors interact to inhibit access to health care, reforms in all the interacting components of the health care system are required.

Policy and legislation

Assess existing policies and services, identify priorities to reduce health inequalities and plan improvements for access and inclusion. Make changes to comply with the CRPD. Establish health care standards related to care of persons with disabilities with enforcement mechanisms.

Financing

Where private health insurance dominates health care financing, ensure that people with disabilities are covered and consider measures to make the premiums affordable. Ensure that people with disabilities benefit equally from public health care programmes. Use financial incentives to encourage health-care providers to make services accessible and provide comprehensive assessments, treatment, and follow-ups. Consider options for reducing or removing out-of-pocket payments for people with disabilities who do not have other means of financing health care services.

Service delivery

Provide a broad range of modifications and adjustments (reasonable accommodation) to facilitate access to health care services. For example changing the physical layout of clinics to provide access for people with mobility difficulties or communicating health information in accessible formats such as Braille. Empower people with disabilities to maximize their health by providing information, training, and peer support. Promote community-based rehabilitation (CBR) to facilitate access for disabled people to existing services. Identify groups that require alternative service delivery models, for example, targeted services or care coordination to improve access to health care.

Human resources

Integrate disability education into undergraduate and continuing education for all health-care professionals. Train community workers so that they can play a role in preventive health care services. Provide evidence-based guidelines for assessment and treatment.

Data and research

Include people with disabilities in health care surveillance. Conduct more research on the needs, barriers, and health outcomes for people with disabilities.

WHO response

In order to improve access to health services for people with disabilities, WHO:

- guides and supports Member States to increase awareness of disability issues, and promotes the inclusion of disability as a component in national health policies and programmes;
- facilitates data collection and dissemination of disability-related data and information;
- develops normative tools, including guidelines to strengthen health care;
- builds capacity among health policy-makers and service providers;
- promotes scaling up of CBR;
- promotes strategies to ensure that people with disabilities are knowledgeable about their own health conditions, and that health-care personnel support and protect the rights and dignity of persons with disabilities.

For more information contact:
WHO Media centre. Telephone: +41 22 791 2222;
E-mail: mediainquiries@who.int