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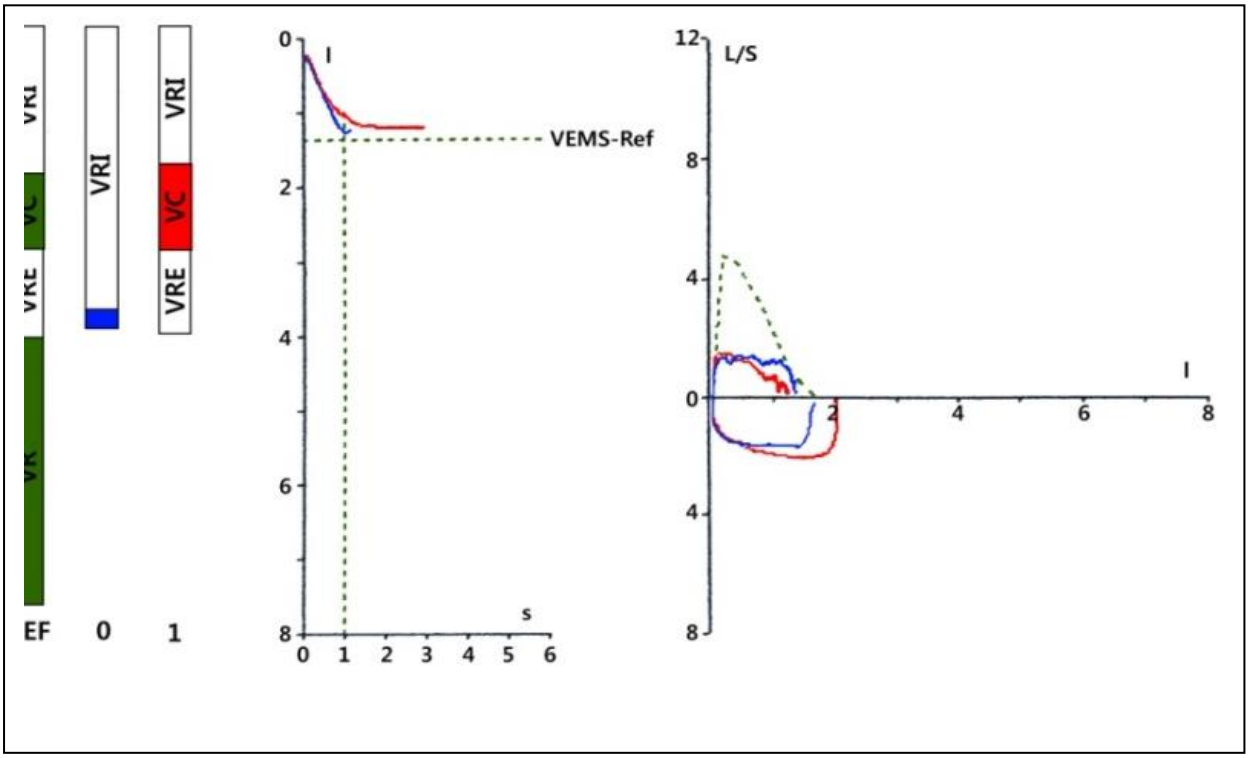

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CONTENTS

VITAMIN D ESTIMATION: PROTOCOLS, CHALLENGES AND RECOMMENDATIONS

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ABSTRACT

Vitamin D, a pro-hormone, is not only important for bone health, but is also involved in other diseases such as multiple sclerosis, irritable bowel syndrome, type I diabetes, cardiovascular disorders and a variety of cancers. These findings have emphasized the need for determining vitamin D status in a convenient and cost-effective way. Measurement of vitamin D is not an easy task or straightforward procedure. There are many issues/challenges related to the testing procedure like different sources and metabolites, lack of harmonization between different methods and structural problems. In this context, present review highlights the importance of vitamin D determination in human health and diseases related to its deficiency. Problems associated with vitamin D measurements are also being described. Available methods of vitamin D determination were critically compared in order to gather logical suggestions for reliable and accurate determination. According to the reviewed literature in this regard, inexpensive and high output methods like Diasorin Liaison Total can be employed for routine use, however, low readings need to be repeated by LCMS, as the performance of Diasorin Liaison Total drops significantly with very low reading. In addition, more work should be done on standardization.

KEYWORDS: Vitamin D, LCMS, Diasorin Liaison Total

INTRODUCTION

Vitamin D is a pro-hormone which was discovered in 1922[1]. Vitamin D can be obtained from food sources as well as produced by human skin via sun exposure. In the past, vitamin D serum status was linked only to bone metabolism and bone related diseases. In contrast, since years ago, the importance of vitamin D in many other body functions has been discovered. For example, vitamin D was found to have a role in cell proliferation and body immunity[2]. In addition, relation between vitamin D deficiency and many diseases have been reported. For example, vitamin D deficiency was found to be associated with multiple sclerosis, irritable bowel syndrome, type I diabetes, cardiovascular diseases and various forms of cancers[3]. Moreover, researchers found that vitamin D deficiency may be linked with increased risk of myocardial dysfunction in type 2 diabetic patients. However, it was also suggested that vitamin D supplements might be useful in asthma and chronic obstructive pulmonary disease (COPD)[4,5]. At the same time, wide population spectrum has been diagnosed as vitamin D deficient. Due to its importance, vitamin D is being focused as vital research topic[6]. In parallel, laboratory requests for vitamin D estimation have been increasing because of its pronounced biological roles as well as associated deficiency diseases. Vitamin D testing has been recognized as routine. For example, according to CLN survey which was done in USA, more than 25% of labs reported that vitamin D requests increased by 100% or more between 2006 and 2008 while more than 50% increase was reported by half of labs at same period. In addition, MyoClinic lab reported that 61,000 tests per month were done in 2008 compared to 19,000 tests in 2006[7]. Moreover, 200% increase was reported by Aga Khan University clinical laboratory in Pakistan from 2005 to 2008[8]. The increase in annual requests of vitamin D was even more in Auckland, New Zealand, where four times increase was reported between 2000 and 2010[9]. By this explosion of vitamin D interests, proficiency of vitamin D testing has been a matter of clinicians and scientists' concern. For instance, participants in the International Vitamin D External Quality Assessment Scheme (DEQAS) were increased from 141 labs in 2001 to 670 labs in 2009[10]. Overall, high number, well performed tests are needed to be done in shorter time periods which is not an easy task. Testing of vitamin D faces many difficulties and challenges. In this review, information on some important aspects of vitamin D estimation and accompanied analytical challenges is being presented. Furthermore, details of few common methods are also discussed. Review of literature is concluded by providing recommendations for better testing practice.

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CHEMISTRY OF VITAMIN D

Vitamin D is a hydrophobic molecule with steroid like characters. It is found in two forms which are vitamin D2 known as ergocholecalciferol and vitamin D3 named cholecalciferol. Ergocholecalciferol is usually classified as plant form because it is obtained from plant food sources and supplement medicines. On the other hand, cholecalciferol can be either obtained from animal food and supplementations or produced by skin sun exposure. Vitamin D3 is known as animal form and sun exposure regarded as its important

source[11,12]. Vitamin D (D2 and D3) is biologically inactive. Vitamin D is metabolized in liver by hydroxylation and converted to 25(OH) D which is also an inactive metabolite. The 25-Hydroxylated vitamin D regarded as the body pool of vitamin D where it is the most common form in the body. Then, 25(OH)D is activated in the kidneys by additional hydroxylation step at position 1 to produce the active $1,25(OH)_2$ D form. This active form only exists for very short time. Additionally, $24,25\ (OH)_2$ D which has no biological importance is also formed at lesser extent[11,13]. Overall, vitamin D obtained from different sources and exists in different forms inside the body. In addition, both VitD2 and VitD3 are used in supplementation.

CHALLENGES OF VITAMIN D ANALYSIS

Different sources and metabolites

Presence of different forms or/and metabolites in addition to dual sources of vitamin D contribute in many analytical challenges. Two of these difficulties will be focused. Firstly, absence of clear cut off for insufficiency and recommended doses or recommended sun exposure time. Many other variations also contribute in this issue as seasonal variation, skin pigmentation and racial differences. In this regard there is a controversy about who can be categorized as insufficient, deficient, and optimal. However, person with serum level below 25nmol/l or 10ng/ml is classified as deficient while serum level 25 to 50nmol is classified as insufficient. Nevertheless, some studies nominate 75-87.5 nmol as recommended level[11,14]. The debate about optimal and sup-optimal ranges may result in different clinical classifications hence different clinical outcomes.

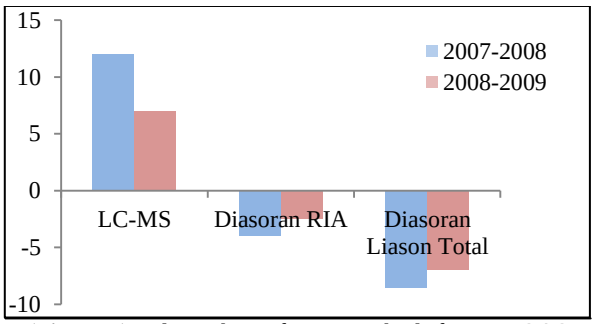
The other issue is defining which metabolites/form should be measured. Although 25(OH) D is the commonly used indicator for vitamin status, 25(OH) D2 and 25(OH) D3 separately or as a whole is still a debatable point. On one hand, Vitamin D2 is also activated and commonly used in many countries as supplement. Therefore reporting of only D3 is regarded as an incomplete picture. On the other hand, vitamin D2 has only one third activities compared to vitamin D3 and reporting them as one analyte could be misleading[15]. In addition, these forms cross react and form specificity issue in many testing principles. According to CLN survey, most of labs report total vitamin D[7]. This is not regarded a problem in normal situations as the concentration of vitamin D2 is quite low in compare to D3. Nevertheless, this point needs to be considered in many cases such as people use vitamin D2 as supplement. Theoretically reporting of each form separately seems to be the proper way especially many available methods measure fractionated D2 and D3. However, the interpretation problems and reference ranges are still the important limitations.

Lack of harmonization

In addition to the controversial reference ranges, there is some lack of agreement between labs, this was reported by many programs and clinical societies like vitamin D metabolites quality assurance program which was established in USA by the National Institute of Standards and Technology (NIS) in collaboration with the National Institutes of Health Office[16].

The use of different method could be the main cause. For instance, High Performance Liquid Chromatography (HPLC) gives higher results than Radio Immunoassay RIA and ELSIA for $25(OH)D_2$ while the opposite for $25(OH)D_3$[17]. These variations may result in different clinical classifications also between labs use same cut offs or even within the same lab that uses two different methods[18]. This problem is a recognized one and not uncommon. For example, in UMass Memorial Medical Center, by testing vitamin D for group of people by immunoassay and by Liquid Chromatography Mass Spectrum (LCMS) , more than two third of tested individuals classified as insufficient by immunoassay while less than one third in the case of LCMS[7].

These variations have been narrowing and better agreements are being achieved due to many factors. One of these factors is the International Vitamin D External Quality Assessment Scheme (DEQAS) which was implemented in 1989. This quality assurance program was founded as a response of poor vitamin D proficiency reported in many studies. Since that date, the participants increase while coefficient of variation between them declines. A 17% decrease in inter-laboratories imprecision in 15 years-time (1994-2009) was reported[10,19]. However, CV is still 15.3%, which does not meet the needed CV according to experts' opinion that states 10% as target coefficient of variation (CV) for routine measurements[20]. In addition, deciding which one of varied methods is more precise sill undoable because of absence of a certain gold standard protocol to which other methods can be compared and lack of standardization[10]. Some differences are shown in (figure 1) below.



(Figure 1) Relative bias of some methods from DEQAS calculated mean According to data obtained from two different cycles[10]

Structure related problems

Vitamin D is a hydrophobic molecule for this reason it needs to bind to a carrier protein in order to be transported as 85% of vitamin D attaches to vitamin D binding protein and the other portion to albumin. There is a very small free amount. 25(OH)D form

which usually is measured while the other portion is strongly binds to the binding protein.

This property adds some challenges. For example, in many used protocols, vitamin D needs to be extracted. In this aspect, extraction of vitamin D is not challenge free process because it is very stable in serum and labile in other fluids. In addition, it is insoluble in aquatic phases. Therefore, extraction in organic phases is needed which may need some drying steps. However, some methods which do not need an extracted sample have been developed but their results might be affected by the used agents which is known as matrix effect[21,22].

In addition to the above structural issues, the variability in the percentage of free 25(OH) D levels in compare to total vitamin D among different clinical population was also highlighted in some studies and it might have a clinical significance[23]. Moreover, the orientation change of hydroxyl group at carbon 3 of the steroid nucleus was reported and its biological importance has been questionable[24].

CURRENTLY USED METHODS

Historical background

First vitamin D assay was designed on protein binding competition in 1970. Then HPLC was founded in 1978. Later, in 1985 Radio immunoassay (RIA) have been commercially available. Then other methods were introduced like Enzyme Immunoassay (EIA), Automated RIA, and mass spectrum[8].

Immunoassays

There are manual and automated available immunoassays and most of them are competitive. Manual immunoassays usually have simple procedures which are easy to follow. But the long incubation time, low throughput specificity issues and inappropriate extraction techniques are important limitations. Manual Radioimmunoassay (RIA) like the one designed in 1985 by the diagnostic company Diasorin is a very common used example of this type. However, some other manual immunoassays do not need an extraction step such as Direct EIA. In this procedures turnaround time can be diminished, also simpler and inexpensive procedure is applied. Nevertheless, matrix effect is the main problem in addition to low throughput[25,26].

On the other hand, automated procedures offer important advantages. For example, Diasorin company developed in 2004 a fully automated Chemiluminescent Immunoassay (CLIA) named Liaison Total, this method is widely used nowadays due to the many offered advantages. It is an extraction free method that can run a large number of tests and gives the results in about 65 minutes. These benefits are important to cope with the tremendous increase in the request numbers. Diasorin Liaison Total is also technically simple. However, matrix effect is still a limitation. In addition, low sensitivity is another issue faced by this technique. Evidently, according to RCPAQAP program-cycle number 33 lower limit of detection for this device is 33 nmol/ml[26,27,28,29,30].

Physical detection methods

The more common non-immunological principles which are used in vitamin D testing are HPLC and LCMS. HPLC method has very good performance and it can be automated. In addition, HPLC is high sensitive with low detection limit. However, there are some limitations like low throughput and large sample size. Moreover, skillful operator is needed[30,31,32].

Liquid Chromatography Mass Spectrum LCMS is another sensitive method which is regarded as a golden standard in some practices. Matrix effect is minimized and standardization can be controlled by the operator. Moreover, LCMS automation is also available which help to alleviate the operator's effect. In the other side, low throughput, high establishment cost and needing of skilled operator are the main problems faced by technique. In addition, positive bias compared to many other methods is documented[7,27,30,31].

Suggestions for better practice

For current practice, method like Diasorin Liaison Total can be used for routine use as it offers inexpensive, high number of tests and good performance except for too low readings. In parallel, lower readings can be repeated on LCMS especially vitamin D tests are usually not urgent.

For future work, although the agreement between used methods is now increasing, lack of standardization is the most issue in vitamin D testing practice. Likewise, work in standardization is the most urgent. In addition, national compulsory proficiency programs need to be implemented and new programs also need to cooperate with DEQAP which is an international and non-mandatory program. The promising picture that supports that is the decline in CV since DEQAP has been implemented.

CONCLUSION

Discovered biological roles of vitamin D drastically increased number of the requested lab tests to check vitamin D status. Measuring of vitamin D is not an easy task or straightforward procedure. This is because of many issues faced by this testing process. Although some improvement like CV decline and closer agreements between methods have been achieved in the last years, different metabolites and sources, structural nature and lack of standardization still exist as important issues. In the future, more proficiency testing programs need to be implemented. Moreover, working cooperatively between implemented procedures on standardization issue should be the priority.

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ADMISSION PATTERNS AND OUTCOMES OF YOUNG INFANT IN RESOURCE DEFICIENT HOSPITALS

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ABSTRACT

To calculate incidence of admission and mortality pattern in admitted young infants and to identify measures to assess and evaluate performance to the existing hospital services to improve facilities and inpatient care. This was a descriptive study (Longitudinal hospital based study) in Paediatric Department, Misurata teaching hospital, from January 2012-December 2012. All hospital admissions, of young infant who presented to paediatric department with clinical symptoms justifies admission are included in the study. Sick infants were routinely investigated according to a standard protocol. The clinical care during admission was supervised by a consultant paediatrician who was also responsible for assessment and assigning the final diagnosis at the end of the admission after review of the case notes and the results of all relevant investigations. There were a total of 384 young infant admitted into the paediatric department during the study period. Thirty four infant deaths were recorded (8.9%) from the total young infant admitted during this study. Presumed serious infections were the commonest cause of admission among infants <2 months of age (41%), followed by Pneumonia (aged 30–59 days) at 30.7% from total admission of young infants. Mortality in severe infection was 12.6% from total admitted cases of this group but account for 58.8% from total mortality in young infant. our data suggest that strategies to tackle the problem of infection in young infant by prevent or treat infection may be of great benefit if we consider value of community based diagnosis and care. I believe that the discussion of mortality cases provides an adequate means of changing practice patterns which needed to reduce the mortality in young infant.

KEY WORDS: Resource Deficient Hospitals, Mortality, Young infant, Severe infection.

INTRODUCTION

Children hospitals are adept at managing the medical needs of ill children, providing continuity of care, and developing effective relationships with other health care team members. Ideally, specialists significantly enhance the quality of health care provided to individual children. In response to the increasing emphasis on delivering cost-effective and high-quality health care, many hospitals have implemented clinical pathways and protocols that rely on evidence-based guidelines for a variety of common, predictable inpatient illnesses and procedures. Hospitals with low resources need continuous evaluations to develop practical and sensible guidelines according to the facility provided to improve the quality of health care delivered to children in the inpatient setting.

Quality of care has assumed its rightful place as a central focus of health care delivery and management. The increased attention to quality arose from abundant evidence that health care in developing countries suffers from serious and pervasive quality-related problems that have staggering effects. When we talk about quality of care we should define six specific aims for the health care system, now widely conceived as the critical dimensions of quality. Health care should be: Safe, Effective, Efficient, Patient centered, Timely, and Equitable[1]. Effectiveness refers to the reliable delivery of care that is likely to achieve desired results (i.e., care consistent with evidence). Evidence-based medicine and clinical practice guidelines, respectively, provide an orientation to the delivery of effective care. Guidelines must be coupled with effective strategies to incorporate evidence into clinical practice[2,3].

The work in resource deficient hospital is totally different. Ideally, measures should be derived from data collected routinely in the course of care, such as health records or ongoing patient surveys, but in most cases, it must be supplemented by project-specific data collection and analysis. Importantly, data should be plotted and tracked over time but they should not be kept hidden for evaluation-oriented before-and-after studies. A typical improvement studies uses some important measures, including measures of the processes of care (was the right thing done?), the outcomes of care (did the right result occur?), and potential adverse outcomes (was there unintended harm?). In hospitals with limited resources, efforts to improve pediatric patient safety are important which have been hampered by different factors. Although many mecha-

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nisms exist by which patient safety principles can be taught, one of the most effective may be the morbidity and mortality (M&M) review process. These reviews had been a part of some hospital practice for generations, and it is to discuss adverse outcomes.

There is no standard blueprint for the ideal pediatric M&M review process. One must take into account the size and type of hospital, the policies of the institution, the time and resources available. As we talk about our limited resource hospital, we are in a weak position to deal with some of these issues. Studying the outcomes and effectiveness of M&M reviews is important and can serve as a vehicle for introducing changes.

Young infant mortality is well recognized world wide. Every day, more than 26,000 children under the age of five die around the world, mostly from preventable causes[4]. The vast majority of them live in the developing countries and more than one third of these children die during the first month of life[4]. In addition World Health Organization 2000–2003 report, estimate that young infant sepsis and pneumonia are responsible for about 1.6 million deaths each year, mainly in resource-poor countries[5].

AIM OF STUDY

This study is aimed at evaluating the mortality pattern in young infant in our Hospital and to identify measures to assess performance. The information obtained from this study would be used in re-evaluating existing services and in improving facilities and patient care.

To calculate incidence of admission and mortality pattern in admitted young infants and to describe the factors that probably affect the mortality rate in our hospital.

PATIENTS AND METHODS

This was a descriptive study (Longitudinal hospital based study) in paediatric department, Misurata teaching hospital, from January 2012-December 2012. All hospital admissions, of young infant (under the age of two month) who presented to paediatric department with clinical symptoms justifies admission are included in the study. Prospectively collected data on admitted cases include; history, clinical examination, investigations, and treatment (Details of relevant clinical information, investigation, and treatment are recorded on a data collecting form). Data from 200 young infant are expected to be available for analysis (190 subjects are estimated, with precision of ±5 % using a 95 % confidence interval).The sample size is increased to allow for possible loss. The SPSS is used for data analysis.

Young infant admitted to hospital department are presented to hospital paediatric outpatient department (OPD) transferred usually from dispensary, private hospital or clinic or directly presented with their parents to hospital paediatric OPD.

In our study the following definitions were adapted:

Young infant are infant less than 60 days old. The neonatal period begins with birth and ends 28 complete days after birth.

Prematurity includes children admitted up to the age of 30 days for whom their immaturity was considered the major problem. (Preterm Less than 37 completed weeks (less than 259 days) of gestation).

Term From 37 completed weeks to less than 42 completed weeks (259 to 293 days) of gestation.

Post-term 42 completed weeks or more (294 days or more) of gestation. Low birth weight (LBW) Less than 2500g (up to and including 2499g). Sepsis diagnosis was based on the clinical features with or without positive culture or abnormal biochemical analysis. Severe infection includes the clinical categories, neonatal sepsis, severe infection/pneumonia, and meningitis. Pneumonia includes children for whom the clinician felt able to make a firm clinical diagnosis of pneumonia rather than the less specific "severe infection".

Criteria of admitted young infant babies in paediatric department, Misurata Teaching Hospital:

1- Presence of respiratory distress signs whatever the birth weight or gestational age.
2- Clinical signs suggestive of a coexisting acute systemic illness (e.g. meningitis, sepsis).
3- Birth weight less than 2KG.
4- Neonate with presence of maternal risk factors which include, evidence of chorioamnionitis (laboratory or clinically), prolonged premature rupture of membrane (PPROM) > 24.
5- Young infant with pyrexia.
6- Major congenital malformation.
7- Symptomatic congenital heart diseases.
8- Infant of diabetic mother.
9- Pathological jaundice or jaundice with positive family history of exchange transfusion.
10- Birth Asphyxia [1, 5- minute Apgar score of 0-3, hypoxic ischemic encephalopathy (altered tone, depressed level of consciousness)].

We adapt the WHO clinical signs that predict severe infection in infants presenting to our hospitals[6].

These included

1- Fever, hypothermia, inability to suck.
2- History of convulsions.
3- Lower chest indrawing, crepitations, sustained fast breathing or cyanosis.
4- Failure to arouse with minimal stimulation, history of change in activity.

Interventions

Sick infants were routinely investigated according to a standard protocol with a full blood count, blood culture, plasma electrolytes, creatinine, and glucose. Total serum bilirubin was measured in all visibly jaundiced infants. Lumbar puncture was performed as part of the routine "septic screen" in all neonatal admissions with suspected sepsis and otherwise according to locally agreed clinical criteria based on those used in the WHO multicentre study of young infants[7]. Chest radiography was done when indicated clinically.

Hospital treatment available

Included oxygen, antibiotics, intravenous fluids (not parenteral nutrition), nasogastric feeding of expressed breast milk, phototherapy, and exchange transfusion. During the study an incubator was routinely available. Empiric management of suspected severe infection was with 3rd generation cephalosporin and gentamicin.

The clinical care during admission was supervised by a consultant paediatrician who was also responsible for assessment and assigning the final diagnosis at the end of the admission after review of the case notes and the results of all relevant investigations. Determining the precise diagnosis in young infants is problematic sometimes. Thus severe illness in a premature infant may be due entirely to immaturity (for example, the development of respiratory distress) or secondary to infection to which they are predisposed on account of their immaturity. The final diagnosis assigned represents an experienced pediatrician's view of the most probable primary pathological event on which secondary pathological events might be superimposed. All young infants were invited back after discharge for a follow up appointment according to their discharge diagnosis.

RESULTS

There were a total of 384 young infant admitted into the paediatric department during the study period. Based on the results, these young infants represented 32.5% of all paediatric admissions (1182 patients) and 58.6% of paediatric deaths during this period. Thirty four young infant deaths were recorded (8.9%) from the total young infant admitted during this study. These were made up of 18 males and 16 females giving a ratio of 1.1:1.

Fifty eight children in all age groups died in our hospital during the study period which account for 4.9% from total hospital admission. Accepting the inherent limitations in the diagnostic process, the observed Although 30.7 % of all admissions less than 2 months of age were diagnosed as Pneumonia (aged 30–59 days) (table 1) but infant death account for only 1.7% from total admission in patient diagnosed with pneumonia in age 30-59 days (table 2). Fourty patients were admitted as cases of birth asphyxia which approximately 10.4% from the total hospital admission of young infant (table 1) and about 7.5% of these patients were died (table 2).

DISCUSSION

Child mortality is a sensitive indicator of a country's development and telling evidence of its priorities and values[8]. Deaths have been reported to be more in poor resource hospital settings on which malnutrition and infection-related diseases have resulted in childhood deaths.

Since 1990, impressive progress has been made in improving the survival rates and health of children, even in some of the poorest countries[9]. However it is worrisome to note that high rate of infant and child cause specific patterns of admissions and mortality are presented in (table 1) and (table 2). Presumed serious infections were the commonest cause of admission among infants <2 months of age (41%) (table1), followed by Pneumonia (aged 30–59 days) at 30.7% from total admission of young infants.

(Table 1) Prevalence of major diseases in admitted young infant <60 days of life

Disease	% & No.
Severe infection	41 (158)
Prematurity	7.5 (29)
Pneumonia (aged 30–59 days)	30.7 (118)
Birth asphyxia	10.4 (40)
Major congenital abnormalities	3.3(13)
Others	6.8(26)

In the majority of cases of severe infection, it was not possible to identify a focus of infection. However, clinicians felt more confident distinguishing pneumonia from other infections in infants older than 1 month.

Mortality in severe infection group account for 58.8% from total mortality in young infant. Premature infants in this group accounted for 7.5% from the total hospital admission of young infant (table 1), and 24% of them were died (table 2) but only represent 20.5% from deaths in those under 2 months of age.

(Table 2) Prevalence of mortality in admitted young infant <60 days of life

	No. of admitted cases	% of mortality & No.
Severe infection	158	12.6 (20)
Prematurity	29	24 (7)
Pneumonia (aged 30–59 days)	118	1.7 (2)
Birth asphyxia	40	7.5 (3)
Congenital abnormalities	13	15.4 (2)

morbidity and mortality is still one of the greatest challenges facing most of the developing countries[8]. In our hospital department, total mortality in different age group during the study period is 4.9 % which lower than the 6.8 % observed in other developing countries[10].

Although infants less than 2 months of life comprise a 32.5% of our hospital admissions, they contribute disproportionately to 58.6% of paediatric deaths to inpatient paediatric mortality. Thirty four young infant deaths were recorded (8.9%) from the total young infant admitted during this study. If we compare it to other studies that shows that mortality rates for young infants in developing countries depend partly on the level of hospital resources and health facility, ranging from 5.4% in the WHO young infant study[7] to18% among those admitted to district or provincial hospitals[11,12]. Higher rates of mortality might be expected in referral hospitals because in general sicker infants will be referred.

Pneumonia (aged 30–59 days) are seen in 30.7% of young infant admitted to hospital (table 1) and mortality in this group is rare, which about 5.8% from total mortality in young infant(table 2). Birth asphyxia is a less common problem attributed to young infant mortality in our setting than might be anticipated (table 2). This is probably because, some of asphyxiated infants die in private hospital before transferred to our hospital, is possible explanation.

If we look to our study we found severe infection is the commonest reason of admission in young infant (table 1) and the mortality in these group about 58.8% from total mortality in young infants (table 2). In part this high mortality may be explained by the difficulties of sustaining even appropriate, basic levels of supportive care with limited personnel and resources in a setting designed to cope with less than half the number of admissions than are actually received.

Analysis of discharge data from more than 5 million pediatric hospitalizations revealed that sepsis and infection were common events among hospitalized children[13]. Children who had infections were found to have an increased median length of hospital stay, higher direct health care costs, and greater in-hospital mortality. These findings persisted even after adjustment for patient and hospital characteristics. The true burden of bacterial infections in our hospital settings is also unclear, because many clinical bacterial infections may present with RDS or in preterm babies and birth asphyxia who can acquire hospital infections which account for high rate of mortality.

Studies have reported rates of hospital infections that are 3–20 times higher in resource poor than resource-rich countries[14].The most common reported organisms are Gram-negative bacilli and S aureus[14]. Nosocomial infections are the single most common adverse event experienced by hospitalized children especially young infant. Recent data suggest that as many as 10% of patients develop nosocomial infections during admission to an acute care hospital[15]. Hospital-acquired infections increase morbidity, extend hospital stays, and raise hospital charges, and they are also associated with substantial increases of in-hospital mortality. To prevent these infections, however, a number of simple care practices that can reduce the probability of an infant developing a hospital-acquired infection. These include elimination of overcrowding and understaffing, careful preparation and storage of infant formulas, decreasing the number of venipuncture, sterilization of resuscitation bags and masks, and use of sterile suctioning techniques. Because many episodes of bacteremia are associated with indwelling lines or mechanical ventilation, common sense dictates avoiding their use or minimizing the number of catheter or ventilator days. All what we mention before are difficult to apply in our resource deficient hospital. What we can do to prevent infection in our hospital probably are the care practices that are likely intended to start early enteral feedings, use of human milk feedings, sterile insertion techniques by skilled personnel and dressing changes with careful disinfection of the insertion site and care of the hub, careful preparation of intravenous fluids and blood products. Hand washing and degerming (using an alcohol-based hand rub with emollient) remain the simplest and most effective methods of preventing transmission of infection from clinicians to young infants which usually not done.

There are problems in assigning a single diagnosis to sick young infants, particularly where facilities for investigation are limited. In addition one of the possible limitations of this study was the inability to identify the agents of infections in our hospital and their antibiotic susceptibility patterns because the majority of treated young infant are clinically septic babies but with negative blood culture. Therefore, while it is possible that absence of this data means the "cause" of death or illness is misclassified in some cases. We feel the spectrum of disease presented here is likely to be representative of that in district hospitals in many areas of Africa with a similar hospital sitting. While accepting that some misclassification is inevitable in our study, we believe our data provide valuable insight into the clinical challenge of caring for sick young infants faced by similar resource deficient district hospitals in the region.

In previous study in our hospital, 2005 (unpublished) shows preterm sepsis account for the bulk of preterm death in our neonatal unit. About 53% of preterm death associated with sepsis and commonly associated with hospital-acquired neonatal infections. Whilst poor hospital facility, shortage of nurses, and heavy resistant microbial colonization are major risk factors for young infants infections. Young infant who were infected require prolonged hospital admission with high risk of mortality. There is no doubt that use of antibiotic is effective and important to reduce the young infant mortality, but treatment strategies had not been implemented widely and consistently in our hospital.

Other factors that probably increase mortality in infected young infant is likely the resistance that present to the usual antibiotic used in treating infection. Antibiotic resistance is an important problem in resource poor countries[14,16,17,18].

A number of studies in health maintenance organizations, academic medical centers, and children's hospitals comparing hospitalist programs to traditional inpatient care systems in preventing and treating infection have shown a decrease in hospital charges, costs, and length of stay[19,20,21,22].

Our hospital had limited diagnostic and treatment resources (e.g. new generation antibiotics, mechanical ventilator, presence of surfactant, lacking of diagnostic laboratories and radiological facility) which all underprovided and probably increase the burden of mortality in young infant.

Young infant mortality reports are very important. In our hospital we have no mortality reports (MR). Barriers to performing appropriate MR reviews include the

anxiety of acknowledging individual error, potential loss of respect, and fear of legal action. Learning from one's errors is important, but confronting them is difficult, especially in front of a group of peers. Harbison and Regehr believe that MR reviews could be improved by decreasing defensiveness and blame[23]. MR reviews should be mandatory for all inpatient pediatric units to ensure that the care provided was timely and appropriate, to learn from the event, and to develop new knowledge and improved systems of care. Reviews should emphasize learning and the prevention of similar occurrences. Every mortality and significant morbidity should be reviewed in a timely manner. Cases should be selected both for their individual educational value and to expose attendees to a broad range of patient safety themes. Speculation and the language of blame should be avoided; reviews should emphasize "systems" rather than "individuals," and should be "confidential."

CONCLUSIONS AND RECOMMENDATION

Our hospital based study measures the admission patterns and outcomes of young infants which probably a reflection of what is obtainable in a community at large. Therefore, data obtained from our study is important in re-evaluating existing services and in improving facilities and patient care.

The vast majority of young infant's mortality is secondary to severe infection like sepsis, which usually increased when resources are deficient. Targeting the causes of young infant mortality is very important issues to reduce the mortality rate. However, although it is true that dysfunctional health systems is adversely affect child health in many hospitals (including our hospital), this is relatively difficult to change in the short term.

Although our study is hospital based, our data suggest that strategies to tackle the problem of infection in young infant by prevent or treat infection may be of great benefit. In addition, gaps in the system of communication and referral from primary health centre and private clinics to our hospital should be addressed.

To achieve the goals of improving patient safety and effectively educating staff, relevant mortality cases need to be presented and discussed in an appropriate manner. Often, minimal attempts are made to ensure the complete identification and reporting of complications. I believe that the give-and-take of the discussion of mortality cases constitutes effective peer review and this provides an adequate means of changing practice patterns when needed.

Systems for developing both clinical practice guidelines and associated outcome measures will act to create evidence-based cultures that improve the quality of health care delivered on pediatric inpatient services in low resource hospitals.

In addition the results of this study offers compelling support for using further researches to identify the more effective measures to save young infant lives, for example hand washing, reducing overcrowding of patients and provide adequate number of paediatric nurses, careful preparation of infant formula, decreasing the number of venipuncture, use of sterile suctioning techniques, early enteral feedings with human milk feedings, careful disinfection of the insertion site, careful preparation of intravenous fluids and blood products. These measures should be applied in our clinical practice and further researches should be done to see the effect of these practice changes in reducing hospital infection and mortality in young infant in our hospital.

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COLD CHAIN STATUS AND VACCINATION ACTIVITIES AT VACCINATION CENTERS IN TRIPOLI, LIBYA (2015)

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ABSTRACT

Effective immunization program requires a stable cold chain to maintain potency of vaccines from national stores through to delivery sites. The integrity of the cold chain is depend on not only the equipment used, but also the people involved and the practices they undertake. To assess the condition of cold chain equipment and the practices adopted for cold chain maintenance by the vaccinators. The study was designed as cross-sectional, conducted at the vaccination centers in Tripoli. Cold chain equipments were assessed with regards to their condition, along with the practices of vaccine providers. The study was conducted during the period from December 2014 to February 2015. The data was analyzed using SPSS program, and results were presented as frequency and percentage. All vaccination centers in Tripoli were assessed, according to World Health Organization recommendations, 95.7% of refrigerators had proper site, appropriate vaccine packing was detected in 55.3% and proper temperature was found in 42.6% of refrigerators. During vaccination session 66% of nurses used to wash their hands, most of them were handling the child properly, while all of them checking the type, the dose of vaccine and reconstitute the vaccine as it should be. Only 10.6% of nurses did not counsel the mothers about the side effects of vaccine and did not remind them about the time of the next visit, and 95.7% of the nurses handle the needles and syringes safely. Cold chain maintenance and practice need improvement; regular staff training and supervision.

KEY WORDS : Immunization, Vaccine, Cold chain, Vaccine providers, Assessment.

INTRODUCTION

Immunization is the most successful global health intervention and one of the most cost-effective ways to save lives and prevent diseases[1-3].

The number of deaths caused by vaccine preventable diseases have fallen from an estimated 0.9 million in 2000 to 0.4 million in 2010[4].

Vaccines have the power not only to save, but also to transform lives giving children a chance to grow up healthy, go to school and improve their life prospects[5].

Vaccine storage and handling errors can result in the loss of vaccines worth millions of dollars. The administration of mishandled vaccine can affect a large number of patients. Failure to adhere to required protocols for storage and handling can reduce vaccine potency, resulting in inadequate immune responses, as well as inadequate protection against disease[6].

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The system of transporting and storing vaccines within recommended temperature range of $+2C^0$ to $+8C^0$ from the place of their manufacture to the point of vaccine administration is called the cold chain[7-10].

The key elements of cold chain are personnel to manage vaccine storage and distribution; equipment to store and transport vaccine; and procedures to ensure that vaccines are stored and transported at appropriate temperature[11].

All staff members who handle or administer vaccines should be familiar with the storage and handling policies and procedures at their facility. This includes not only those who administer vaccines, but also anyone who delivers or accepts shipments or who may have access to the units where vaccines are stored[6].

The vaccine refrigerator should be placed in a cool room, away from direct heat or sunlight, at least 10cm to 20cm from the wall and with at least 40cm of clear space above. The room should be well ventilated so that the heat from the refrigerators and freezers will not make the room too hot. If several refrigerators or freezers are kept in one room, they should be properly spaced, at least 30cm from each other[10-12].

Adequate cold air circulation helps each vaccine reach a consistent temperature throughout its mass, and is necessary for the storage unit to maintain a consistent temperature. Packing any vaccine storage unit too tightly can negatively affect the temperature[6].

A storage unit is only as effective as the temperature monitoring system inside. Accurate temperature history that reflects actual vaccine temperatures is imperative to effective vaccine management[6-12].

As recommended that do not keep food and drink in a refrigerator used for vaccine storage. Frequent opening of the refrigerator to retrieve food items can affect the temperature of the unit and thus affect the efficacy of the vaccines. It may also result in spills and contamination inside the unit[6-12].

With the exception of Bacillus Callmette- Guérin (BCG) vaccine, injectable vaccines are administered by the intramuscular or subcutaneous route. Deviation from the recommended route of administration might reduce vaccine efficacy or increase the risk for local adverse reactions[13].

For the majority of infants, the anterolateral aspect of the thigh is the recommended site for injection because it provides a large muscle mass[13].

To prevent inadvertent needle-stick injury or reuse, safety mechanisms should be deployed after use; needles and syringes should be discarded immediately in labeled, puncture-proof containers located in the same room where the vaccine is administered[13].

So, this study was conducted with the aim to assess the condition of cold chain and the practice of vaccine providers at vaccination centers.

MATERIALS AND METHODS

This study is a descriptive, cross-sectional type; conducted to assess all vaccination centers in Tripoli. Administrative approval was obtained from primary health care office in Tripoli. The list of vaccination centers was prepared and the time schedule to visit all vaccination centers was decoded. The study was carried out during the period from December 2014 to February 2015. Cold chain equipment was assessed using a pre-constructed checklist, regarding to their condition and practices of health personnel for cold chain maintenance. A vaccination session was observed to assess the performance of vaccine providers at the time of vaccine administration.

The study tool was a pretested questionnaire, designed according to cold chain criteria set by world health organization (WHO)[5], which consisted of two sections; section one includes a checklist to assess the vaccination room, refrigerator, cold box and vaccine carriers; the second section deals with questions to assess the practice of those providing immunization and managing the cold chain at vaccination centers.

SPSS software version16 was used for data analysis, descriptive statistics were used and results presented as frequency and percentage.

RESULTS

Vaccination activities in Libya are provided in all health care levels, in different health units and for every one free of charge. Vaccination centers in Tripoli according to the list obtained from primary health care office were evaluated in this study, and (table 1) shows their distribution according to the type.

(Table 1) Distribution of vaccination centers according to the type of health facility in Tripoli (2015)

Type	Frequency	%
MCH	2	4.2
Dispensary	3	6.4
Health center	31	66
Polyclinic	6	12.8
Hospital	5	10.6
Total	47	100

This study showed that the majority of vaccination rooms had proper waiting facility (72.3%), appropriate ventilation (78.7%), and suitable washing facility (70.2%). Most of vaccination rooms (89.4%) were clean and all centers have proper disposal facilities that include puncture proof containers and safe boxes (table 2).

(Table 2) Situation of vaccination room at vaccination centers in Tripoli (2015)

Character	Proper	Improper	Total
Waiting facility	34 (72.3%)	13 (27.7%)	47 (100%)
Ventilation	37 (78.7%)	10 (21.3%)	47(100%)
Light	39 (83%)	8 (17%)	47(100%)
Washing facility	33 (70.2%)	14 (29.8%)	47(100%)
Disposal facility	47 (100%)	0	47(100%)
Cleaning	42 (89.4%)	5 (10.6%)	47(100%)

The study revealed that all vaccination centers had refrigerators and 87.2% had deep freezer, only 2.1% of vaccination centers had shortage in injection equipment.

Daily electricity failure was noted in 85.1% of vaccination centers and only 38.3% had stand-by generator and fuel was available in 21.3% of them (table 3).

(Table 3) Cold chain equipment in vaccination room in Tripoli (2015)

Equipment	%	Not %	Total
Refrigerator ILR Domestic	36 (76.6%) 11 (23.4%)	0	47(100%)
Deep freezer	41 (87.2%)	6 (12.8%)	47(100%)
Injection equipment	46 (97.9%)	1 (2.1%)	47(100%)
Vaccination poster	8 (17%)	39 (83%)	47(100%)
Electricity failure	40 (85.1%)	7 (14.9%)	47(100%)
Generator	18 (38.3%)	29 (61.7%)	47(100%)
Fuel	10 (21.3%)	37 (78.7%)	47(100%)

Regarding the refrigerator state, 76.6 % of refrigerators were of ice lined type (ILR), 95.7% of refrigerators were placed at proper site that away from direct sun light exposure and 85.1% had appropriate distance away from the wall as recommended by WHO. Proper vaccine packing was observed in 55.3% and proper temperature (2°C – 8°C) was seen in only 42.6% of

refrigerators in vaccination centers which make the vaccine potency in that centers questionable (table 4).

(Table 4) Status of refrigerators at vaccination centers in Tripoli (2015)

Status of refrigerator	Proper	Improper	Total
Site	45 (95.7%)	2 (4.3%)	47(100%)
Distance	40 (85.1%)	7 (14.9%)	47(100%)
Temperature	20 (42.6%)	27 (57.4%)	47(100%)
Vaccine packing	26 (55.3%)	21 (44.7%)	47(100%)
Ice pack freezing	11 (23.4%)	36 (76.6%)	47(100%)

In present study, thermometer was found in only 48.9% of refrigerators, 8.5% of refrigerators were leaked and temperature recording sheet and vaccine expiry sheet were absent in 78.7% and 57.4% of refrigerators respectively. Food was present in 4.3%of refrigerators. Diluents which needed for reconstitution of vaccine were present inside 72.3% of refrigerators at vaccination centers (table 5).

(Table 5) Storage requirement of refrigerator at vaccination centers in Tripoli (2015)

Storage requirements	%	Not %	Total
Thermometer	23 (48.9%)	24 (51.1%)	47(100%)
Leaking	4 (8.5%)	43 (91.5%)	47(100%)
Temperature recording sheet	10 (21.3%)	37 (78.7%)	47(100%)
Expiry date sheet	20 (42.6%)	27 (57.4%)	47(100%)
Food	2 (4.3%)	45 (95.7%)	47(100%)
Vaccine Diluents in refrigerator	34 (72.3%)	13 (27.7%)	47(100%)

The study demonstrated that 97.9% of cold boxes were in good condition, there were no thermometers inside cold boxes during our visit. 36.2% of ice packs were arranged improperly in cold box and the temperature inside these cold boxes was not known if within recommended range or not (table 6).

(Table 6) Characteristics of cold boxes at vaccination centers in Tripoli (2015)

Character	Proper	Not proper	Total
Condition	46 (97.9%)	1 (2.1%)	47(100%)
Ice packs arrangement	30 (63.8%)	17 (36.2%)	47(100%)
Vaccine packing	45 (95.7%)	2 (4.3%)	47(100%)
Thermometer inside cold box	0	47 (100%)	47(100%)
Closed tightly	46 (97.9%)	1 (2.1%)	47(100%)

During vaccination session only 66% of nurses wash their hands before administration of vaccine, most of them (97.9%) were handling the child properly, all of the vaccine providers were inspecting the type of vaccine, checking if vaccine frozen and only 48.9% of them read the vaccine vial monitor (VVM), to know whether the vaccine has been damaged by heat or not. Also during the same session, all the nurses reconstitute the vaccine properly, vaccinate the child at correct site and route and were given the correct dose of Polio and Rota vaccines and recorded all information in immunization card and vaccine register files.

Only 10.6% of nurses did not counsel the mothers about the side effects of vaccines and did not remind them about the time of next visit. Most of nurses (95.7%) were handling the syringe safely and all of them were disposing the needle and vaccine vial properly (table 7).

(Table 7) Nurses' performance during vaccination session at vaccination centers in Tripoli (2015)

Practice	Yes	No	Total
Washing hands	31 (66%)	16 (34%)	47(100%)
Proper child handling	46 (97.9%)	1 (2.1%)	47(100%)
Checking type of vaccine	47 (100%)	0	47(100%)
Checking frozen vaccine	47 (100%)	0	47(100%)
Reading VVM	23 (48.9%)	24 (51.1%)	47(100%)
Proper reconstitution	47 (100%)	0	47(100%)
Proper handling of syringe	45 (95.7%)	2 (4.3%)	47(100%)
Proper Cleaning technique	37 (78.7%)	10 (21.3%)	47(100%)
Correct site	46 (97.%)	1 (2.1%)	47(100%)
Correct route	47 (100%)	0	47(100%)
Correct polio dose	47 (100%)	0	47(100%)
Correct Rota vaccine dose	47 (100%)	0	47(100%)
Recording	47 (100%)	0	47 (100%)
Health education	42 (89.4%)	5 (10.6%)	47(100%)
Proper Disposal	47 (100%)	0	47(100%)

DISCUSSION

Failure to adhere to recommended specifications for storage and handling of immunobiologics can reduce or destroy their potency, resulting in inadequate or no immune response in the recipient. Inadequate vaccine storage also can result in the loss of thousands of dollars' worth of vaccine inventory and the cost of inventory replacement[13].

To provide any health service, proper waiting facility should be available in each health unit to relive anxiety and to decrease over crowding at doors, hence provision of good services by health personnel. Each vaccination room should be well ventilated, with suitable lighting and proper washing facility to conduct safe immunization activities. In current study, some of vaccination rooms lack these requirements because of lack of continuous maintenance.

In this study, vaccination centers showed remarkable improvement in cold chain management, as compared with previous studies conducted by Omar (1996)[14], Ehmadi (2000)[15], Ehmadi (2003)[16]. But some vaccination centers suffered from shortcomings, which may affect immunization program these include failure to adhere to expanded program on immunization recommendations and guidelines for cold chain and vaccination activities.

In the present study, 76.6 % of refrigerators were of ice lined type (ILR) and they were placed in proper site and had proper distance away from the wall. Similar results found in a study done by Naik AK in western India[17].

Presence of thermometers in vaccine fridge is one of the cold chain recommendations that measure the temperature, which should be maintained between 2°C- 8°C, if there is no thermometer in the fridge, the vaccine is in danger. In this study, nearly the half of refrigerators had thermometers and proper temperature was available in 42.6% of refrigerators. Similar results confirming this study were achieved by national cold chain assessment 2008 in India; they reported that Cold chain management was poor in some places (including private practices), particularly for temperature recording and risk of freezing the freeze-sensitive vaccines[18].

As the results showed that more than two thirds of refrigerators deficient in temperature recording sheet, this explains lack of responsibility and supervision.

Study done by Ministry of health in Malawi, from 2011 to 2015 revealed that, of the 1,045 working refrigerators at the time of the survey, 88.4% had at least one temperature monitoring device[19].

In a study conducted in Cameron by Atendjieu et al.,2013, It was noted that the temperature was not systematically recorded on charts twice daily as required in 11 (40.7%) of the health facilities[20].

Other study, done by Widsanugorn et al., 2011 in Thailand, revealed that the findings from direct observation about equipment and practices regarding the cold chain system in primary care units were 86.7% of them, the temperature inside refrigerators was in the range of 2–8°C[21].

Vaccine loading was as recommended in 55.3% of refrigerators in present study. Proper storage of vaccine was in 78.6% of refrigerator in study done in Cameron[20] and 90% in a study done by Rao et al., at costal south of India[22].

Presence of other item with vaccine as Food and drug was in only 4.3% of refrigerators in this study; hence unnecessary opening of doors which leads to fluctuation of temperature was avoided. Other studies were conducted in different countries, were getting similar finding[17,22].

In current study the electricity failure, which may harm immunization program was present in 85.1% of vaccination centers, only 5 hospitals and 2 polyclinics had continuous electricity supply; generators were available in 38.3%, and fuel was accessible only in 21.3% of health centers. But, most of refrigerators were ice landed refrigerators (76.6 %), so the cold chain will not be affected by the electricity failure for 48-72 hours. While, the results in the previous study conducted by Ehmadi demonstrated that electricity failure was rare or none in 90% of vaccination units[15].

In study done in India out of the 574 sites assessed, generators were available at 173 sites[23]. Same finding was in other study conducted in western India the lack of generators was in 85% of health centers[17].

Persons administering vaccinations should follow appropriate precautions to minimize risk for spread of disease. Hands should be cleansed with an alcohol-based waterless antiseptic hand rub or washed with soap and water before preparing the vaccine and between each patient contact. Occupational Safety and Health Administration (OSHA) regulations do not require gloves to be worn when administering vaccinations, unless persons administering vaccinations are likely to come into contact with potentially infectious body fluids or have open lesions on their hands. If gloves are worn, they should be changed between patients[13].

If an alcohol swab is used, it must be allowed to dry for at least two minutes, otherwise alcohol may be tracked into the muscle, causing local irritation and alcohol may also inactivate a live attenuated vaccine[10].

The vaccine providers were observed during vaccination of the children only 66% of them washed their hands before or after vaccination, this contribute to lack of washing facility in some vaccination rooms and absence of this habit from the nurse practice. 78.7% of nurses practice correct cleaning technique and allow skin to be dry before injection of the vaccine. Study done in Dammam by Mugarbel et al in 2007, found that hand washing was practiced by 18.2% of government health facilities[24].

This study reported remarkable improvement in the practice among vaccine providers when compared to a study done in Tripoli in 2003[16], regarding reconstitution and administration of vaccine in correct dose, site, route and following safe mechanism of needle and syringe disposal as recommended by WHO and center of disease control (CDC); this improvement contributed to good training program which conducted under supervision of national center for disease control and primary health care office in Tripoli.

CONCLUSION

In conclusion, there were some gaps in maintenance and practices regarding the cold chain system among health care workers in vaccination centers at Tripoli. Continuous training and regular supervision on national immunization program and the cold chain system are necessary to ensure optimal immunization effectiveness.

RECOMMENDATIONS

All healthcare providers who administer vaccines should evaluate their vaccine cold chain procedures to ensure that vaccine storage and handling best practices are being followed; organize to prevent power interruption in health facilities by stocking alternative sources of power; and training should occur whenever recommendations are updated and when new vaccines are added to maintain staff competency and to enhance practice skills for the management of cold chain.

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EFFICACY OF LOW DOSE HEAVY BUPIVACAINE WITH FENTANYL IN SPINAL ANESTHESIA FOR CAESAREAN DELIVERY

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ABSTRACT

Spinal anesthesia is a preferred anesthetic technique for elective caesarean deliveries, for which hypotension remains a significant side effect. We designed the present randomized trial to test the hypothesis that reducing the spinal dose of local anesthetics results in equally effective anesthesia and less maternal hypotension. One hundred patients with American Society of Anesthesiologists physical status (ASA) I–II, age 19 to 38 years, were randomized into two groups. The studied cases were admitted in Al-salam hospital, Misurata and Misurata central hospital.

Patients in group A (n=50) were given spinal anesthesia using 10 mg heavy Bupivacaine with 25 µg fentanyl. Patients in group B (n=50) were given spinal anesthesia using 7.5 mg heavy Bupivacaine with 25 µg fentanyl. Vital signs were monitored, the time it took to reach the T3 dermatomal level, duration of cesarean delivery, duration of adequate anesthesia. The Apgar score of the newborn were compared between the two groups. Duration of adequate anesthesia was longer in A group, more patients in the group experienced hypotension. However, Neonatal outcomes were similar in both groups. We conclude that small-dose spinal anesthesia (group B) better in preserving maternal hemodynamic stability with equally effective anesthesia that for shorter duration, it may be feasible only when the block can be reinforced using a functional epidural catheter.

KEY WORDS: Bupivacaine, Caesarean delivery, Fentanyl, Spinal Anesthesia, Hypotension.

INTRODUCTION

There are two general types of regional anesthesia for cesarean section and these are the spinal and epidural techniques. Both these techniques are commonly used to reduce the complications associated with general anesthesia such as pneumonia, post-operative pain, etc. Spinal anesthesia is simpler to place and it works fast enough to obtain effective sensory and motor block and so its use increase[(1)]. Many physiological and anatomical changes during pregnancy affect spinal anesthesia. The hormonal and mechanical factors make pregnant women require less local anesthetic than nonpregnant women to attain the same level of spinal anesthesia[(2)]. The factors that affect the sensorial blocked are baricity, dose, volume and concentration of local anesthetics, barbotage, and demographic properties of patients such as weight, height or age. Baricity is the most important factors for local anesthetic distribution. According to baricity conception, isobaric solution remains in proximity of the injection site and hyperbaric solution gravitate to dependent areas[(3)]. Bupivacaine is an amide local anesthetic with a moderately rapid onset and long duration of action, hyperbaric bupivacaine in 8% glucose has a specific gravity of 1021 at 37°C. Both isobaric and hyperbaric bupivacaine have been used for spinal anesthesia with good results[(4)]. The addition of opioids to local anesthetics for spinal anesthesia is increasingly common both to enhance anesthesia and to provide postoperative analgesia[(5)]. Among the synthetic opioids, fentanyl is favorable due to greater potency, faster onset of action and rapid redistribution with an associated decrease in the plasma concentration of the drug[(6)] and thus enhancing the early postoperative analgesia[(7)]. The present randomized, double-blind trial was designed to compare the hemodynamic effects and anesthetic efficacy of two intrathecal mixtures combining two doses of bupivacaine, each with 25 µg fentanyl.

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PATIENTS AND METHODS

With the approval of the hospital research ethics committee and written informed patient consent, 100 patients were enrolled from the admitted cases in Al-salam hospital, Misurata and Misurata central hospital. All enrolled patients with American Society of Anesthesiologists (ASA) physical status I and II, aged 19 to 38 years scheduled for elective caesarean section. Patients were randomized into two groups.

Patients in group A (n=50) were given spinal anesthesia using 10 mg heavy Bupivacaine with 25 µg fentanyl. Patients in group B (n=50) were given spinal anesthesia using 7.5 mg heavy Bupivacaine with 25 µg fentanyl.

Patients with preexisting hypertension or pregnancy induced hypertension requiring treatment, those with cardiac/renal or other end-organ disease, patients in active labor, multiple pregnancy, placenta previa and those with contraindication to neuraxial block were

excluded from the study. Obese patients (BMI>30) and patients with extreme height (<140 cm or >180 cm) were also excluded from the study.

Before the spinal block, a peripheral venous cannula 18-G was placed and intravenous infusion 10 ml/Kg Normal saline (0.9% sodium chloride) before induction. No vasopressors were administered before the procedure.

Under aseptic conditions, lumbar puncture was performed in a sitting position using a 25 gauge spinal needle at the level of the L3-4 interspaces. After the free flow of cerebral spinal fluid the specified drug in each group was injected slowly over 20 s, with the orifice of the spinal needle pointing cephalic. Patients were positioned immediately in supine position. The wedge was placed under patient's right buttock to avoid the supine hypotension syndrome. Oxygen was supplemented by face mask

Standard monitors such as electrocardiography, Pulse oximetry and noninvasive blood pressure cuff were applied.

Systolic and diastolic blood pressure were recorded every 2 min for the first 30 min and thereafter for every 5 min intraoperatively. A decrease of systolic blood pressure <95 mmHg or decrease >20% from baseline was considered as hypotension and treated with 6-9 mg of ephedrine. Sensory level of the block was assessed by loss of cold sensation bilaterally at 2 min intervals and confirmed by a pinprick method. Adequate anesthesia was defined as an upper sensory spread (absence of sensation to cold) to a level of T3. We measured the time it took to reach the T3 dermatomal level, duration of caesarean delivery and duration of adequate anesthesia (time from the start of spinal anesthesia to the time breakthrough pain occurred or the upper sensory level decreased to bellow T3).

If a bilateral T3 sensory level was not attained within fifteen minutes after the administration of the intrathecal drug, the patients were excluded from the study and given general anesthesia. If intraoperative pain persists after delivery, the treatment options are intravenous fentanyl 50 – 100 µg, A 50: 50 mixtures of nitrous oxide and oxygen given through the anesthetic machine.

Each newborn was examined by a pediatrician and was given an Apgar score.

Data Analysis:

The t-test was used to compare the results in the two groups, A P value < 0.05 was considered statistically significant.

RESULTS

(Table 1) shows no significant differences between groups regarding their age, weight, height or duration of surgery (P > 0.05).

All patients had satisfactory anesthesia, with the exception of only one case in Group B, converted to

(Table 1) Demographic Data of patient undergoing C\S using spinal anesthesia

Parameters	Group A (mean±SD)	Group B (mean±SD)
Age (years)	31± 4.8	33.2±5.4
Weight (Kg)	76.3± 10	78± 12.5
Height (Cm)	162.1± 4.2	160± 8.3
*Duration of surgery (min)	62± 9	61± 13

*Duration of surgery = time from the start of spinal injection and the end of surgery.

Thirty nine of the fifty patients in Group A had hypotension (systolic arterial pressure {SAP} dropped >20%). The incidence of hypotension in Group A was 78% (table 2).

Six of the forty nine patients in Group B had hypotension (SAP dropped >20%). The incidence of hypotension in Group B was 12.24% (table 2).

The t test was used to compare the incidence of hypotension in both groups. P value < 0.05 (significant).

(Table 2) Hemodynamic Data and Satisfactory for anesthesia of patient undergoing C\S using spinal anesthesia

Group	Total Number of patients	Number of Patients Satisfactory for Anesthesia	Number of Patients who Developed Hypotension
A	50	50	39 (78%)
B	50	49	6 (12.24)

The computed mean time in minutes required to achieve adequate anesthesia was 4.9± 1.3 SD in Group A versus 7.8±2 SD in group B (table 3) (P<0.05). The mean duration of adequate surgical anesthesia was significantly shorter in group B (low dose) {66±12 SD than 96±17 SD in group A, P < 0.05} (table 3). Four patients in group B required analgesia for control of pain, P < 0.05} (table 3).

(Table 3) Anesthetic and Surgical Data of patient undergoing C\S using spinal anaesthesia

	Group A	Group B
Time to T3 (min)	4.9±1.3	7.8±2
*Supplement required before delivery	0	0
Supplement required after delivery	0	4
**Duration of adequate anesthesia (min)	96±17	66±12

Time to T3 = Time required to reach dermatomal level T3 as assessed by cold discrimination.*

*Supplement required = the treatment option are intravenous fentanyl 50 – 100 µg, A 50: 50 mixture of nitrous oxide and oxygen.

*Duration of adequate anesthesia = the time from the start of spinal anesthesia to the time breakthrough pain occurred or the upper sensory level decreased to bellow T3.

There was no difference in neonatal Apgar scores in both groups at 1 min and 5 min after birth.

DISCUSSION

Spinal anesthesia is the preferred method for elective caesarean section as being simple to perform, econom-

ical and producing rapid onset of anesthesia with complete muscle relaxation. It carries high efficiency, involves less drug doses, minimal neonatal depression and lesser incidences of aspiration pneumonia. However, it also produces a fixed duration of anesthesia, lesser control of block height, postdural puncture headache and hypotension[2,8,9]. Subsequently, hypotension is known to result in maternal morbidity, nausea, vomiting, dizziness and can also directly influence the neonate well-being by reducing uteroplacental blood flow[2,10]. The link between the extent of sympathetic block and the incidence of hypotension has led to numerous attempts at reducing the dose of local anesthetic and also the addition of opioids due to their synergistic action with local anesthetics on the sensory block without increasing sympathetic block for cesarean section[2,11]. Several research papers have argued that the addition of various opioid to local anesthetic showed improved the intra and post-operative analgesic effect[12,13,14,15].

We observed that the systolic blood pressure was decreased significantly in group A (High dose) when compared to group B (low dose), mostly due to more sympathetic blockade by higher doses of bupivacaine in group A. Similar findings were observed by Himabindu et al and Bogra et al[2,16].

Our results revealed that the time required for the onset of sensory blockade up to T3 was faster in group-A than in group-B and is statistically significant with ($P < 0.05$).

The low dose bupivacaine combined with fentanyl in present trial produced adequate anesthesia, although of limited duration. Low dose spinal anesthesia is only feasible if epidural catheter backup is possible, as with a combined spinal- epidural technique.

CONCLUSION

In this study, we concluded that low dose spinal anesthesia with bupivacaine and fentanyl better preserves maternal hemodynamic stability while resulting in equally effective anesthesia. However, duration of adequate surgical block is limited, suggesting that these low doses only be used when the block can be reinforced with a catheter.

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EFFICIENCY OF LATERAL INTERNAL ANAL SPHINCTEROTOMY BY CLOSED METHOD UNDER LOCAL ANAESTHESIA AS AN OUT PATIENT PROCEDURE

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ABSTRACT

Chronic anal fissure is one of the main proctological disorders encountered in surgical outpatient departments, due to its high prevalence and the great discomfort involved.Though, the exact aetiology of primary anal fissure is still unknown, high resting anal pressure caused by increased internal sphincter tone appears to be the underlying pathological factor. So, the aim of this study is to determine the efficiency of the procedure of lateral internal sphincterotomy by closed method under local anaesthesia as an outpatient procedure. The clinical study was undertaken in all patients (70 patients, mean age 35 years) undergoing lateral closed sphincterotomy for chronic anal fissure (defined as anal fissure with > 6 weeks symptoms duration) from June 2005 to May 2006 who presented to Surgical OPD, in our hospital. Among 70 studied patients, 41 (58.5%) were females and 29 (41.4%) males. Age ranged from 16-63 years with the mean age of 35 years. Post-operatively, early complications included minor bleeding in two patients (3.4%) and incontinence of flatus in five patients (8.6%). In all the patients in our study lateral internal sphincterotomy was performed under local anesthesia and they were followed up for 4 months. 88% of patients were cured of their symptoms while only in 12% the fissure failed to heal. Lateral internal anal sphincterotomy by closed method under local anesthesia as an outpatient procedure has very good results in patients with chronic anal fissure who do not respond to conservative treatment.

KEY WORDS : Lateral internal anal sphincterotomy, Chronic anal fissure.

INTRODUCTION

Anal fissure results from longitudinal tear in the squamous epithelium of anal canal. Ninety percent are situated posteriorly and 10% anteriorly[(1)]. Chronic anal fissure is characterized by skin tag and hypertrophied anal papilla[(2)]. Though, the exact aetiology of primary anal fissure is still unknown, high resting anal pressure caused by increased internal sphincter tone appears to be the underlying pathological factor[(3)]. There is a vicious cycle beginning from a tear in the anoderm from forceful dilatation of the anal canal during defecation exposing the underlying internal sphincter muscle that eventually goes into spasm and fails to relax during next bowel movement. Further tearing results in persistent muscle spasm leading to relative ischemia of the anoderm causing persistence of symptoms and impairment of healing. The clinical history is typically cyclical; periods of acute pain are followed by temporary healing only to be followed by further acute pain. Inspection of perianal area is confirmatory in diagnosis. Digital examination is usually not possible because of severe pain. Lateral internal sphincterotomy emerged as the operation of choice for uncomplicated chronic anal fissure[(4)]. It is of two types, open and closed. Lateral internal sphincterotomy by closed method can be done under local anaesthesia[(5)], with less postoperative period of hospital stay and complications[(6)].

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AIM OF THIS STUDY

It is to determine the efficiency of the procedure of lateral internal sphincterotomy by closed method under local anaesthesia as an out patient procedure

PATIENTS AND METHODS

A clinical study was undertaken in all patients (70 patients, mean age 35 years) undergoing lateral closed sphincterotomy for chronic anal fissure (defined as anal fissure with > 6 weeks symptom duration) from June 2005, to May 2006 who presented to Surgical OPD,. Among patients, 29 (41.4%) were men and 41 (85.6%) were women. Atypical fissures associated with inflammatory bowel disease, cancer, or anal infections were excluded from the study. Exclusion criteria, also, were previous sphincterotomy or anal dilation and suspicion of malignant fissure or ulcer. The main complaints reported by all patients were persistent pain connected with defecation, small rectal bleedings, discharge and pruritis. In all of the patients conservative treatment had failed (lidocaine, hydrocortisone, glycerine trinitrate, sitz bath, and luxuatives). Closed lateral sphincterotomy was performed in all cases under local anesthesia using a short stab incision and blind division of the internal sphincter guided by the surgeon's finger. All operations were performed as a day case procedure in the Surgical OPD,

Ibn Sena Hospital, with no readmissions. In this series, 58 of the 70 patients were able to be followed up on regular basis for up to 4 months postoperatively and fissure healing was assessed by physical examination during patients' clinic visits after operation. The other 12 patients were lost and excluded from the study. Postoperative stay, relief of symptoms, symptoms of incontinence, time to fissure healing and complications were assessed.

RESULTS

Among 70 patients, 41 (58.5%) were females and 29(41.4%) males.

Age ranged from 16-63 years with the mean age of 35 years.

The maximum inciden of anal fissure was noted between 31-40 years (table 1).

(Table 1) Age range of patients

Age (years)	Frequency	%
10-20	7	10%
21-30	16	22.8%
31-40	23	32.8%
41-50	14	20%
51-60	8	11.4
61-70	2	2.8%

Pain, especially during defecation, was the principal symptom present in all the patients, more than 4 weeks in most. Bleeding per rectum in 18 patients (25.7%) and perianal swelling in 10 patients (14.2%). The anal fissure had been able to be seen in the posterior wall of the anal canal in 57 patients (81.4%) (table 2).

(Table 2) Presenting symptoms

Symptoms	Frequency	%
Pain	38	54.2%
Bleeding	18	25.7%
Perianal swelling	10	14.2%
Pruritis	4	5.7%

Post-operatively, early complications included minor bleeding in 2 patients (3.4%) and incontinence of flatus in 5 patients (8.6%) (table 3).

(Table 3) Early post-operative complications of Lateral Internal Anal Sphincterotomy. (n= 70)

Complication	Frequency	%
Bleeding	2	3.4%
Incontinence of flatus	5	8.6%

DISCUSSION

Chronic anal fissure is one of the main proctological disorders encountered in surgical outpatient departments, due to its high prevalence and the great discomfort involved. There were 70 patients in our study. The age range of these patients was 16-63 years with the mean age of 35 years. Thirty three percent of patients were in 31- 40 years age group followed by patients in the age range of 21-31years. Shafiqullah et al[7] reported 32% in 20-30years and 46% in 31-40 years age groups. Mean age reported in different studies range from 30-45years[8] but Cho DY noticed that confounding effects of age, gender, body weight, and height were not significant[9]. Among the seventy patients in our study, 57(81.4%) patients had posterior midline fissure while 11 (15.7%) were found to have anterior midline fissure. The increased number in posterior fissure support the fact that posterior fissure is more common than anterior one. Ninety per cent of acute fissures respond to conservative treatment with a fibre-rich diet and warm sitz baths. However, many acute fissures persist for several weeks and may become chronic. Conservative methods of treatment of chronic anal fissure have been proposed such as botulinum toxin[11-16], nitrate preparations[10,17], and nifedipine[18] and surgical treatments such as anal dilatation[19, 20], sphincterotomy[21-24], and advanced flap[22]. All these techniques aim at a high rate of healing in association with a low morbidity rate. Internal lateral sphincterotomy has been proven the procedure of choice in various comparative studies, since it exhibits the highest rate of healing associated with the lowest indexes of incontinence. Two types of internal lateral sphincterotomy have been widely discussed in the literature: open sphincterotomy, first described in 1951 by Eisenhamer[25], and closed or subcutaneous sphincterotomy, first described in 1971 by Notaras[26]. In all the patients in our study, lateral internal sphincterotomy was performed under local anesthesia and were followed up for 4 months. 88% of patients were cured of their symptoms while only in 12% the fissure failed to heal, although the symptoms had decreased in severity and the patients were not willing for further operations. Post-operative impairment of continence is not uncommon. Lewis et al[27] found some degree of incontinence in 17% of their patients; in two thirds of these patients, this complication was only temporary. Khubchandani and Reed reported postoperative soiling in 22% and grade-I incontinence in 35 % of patients after sphincterotomy[28]. In the present study, 8.6 % had mild soiling which resolved within 2 to 3 months. All of the above mentioned results are close to our results in term of success rate and rate of complications.

CONCLUSION

Lateral internal anal sphincterotomy by closed method under local anesthesia has very good results in patients with chronic anal fissure who do not respond to conservative treatment.

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END-STAGE RENAL DISEASE IN MISURATA

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ABSTRACT

The prevalence of End-stage renal disease (ESRD) has been continuously increasing in most of countries. ESRD requiring renal replacement therapy poses a tremendous burden on health care budgets. Unfortunately, there are no studies on the epidemiology and prevalence of ESRD in Misurata city, hence, our study was conducted to assess the prevalence, etiology and risk factors for ESRD patients on haemodialysis (HD) at Misurata city during the year 2005. This is a descriptive study conducted retrospectively by reviewing files of all patients attending haemodialysis unit at Misurata Central Hospital during 2005. The total number of ESRD patients undergoing haemodialysis from January 2005 to December of the same year was 70 patients. Their mean age was 36.4±17.7 years, and of median 37.7 (range 3-69). The male constituted 55.7% while female patients were 44.3% with male to female ratio of 1.25:1. The estimated prevalence of ESRD was 34.71% patients per 100.000 populations. The most common causes of ESRD were diabetes mellitus in 28.5% and hypertension in 17.1% followed in order by undetermined causes in 15.7%, glomerulonephritis in 14.3%, chronic pyelonephritis in 8.6%, drug nephrotoxicity in 5.7%, other less common causes like obstructive uropathy, polycystic kidney disease, gout and IgA nephropathy also was reported in our study. The most common causes of ESRD were found to be DM and HTN, affecting young- age population. This suggests that we need to improve our health care system and implementation of effective reno-protective strategies.

KEY WORDS: ESRD, prevalence of dialysis, renal replacement therapy, ESRD risk factor, Misurata.

INTRODUCTION

Chronic Kidney Disease (CKD) is a common condition that is often unrecognized until the very advanced stages occur. The incidence of CKD is rising due to the aging of population and higher incidence of diseases, such as Diabetes mellitus (DM) and Hypertension (HTN) in the adult population[(1-4)].

DM and HTN are emerging as the most common causes of CKD[(5)]. According to the international guideline[(6)], strict blood pressure control, regulation of calcium /phosphate metabolism and maintaining an optimum hemoglobin concentration are three main essential treatment for Reno-protection and better prognosis in CKD patients.

Since renal replacement therapy (RRT) for end-stage renal disease (ESRD) became widely available in 1960s, the number of prevalent patients on RRT has continued to rise at an alarming rate[(7)].

The prevalence of ESRD has been continuously increased in most of countries: it is currently higher than 2000 pmp in Japan, about 1500 pmp in the US, and about 800 pmp in the European Union. Yet, in the developing countries, the figures vary from less than 100 pmp in sub-saharan Africa and India to about 600 pmp in Saudi Arabia[(8)]. ESRD requiring RRT poses a tremendous burden on health care budgets, even for highly developed countries[(9)]. In the developing countries the real prevalence of Chronic Renal Failure (CRF) is difficult to be determined since medical facilities are limited. In the absence of a central medical registry, the only data available are center-based[(10)].

Unfortunately, there are no studies on the epidemiology and prevalence of CRF in the city of Misurata. Haemodialysis (HD) represents the only mode of renal replacement therapy in our area.

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AIM OF THE STUDY

The aim of this study is to assess the prevalence, etiology and risk factors for ESRD patients on HD at Misurata city during the year of 2005.

PATIENTS AND METHODS

This study was conducted at Misurata Central Hospital, a 500-bed capacity teaching hospital established in 1973. The hospital has a catchment population of approximately 350,000 persons.

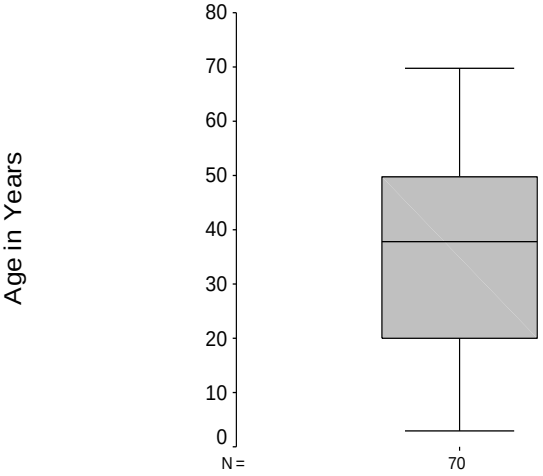
This is a descriptive study done retrospectively by reviewing the files of all patients attending Haemodialysis unit at Misurata Central Hospital during the year of 2005. There were 24 haemodialysis stations serving over 210 sessions per week. A total of 70 pa-

tients were on haemodialysis programmed at the time of the study with a rate of 3 sessions per week of 3-hours duration. Data of the study include age, sex, and other risk factors like diabetes mellitus, hypertension, family history of renal failure and history of other diseases of genetic and autoimmune basis were obtained. Renal biopsy had been performed in only 2 cases (2.8%) at some time in the course of the disease and both were performed out of the hospital.

All data were analyzed by using the statistical package for social science (SPSS program). Data were expressed as frequency and percentage and then displayed in appropriate tables and figures.

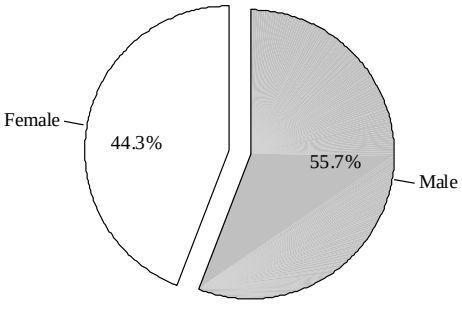
RESULTS

The results showed that all the 70 patients were on regular haemodialysis at the rate of 3 times/week. Their ages ranged from 3 to 69 years with median age at starting HD 37.7 with mean ± standard deviation of 36.4± 17.7 as shown in (figure 1).



(Figure 1) Age distribution of patients at starting haemodialysis

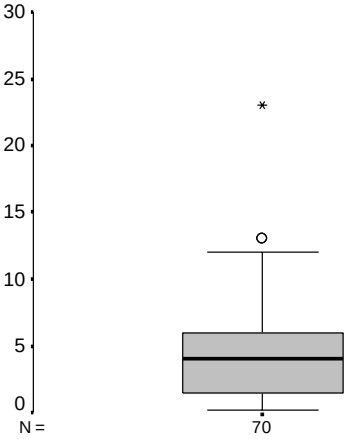
The male group constituted 55.7% (39 patients) of the study population and the female group 44.3%



(Figure 2) Distribution of gender among the studied group

The estimated prevalence of ESRD was 34.71 patients per 100.000 population.

The result showed that the minimum duration of haemodialysis is about 6 weeks and the maximum is 23 years with mean ± standard deviation duration of 4.65± 3.99 years and median of 4 years as can be seen in (figure 3).



(Figure 3) Duration of haemodialysis among the studied group

(Table 1) shows that history of diabetes mellitus (DM) and hypertension (HTN) were obtained from 28.5% (20 patients), 17.1% (12 patients) respectively and they were considered the most prevalent among patients with ESRD on regular HD. Other important causes are chronic glomerulonephritis, chronic pyelonephritis and drug nephrotoxicity (14.3% , 8.6% and 5.7%) respectively. Other less common causes include obstructive uropathy, polycystic kidney disease, gout, and IgA nephropathy(4.3% , 2.8% , 1.4% and 1.4%) respectively. The etiology of ESRD was not known in 15.7% of all the patients.

(Table 1) Causes of ESRD among the studied group

History of risk factor	Frequency	%
Diabetes	20	28.5
Hypertension	12	17.1
Undetermined	11	15.7
Ch G.N	10	14.3
Chronic Pyelonephritis	6	8.6
Drug ephrotoxicity	4	5.7
Obstructive ropathy	3	4.3
poly cystic Kidney	2	2.8
Gout	1	1.4
IgA Nephropathy	1	1.5
Total	70	100%

DISCUSSION

This epidemiological study provides the first retrospective evaluation of ESRD undergoing haemodialysis in Misurata area. Intermittent haemodialysis is the only option of renal replacement therapy available. There is no use of other modalities of dialysis like peritoneal dialysis, due to shortage in training for this kind of treatment and renal transplant is also limited because of the shortage of donors.

Renal biopsy is not practiced in our hospitals due to the lack of facility. The two biopsies that were reported in this study had been performed abroad.

The prevalence rate of ESRD on HD in Misurata area can be estimated after adding 33 patients from Alzarouk dialysis center and the total of Misurata population according to the last national population census of the year 2004 which was 296.735[11].

The prevalence rate is approximately 34.71 per 100.000 populations. This rate if adjusted to millions of population will be near that estimated for the Mediterranean region of 312 to 352 pmp[12, 13], but higher than that reported in Egypt (El-minia Governorate) 260 pmp in 2005[14]. It was less than that reported in the US, European union and Saudi Arabia which were found to be 1500, 800, 600 pmp, respectively[8].

These international differences in the prevalence rate could be explained by medical factors (e.g. Prevalence of DM and HTN) or by non medical factors (e.g. Non referral to nephrologists)[7]. The etiology of ESRD was unknown in our results with 15.7% of the patients, which coincides with that in Iraq (14%), Qatar (14%) and Iran (14.8%)[15]. It was less than reported in Egypt (27%)[16], but higher than that reported in the US (3.7%)[17].

This marked difference reflects the late referral of the patients by treating doctors to nephrology centers as well as the patients lack of education about the proper time to seek medical advice. Late referral to nephrologist is associated with increasing the risk of death[18].

In the current study, the surprising and alarming result was that ESRD affecting the young population with mean age of 36.4± 17.7, especially when compared to that reported in the USA (60 years)[19], or that reported in France (70.4 years)[20]. This marked increase in mean age in patients from these countries may reflect the improvement in ESRD care, while in our country the disease is affecting young people at their productive period of life. Therefore it is important to have future strategy in order to reduce morbidity and to save resources.

In our study, the prevalence of ESRD was higher in the male group than in female group (55.7% vs. 44.3%, respectively), which was observed in other countries too[16,21-24].

In this study DM (28.5%), HTN (17.1%) were the most common causes of ESRD followed by Glomerulonephritis (14.3%) and chronic pyelonephritis (8.6%). DM and HTN also reported as the commonest causes of ESRD in USA, where DM constitutes 44.4% of the causes of ESRD followed by HTN in 26.6 %[25]. This could be due to steady increase in the prevalence of diabetes[26] and hypertension[27] in general population.

Diabetic nephropathy was the most frequent cause among new ESRD patients in Qatar (48%)[28], while hypertension was the commonest cause of ESRD in Egypt (20%)[13] and in Iran (30.5%)[29]. We also found out that 4.28% of ESRD was because of obstructive uropathy which is not far from what was reported in Qatar (5%)[28] and in Aleppo-Syria (6%)[30], but less than that reported in Iraq (17.3%)[15].

Drug nephrotoxicity was seen in 5.7%, while in the US was only 0.2 %[17], which reflects poor education regarding the hazard of excessive use of analgesics in our locality. The prevalence of Glomerular disease as a cause of ESRD in this study (14.28%) was higher than the result from Qatar (13%)[28], the USA (9.9%)[25] and the KSA (9.9%)[31]. Such high result need more evaluation, it could be overestimated because of the suggestive presentation of chronic glomerular disease or biopsy proven cases which included in this study. However biopsy is not practiced in our hospital.

Among other causes of ESRD, Pyelonephritis occurred in 8.57% which is higher than the prevalence reported in Iran (4.6%)[32] and Iraq (4.7%)[15], which may reflect high prevalence of infections.

CONCLUSION

In conclusion, this study found out that ESRD is affecting young people and the two most important leading causes of ESRD were Diabetes and Hypertension. This disease is threatening our health system that should stimulate further action to control its progression by efforts to improve early nephrological referral of renal patient, aggressive approaches to control blood glucose and blood pressure, and also by implementation of effective Reno-protective strategies. However, those patients with undetermined causes were high in this result, which reflects some diagnostic limitations.

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LAPAROSCOPIC OVARIAN DRILLING TREATMENT OPTION FOR POLYCYSTIC OVARY AND INFERTILITY

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ABSTRACT

To find out the effectiveness of laparoscopic ovarian drilling (LOD) in patients clinically and radiologically diagnosed as Polycystic Ovarian Syndrome (PCOS) suffering from infertility and to find out factors that may predict the outcome of LOD. This prospective study included 186 patients with anovulatory infertility due to PCOS who underwent LOD during the period from January 1st 2007 to December 31st 2008. Diagnosis was made according to the European Society of Human Reproduction and Embryology (ESHRE) criteria for PCOS. Body Mass Index (BMI), serum Testosterone level and serum LH was taken from the patients. All patients were followed up till they got pregnant or for a period of 12 months after the procedure. Out of 186 patients, 102 (55%) conceived after long term infertility ranged from 3-15 years, Antenatal complications were not significant as there was 1 twins pregnancy, 3 miscarriages and 1 ectopic pregnancy, Patients with Body Mass Index $\geq$ 35 kg/m^2 and serum testosterone level $\geq$ 4.5 nmol/l seems to be poor responders for LOD, meanwhile those with Serum LH level > 10 IU/L appears to be associated with higher pregnancy rate after LOD. LOD gave good fertility rates in patients with PCOS in which medical ovulation induction failed, marked obesity and hyperandrogenism are a marked predictor for resistance to LOD, while high level of LH predicts to a higher probability of pregnancy.

KEY WORDS: Laparoscopic Ovarian Drilling, Polycystic Ovarian Syndrome, anovulation, infertility.

INTRODUCTION

Polycystic ovarian syndrome (PCOS) is one of the most common female endocrine disorders affecting approximately 5 -10 % of women of reproductive age (12–45 years old) and is thought to be one of the leading causes of female sub-fertility.

It comprises a heterogeneous mixture of clinical and diagnostical findings. Polycystic ovarian syndrome (PCOS) is the most common cause of anovulatory infertility, being found in 75% of cases[1,2,3,4].

The pathology of polycystic ovarian disease (PCOD) was described by Stein and Leventhal in 1935. It is characterized by infertility, oligomenorrhoea or amenorrhea, hirsutism, acne, and bilaterally enlarged cystic ovaries sonographic appearance of polycystic ovary (figures 1& 2).

The principal features are obesity, anovulation (resulting an irregular menstruation or amenorrhea), acne, and excessive amounts of androgenic (masculinizing) hormones[5].

The aetiology of the PCOS is based on two major concepts, hyperandrogenism and insulin resistance. The classical hypothesis as proposed by Yen postulates an initial androgen excess. Androgens are aromatized in peripheral tissue to estrogens, resulting in an imbalance of luteinizing hormone (LH) and follicle stimulating hormone (FSH) secretion on the pituitary level with endogenous hyper secretion of LH. The LH strongly stimulates the intra ovarian androgen production. This classical concept has been extended by the role of hyperinsulinaemia in PCOS patients. Insulin resistance can be found in up to 50% of women with PCOS. Insulin like LH stimulates directly the ovarian biosynthesis of steroid hormones, in particular, of ovarian androgens. Furthermore, insulin decreases the sex-hormone-binding globulin (SHBG) production in the liver, thus, further elevating free androgen levels. Therefore, both pathways end in the stimulation of ovarian theca cells with elevated ovarian androgen production, resulting in disturbed folliculogenesis, cycle disorders and chronic anovulation. This pivotal role of the ovary for the aetiology of the PCOS has favored therapeutical concepts, which might directly correct the intra ovarian pathology[6].

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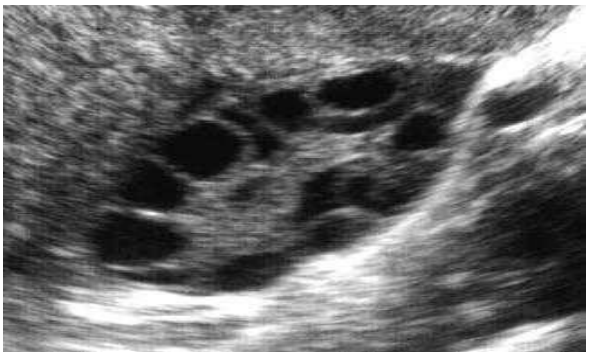
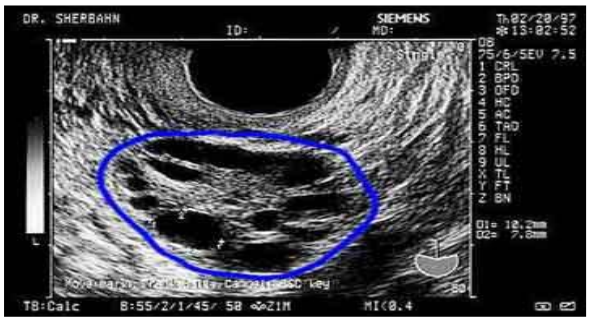


(Figure 1) Sonographic appearance of polycystic ovary



(Figure 2) Sonographic appearance of polycystic ovary

Laparoscopic ovarian drilling (LOD) has been widely used to induce ovulation in PCOS women after failure of treatment with Clomiphene Citrate (CC) and Human menopausal Gonadotropin (HmG)**.** Laparoscopic drilling of the ovaries is an alternative treatment for patients with clomiphene citrate resistant polycystic ovary syndrome. This involves a single procedure, which has minimal morbidity, which can lead to consecutive ovulations with minimal risks of multiple pregnancy. Patients may also respond to clomiphene citrate after this treatment **.** The mechanism of action of LOD is not fully understood and therefore it is not exactly clear why some PCOS patients fail to respond to this treatment. A possible explanation is that the amount of ovarian tissue destroyed during LOD is not sufficient to produce an effect in some patients. However, others believe that ovarian diathermy works by increasing the sensitivity of the ovaries to endogenous FSH. Hence another possible explanation of failure to respond is an inherent resistance of the ovary to the effects of drilling[7,8,9,10].

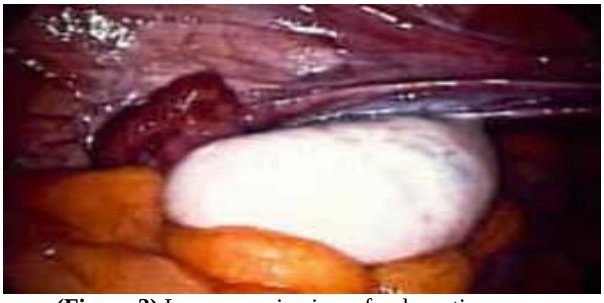
If it were possible to identify the factors that determine the sensitivity of PCOS patients to LOD, then fruitless treatment could be avoided and success rates improved[11,12].

MATERIALS AND METHODS

Between January 1st 2007 to December 31st 2008 186 patients with primary or secondary infertility due to PCOS underwent LOD at the Infertility Unit, department of Gynecology, Misurata Oncology Center. All patients were evaluated clinically, radiologically and biochemically and BMI was calculated. All patients had infertility of > 1 year duration, 154 had been treated with Clomiphene Citrate (CC) up to 200 mg / day for 5 days from D2 – D6 and for a period of 6-12 months, while 32 patients were induced with Human menopausal Gonadotropin and failed to conceive.

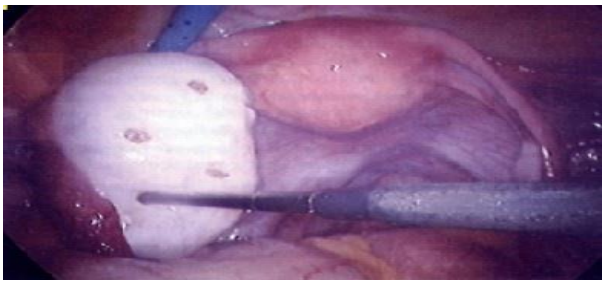
Diagnosis of PCOS was made according to the ESHRE criteria for diagnosis of PCOS: The main criteria are chronic anovulation, clinical and / or biochemical signs of hyperandrogenism and polycystic ovaries by ultrasound. At least two out of these three criteria must present. Furthermore, other etiological factors like cushing syndrome, androgen-producing tumors or congenital adrenal hyperplasia are excluded. Serum hormonal concentrations (FSH, LH and Testosterone) were all measured prior to the procedure using well established assays. All patients underwent transvaginal scanning prior to LOD using Aloka 1500 with a convex 6.5 MHz transvaginal probe.

Laparoscopic view of polycystic ovary as shown in (figure 3).



(Figure 3) Laparoscopic view of polycystic ovary

LOD was done bilaterally using monopolar electrosurgical unit**.** Coagulation current at 35 W power setting was used, 4-5 punctures made for each ovary in different areas with a 5 seconds puncture duration**.** Laparoscopic ovarian drilling as shown in (figure 4).



(Figure 4) Laparoscopic ovarian drilling

Postoperative monitoring; patients were asked to keep a record of their menstrual cycle, then they were followed up by ultrasound and by investigations to find out if spontaneous ovulation happed or not, if not then ovulation induction medication was added and patients were followed up till they conceived or for a period of 12 months.

Analysis of Data

The data were entered into the Statistical Package for Social Science (SPSS) for windows version 11.

Data were tabulated using frequency distribution tables and analyzed using proportions and chi square

test. A p-value of less than 0.05 was taken as the level of statistical significance.

RESULTS

The influence of patients preoperative characteristics including age, BMI duration of infertility, presence or absence of acne or hirsutism, menstrual pattern, serum FSH, serum concentrations of LH and testosterone were studied. As shown in (table 1) and (table 2).

(Table 1) Blood LH and testosterone levels were divided into three categories: normal , moderately elevated and markedly elevated

	Normal	Moderately elevated	Markedly elevated
LH (IU/L)	< 10	10 – 19.9	≥ 20
Testosterone (nmol/L)	< 2.6	2.6 – 4.4	≥ 4.5

(Table 2) The characteristics of all 186 patients whom underwent LOD for infertility were as follows

(Table 2-A)

Characteristic	Patient No.	Mean	S.D.
Age (years)	186	32.1 yrs	(4.1)
BMI (kg/m^2)	186	33.4	(5.2)
Duration of infertility (years)	186	3.3 yrs	(2.1)
S. LH (IU/L)	162	13.1	(6.3)
S. FSH (IU/L)	162	5.2	(1.3)
S. Testosterone (nmol/L)	112	2.9	(1.4)

(Table 2-B)

	Patient No.	%
Menstrual Pattern	186	
- Regular	35	19
- Oligomenorrhoea	151	81
Hirsutism	186	
- Yes	121	65
- No	65	35
Acne	186	
- Yes	113	61
- No	73	39
Infertility	186	
- Primary	132	71
- Secondary	64	29
evidence of PCO	186	
- U/S evidence	153	82
- Biochemical Criteria for PCO.	33	18

Menstrual pattern definition: regular cycles: cycle length between 25 and 35 days; oligomenorrhoea: cycle length > 35 days

A total of 186 patients with anovulatory infertility associated with PCOS who underwent LOD were included in this study. The characteristics of this group of women are shown in (table 2).

Among the 186 patients included in the study, 108 (58%) ovulated after LOD with the addition of Clomiphene Citrate and 17 (9%) ovulated spontaneously giving an overall ovulation rate of 125 (67%) patients, 102 (55%) conceived. One patient conceived with twins, giving a multiple pregnancy rate of (1%). Of the 102 pregnancies, three (3%) ended in miscarriages and one (1%) was ectopic pregnancy.

The results in (table 3) shows that women with over weight (BMI ≥ 35 kg/m2) achieved significantly less pregnancy rates (13%, respectively) compared with obese (BMI 29.1-34.4 kg/m2) women (49%) and with women with normal/ underweight (BMI < 29 kg/m2) (52%).

(Table 3) Factors affecting the success rates of LOD

	Category	N	Pregnancy Rate %	Chi square with p value
Age	≤ 35	174	46	X^2_{df-1} 0.073, p-value >0.05
	> 35	12	49	
BMI (kg/m^2)	< 29	107	52	X^2_{df-2} 8.922, p-value <0.05
	29.1 – 34.4	63	49	
	≥ 35	16	13	
LH (IU/L)	< 10	48	36	X^2_{df-2} 1.208, p-value >0.05
	10.1 – 19.9	83	44	
	≥ 20	31	45	
Testosterone (nmol/L)	< 2.6	56	54	X^2_{df-2} 4.732, p-value >0.05
	2.6–4.4	48	47	
	≥ 4.5	8	10	

As far as the androgens are concerned, ovulation and pregnancy rates showed significant reduction with increasing androgen levels: in women with testosterone levels ≥4.5 nmol/l, the rate was 10%, which were significantly lower than those (47%) of women with moderately elevated testosterone (2.6–4.4 nmol/l). Patients with normal serum testosterone levels (< 2.6 nmol/l) showed higher pregnancy rate (54%) than the other groups.

There was a trend towards higher conception rates with increasing levels of LH. Further analysis revealed that once ovulation was achieved, serum LH levels had a statistically significant impact on the pregnancy rate: LOD responders with pre-treatment serum LH concentrations ≥10 IU/l achieved a significantly higher pregnancy rate than that of responders with serum LH concentrations <10 IU/l.

DISCUSSION

Common symptoms of PCOS includes Oligomenorrhoea, amenorrhea irregular or absent menstrual periods, infertility generally resulting from chronic an ovulation (lack of ovulation).

Hirsutism, excessive mild symptoms of hyperandrogenism such as acne. In most instances, these symptoms are transient and only reflect the immaturity of the hypothalamic-pituitary-ovarian axis during the first years following menarche. Approximately three-fourths of patients with PCOS (by the diagnostic criteria of NIH/NICHD 1990) have evidence of hyperandrogenemia**.** PCOS can present in any age during the reproductive years. Due to its often vague presentation it can take years to reach a diagnosis, Serum insulin, insulin resistance and homocysteine levels are significantly higher in subjects having PCOS but have no significant effect on fertility[13].

Not all women with PCOS have polycystic ovaries (PCO), nor do all women with ovarian cysts have PCOS. Although a pelvic ultrasound is a major diagnostic tool, it is not the only one. The diagnosis is straightforward using the Rotterdam criteria, even when the syndrome is associated with a wide range of symptoms.

Standard diagnostic assessments

History-taking, specifically for menstrual pattern, obesity, hirsutism, and the absence of breast development. A clinical prediction rule found that these four questions can diagnose PCOS with a sensitivity of 77.1% (95% confidence interval [CI] 62.7%–88.0%) and a specificity of 93.8% (95% [CI] 82.8%–98.7%)[14]. Gynecologic ultrasonography, specifically looking for small ovarian follicles. These are believed to be the result of disturbed ovarian function with failed ovulation, reflected by the infrequent or absent menstruation that is typical of the condition. In normal menstrual cycle, one egg is released from a dominant follicle essentially a cyst that bursts to release the egg. After ovulation the follicle remnant is transformed into a progesterone producing corpus luteum, which shrinks and disappears after approximately 12–14 days. In PCOS, there is a so called "follicular arrest", i.e., several follicles develop to a size of 5–7 mm, but not further. No single follicle reach the pre ovulatory size (16 mm or more). According to the Rotterdam criteria, 12 or more small follicles should be seen in an ovary on ultrasound examination. The follicles may be oriented in the periphery, giving the appearance of a 'string of pearls Laparoscopic examination may reveal a thickened, smooth, pearl-white outer surface of the ovary. (This would usually be an incidental finding if laparoscopy were performed for some other reason, as it would not be routine to examine the ovaries in this way to confirm a diagnosis of PCOS). Blood level of androgens including androstenedione and testosterone may be elevated[15]. The free testosterone level is thought to be the best measure with ~ 60% of PCOS patients demonstrating supra normal levels. The Free androgen index of the ratio of testosterone to sex hormone-binding globulin (SHBG) is high, is meant to be a predictor of free testosterone, but is a poor parameter for this and is no better than testosterone alone as a marker for PCOS, possibly because FAI is correlated with the degree of obesity. Some other blood tests are suggestive but not diagnostic[16].

The ratio of LH (Luteinizing hormone) to FSH (Follicle stimulating hormone) is greater than 1:1, as tested on Day 3 of the menstrual cycle. The pattern is not very specific and was present in less than 50% in one study. There are often low levels of sex hormone binding globulin, particularly among obese women[17].

Pathogenesis

Polycystic ovaries develop when the ovaries are stimulated to produce excessive amounts of male hormones (androgens), particularly testosterone, either through the release of excessive luteinizing hormone (LH) by the anterior pituitary gland or through high levels of insulin in the blood (hyperinsulinaemia)[18]. In women whose ovaries are sensitive to this stimulus. The syndrome acquired its most widely used name due to the common sign on ultrasound examination of multiple (poly) ovarian cysts. These "cysts" are actually immature follicles, not cysts ("polyfollicular ovary syndrome" would have been a more accurate name), the follicles have developed from primordial follicles, but the development has stopped ("arrested") at an early antral stage due to the disturbed ovarian function. The follicles may be oriented along the ovarian periphery, appearing as a 'string of pearls' on ultrasound examination. The condition was first described in 1935 by Dr. Stein and Dr. Leventhal, hence its original name of Stein-Leventhal syndrome[5]. PCOS is characterized by a complex set of symptoms, and the cause cannot be determined for all patients. However, research to date suggests that insulin resistance could be a leading cause. PCOS may also have a genetic predisposition, and further research into this possibility is taking place. No specific gene has been identified, and it is thought that many genes could contribute to the development of PCOS. A majority of patients with PCOS have insulin resistance and/or are obese. Their elevated insulin levels contribute to or cause the abnormalities seen in the hypothalamic-pituitary-ovarian axis that lead to PCOS[18]. Adipose tissue possesses aromatase, an enzyme that converts androstenedione to estrone and testosterone to estradiol. The excess of adipose tissue in obese patients creates the paradox of having both excess androgens (which are responsible for hirsutism and virilization) and estrogens (which inhibits FSH via negative feedback)[19].

Also, hyperinsulinaemia increases GnRH pulse frequency, LH over FSH dominance, increased ovarian androgen production, decreased follicular maturation, and decreased SHBG binding; all these steps lead to the development of PCOS. Insulin resistance is a common finding among patients of normal weight as well as those overweight patients. PCOS may be associated with chronic inflammation, with several investigators correlating inflammatory mediators with an ovulation and other PCOS symptoms[20]. 20 to 30% of ovulatory PCOS women fail to respond to LOD. It may be due to the amount of LOD is not sufficient to produce an effect in patients. But studies revealed that LOD increases the endogenous FSH and only a minimal amount of thermal energy is required. Another possible explanation may be failure to respond is an inherent resistance ovary to the effects of drilling[21]. Another cause may be hyperprolactaenaemia observed in some patients after LOD. It is important to monitor the patients for prolactin levels after LOD. The drawback with LOD is to quantify the dose of diathermy to a particular patient. It is difficult to decide the dose for a particular patient without knowing the dose re-

sponse. There is a need to optimize the dose of LOD in response to ovarian size. However the predictors of success of LOD depends on the body mass index, serum testosterone concentration and duration of infertility. These predictors will help in selection patients for LOD with infertility more than 3 years, high testosterone levels are advised to take gonadotrophin therapy and IVF. In this study, we have evaluated the impact of various clinical, biochemical and Ultrasonographic features of PCOS on the clinical outcome of LOD in 186 PCOS women. In addition, we have also reported on the factors affecting the duration of the beneficial effects of LOD. Eighteen percent of PCOS women in this study had apparently regular menstrual cycles prior to LOD. Although chronic anovulation in women with PCOS is usually associated with menstrual irregularities, several authors have reported that 16–24% of these women do have apparently regular menstrual cycles. Furthermore, many anovulatory PCOS patients ovulate occasionally and some may resume regular menstrual cycles for variable periods of time. This explains why some anovulatory PCOS patients conceive spontaneously while being investigated for infertility or waiting for treatment[22]. Our data showed three main factors to have a significant impact on the efficacy of LOD, namely BMI, hyperandrogenism and serum LH levels. Women with marked obesity (BMI $\geq$ 35 kg/m2), marked hyperandrogenism (testosterone $\geq$ 4.5 nmol/l) and low serum LH seem to be resistant to LOD. With regards to LH levels, once ovulation was achieved, LH levels had a significant impact on the pregnancy rates. Not all women with PCOS have difficulty becoming pregnant. For those who do, anovulation is a common cause. Ovulation may be predicted by the use of urine tests that detect the preovulatory LH surge, called ovulation predictor kits (OPKs). However, OPKs are not always accurate when testing on women with PCOS[23]. Charting of cervical mucus may also be used to predict ovulation, or certain fertility monitors (those that track urinary hormones or changes in saliva) may be used. Methods that predict ovulation may be used to time intercourse or insemination appropriately. While not useful for predicting ovulation[24]. basal body temperatures may be used to confirm ovulation. Ovulation may also be confirmed by testing for serum progesterone in mid-luteal phase, approximately seven days after ovulation (if ovulation occurred on the average cycle day of fourteen, seven days later would be cycle day 21). A mid-luteal phase progesterone test may also be used to diagnose luteal phase defect. Methods that confirm ovulation may be used to evaluate the effectiveness of treatments to stimulate ovulation[25]. For overweight women with PCOS, who are anovulatory, diet adjustments and weight loss are associated with resumption of spontaneous ovulation. For those who after weight loss still are anovulatory or for anovulatory lean women, CC and FSH are the principal treatments used to help infertility. Previously, even metformin was recommended treatment for anovulation. But in the largest trial to date, comparing clomiphene with metformin, clomiphene alone was the most effective[26]. The most drastic increase in ovulation rate occurs with a combination of diet modification, weight loss, and treatment with metformin and clomiphene citrate[27]. It is currently unknown if diet change and weight loss alone have an effect on live birth rates comparable to those reported with clomiphene and metformin. For patients who do not respond to clomiphene, diet and lifestyle modification, there are options available including assisted reproductive technology procedures such as controlled ovarian hyperstimulation with FSH injections and in vitro fertilization (IVF)[28]. Ovarian stimulation with FSH followed by hCG has an associated risk in women with PCOS of ovarian hyperstimulation syndrome — an uncomfortable and potentially dangerous condition with morbidity and rare mortality[29]. Thus recent developments have allowed the oocytes present in the multiple follicles to be extracted in natural, unstimulated cycles and then matured in vitro, prior to IVF. This technique is known as In vitro maturation (IVM). The RCOG (The Royal College of Obstetricians and Gynecologists) published an opinion paper on "Metformin therapy for the management of women with polycystic ovary syndrome", The paper concluded that while initial studies appeared to be promising, more recent large randomized controlled trials have not observed beneficial effects of metformin either as first-line therapy or combined with clomiphene citrate for the treatment of the anovulatory woman with PCOS. Most work has been undertaken in the management of anovulatory infertility and there are no good data from randomized controlled trials on the use of metformin in the management of other manifestations of PCOS. It is clear that the first aim for women with PCOS who are overweight is to make lifestyle changes with a combination of diet and exercise in order to lose weight and improve ovarian function.

The European Society for Human Reproduction and Embryology and American Society for Reproductive Medicine consensus on infertility treatment for PCOS concluded that there is no clear role for insulin sensitizing and insulin lowering drugs in the management of PCOS, and should be restricted to those patients with glucose intolerance or type 2 diabetes rather than those with just insulin resistance. Therefore, on current evidence that metformin is not a first line treatment of choice in PCOS(RCOG Dec. 2008)

CONCLUSION

LOD gives good fertility rates in patients with PCOS in which medical treatment failed,

Obesity and hyperandrogenism seems to predict resistance to LOD, while high level of LH appears to predict higher probability of pregnancy.

LOD is a safe and cost effective procedure. A single treatment results in uni- follicular ovulation.

No need of continuous monitoring as seen with hormonal treatment and no fear from ovarian hyperstimulation. Correction of hormonal levels prevents miscarriages. LOD increase the sensitivity to Gonadotropin and it is effectiveness in PCO.

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LATENT HSV-1 INFECTION CAN BE ESTABLISHED IN KERATINOCYTE CELLS FOLLOWING TREATMENT WITH MITOTIC INHIBITORS

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ABSTRACT

Herpes simplex virus type 1 (HSV-1) infection of murine keratinocyte cell lines (HEL-30 and PAM-212) treated with mitotic inhibitors leads to silencing of virus replication. At 0.1 (Multiplicity of infection) MOI, PAM-212 keratinocytes showed some cell lysis; and viral plaques were seen in HEL-30 keratinocyte cultures. PAM-212 keratinocytes, infected at 0.01 MOI, were more susceptible to the lytic effect of HSV-1 than were HEL-30 cells. In this study, 5-fluoro-2'-deoxyuridine (FUDR) treatment of both keratinocyte cell lines permitted an increase survival of HSV-1- infected keratinocytes especially for PAM-212 cell line which was further examined for the presence of sequestered virus after treatment with FUDR and infection with HSV-1. In this post-mitotic state, HSV-1-infected keratinocytes appeared to contain latent virus as suggested by the lack of virus plaques or cytopathic effect (CPE). After infection, these cells were examined for the presence of replicating HSV-1 in Vero cell overlays. Virus plaques were found suggesting that latency may have been established.

KEYWORDS: HSV-1, Mitotic inhibitors, FUDR, Taxol.

INTRODUCTION

Herpes simplex virus type 1 (HSV-1) causes serious ocular disease that can lead to blindness in both developed and underdeveloped countries[(1)]. In spite of a plethora of information concerning HSV-1 pathogenesis and latency, recurrent ocular infections reactivated from virus latent in trigeminal nerve neuronal cells lead to eventual loss of vision. Keratinocytes are chosen in this study because they are the primary site of infection for HSV-1 and the infection occurs via an endocytic process[(2,3)].

Noted that both HSV-1 and interferon-gamma (IFN-γ) rendered keratinocytes susceptible to the lytic effect of the virus and a concomitant increase in expression of suppressor of cytokine signaling-1 (SOCS-1). To render the keratinocytes susceptible to the antiviral action of interferon-gamma (IFN-γ) or its peptide mimetic and protect from HSV-1-induced lysis, the keratinocytes were pretreated with either SOCS-1 small interfering RNA (siRNA) or a peptide antagonist of SOCS-1 (pJAk2). The SOCS-1 antagonist has both an antiviral effect against HSV-1 in the keratinocyte as well as a synergistic effect on IFN-γ induction of an antiviral state and it plays an important role in the inhibition of the antiviral effect of IFN-γ in keratinocytes infected with HSV-1[(3)]. The present study aims to investigate whether SOCS-1 antagonists can be used to abrogate this refractoriness in vivo. Paradoxically, post-mitotic neuronal cells from the trigeminal ganglion of HSV-1-infected mice, in which HSV-1 lies latent, express high levels of SOCS-1 in response to IFN-γ[(4)] similar to that of keratinocytes[(3)]. The SOCS-1 peptide antagonist could permit reactivation of HSV-1 infection. To resolve this problem, responses of cultured neuronal cells to HSV-1 have to be determined.

The hypothesis for this study was: HSV-1 infection of murine keratinocyte cell lines (HEL-30 and PAM-212) treated with mitotic inhibitors leads to silencing of virus replication. In this post-mitotic state, the question was raised whether HSV-1 latency could be established in the treated keratinocytes. HSV-1-infected keratinocytes appeared to contain latent virus as suggested by the lack of virus plaques or cytopathic effect (CPE) after infection. To demonstrate this result, keratinocytes were examined for the presence of replicating HSV-1 in Vero cell overlays to rescue virus.

MATERIALS AND METHODS

Virus, cell lines and cell culture. HSV-1 (syn17+) (obtained from Children's Hospital Medical Center, Cincinnati, OH) was titrated in Vero cells (CCL-81, American Type Culture Collection). HEL-30 keratinocytes, derived from C3H mice, (Wright Patterson Air Force Base) and PAM-212 keratinocytes, derived from BALB/c mice, (American Type Culture Collection), were cultured in Dulbecco's Modified Eagle Medium (DMEM) (Fisher Science, Pittsburgh, PA) supplemented with 10% bovine calf serum and 1µl/ml gentamicin sulfate solution. The cells were grown on 100 mm^2 tissue culture dishes were used to plate the cells which were incubated in a humidified incubator at 37 °C, 5% CO_2, and 95% air.

Mitotic inhibitors: 5-Fluoro-2'-deoxyuridine (FUDR) (Fisher Scientific, Pittsburgh, PA) and Paclitaxel

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(Taxol) (Fisher Science, Pittsburgh, PA) were used to induce a post mitotic state in keratinocytes. FUDR was dissolved in 2% DMEM and a stock solution of 1µg/ml was made. The stock was further diluted depending on the experiment. Paclitaxel was dissolved in DMSO as 5µg/ml stock solution.

Cytopathic effect (CPE) assay: This assay was used to determine the effect of HSV-1 treated with various concentrations of IFN- γ, FUDR, or Taxol or when FUDR or Taxol were used with IFN- γ to treat HEL-30 or PAM-212 keratinocytes. Cells were counted using a hemacytometer and plated in 96 well plates at densities of 2.0 x 10^4 to 3.0 x 10^4 per well; plates were incubated until the cells were 70-100% confluent. At that point, cells were treated with different concentrations of mitotic inhibitors. Cells were then incubated for various amounts of time depending on the experiment design before infection with virus. Virus was removed two hours later and the plates incubated for 48h in DMEM supplemented with 10% FBC. The cells were rinsed with DMEM after the end of each incubation period. Cells then were washed with phosphate-buffered saline, pH 7.4 (PBS), fixed using 10% formalin and stained with 0.05% crystal violet. Plates then were washed with H_2O and dried overnight. Plates were scanned using a ScanJet 5300C and the images were examined using NIH image J to calculate the density of cells in each well. These experiments were performed in triplicate and the results were analyzed statistically using SigmaPlot 11.2 (Systat Software, Inc., San Jose, CA)

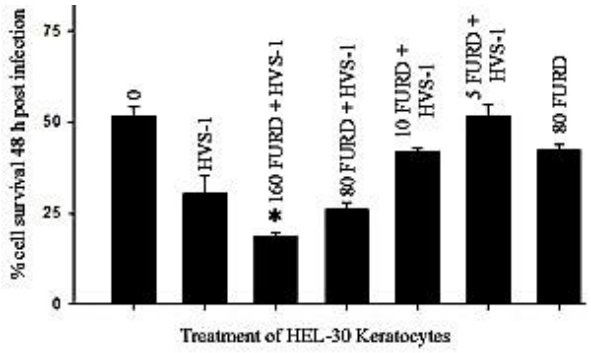
Plaque assay: After treating cells with mitotic inhibitors and infecting them with HSV-1, the virus was rescued by adding 1 X 10^5 Vero cells in DMEM containing 10% CS and the 96-well culture plates incubated for 24h at 37 ^oC in 5% CO_2 ; plaques were detected by methyl cellulose-containing overlay media (Fisher Science, Pittsburgh, PA). The plates were stained with 0.02% crystal violet, scanned using an HP ScanJet 5300C, and the scans examined by Image J. The results were analyzed using SigmaPlot 11.2.

RESULTS AND DISCUSSION

Selection of Dosages of Mitotic Inhibitors

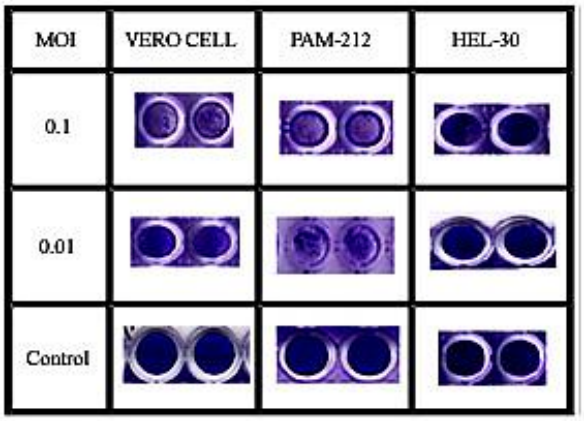
In preliminary titrations (data not shown), concentrations of FUDR above 10µg/ml were toxic to the keratinocyte cell lines. Titrations of FUDR from 160 to 2.5µg/ml were added to the keratinocytes. In (figure 1), concentrations of FUDR 160µg/ml, 80µg/ml, 10µg/ml, and 5µg/ml were used. After infection with HSV-1 at an MOI of 0.1, fewer than 25% of HEL-30 cells survived these treatments. ($p>0.001$ by ANOVA; * $p= 0.004$) (figure 1).

High concentrations of FUDR induced cell death (*). For all subsequent experiments, concentrations of 5-10µg/ml of FUDR were used because each of them was non-toxic and inhibited replication of virus. Note that the 0 bar denotes the viability in culture of untreated, uninfected cells. Since Pushkarev and others found that high concentrations of paclitaxel led to cell cycle arrest in G2/M phase[5], an initial concentration of 5µg/ml was added to keratinocytes for 30 min prior to HSV-1 infection. Different HSV-1 MOI's used to infect keratinocyte cell lines.



(Figure 1) the effect of high concentrations of FUDR on HEL-30

HEL-30 and PAM-212 keratinocytes were plated in 96 well plates and infected with 0.01 or 0.1 MOI HSV-1 for 2 hours to permit adsorption of virus. The virus was then removed and fluid replaced with DMEM containing 10% CS. The keratinocyte cell lines were compared with Vero cells infected with these two MOI's. In (figure 2), note that at 0.1 MOI, each of the cell lines showed cytopathic effects; PAM-212 keratinocytes and Vero cells showed cell lysis; and viral plaques which represented in the figure as clear areas were seen in HEL-30 keratinocyte cultures. PAM-212 keratinocytes and Vero cells, infected at 0.01 MOI, were more susceptible to the lytic effect of HSV-1 than were HEL-30 cells which appeared as dark blue, stained areas with the lack of any clear spots. These results were similar to those reported by Frey[3].

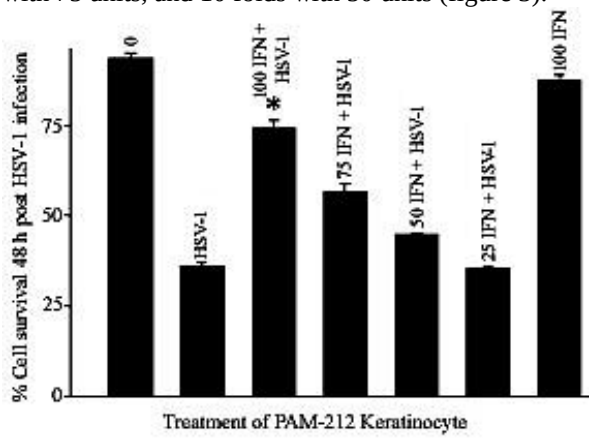


(Figure 2) cells response to 0.1 and 0.01 MOI of HSV-1

Vero cells, HEL-30, and PAM-212 were infected with different MOI of HSV-1. Cells were stained with crystal violet in 70% methanol. Arrows denote to the viral plaques. The effect of IFN-γ on HEL-30 and PAM-212 keratinocytes (figure 2).

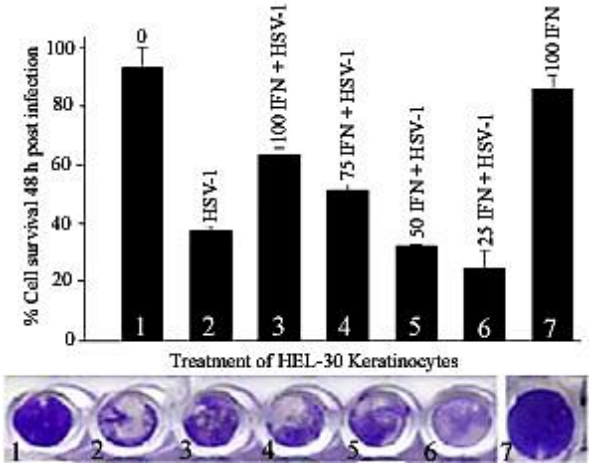
As known that IFN- γ has an antiviral effect, we attempted to protect HEL-30 & PAM-212 keratinocytes by treating them with different concentrations of IFN-

γ. These cells showed different response to IFN-γ treatment. The antiviral effect of IFN- γ was greater in PAM-212 cells which showed about 40 folds increase in the cells viability with the use of 100 unit, 25 folds with 75 units, and 10 folds with 50 units (figure 3).



(Figure 3) Effect of IFN-γ on HSV-1-infected PAM-212 keratinocytes

However, HEL-30 cells did not show much difference in the cell survival even with the use of high concentrations of IFN- γ (20 folds with 100 and 10 folds with 75 units) (figure 4). Moreover, higher concentration of IFN-γ provided more protection as seen by increased cell density.



(Figure 4) Effect of IFN-γ on HSV-1-infected HEL-30 keratinocytes

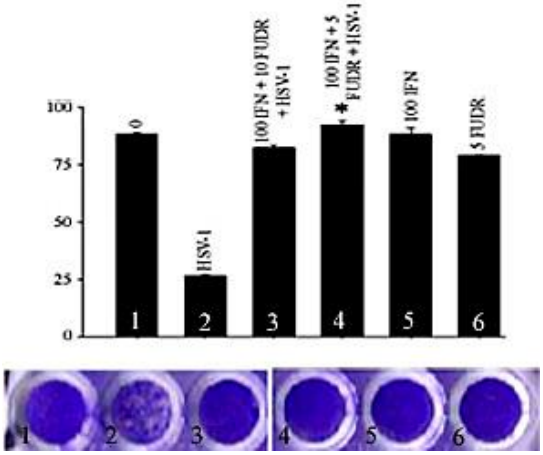
Cells were treated with various concentrations of IFN-γ for 24h then infected with 0.01MOI HSV-1 for 2h. 24h after infection. The cells were stained and image J was used to count the cells viability. Error bars indicate standard error of the means. There were about a 40 fold differences between cells treated with100 IFN-γ unit (*) and untreated, uninfected cells (0) ($p < 0.001$). Note that the 0 bar denotes the viability in culture of untreated, uninfected cells.

HEL-30 were treated with various concentrations of IFN-γ for 24h then infected with 0.1 MOI of HSV-1 for 2h. 24h after infection, the cells were stained and the images analyzed using the Image J program to determine cell density (viability). Error bars indicate standard error of the means. There were no significant differences between the viability of IFN-γ treated cells and untreated, infected cells (0). The cell viability after treatment with 100ug/ml IFN-γ increased 25-fold relative to virus infected cells ($p < 0.001$). None of the differences among the HSV-1 infected cells was statistically significant. Note that the 0 bar denotes the viability in culture of untreated, uninfected cells. These results mirror those observed by Frey et al., for the PAM-212 keratinocytes after infection with 0.1 MOI of HSV-1. A difference from the Frey study was seen for the HEL-30 cells in which approximately 20% of the keratinocytes survived HSV-1 infection with 0.1 MOI of virus. In Frey's study, none of the keratinocytes survived an MOI of 0.1. This difference may reflect differences in the source of HEL-30 cells.

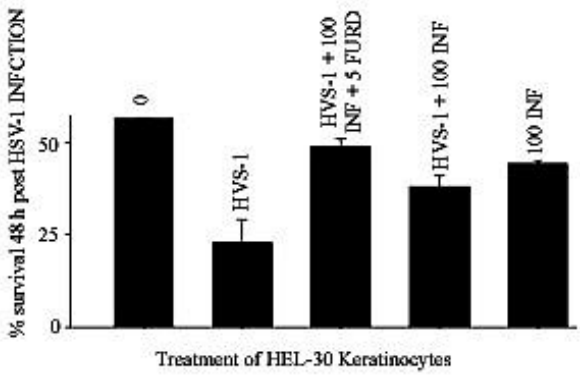
The HEL-30 cells in this study were derived from a stock received from WPAFB, while Frey's were supplied by National Institutes of Health. The two mitotic inhibitors induce differences in the keratinocyte cell lines in a time and concentration-dependent manner. The effect of FUDR on HEL-30 and PAM-212 Keratinocytes. Since FUDR acts as a mitotic inhibitor, the expectation was that the HSV-1 infection would not cause a cell death for the FUDR-treated cells. FUDR treatment would promote a cell proliferation. To determine the effect of FUDR on keratinocytes, cells were treated with 100 units of IFN-γ for 24h, followed by exposure to either 10 or 5μg/ml FUDR before viral infection. The 5 μg/ml concentration permitted about 65 fold increase in PAM-212 cell viability comparing to untreated cells (figure 5) with less activity on HEL-30, (figure 6). These variations in the response could due to the fact that different keratinocytes differ in their susceptibility to HSV-1 infection.

PAM-212 keratinocytes were plated in 96 well plate, and treated when they were about 80% confluence with 100 u/ml of INF-γ for 24h followed by 5 or 10μg/ml of FUDR treatment for an hour before infection with the 0.01 MOI of HSV-1.

There were statistically significant differences between 100 u/ml IFN-γ and 5 μg/ml FUDR treated cells (*) and untreated, uninfected cells (0) ($p < 0.001$). Note that the 0 bar denotes the viability in culture of untreated, uninfected cells.

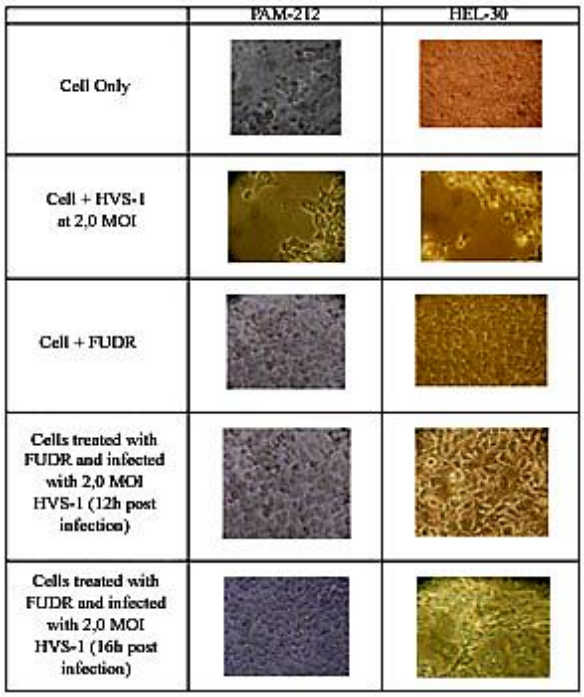


(Figure 5) The effect of FUDR on PAM-212 keratinocyte



(Figure 6) The effect of FUDR on HEL-30 keratinocyte

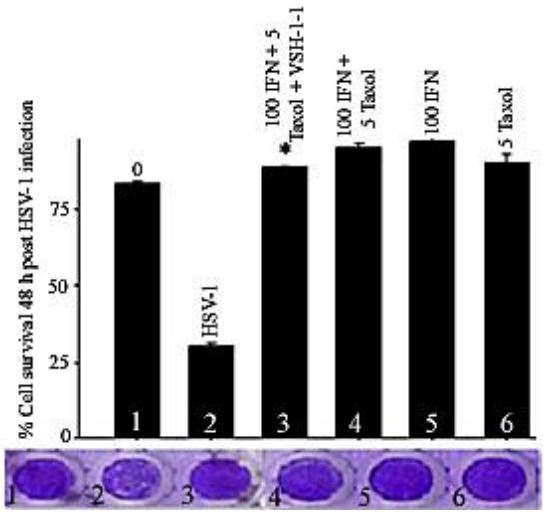
HEL-30 keratinocytes were plated in 96 well plates, and treated with 100µg/ml of IFN-γ when the cell confluence was about 80% for 24 hours. Then 5 µg/ml of FUDR was added for an hour, followed by infection with the 0.1 MOI. There was a 25 fold difference between IFN-γ and FUDR treated cells (*) and untreated, uninfected cells (0) ($p = 0.013$). Note that the 0 bar denotes the viability in culture of untreated, uninfected cells. As shown in (figure 7), PAM-212 treated with FUDR maintains its cell morphology and the percentage of growth. However, HEL-30 treated cells showed some decrease in the rate of proliferation compared to untreated cells. Moreover, HEL-30 cells formed more regular polygons.



(Figure 7) The effect of FUDR on PAM-212 and HEL-30 morphology and proliferation

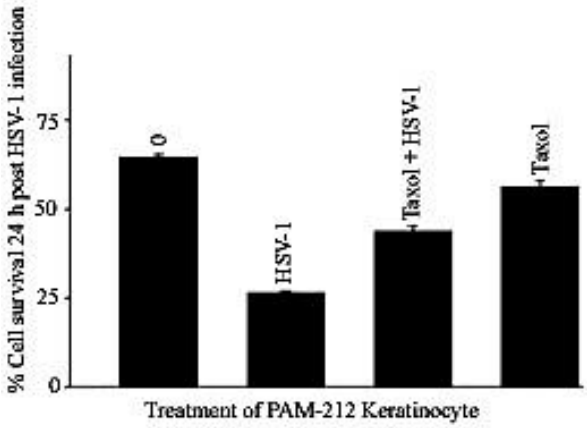
These pictures were taken with a 10X objective lens. The effect of paclitaxel on PAM-212 and HEL-30.

To examine the effect of paclitaxel on PAM-212 keratinocytes, cells were treated with IFN-γ and paclitaxel before HSV-1 infection. PAM-212 treated cells showed 50 folds increase in the cell growth compared with untreated cells (figure 8).



(Figure 8) the effect of Taxol on PAM-212 keratinocytes

To see if this effect was related to the paclitaxel or IFN-γ, the cells were treated with paclitaxel only. As shown in (figure 9), paclitaxel induced cell proliferation (20 folds increase) even in the absence of IFN-γ. These results indicate that paclitaxel can inhibit the cell death caused by HSV-1.

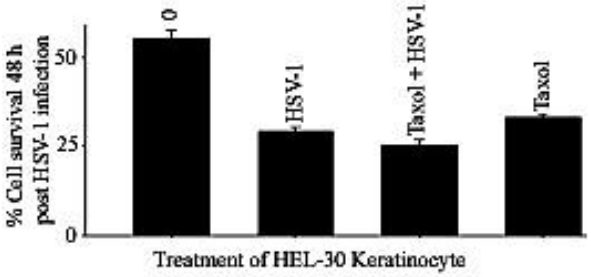


(Figure 9) The effect of Taxol on PAM-212 keratinocytes without the IFN- γ treatment

PAM-212 keratinocytes were plated in 96 well plate, and treated when they are about 80% confluence with 100u/ml of IFN-γ for 24h followed by treatment with 5 µg/ml taxol for an hour before infection with the virus at 0.1 MOI. There were statistically significant differences between IFN-γ and FUDR treated cells (*) and untreated, uninfected cells (0) ($p < 0.001$). Note that the 0 bar denotes the viability in culture of untreated, uninfected cells.

PAM-212 cells were treated with 5µg/ml of Taxol for 30 min before HSV-1 infection. Taxol- treatment provided a 20 fold increase (*), even in the absence of IFN-γ ($p = <0.001$). Note that the 0 bar denotes the viability in culture of untreated, uninfected cells. Because IFN-γ potentiated the lytic effect in HEL-30 cells at an MOI of 0.1 as showed in (figure 3), this cell line was not examined further following treatments with paclitaxel and IFN-γ. As shown in (figure 10), paclitaxel had a toxic effect on HEL-30 which ap-

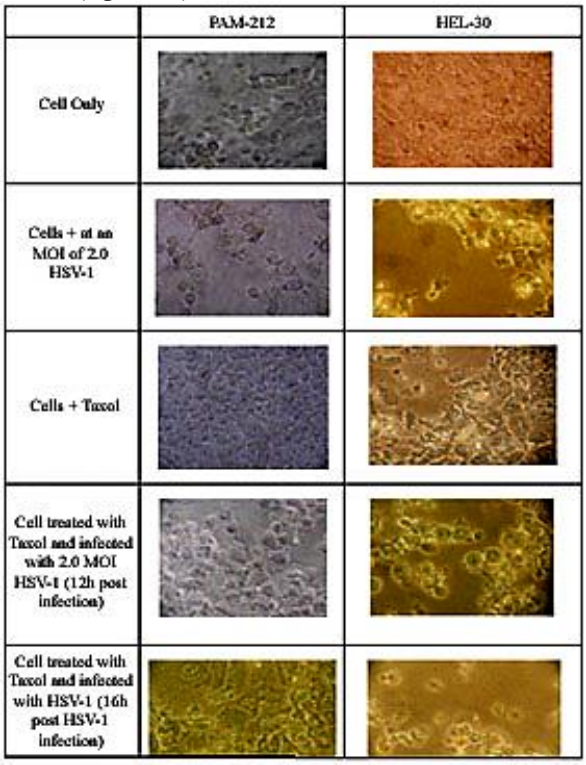
peared by the decrease of cell survival by 20 folds even in the absence of HSV-1.



(Figure 10) The effect of paclitaxel/taxol on HEL-30 keratinocyte

HEL-30 keratinocytes were plated in 96 well plates. When they were about 80% confluent, the cells were treated with 5µg/ml of taxol for 30 min, followed by infection with the 0.1 MOI of HSV-1. Taxol treatment had a toxic effect on HEL-30 cells (*) compared to untreated, uninfected cells ($p = <0.001$). Note that the 0 bar denotes the viability in cultures of untreated, uninfected cells.

In cultures of paclitaxel-treated keratinocytes, changes in the proliferation rate and morphology were observed (figure 11).

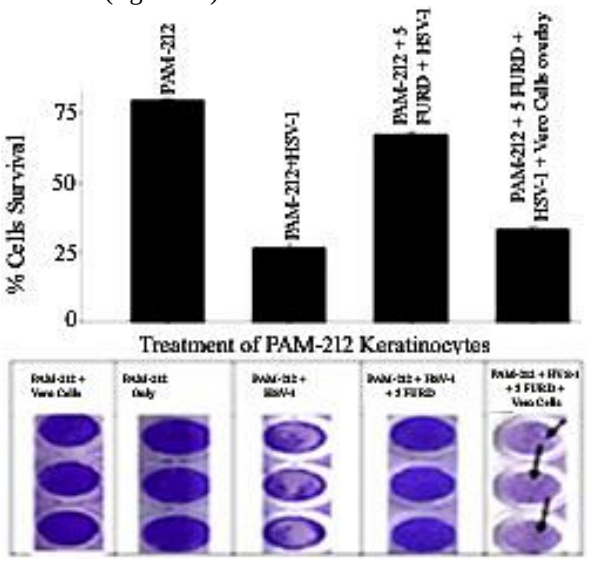


(Figure 11) The effect of paclitaxel/taxol on PAM-212 and HEL-30 morphology and proliferation

These changes which were different depending on the cell line were anticipated because paclitaxel causes microtubule's alteration. HEL-30 cells were less susceptible to the anti-mitotic effect of paclitaxel than were PAM-212 cells. This may be due to the reaction level between the cells and the paclitaxel or any other treatments depending on the tumor type which is erythroleukemia in HEL-30 and cutaneous squamous cells carcinoma in PAM-212 cell line. It also could due to the variations in the degree of cell–cell contact formation, depending on cell density in the culture dish[6].

HEL-30 keratinocyte exhibited some changes in their morphology; these cells were more rounded than untreated, uninfected cells and lost their plastic adhesion. These observations were made microscopically 24h after treatment, as well as 12h and 16h after HSV-1 infection with an MOI of either 0.1.or 2.0 in which about 25%, 60% and 80% respectively of cells were dead. Nevertheless, PAM-212 keratinocytes were much less affected by the apoptotic effect and showed that they were more likely to go toward cell cycle arrest (figure 12). These results were comparable to results reported by Kim and his colleagues' using different cell lines[7].

These pictures were taken with a 10X objective lens Attempt to rescue virus from FUDR-treated PAM-212 cells[8]. Overlayed single cell suspensions of trigeminal neuronal cells with fibroblasts to rescue latent HSV-1 virions from the trigeminal neuronal cells. Based on this observation, susceptible Vero cells were used to overlay the PAM-212 cell cultures infected with HSV-1 in attempt to release the virus from PAM-212 cells (figure 12).



(Figure 12) Effect of HSV-1 infection on FUDR-treated PAM-212 keratinocytes

If the virus established latency inside HSV-1- infected, FUDR- treated PAM-212 cells, we will have a decrease in the cell survival as a result of Vero cells overlay. Note that viral plaque formation is apparent (marked with arrows) in the Vero cells overlayed onto HSV-1- infected, FUDR- treated PAM-212 cells. An alternate explanation for this observation may be that the virus exiting from the PAM-212 cells to infect the Vero cells causes trauma to the PAM-212 cells. The staining of this set of wells was lighter and the Vero cells overlay induced 40 fold decrease in the cell survival compared with the un-overlayed cells. These results suggest that the infected Vero cells may be releasing enzymes which damages the PAM-212 cells.

Further experimentation is needed to confirm that this viral infection reflects latency rather than surface contamination with live virus. Polymerase chain reaction has to be done looking for LAT, which is the main sign of latency.

Fewer cells survived after Vero cells overlay (*) compared to FUDR treated- HSV-1 infected cells (p= <0.001). Note that the 0 bar denotes the viability in culture of untreated, uninfected cells.

CONCLUSION AND RECOMINDATION

Primary infection, latent infection, and reactivation are the main stages that characterized HSV-1. However, the stages leading to HSV-1 latency is still unclear. If it is possible to develop a latent stage in keratinocytes, then it may be possible to dissect these events to understand progression from initial infection to latency as seen in neuronal cells. Since most of the antiviral drugs target the lytic state, targeting the virus in the latent state is considered one of the new approaches for potential treatments. In this study, two mitotic inhibitors were used to render the keratinocytes susceptible to a latent HSV-1 infection.

In this experiment , FUDR treatment of both keratinocyte cell lines permitted an increased survival of HSV-1- infected keratinocytes, especially for PAM-212 keratinocytes. This cell line was further examined for the presence of sequestered virus after treatment with FUDR and infection with HSV-1. Knickelbein et al. were abled to rescue HSV-1 from latency in murine trigeminal ganglia by co-culture with susceptible fibroblasts. As shown in (figure 12), viral plaques were seen in PAM-212 cells 48h after infection with HSV-1 and 24h after overlay with susceptible Vero cells suggesting that this approach warrants further study. This study sets the stage for future work in the laboratory confirming the usefulness of the latency model[8].

Further examination of the effect of FUDR on keratinocytes using different times of exposure (2h, 4h, 6h, and 24h) is needed. Since Rich and his colleagues found that the inhibitory effect of FUDR is reversible[9], HSV-1 infection of keratinocytes should be examined at different times after FUDR treatment. Paclitaxel was also used as a mitotic inhibitor in these keratinocyte cells line in attempts to induce viral latency. The concentration of paclitaxel used (5μg/ml) was toxic to both cell lines. Since Choritz et al., have found that the growth and migration inhibition resulted from the exposure to paclitaxel/taxol are a dose and time dependent. Low concentrations of paclitaxel induce less cell death, further investigation with lower concentrations of paclitaxel (1μg/ml, 0.5 μg/ml, 0.01 μg/ml or lower) at different time of exposure is needed to see if these low concentrations could induce a mitotic inhibition instead of cell death[10].

In the latency process, silencing the lytic gene expression and blocking the host cellular and humoral immune response have to be considered to achieve this goal. If treatments of keratinocyte cell lines with these mitotic inhibitors render the cells susceptible to herpes virus latency, expression of latency-associated transcript (LAT) must be demonstrated in these cells. Future studies should include determining the polymerase chain reaction products for early viral genes (ICP4 and ICP0) as well as latent-associated transcript (LAT) in the keratinocyte when they are in the post mitotic state. Initial attempts to demonstrate LAT in PAM-212 following treatment with FUDR and HSV-1 infection were performed at 12h and 16h post infection. Since ICP0 and ICP4 genes (immediate early, IE) are expressed early in infection time points of 5h and 16h post infection should be examined. ICP0 and ICP4 expression should predominate in the 5h samples and LAT, if present, should predominate in the 16h sample to demonstrate latency. Future studies should include determining the polymerase chain reaction products for early viral genes (ICP4 and ICP0) as well as latent-associated transcript (LAT) in the keratinocyte when they are in the post mitotic state.

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MACROSOMIA , PREDICTION AND MODE OF DELIVERY

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ABSTRACT

The concept of fetal macrosomia and its adverse outcomes has been recognized in medicine and literary reports throughout the ages , Attempts at perinatal diagnosis of macrosomia have been useful in some cases. The mode of delivering a borderline macrosomia is a matter of discrepancy. Fetal macrosomia has been defined in several different ways including birth weight of [4000-4500 gm] or birth weight greater than 90% for gestational age after correcting for sex and ethnicity. Based on these definitions macrosomia affect 1- 10 % of pregnancies. It`s an analytic study aims to detect the possibility of antenatal prediction of fetal macrosomia and the decision for the safe mode of delivery . The study was done at the obstetric unit of Misurata Teaching Hospital–Libya, over a period of two years from the first of January 2010 till December 2011. During this period, a total of 17234 deliveries occurred. 100 patients whom delivered babies weighing >4, 500 kg were included in this study. They were randomly selected. maternal complications were observed. The 100 macrosomic infants delivered in the study period were their birth weight >4500 gm constituted 0,7% of all deliveries; There was a statistically significant increased incidence of macrosomia in the age group 30–40 years which is 50%. The highest incidence of macrosomic pregnancy in women P1 to P3 41% and then P4 to P6 which is 32% and the incidence decreases. In grand multiparous women and also in primigravida were it 13% in both, The complications were recorded in 20% of all deliveries ,in particular shoulder dystocia 4% of all macrosomic births, various bone fracture is 3%of all deliveries which occurred more frequently with operative vaginal deliveries. The ability to estimate the fetal weight appears to be of great importance in identification of macrosomic fetus Clinical estimation along with ultrasound estimation can serve a useful guide to prevent maternal and fetal complications. Most of complicated cases of macrosomic deliveries are from the unpredicted group.

KEY WARDS: fetal macrosomia, maternal and fetal complications, multiparity, diabetes mellitus.

INTRODUCTION

Historical Background

The concept of fetal macrosomia and its adverse outcomes has been recognized in medicine and literary reports throughout the ages. The 16th century monk and physician, Francois Rabelais, told the story of the birth of Gargantua, (a giant baby). Several years later, Gargantua's wife died giving birth to Pantagruel "for he was so amazingly large and so heavy that he could not come into the world without suffocating his mother[1]. In 1891 Ortega reported the birth of a 24.13pound (10.9 kg) male infant. In 1916, Belcher claimed to have delivered the largest infant, 25-pound (11.3 kg) stillborn[1,2,3].

Definitions& Associations

The term macrosomia is used to describe new born with excessive birth weight (> 4.500 kg). Attempts at perinatal diagnosis of macrosomia have been useful in some cases. The mode of delivering a borderline macrosomia is a matter of discrepancy[4,5] The accurate diagnosis of fetal macrosomia can be made by measuring birth weight after delivery, therefore the condition is confirmed retrospectively, i.e. after delivery of infant.

Fetal macrosomia has been defined in several different ways including birth weight of [4000-4500 gm] or birth weight greater than 90% for gestational age after correcting for sex and ethnicity. Based on these definitions macrosomia affect 1-10 % of pregnancies[1]. The pathophysiology of macrosomia is related to the associated maternal and fetal condition that accounts for its development[6,7,8].

In general poorly controlled diabetes ,maternal obesity and excessive maternal weight gain during pregnancy are all associated with fetal macrosomia[13,14,15,16,17].

Strategies to predict macrosomia

The three major strategies used to predict macrosomia are *clinical risk factors, *clinical estimation by Leopold's maneuvers and *ultrasonography. But each method has substantial limitations.

1) Clinical risk factors for fetal macrosomia

A number of risk factors for fetal macrosomia have been recognized. the strongest risk factor is maternal diabetes which result in a twofold increase in the incidence of macrosomia. Many risk factors are highly prevalent among parturient even when two of these risk factors are present, the risk of macrosomia is only 32%. Furthermore, 34%of macrosomic infants are born to mothers without any risk factors and 38% of

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pregnant women have at least one risk factor[18,19,20]. These risk factors include. Maternal Diabetes, Excessive weight gain, Male fetus, Multiparty, Previous macrosomia, Prolonged gestation, Maternal obesity, Family history of big baby, Parental stature and Maternal impaired glucose tolerance, prolonged 2nd stage[9,10,21]. Clinical estimation of fetal macrosomia, the volume of amniotic fluid, the size and the configuration of the uterus and the maternal body habits. Regarding Clinical estimation of the size of the fetus by manual palpation through the abdominal wall, several studies have documented mean error of about 300gm[10,11, 21,22].

2) Leopold maneuvers

Are techniques developed to determine fetal presentation, lie and size. They are also limited by many factors as mentioned before for fundal height measurement, however these maneuvers provide the clinical with the general appreciation of fetal size and other important information.

Previous studies designed to evaluate Leopold maneuver with fundal height measurement for prenatal diagnosis of possible macrosomia report sensitivities of 10-43%. Specificities of 99-99.8 % and positive predictive value of 28-53 %[12].

3) Ultrasonography

Ultrasound scans for assessment of fetal growth usually starts at the end of second trimester and is repeated there-after every 4 weeks or more if needed Baseline measurement of fetal abdominal circumference at 26 weeks expressed as a percentile can be compared with later scans to provide evidence for growth acceleration[8].

Ultrasonographic measurements to obtain estimated fetal weights are indicated when clinical assessment indicate a uterine size greater than that expected for the gestational age .An examination within 1-2 weeks of delivery showing an abdominal circumference of 35cm or larger should alert the clinician to anticipate a fetus with birth weight of 4,000gm or more.

The definitive diagnosis can only be made after delivery of the neonate. Ultrasonography of the fetus and its size can be useful for identifying macrosomic infants. In 1999 jazayeri et al showed that abdominal circumference measurements made within 2 weeks of delivery can be predictive of a birth weight greater than 4,000gm[27].

A measurement of 35 cm or more identified more than 90% of neonates with birth weight greater than 4000gm and occurred in only 18% of the population. An abdominal circumference measurement within two weeks of delivery had a sensitivity & specificity & positive and negative predictive values of approximately 90%. Abdominal circumference measurement in patients at risk for macrosomia can provide some clues to the size of the fetus and thus allows appropriate preparation for delivery. Recent studies have confirmed that appropriately performed abdominal circumference by ultrasonography in the third trimester is the best way of predicting fetal weight. Measurements without doubt, the usefulness of this technique depends on the care used to measure the variable & the quality of the image obtained in late third trimester and the cut off used to define the neonates at risk[28].

The term (fetal macrosomia) is misleading, because birth weight never known with certainty until after delivery, the most commonly proposed criteria for macrosomia is birth weight greater than either 4000gm or 4500gm this represented.

10.9 % and 1.8% of infants born in USA respectively . The most clinically useful definition of macrosomia is a weight below which macrosomic complications such as shoulder dystocia doesn't occur. Unfortunately, studies showed that one half of all cases of shoulder dystocia occur at birth weight of less than the commonly used cut-off 4000gm[25]. Furthermore, almost one half of all cases of permanent brachial plexus injuries occur in infants weighing less than 4500gm[2]. The predictive accuracy of fetal weight estimates is poor at greater than 5000gm, most authors agree that prophylactic cesarean section should be offered[26,27].

AIM OF THE STUDY

It`s an analytic study aimed to detect the possibility of antenatal prediction of fetal macrosomia and the decision for the safe mode of delivery in Misurata Teaching Hospital, Misurata-Libya.

MATERIAL AND METHODS

The study was done at the obstetric unit of Misurata Teaching Hospital-Libya, over a period of two years from the first of Jan. 2012 till the end of Dec 2013. During this period, a total of 17234 deliveries occurred .

100 patients whom delivered babies weighing >4, 500 kg were included in this study and they were randomly selected. maternal complications were observed and analyzed macrosomia expectation based upon estimated fetal weights by Leopold maneuvers or by USS estimation or previous macrosomia or family history of macrosomia or mixed factors. Gestational age at delivery was calculated from the last menstrual period or ultrasonic estimations carried out before the twenty weeks of gestation. The delivery of the baby was conducted by specialized obstetrician. The delivery of the macrosomic infant was attended by apediatrician. After birth the baby was transferred to neonatology unit where a careful assessment made on the basis of Apgar score. A good physical examination for the major congenital anomalies, birth weight detection, and a specimen of cord blood was obtained for glucose determination to exclude hypoglycemia.

RESULTS

The 100 macrosomic infants delivered in the study period were their birth weight >4500gm constituted 0,7% of all deliveries; 100 of their mothers were booked patients ,and the other were un booked or their information were not complete. (Table 1) sets out the

identified characteristics of the mothers in the study. There was a statistically significant increased incidence of macrosomia in the age group 31–40 years which is 50% which is slightly higher in compare with other study SAMJ 1995 the peak incidence at 30-39 yr were 39,9%. It may be due to the increase in maternal age associated with increased medical disease such as diabetes mellitus which is one of most common cause of foetal macrosomia. The parity distribution as we seen below in (table 1&2). The highest incidence of macrosomic pregnancy in women P1 to P3 41% and then P4 to P6 which is 32% and the incidence decrease In grand multiparous women and also in primigravida were it 13% in both, were the incidence is 63,9% in P1-P4 in the above study which is higher than our result.

(Table 1) Maternal characteristics

Maternal age	**No. of patients**
<20yr	1
20-25yr	10
26-30yr	37
31-35yr	25
36-40yr	25
>40yr	2
Maternal parity	**No. of patients**
PG	13
P1 –P3	41
P4 –P6	32
P7 –P10	13
>P10	1
Family history of macrosomia	**No. of patients**
Positive F/H	64
Negative F/H	36

In most of the cases the weight gain during pregnancy is 10kg -16kg (81%), as shown in (table 2).

(Table 2) Maternal weight pre pregnancy, at term and weight gain during pregnancy

Maternal wt. (No.)	**Patient wt. Pre-pregnancy (No.)**	**Patient Wt. at term (No.)**
<70kg	15	0
71kg-80kg	51	7
81kg-90kg	23	33
91kg-100kg	10	44
>100kg	1	16

Wt. gain during pregnancy	**No. of patient**
<10 kg	2
10kg -15kg	43
16kg -20kg	38
21kg -25kg	13
>25 kg	4

The most common medical disorder that associated with fetal macrosomia is Diabetes mellitus which is 32% of cases in this study mostly Gestational DM. (Table 3) illustrate the incidence of other medical disease which is less frequent, HTN is about 5% but it in most of cases is essential hypertension, thyroid disease 1 case was hypothyroidism on treatment, 2 cases of renal disorder recurrent UTI, 1case asthmatic mild and 3 cases of blood disorder. From (table 3), 17% of diabetic pregnancies on insulin and 11% on diet control, most of these patient weren`t to be diabetic pre pregnancy and 3% diagnosed intrapartum.

(Table 3) Medical disorders and type of DM control

Medical disease	**No. of patient**	**Type of DM control**	
Diabetes	32	Diet	11
		Insulin	17
HTN	5		
Thyroid D.	1		
Renal D.	2		
Br. Asthma	1		
Blood D.	3		

The prolonged pregnancy increase incidence of fetal macrosomia because continued delivery of nutrient and oxygen to the fetus, we found the incidence was 51% GA from 37wk to 40wk and 43% in GA from 40wk to 42wk so we found about half of macrosomic babies are postdate (table 4).

(Table 4) Gestational age at time of delivery, mode of delivery, birth weight and fetal sex

Time of delivery	**No. of patient**
<37wk	3
37wk-40wk	51
40wk-42wk	43
>42wk	3
Mode of delivery	
NVD	43
Vacuum extraction	7
Forceps delivery	4
C/S delivery	46
Fetal weight at delivery	
>4.5 kg -5kg	80
5.1kg -5.5kg	13
5.6kg -6kg	6
>6 kg	2
Fetal sex	
Male	66
Female	34

Forty six percent of fetuses were delivered by cesarean section, 29% were elective because of big baby or for excess of another causes, and 17% were emergency cesarean section and most of them unpredicted, vaginal delivery 54%, 43% normal vaginal delivery (NVD) in this group the patients were higher birth order and had H/O delivery of macrosomic baby, other operative vaginal delivery occur in 11% of cases which represent 20%of all vaginal delivery, the intervention include vacuum extraction 7% and low forceps 4% (table 4).

The highest incidence of birth weight were 80% the babies weighing more than 4500gm to 5kg, and 13%

birth weight 5.1kg to 5.5kg, above 5.5kg about 8%. As we found in this study most of babies who birth weight more than 5kg delivered by caesarean section. The male fetus heavier than female fetus at any gestational age, in our study the incidence of males 66%, where the females 34%. The complication were recorded in 20% of all deliveries, details are in (table 5).

(Table 5) Feto-Maternal complications

Feto-maternal injury	No. of patient
Dystocia	4
Erb's palsy	2
Bone fracture	3
Birth asphyxia	2
Soft tissue trauma	3
Birth canal injury	7

In our study 39% of patient predicted to be pregnant with macrosomic fetus mainly by clinical assessment in some cases based on the history of big baby or family history of big baby or in combination. Twenty percent of patients were not predicted, as macrosomic until delivery, and majority of these patient has had feto-maternal complications. Eighteen percent were suspected that are macrosomic by mixed factors. In patients had H/O delivery of macrosomia, in only 3% of them were predicted by USS (table 6).

(Table 6) Antenatal prediction of macrosomic foetus

Mode of prediction	No. of patient
USS ass.	12
Clinical ass.	10
History of macrosomia	8
Mixed factor USS + Clinical + H/O big baby	58
Unpredicted	12

DISCUSSION

Macrosomia was associated with wide range of adverse pregnancy outcomes. In order to make the diagnosis of fetal macrosomia antenatally ,it is vital to be aware of predisposing factors in our environment these were found to be as follows; about half of patients in their 3rd decade of life, multiparous, over weight pre-pregnancy, and obese at term (BMI >30kg/m^2).

Weight gain during pregnancy was high 38% gained from 16kg-20kg which is high in comparison with normal weight gain for normal pre-pregnancy BMI, and most of them had history of delivery of macrosomic baby, also we found in our study 43% post-date and 3% post-term[8], the incidence of gestational diabetes mellitus was 32% which is significantly high which is the strongest risk factor for macrosomic baby and other feto-maternal risks as shoulder dystocia, neonatal hypoglycemia, systemic maternal complications of DM[11].

According to the results of this study feto-maternal complications tended to increase in vaginal births, the most serious encountered complications in macrosomic babies were developed Erb's palsy in neonatal period which was 2% of all macrosomic deliveries which was out of 4% of shoulder dystocia, other most serious fetal complication was Birth asphyxia [defined as a one minute Apgar score less than 7] among macrosomic infants delivery was 2% which result due to unpredicted macrosomia prolonged labour fetal distress and end by urgent cesarean section delivery. Maternal complication which was 7% birth canal injury which include extended episiotomy, 1st, 2nd, 3rd, 4th degree perineal tears, 3rd and 4th degree perineal tears were complicated by anal sphincter incontinence later on.

Macrosomia is associated with considerable maternal morbidity and high neonatal mortality and morbidity[8], we found antenatal prediction was associated with an increase incidence of cesarean section delivery which was 46% without decrease in shoulder dystocia and other birth traumas[9].

Cesarean section delivery suggested as the mode of delivery to minimize the risk of birth trauma that associated with macrosomia. Cesarean section did not improve the outcome in uncomplicated pregnancies[8].

The rate of Perinatal and maternal morbidity and mortality can be reduced by the antenatal diagnosis, the risk factors leading to macrosomia must be thoroughly evaluated by the clinician, since majority of factors which lead to delivery of macrosomic babies are preventable[10].

We believed that the unacceptable high Perinatal morbidity rate and maternal morbidity rate can be avoided if midwife and labour room doctors are properly trained in the concept of active management of labour, and early diagnosis of failure to progress, clinical suspicion of large baby, coupled with slow active phase of labour, especially arrest of cervical dilatation over a-2 hour period in the presence of adequate uterine contractions, and constitutes an early sign of failure to progress which should not be ignored. In 2nd stage of labour, intervention is required if there is no descent of the presenting part after 30 minute of bearing down, or patient undelivered after 45 minute of pushing[8].

CONCLUSION

In the study we found out that most of the cases of macrosomia are antenatally estimated. History of previous delivery of big baby and maternal diabetes are significant predisposing factors.

Maternal obesity and weight gain during pregnancy are strongly related to fetal macrosomia. The ability to estimate the fetal weight appears to be of great importance in identification of macrosomic fetus clinical estimation along with ultrasound estimation can serve a useful guide in an experienced obstetrician.

Most of complicated cases of macrosomic deliveries are from the unpredicted group. It is agreed that real-time ultrasound scan give best estimate of fetal weight if available and should be used routinely for any patient whom at risk of having macrosomic fetus.

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PERIOD PREVALENCE OF CRYPTORCHIDISM IN LIBYA

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ABSTRACT

Cryptorchidism is a congenital condition characterized by testicles do not descend to the scrotum .This is a prospective study aimed to predict undiagnosed cases of undescended testicles, its prevalence in the community and to find out the risk factors leading to it; as well as the management of this condition. This comprehensive study is carried out in Alkhadra Hospital, Aljalla Hospital and Zliten Central Hospital over a period from Jan 1 to Dec 31 2013. Included (342) examined cases. Their age ranged between one week to 5 years old; of which 19 cases (5.6%) were found to have cryptorchidism. The poor mothers' knowledge about this condition was another finding. Every male infant should be examined to detect undescended testecls.

KEY WORDS: cryptorchidism, prevalence, diagnosis, risk factors and management.

INTRODUCTION

Undescended testes usually are histologically normal at birth but atrophy and poor development are found by the end of the first year of life. There is a high incidence of infertility, malignancy, untoward psychological effects in adolescence and adulthood, as well as testicle torsion, and hernia[(1)] (figure 1).

It is the most common abnormality of male sexual development, in this condition where one or both testes are not located in the scrotum, can be ectopic, incompletely descended, retractile or absent[(2)]. Bram Abrecht Von Haller who is the one described the anatomical position of fetal testes in 1755. The term cryptorchidism originates from Latin terminology in which crypto means hidden and orchid means testis.

The earliest study on testicular malposition was published in 1786 by John Hunter[(3)].

Normal testes are expected to descend in to scrotum between the 35th and 40th weeks of gestation, therefore infants whose delivered preterm especially before the 35th week of gestation have been reported to have a high incidence of undescended testes[(4)].

The right testis usually descends from the scrotum later than the left testis, and higher in the scrotum[(5)] (figure 2).

For Testes to produce mature spermatozoa the temperature of the local Environment must be (1.5-2°C) below body temperature[(6)].

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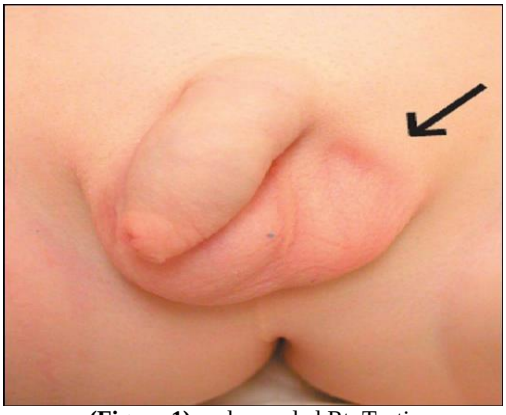
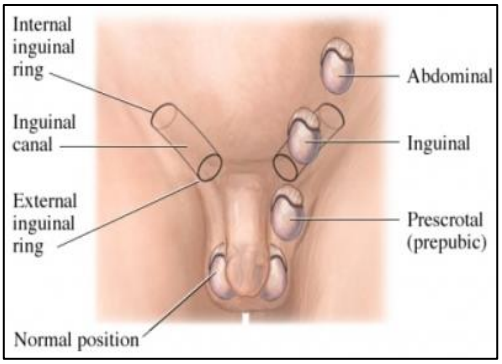


(Figure 1) undescended Rt. Testis

Predisposing factors which may lead to the undescended testicles such as prematurity (delivery before complete 37 weeks gestation) low birth weight (birth weight > 2.5 kg)[(7)] being twin, surgery in the inguinal hernia of preterm, regular alcohol consumption during pregnancy, being born to pregnant woman who drink caffeine at least 3 drinks per day , maternal exposure



(Figure 2) The pathway of testes descendense

to estrogen during the first trimester, preeclampsia, congenital malformation syndromes such as Down syndrome, Noonan's syndrome, Prader Welli syndrome, and Klinefelter syndrome, As well as hypospadias, cerebral palsy, mental retardation, Willms tumor, exposure to pesticides and diabetic mothers.

The first recorded attempt of orchidopexy was performed by Jones Adons in London Hospital in 1871 on an outpatient department[9]. The first successful Orchidopexy by Thomas Annandale was in 1877[10]. Since 1931 the Hormonal therapy Human chorionic Gonadotropin (HCG) has been used for the diagnosis as well as treatment of cryptorchidism. Hormonal therapy is often used to distinguish between retractile testes and true undescended testicles in which 500 microgram HCG intramuscular injection is used twice a week for five weeks[11]. The American Academy of Pediatrics recommended the surgical correction at one year of age. The hormonal therapy by HCG should probably be attempted before then (one year of age)[12].

AIM OF THE STUDY

To determine the prevalence rate of cryptorchidism from birth to 5 years old, in the community as well as the mothers' knowledge about this problem.

PATIENTS AND METHODS

A total number of 684 testes were examined. This comprehensive study was undertaken in Alkhadra Hospital, Aljala Hospital and Zliten Central Hospital; over one year duration from Jan 1st to Dec 31st in the year 2013. Genital examination was carried out to all male patients whose presented to our clinics by deferent illnesses who aged between one week to 5 years. All patients were examined by pediatrician and neonatologist. The data including the age, birth weight, head circumference, length, gestational age, systemic examination, penis, and scrotal examination was checked and collected. In the scrotal examination the patient was relaxed in warm room, and warm hands. Pulling the testis into the inguinal canal, examiner started palpation along the inguinal canal moving from a point just above the inguinal ring toward the scrotum (Milky test)[13], try to entrap the testis between fingers place it on the scrotum. The case was classified as cryptorchidism if the testis is not true palpable or if it cannot be brought into the scrotum. Ultra-sonography examination, CAT scan, MRI have been carried out to document the presence of a non-palpable testis. Information were collected from the family including antenatal, natal and postnatal history, age of the mothers and the fathers, family history of the cryptorchidism, and the level of the mothers education about cryptorchidism. The follow up was performed for all patients till the testis is descended in the scrotum spontaneous, by hormonal therapy or by surgical intervention.

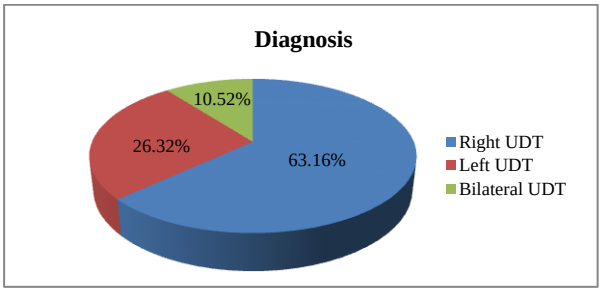
RESULTS AND DISCUSSION

Three hundred forty two male patients who attended the pediatric outpatient clinic in the period from Jan 1st to Dec 31st 2013 for different illnesses underwent the genital examination for undescended testes (table 1). Nineteen (5.6%) male patients have been found to have undescended testes. Diagnosis of cryptorchidism was done by clinical genital examination of cases and its site was confirmed by ultrasonography examination.

The target age was first week to 5 years ,neonatal period (2.9%), 3monthes (1.5%), and between one year and 5 years was (1.2%). Out of the 19 patients who diagnosed as cryptorchidism; right cryptorchidism was (63.16%) and left side was (26.32 %), bilateral cryptorchidism was (10.5%), for this deference no special factors explain this fact (figure 3).

(Table 1) The number of patient according to their age (Table 1 is two Parts)

The Age of Patients in Months	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	**Total No. of Patient**
No. of Patient	71	19	13	11	11	12	9	7	11	10	8	9	8	7	6	7	7	10	
The Age of Patients in Months	19	20	21	22	23	24	25	28	30	32	33	35	38	40	45	50	54	60	**342**
No. of Patient	7	6	8	7	23	6	3	7	8	5	6	4	4	7	4	6	5	7	



(Figure 3) Percentage of cases according to side of Undescended testes

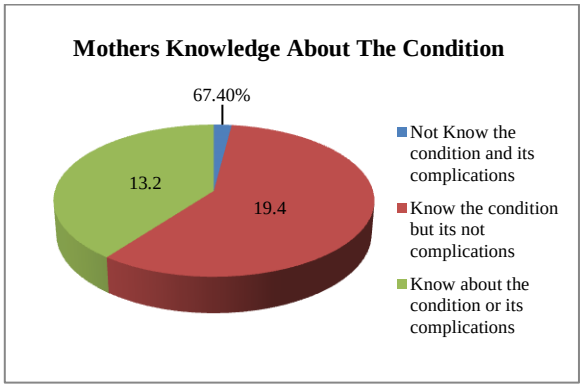
Undescended right Testes was (5%), undescended left testes was (30%), and undescended both testes was (20%)[14].

During the embryonic life the testes form beside the mesonephric kidneys and descend via the inguinal canal to the scrotal sac, if the process is failed, cryptorchid testes may held at any the normal pathway descend (undescended or retractile testes), it may travels off the normal pathway of descent (ectopic) or absent[15]. Cryptorchidism may present in (4%) of boys at birth and there is an even high incidence in

preterm infants. (75%) of undescended testicles well descend within the first 3months of age[16] .
(30%) of preterm male infants , and (3%) of full term male infants. In (80%) of cases testis migrates into correct position without intervention during the first year of life. The condition occurs in both testicles in about (10%) of cases[17].
This study reported the prevalence of cryptorchidism in the community (5.6%) of males between one week and 5 years, the incidence of cryptorchidism in United Kingdom in (1950) was (2.7%), and in (1980) was increased to (4.1). In Denmark was (1.8%) in (1950) and increased in (1990) to (8.4%)[18] in which the result reported by this study was between the above mentioned incidence. In England and Wales was (0.8%)[19,20].
In Jordan the incidence was (2.12%) of the children in the same age group of this study patients which is less than this study result[21]. The prevalence of cryptorchidism in Lithuania newborns at birth (5.7%) in which is higher than this study result, but at one year of age, it was (1.4) which is the same result reported by this study at one year of age[22].
The prevalence of cryptorchidism in United State of America ranged between (3.7%) at birth and (1.1 %) from one year to 5 years old. International prevalence of cryptorchidism (4.6%) at birth, (2.5,%) at 3months of age, (1.5%) at 9 months, undescended testes is identified in (2.8%) of the fathers and (6.2%) of the brothers of the patients with cryptorchidism[23]. The prevalence in New York City Hospital between 1987 and 1990 was (3.7%), the overall rate had declined to (1.1%) by 3 months and (1%) at one year of age[24].
The above 3 results (USA, International, New York) at birth all are greater than the rate of prevalence reported by this study, but at 3months of age in Libya, New York City Hospital and International are fast the same, the incidence in Libya, Lithuania and International are the same at one year of age, at the same time is greater than the result reported in USA and New York City Hospital.
In this study, significant percent of mothers (37.7%) have under university education (table 2), it was discovered that the knowledge of the mothers about cryptorchidism was very poor, as about (67.4%) of mothers did not knew about cryptorchidism or its complication (figure 4).

(Table 2) Mothers education level

Level of education	Number of mothers	%
University graduated	86	26.3%
Under university graduation	240	73.7%



(Figure 4) Mothers Knowledge about Undescended testes and Its Complications

This study is the first in Libya to document the prevalence of cryptorchidism in which similar to that reported in Now York City Hospital, and higher than the prevalence reported in United Kingdom, Jordan, USA and Denmark in (1950), at the same time it was less than the prevalence reported in Lithuania, Denmark in (1990) (table 3), and International prevalence. Cryptorchidism is a very important subject to do researches about, for that reason many researches were carried out worldwide.

(Table 3) The statistical result in some countries

Country	Libya (2013)	United Kingdom (1980)	Denmark (1990)	England and Wales	Jordan	Lithuania	USA
Percentage Of UDT	5.6%	4.1	8.4	0.8%	2.12	7.1	4.8

CONCLUSION AND RECOMMENDATION

This study finding signify the diagnosis value of cryptorchidism to provide the chances of early treatment to avoid series complications, and mothers should be educated to be awareness to this condition and consult the pediatrician as early as possible .

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PREVALENCE AND CAUSES OF CHRONIC DRY COUGH AT A RESPIRATORY CLINIC IN TRIPOLI A PROSPECTIVE STUDY BY

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ABSTRACT

Prolonged dry cough, in the absence of other features that suggest common etiologies, can be a diagnostic challenge. The aim of this study was to examine the prevalence and causes of isolated chronic dry cough among the patients who presented to the respiratory clinic in Tripoli Central Hospital during the period from 1st Jan 2005 to 31st Dec 2009. In this prospective study, data from the patients who met the following inclusion criteria was collected; complaint of isolated dry cough for more than 8 weeks, normal chest radiograph, chest physical examination and basal spirometric values. The post-bronchodilator improvement in the FEV1 was considered significant and suggestive of cough variant asthma if it exceeded 15% of the baseline value. The diagnosis was confirmed if the cough improved or disappeared after a short course of steroid therapy. The diagnosis of reflux associated cough was confirmed if it improved with anti-reflux therapy. The total number of registered patients was 800; 69 consecutive patients (8.6%) met the selection criteria. The mean duration of cough was (± SD) 113 ± 141 weeks (range; 8-720 weeks). Their mean age (± SD) was 32 ± 13.2 years (range; 15-75 yrs). Thirty- nine were females (56.5%), and 8 were current or ex-smokers (11.5%). In 56 patients (81.15%) the likely diagnosis was cough variant asthma (CVA). Out of them; 45 (80%) had associated allergic rhinitis too. All of the CVA patients received a short course of oral steroids in addition to bronchodilator inhalers. In another 7 patients (10.1% of total and mostly males (71.4%)); the likely diagnosis was gastro-esophageal reflux disease (GERD) related cough and they responded to anti-reflux therapy. In the last 6 patients (8.7%) who were male smokers; no clear diagnosis was established. They received bronchodilator therapy and were advised to stop smoking. CVA was highly prevalent cause of chronic cough (81.15%) in the study group. Most of the CVA patients had rhinitis too (80%) and the contribution of post nasal drip to the etiology of cough is difficult to establish. 56.5% of the CVA patients were females and of younger age. GERD related cough was less prevalent (10.1%) and was mostly in males.

KEY WORDS: Chronic dry cough, Cough variant asthma

INTRODUCTION

Chronic cough is defined as persistent cough for more than 8 weeks, and is the sole presenting complaint of 10–38 % of referrals to respiratory physicians[1-3]. It can impair the quality of life, resulting in sleep disturbance, anxiety, fatigue, myalgia, dysphonia, syncope, or urinary incontinence; it also results in a high rate of healthcare utilization[3]. Significant sputum production usually indicates a primary lung pathology .The most common causes of chronic dry cough in non-smoking, non- ACE-inhibitor treated adults with normal chest radiogram are; postnasal drip (PND), gastro -esophageal reflux disease (GERD) and asthma syndromes[5].

Asthma syndromes include; "classic" asthma, cough variant asthma (CVA), non-asthmatic eosinophilic bronchitis and atopic cough. CVA was described in 1979 by Corrao and colleagues[6] as; Air way hyper-responsiveness (AHR) with chronic cough but without wheeze or airway obstruction.

CVA is a possible precursor of classic asthma; it usually improves within 1 week of inhaled bronchodilator therapy. Inhaled corticosteroid therapy improves the cough and may reduce the risk of progression to classical asthma[7, 8].

'Atopic cough' is a bronchodilator resistant chronic dry cough, characterizes by absence of variable airflow obstruction and the presence of atopy[7, 8, 9].

Patients with asthma syndromes may present a diagnostic challenge, awareness of them and the ability to diagnose and treat them early; relieves the patient morbidity and may prevent progression into classic asthma[9]. The aim of this prospective study was to examine the causes, characteristics & outcomes of chronic cough among the registered patients at the outpatient respiratory clinic in Tripoli central hospital during the period from 1st Jan 2005 to 31st Dec 2009.

METHOD & PATIENTS

Patients who presented to the respiratory clinic with the sole complaint of chronic dry cough for more than 8 weeks were included in the study, the following

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were the inclusion criteria; 1) No history of asthma, no therapy with ACEI therapy or beta blockers, 2) Normal chest physical examination, 3) Normal chest radiology, and 4) Baseline forced vital capacity (FVC) more than or equal to 70% of predicted values. 69 consecutive patients were included.

The collected data included; diurnal variation and exacerbating factors of the cough, personal or family history of allergic disease, smoking history, esophageal symptoms and presence of blood and sputum eosinophilia. The response of forced expiratory volume (FEV1) to short-acting beta2-agonist bronchodilator therapy was considered significant if it improved by more than 15%.

Spirometry was performed using the Quark PFT® spirometry system (COSMED) and according to the American Thoracic Society (ATS) guidelines. Spirometry was recorded before and after Ventoline inhalations doses that were repeated at intervals of a minimum of 30 minutes.

Peripheral blood eosinophilia was considered significant if it was more than > 6% of total WBC counts, and sputum eosinophil count was considered significant if was equal to or more than ≥ 3%.

Going with the European society guidelines[1]; CVA suspected patients were prescribed a two weeks course of 20 mg prednisolone and bronchodilator therapy, while GERD associated cough suspected patients were treated with a two weeks course of omeprazole 20 mg tab and bronchodilators .

Data analysis

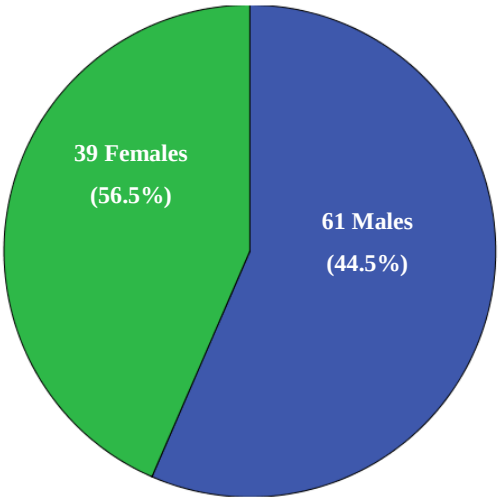
The SPSS software (Statistical Package for the Social Sciences, version 16.0 (SPSS Inc, Chicago, Ill, USA) was used for statistical analysis). Continuous variables are demonstrated as means (±SD), and categorical variables as numbers and percentages. Characteristics of the groups were compared using analysis of variance (ANOVA) for continuous variables& student's t-test for categorical variables. P less than 0.05 was considered significant.

RESULTS

During the study period; a total of 800 patients presented to the respiratory clinic and 69 of them (8.6%) met the selection criteria. As shown in (table 1); their mean age (± SD) was 32 ± 13.2 years (range; range; 15-75 yrs), 39 were females (56.5%) (figure 1), and 9 were current or ex-smokers (11.5%).

The mean duration of chronic dry cough was (± SD) 113± 141 weeks (range; 8-720 weeks). All of them had baseline FVC values more than 70 percent of predicted and FEV1 mean value of (± SD) of 72.4 ± 2.4 percent of predicted. Their mean blood eosinophil count value was 309 ±194 /cmm.

Out of the 69 patients; 56 patients (81.15%) had CVA (figure 2), methacholine inhalation challenge testing was not performed, however; the significant (> 15%) post bronchodilator improvement in FEV1 and the resolution of cough with anti-asthmatic therapy were considered diagnostic[1].

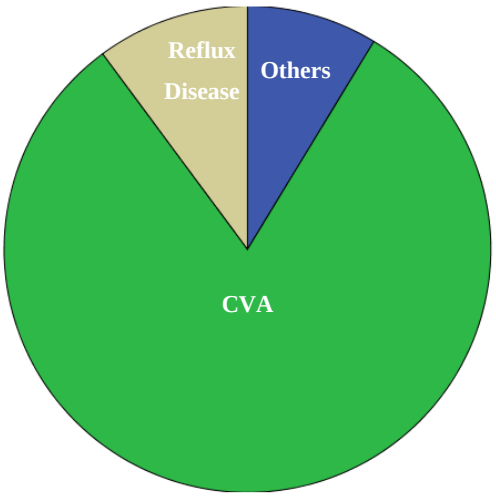


(Figure 1) Gender distribution of the studied patient

(Table 1) Demographic Characteristics of the study patients

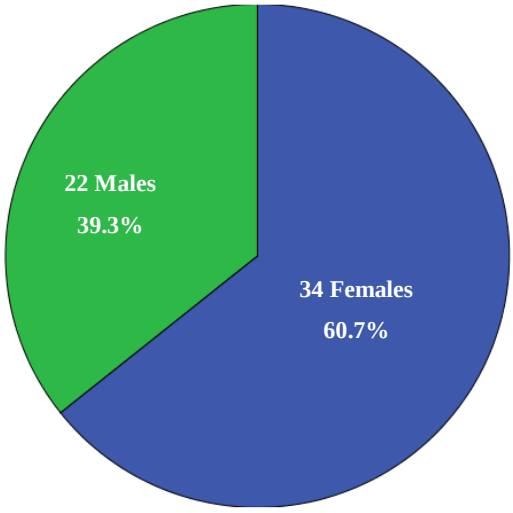
Age (yrs)	**32 ± 13.2**
Gender (female)	56.5%
Cough duration (weeks)	113 ± 141
Diurnal variation (yes)	72.4%
Seasonal variation (yes)	17.3%
Dust intolerance (yes)	68%
Allergic rhinitis (yes)	65.2%
Skin allergy (yes)	11.59%
Food allergy (yes)	5.79%
Conjunctival allergy (yes)	23%
Family history of allergy(yes)	53.6%
Smoking (yes)	13%
Blood Eosinophilia	24.6%
Sputum eosinophils (yes)	49.3%
Baseline FVC(% of predicted)	>70
Baseline FEV1 (% of predicted)	72.4 ± 2.4
Values expressed as % or mean ± SD	

As shown in (table 2); 34 of the 56 CVA patients were females (60.7%) (figure 3), all of them had dry cough, exacerbated by dust and noxious substances exposure, diurnal variations was reported by 49(87.5%) patients (the cough was more sever and frequent night and or early morning). Personal and / or family History of



(Figure 2) Causes of chronic cough

allergic diseases (rhinitis, eczema, allergic conjunctivitis, or food allergies) was reported in 32 (57.1%) and 45 patients (80%) had rhinitis. Fifteen patients had blood eosinophilia > 6% (26.7 %), with a mean value of 603/cmm. Sputum eosinophils were detected in 33 (58.9 %) patients.



(Figure 3) Gender distribution of CVA patient

The post-bronchodilator improvement in FEV1 was attained after the 1st bronchodilator test dose in 23 pts (41%), the 2nd test dose in 27 patients and the 3rd test dose in 6 patients. Seven 7 out of the 69 studied patients (10.1%) had GERD and their cough responded to reflux therapy, 5 of them were males (74.1%). The chronic cough in the other 6 patients (8.7% and all males) was probably related to smoking.

(Table 2) Diagnosis & characteristics' of the studied chronic cough patients

Cough variant Asthma	**81.15%**
Gender (F)	60.7%
Age (yrs)	30.5 ± 12
Cough duration (weeks)	121.5 ± 148.8
CVA only	10.7%
CVA + rhinitis	80%
CVA + history of allergy	57.1%
Diurnal variation (yes)	87.5%
Smoking (yes)	3/56
Blood eosinophilia (/cmm)	324 ± 148.8
Sputum eosinophils	58.9%
Baseline FEV1 (% predicted)	72.4 ± 2.55
Post bronchodilator ↑in FEV1(% predicted)	
↑FEV1≥ 15% after the 1st test dose	41%
↑FEV1≥ 15% after the 2nd test dose	48%
↑FEV1≥ 15% after the 3rd test dose	10.7%
Reflux	10.1%
Gender (Males)	71.4%
Age (yrs)	36.5 ± 7.1
Smoking (yes)	14.2%
Cough duration (weeks)	33 ± 26.7
Cigarette smoking	8.7%
Gender (Males)	100 %
Age	58.25 ± 14.2
Smoking (yes)	100%
Values expressed as % or mean ± SD	

Statistical analysis as shown in (table 3), revealed significant associations between the age of the patient with both the post bronchodilator FEV1 value and the diagnosis of CVA . The mean age of CVA was 30.5 ± 12 yrs, while the mean age of other patients was 42 ± 15 yrs (P .006).

(Table 3) Statistical Correlation findings (determined by Pearson correlation)

Feature	**CVA(n=56)**	**Others (n=13)**	**2-tailed Significance**
Age (yrs)	30.5 ±12	45.2 ± 14.8	0.006
Cough duration (weeks)	121.5±148	64 ± 74	0.239
Eosinophilia/cmm)	324±195.9	224 ± 173	0.136
Baseline FEV1(mean± SD)	72.4±2.55	72.5 ± 1.5	0.879
Post bronchodilator FEV1(mean± SD)	83.3 ± 3.3	79 ± 1.05	0.00

DISCUSSION

Out of the 69 studied patients; 39 (56.5%) were females, which is in agreement with the findings of several studies that showed higher prevalence of chronic cough among females possibly due to an intrinsically heightened cough response[10]. Eight patients (11.6%) were smokers, 7 of them were males (23.3%), and one female (2.5%). We could not be sure of the actual number of the female patients who smoked, as in Libya, smoking in females is considered as a social stigma. CVA was diagnosed in 56 out of the 69 selected patients (81.15%) (figure 2); this was a high ratio when compared with the (6-59%) ratios in other similar studies[7]. This could have been due to the use of strict selection criteria. Diurnal variations were reported in 87.5% of CVA patients (cough more sever and frequent night and or early morning). Blood eosinophilia with a mean value of 603/cmm, was detected in 15 CVA patients (26.7 %). In the western countries; mild secondary eosinophilia often represents an allergic reaction, or exposure to a variety of *drugs. In the developing* world it can also occur in parasitic infestations. During the pulmonary larval migration; patients may complain of cough, malaise, and fever, they are usually anemic and their chest radiography may show transient pulmonary infiltrates [11]. None of our CVA patients had such findings , and the drug history was negative. Sputum eosinophilia is considered as a marker of airway inflammation and was recorded in 33 of the CVA patients (58.9_%). Some studies [12] showed that asthmatics with higher sputum eosinophil count (≥ 3%) were more difficult to control with standard therapy and needed more time to achieve satisfactory FEV1 level. Personal and / or family history of atopic diseases (rhinitis, eczema, allergic conjunctivitis, and /or food allergies) was reported in 32 of the CVA patients (57.1%). Allergic rhinitis and asthma often co-exist and appear to be a continuum of airway disease. The contribution of the

PND to the chronic cough is controversial and may be difficult to establish[13,14]. Allergic rhinitis was recorded in 45 of the CVA patients (80%). None of the studied patients had findings going with "Atopic cough ". GERD is reported to be the second or third most common cause of chronic cough, (30-40%)[11,12]. In our study; only 7 (10.1 %) were diagnosed as GERD associated chronic cough. This low percentage could be explained again by using strict selection criteria**.**

In the remaining 6 (8.7%) patients, who were males & smokers, the cause of cough was not explained. Active and passive Cigarette smoking can enhance the cough response, though; smokers rarely seek medical advice specifically for cough[1]. They were prescribed bronchodilator therapy and were advised to stop smoking.

Study limitations

The cough was not assessed by the quality of life questionnaires that were recommended by the more recent European society guidelines.

It would have been better to use an objective marker for judging the CVA response to therapy; as an example, Bandyopadhyay et al suggested the use of the sputum eosinophil count for the follow up of asthmatic patients[12].

CONCLUSION

The prevalence of isolated chronic dry cough among the patients who presented to the respiratory clinic was 8.6%. CVA was the most common cause (81.15%), most of these patients (80%) had rhinitis too. 56.5% of the CVA patients were females and there was a statistical association with CVA & younger age. GERD related cough was a less prevalent cause (10.1% of total % 71.4% males). The cough in both subgroups resolved or significantly improved with the specific treatment.

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STROKE RISK CLASSIFICATION BY CHADS2 SCORE IN COMMUNITY POPULATION IN ABSENCE OF ATRIAL FIBRILLATION

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ABSTRACT

CHADS2 score is a proven, simply calculated, essential tool for estimating cardioembolic risk (mainly stroke) in patients with nonvalvular atrial fibrillation (AF). The CHADS2 score is used in clinical practice to guide decisions regarding antiplatelet and anticoagulation therapy. The study aimed to evaluat the performance of the CHADS2 score & Community Stroke Risk Classification (CSRC) to classify stroke risk factors in population without AF. This study was conducted as a community based descriptive cross-sectional study in North Africa (North West of Libya), among individuals living in Tripoli area "the capital". It was done by Department of Community & Family Medicine, Faculty of Medicine, University of Tripoli. Duration of the study was five years from 1/1/2010 to 31/12/2014. Data was collected using CHADS2 and CSRC scores; Total of 7497 individuals (52.8% males & 48.2% females) were interviewed by taking detailed histories (present, past, medical, hospital admission), checking of any available investigations, discharge letters and medical reports and perform medical examinations. Among 7497 screened, 64.2 % (4814) had risk factors (RF) of stroke and 35.8% (2682) have no risk on CHADS2 score corresponds to low stroke risk. Among population having CHADS2 risk score, 64.3% (3096) have intermediate risk score, corresponds to intermediate or moderate stroke risk. 1719 (35.7%) had high risk score corresponds to a greater high stroke risk. On Community Stroke Risk Classification (CSRC), majority of the population having stroke risk score grades with one or more risk factors (64.2%). Among 4814 had risk factors of stroke, The analysis showed significant difference in CSRC score grades (P<0.01), the majority of the population having intermediate score grades (1-2 RF)(69.4%)(P<0.001), IRS1 (41.4%) and IRS2 (27.9%). High score prevalence (≥3 RF) was 30.6%, with decrease in percentages with HRS3 (16.5%), HRS4 (9.5%), HRS5 (3.7%) and the lowest is HRS6 (0.9%). Males showed significant raise compared with females in all score grades especially in intermediate score risk (1-2 RF) (P<0.004). Intermediate score (1-2 RF) is dominated in all study age groups compared with high scores (3-6 RF)(P<0.001); 16-49 years (67% for 1-2 RF, 33% for 3-6 RF) and 50-80 years (51.1% for 1-2RF, 48.5% for 3-6RF). Hypertension and Diabetes were the major risk factors of stroke on all scores and highest among intermediate score (1-2 RF) (P<0.001). This study confirmed that stroke is a major public health problem in North Africa. CHADS2 & CSRC scores are very useful and simple method to classify stroke among population without AF.

KEY WORDS: Stroke, CHADS2 score, Prevalence, Risk factors, Classification, Community, Atrial Fibrillation, Africa.

INTRODUCTION

CHADS2 score is a proven and essential tool for estimating cardioembolic risk (mainly stroke) in patients with nonvalvular atrial fibrillation (AF). In this study we analyzed the use of CHADS2 score which adapted to classify stroke risk factors in general public without known atrial fibrillation in a Mediterranean population of Africa (Libya)[(1)].

The CHADS2 score is a validated clinical prediction tool commonly used to estimate the risk of stroke in atrial fibrillation[(2)]. The score is derived from the sum of point values of individual stroke risk factors, one point each for (congestive heart failure (CHF), hypertension, age≥ 70, diabetes, and two points each for prior stroke or transient ischemic attack (TIA)[(2)]. A high CHADS2 score corresponds to a greater risk of stroke, while low CHADS2 score corresponds to lower risk of stroke[(2)].

The CHADS2 score is used in clinical practice to guide decisions regarding antiplatelet and anticoagulation therapy. The simplicity of its calculation has facilitated its widespread adoption and endorsement by national and international society guidelines[(3)].

Although the CHADS2 score and other similar risk stratification schemes have proven useful in populations with known AF, the vast majority (85%) of ischemic strokes occur in individuals without known AF, hence the use of the score in general public[(4)].

North African population at increased risk for stroke. The incidence of stroke varies from 63 to 162 per 100,000 populations, males are affected more than females[(5)]. Furthermore, according to WHO 2014 report, 78% of deaths in North Africa are due to non-communicable diseases, which include stroke and the

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mean age of stroke is within the sixth and seventh decade (varying from 58.5 to 63)[6].

Although CHADS2 score was not used in North Africa, Centre of Disease Control –World Health Organization (CDC-WHO) in 2009 in north Africa (Libya) studied stroke in community survey among 3096 individuals where the risk of stroke among the total population of the that study was very high 99.6% and classified stroke into two categories; category one, representing low grade where population had one or two risk factors of stroke (1-2RF) and high grade where population having three to five risk factors (3-5RF)[7].

CDC-WHO report of that study, showed that high grade (3-5RF) was dominated with 57.6% among study population and the low grade (1-2RF) was 42.4%. Those findings were found among total study population and also among sex; were 37.3% of males had 1-2 RF, 62.7 had 3-5 RF and 48.8% of females had 1-2RF, 52.2% had 3-5RF. CDC-WHO report also confirmed that high grade (3-5RF) was dominated in both age groups , 25-44 years old (48.8% for 1-2RF, 52.2% for 3-5RF) and 45-64 years old (21.9% for 1-2RF, 78% for 3-5RF)[7] .

Each component co-morbidities of the CHADS2 score has been independently associated with stroke in large cohorts of North African population. Therefore, we hypothesized that stroke risk may also be well captured by the CHADS2 score in non-AF general population. To test this hypothesis, the performance of the CHADS2 score for prediction of stroke among general public without AF was evaluated. So, this study was conducted with the aim to analyze the role of the CHADS2 score and Community Stroke Risk Classification (CSRC) to estimate stroke risk factors in community based population without AF in North Africa.

MATERIALS AND METHODS

Study Design and Setting

This study was conducted as a community based descriptive cross-sectional study in North Africa (North West of Libya), among Individuals living in Tripoli area "the capital". It was done by Department of Community & Family Medicine, Faculty of Medicine, University of Tripoli. Duration of the study was five years from 1/1/2010 to 31/12/2014.

Study Population

The study population sample included 7497 randomly selected individuals from population without AF. The study included Adults aged from 16 to > 80 years old.

Methods

History and Medical Examination

Interviewing individuals by taking detailed histories (present, past, medical, hospital admission), medical examinations, checking of any available investigations, discharge letters and medical reports. Known cases of strokes or TIA had been established by medical diagnosis in the past by hospital specialists.

CHADS2 Score Questionnaire

Doctors working in community and family medicine department were trained by Professions to collect data using CHADS2 method; Individuals were interviewed using CHADS2 score questionnaire which adapted to be used among general public with absence of atrial fibrillation[1]. In this study CHADS2 score as well a local Libyan classification of stroke risk factors was used called (Community Stroke Risk Classification-CSRC). CHADS2 score is derived from the sum of point values of individual stroke risk factors {congestive heart failure (CHF), hypertension (HT), age≥ 70, diabetes (DM) (1 point each), and prior stroke or transient ischemic attack (2 points)[2] (table 1). The CHADS2 scoring table which shown below adding together the points that correspond to the condition represents the results in CHADS2 score which used to estimate stroke risk as follows;

Score Zero = No risk = Low Risk Score
Score 1 & 2 = Intermediate Risk Score
Score ≥3 = High Risk Score

(Table 1) showing CHADS2 score Questionnaire used in the study

Condition	Points
C: Congestive heart failure	1
H: Hypertension	1
A: Age ≥70 & sex	1
D: DM	1
S: Prior Stroke or TIA	2

Community Stroke Risk Classification-CSRC

This classification depends on calculation of numbers of risk factors (RF), each Risk factor used in study as age ≥ 70, DM, Hypertension, CHF, TIA and prior stroke were given one number for each condition among each individual participated and the score was a result of summation of those risk factors as shown in (table 2).

(Table 2) showing CSRC score used in the study

Level	Score	No. of Risks	Abbreviation
Low risk	score of zero	No risk factor	LRS 0
Intermediate risk	score of one	One risk factor	IRS 1
	score of two	Two risk factors	IRS 2
High risk	score three	Three risk factors	HRS 3
	score four	Four risk factors	HRS 4
	score five	Five risk factors	HRS 5
	score six	Six risk factors	HRS 6

Statistical Analysis

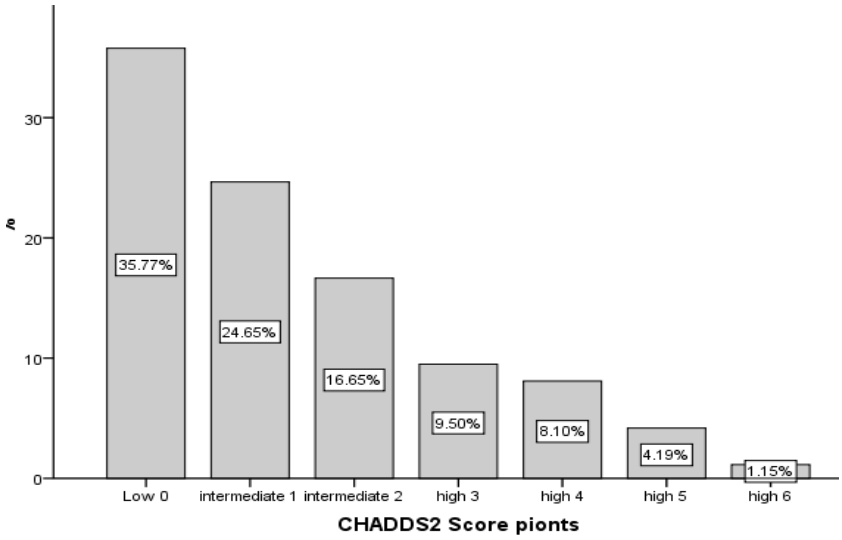
Statisticians were gathering, scoring CHADS2 and CSRC grades, analyzing all information and calculating T-test & P value by using SPSS package version 19- USA.

RESULTS

Among total population (7497), males were 52.8% (3881) and females were 48.2% (3616) with mean age of 52, which is also reflected on different age groups selected in the study and this age/sex structure in the study was agreed with Libyan census of 2010 (51% males & 49% females).

CHADS2 score among study population

Among 7497 individuals screened, 64.2 % (4815) had risk points (RP) of stroke and 35.8% (2682) have no risk on CHADS2 score corresponds to low stroke risk (Low risk score, LRS0). The CHADS2 score grades are gradually decreased in percentages from low to high, intermediate score (3096, 41.3%) is predominant (P<0.01) compared to high scores (1719, 22.9%). IRS1 (24.65%) having one risk point, IRS2 (16.65%) having two risk points. High scores, HRS3 (9.5%) having three risk points, HRS4 (8.1%) having four risk points, HRS5 (4.19%) having five risk points and HRS6 (1.15%) having six risk points (figure 1). Among population having CHADS2 risk score (4815 individuals), 64.3% (3096) have intermediate score risk, corresponds to intermediate or moderate stroke risk where individuals have one or two risk points. 1719 (35.7%) had high risk score corresponds to a greater high stroke risk, with three risk points or more.



(Figure 1) Showing CHADS2 score among total population

Community Stroke Risk Classification among study population

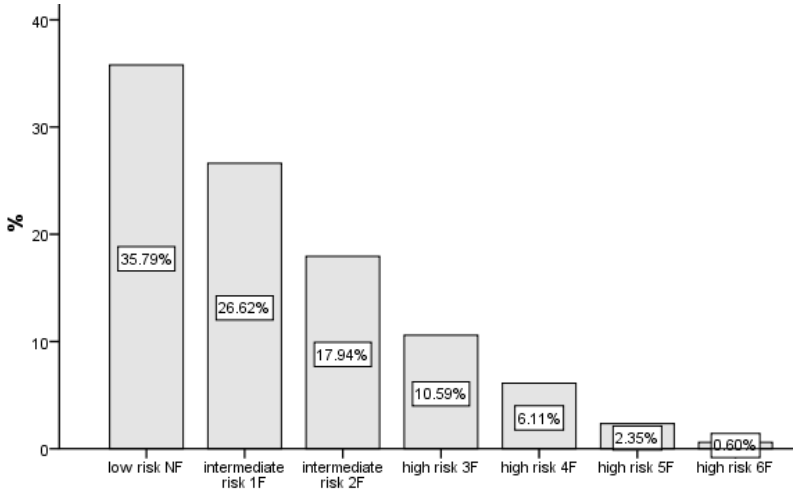
Among total population screened in the study (7497 individuals), 4814 (64.2%) have risk factors on CSRC. 2683 (35.8%) have no risk on CRSC score (LRS0). From those who have risk factors, 3341 (44.6%) have intermediate score risk (IRS 1&2), where individuals have one or two risk factors. 1473 (19.6%) have high risk score (HRS 3,4,5,6) with three risk factors or more.

The CRSC score grades is gradually decreased in percentages from low to high grades, intermediate sore is predominant (P<0.01) compared to high scores specially IRS1 (1996, 26.6%) having one risk factor, and IRS2 (1345, 17.9%) having two risk factors. High scores, HRS3 (10.6%, 794) having three risk factors, HRS4 (6.1%, 458) having four risk factors, HRS5 (2.3%, 176) having five risk factors and HRS6 (0.6%, 45) having six risk factors (figure 2).

Among 4814 individuals had risk factors of stroke, The analysis showed significant difference in CSRC score grades (P<0.01), the majority of the population having intermediate score grades (69.4%, 3341)(P<0.001), IRS1 (41.4%) and IRS2 (27.9%). High grade prevalence was 30.6% (1473), with decrease in percentages with HRS3 (16.5%), HRS4 (9.5%), HRS5 (3.7%) and the lowest is HRS6 (0.9%).

Age grouping & the classification scores

This result showed that a complexity of risk factors increased with increase of age. All age groups were affected with risk scores which increases from forty years old and most ages having the highest scores with multiple risk factors was, 50, 55 ,60, 70, 75 & 80 years old. Concerning age groups which showed higher score risk more than others were 30-49, 50-59, 60-69 with the highest prevalence in 50-59. Though risk scores still high among 70-79 and ≥80 years old. With age grouping, the most prominent scores were the intermediate score (IRS1 & IRS2) (P<0.001).



(Figure 2) Showing CSRC score grades among total population

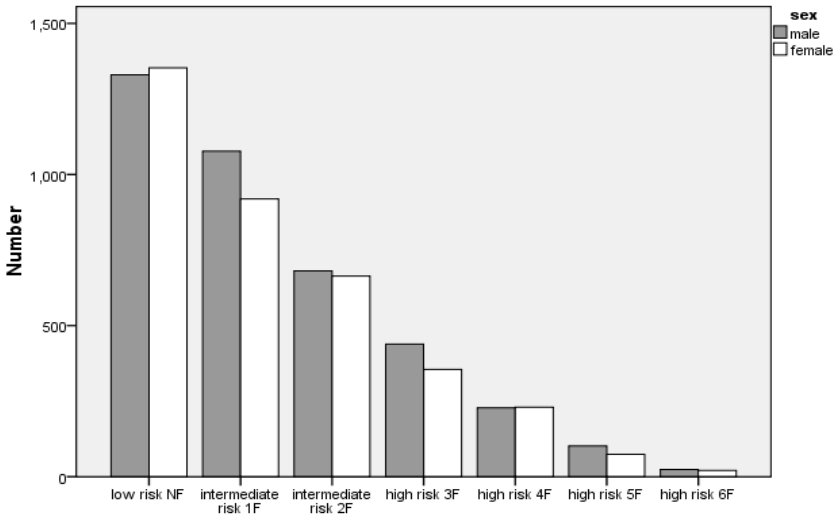
If we divide the age groups into two groups, 16-49 years old and 50->80 for simplicity , 25.6% of population had risk was among 16-49 and 74.4% among 50->80 (P<0.001), also we found that intermediate score (1-2-RF = IRS 1,2) is dominated in both age groups compared with high scores (3-6RF = HRS 3-6) with 69% (1-2 RF) & 31% (3-6RF) respectively (P<0.001), in 16-49 years (88.3% for 1-2RF, 11.7% for 3-6RF) and in 50->80 years (63.8% for 1-2RF, 36.2% for 3-6RF).

Sex & the classification scores (CHADS2 & CSRC score)

65.7% (3160) of male participant in this study had risk points (from 1 to 6 RP), and 62.6% (2718) of female participant had risk points of stroke. Among study population having risk points (4814), males constitute 53% and females 47%. Among males, 63.4% had intermediate score risk with 1-2 RP, 36.5% had high score with 3-6 RP, and among females 65.2% had 1-2 RP, 34.8% had 3-6 RP.

65.7 (2551) of male participant in this study had risk factors (RF) (from 1 to 6 RF), and 62.6% (2263) of female participant had risk factors of stroke. Among study population having risk factors (4814), males constitute 53% and females 47%. Among males, 68.9% had intermediate score risk with 1-2 RF, 31.1% had high score with 3-6 RF, and among females 70% had 1-2 RF, 30% had 3-6 RF.

Males showed significant raise compared with females in all score grades specially in intermediate CHADS2 & CSRC score risk 1-2 RF (P<0.004) (figure 3).



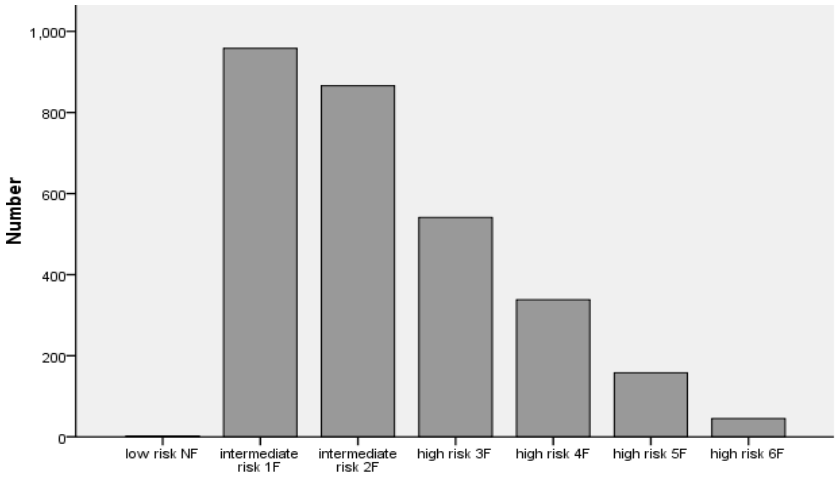
(Figure 3) Showing CSRC score grades and sex

Diabetes Mellitus (DM) & the classification scores

The prevalence of DM among study population over five years was 39%, 54.1% among males and 45.9% among females. DM present in all score risks with highest prevalence in IRS1 (33%) and IRS2 (30%) (P<0.001). DM showed decrease in HRS3 (18.6%), HRS4 (11.6%), HRS5 (5.4%) then declined to the lowest prevalence (1.5%) in HRS6 (figure 4). Males were slightly dominated over females in all scores and age groups.

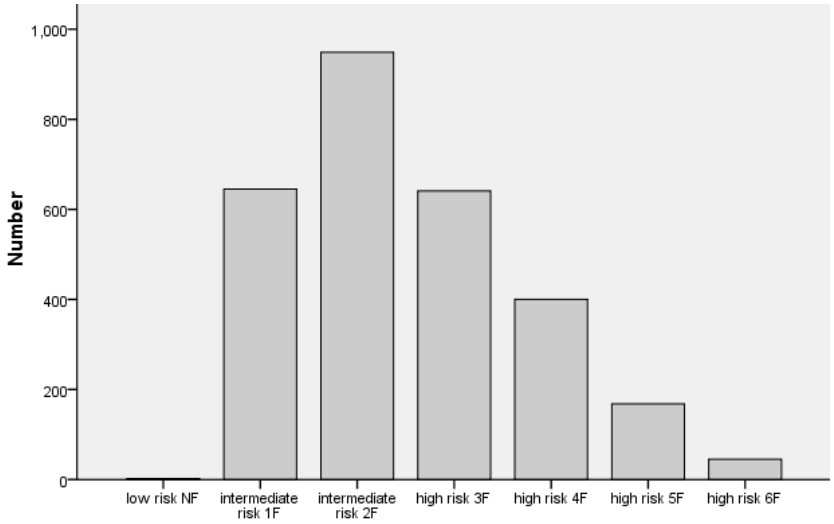
Diabetic patients were distributed all over the age groups but the highest prevalence was found in age

groups over forty (40-49, 50-59 & 60-69) with predominance in intermediate score (IRS1 & 2).
This result confirms that DM is major risk factor of stroke, usually come alone or with hypertension as risk factor and with less account with other risk factors in multiple high score pattern.



(Figure 4) Showing Diabetes Mellitus & CSRC score

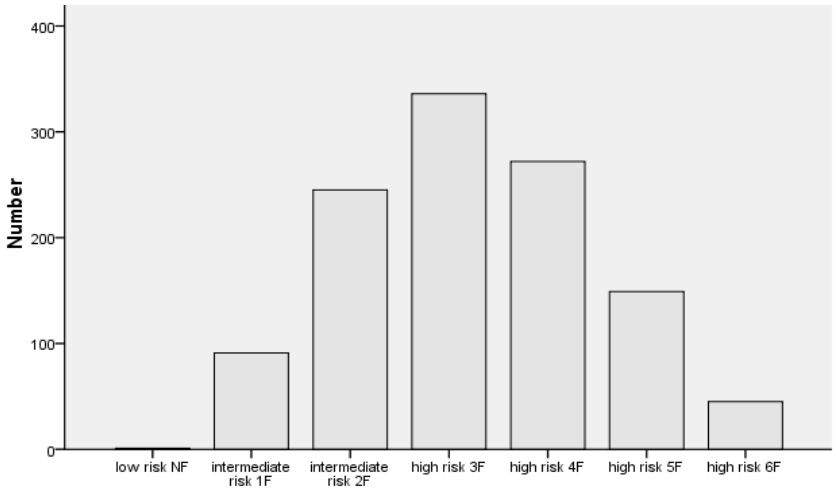
Hypertension (HT) & the classification score
The prevalence of HT among our participants was 38%, among males and females were 50.2% and 49.2% respectively. HT is a major risk factor present in all scores, especially IRS2 (33.3%) then lowered to 22.6% in IRS1, HRS3 (22.3%), HRS4 (14%), HRS5 (5.9%) then declined to the lowest in HRS6 (0.8) (figure 5).
Hypertensive females were generally higher than males in most sores except in high scores HRS3, HRS5 & HRS6. Female predominated in middle age groups (40-59), and males dominated in younger age groups 16-39 and in older ages >60. HT prevalence increase with age, shows higher prevalence in IRS1, IRS2 in age >40 (P<0.001).
This result showed that HT associated with stroke in more than one third of the study population, which is coming alone or with DM forming intermediate risk score of stroke, and also to less extent can be accompanies other risk factors to form multiple risks in higher scores



(Figure 5) Showing Hypertension & CSRC score

Congestive heart failure (CHF) & the classification score
Prevalence of CHF among study population was 15.2%, 51.2% males and 48.8% females. CHF is distributed over all scorers with high prevalence in IRS2 (21.5%), HRS3 (29.5%), HRS4 (23.9%), HRS5 (13.0%), its less in HRS1 (7.9%) and lest in IRS6 (3.9%). Males were dominated in all scores (P<0.001) except in HRS4 where females were higher (figure 6). CHF in all score grades is concentrated in age groups

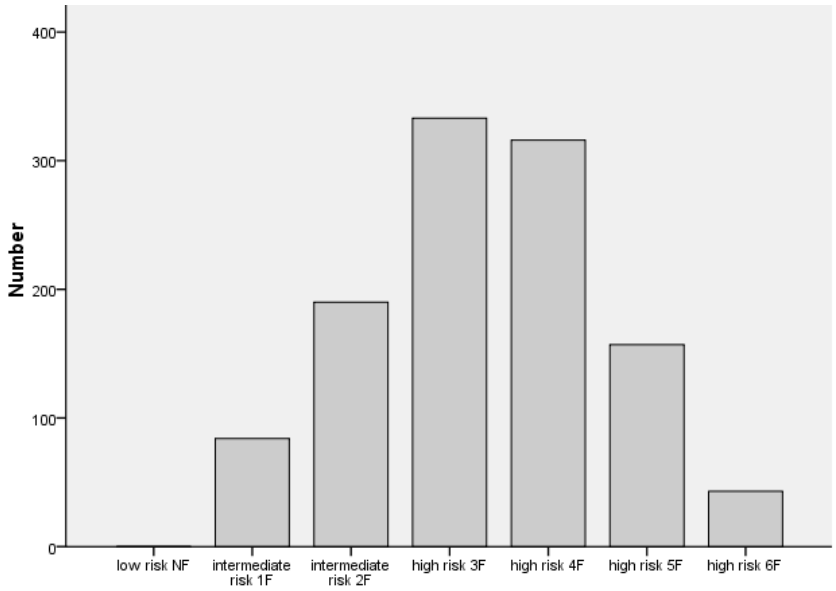
over forty and predominated in 60-69 & 70-79. This result showed that CHF usually come with or as result of other risk factors to form multiple risk factors in higher scores.



(Figure 6) Showing Congestive heart failure & CSRC score

Transit Ischemic Attack (TIA) & the classification score

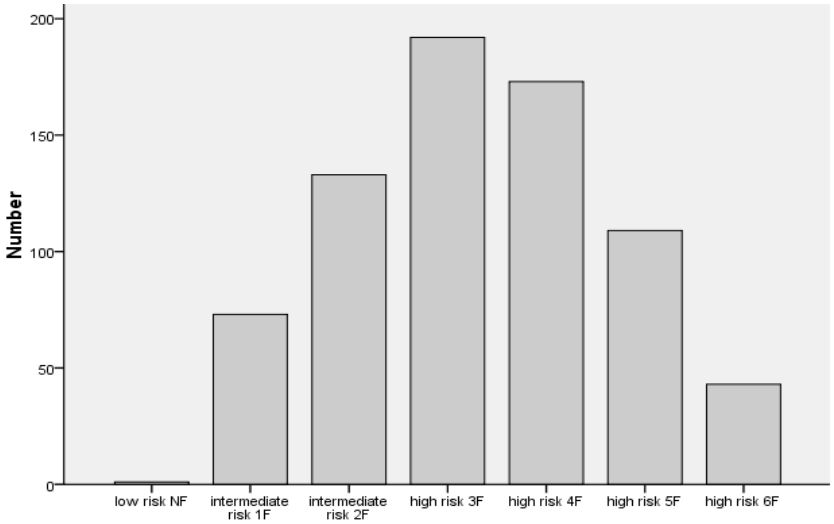
The prevalence of TIA among study population was 15% (1521), 58.2% males and 41.8% females. TIA is present in all risk scores but highest in HRS3 (29.7%), HRS4 (28.1%), HRS5 (13.9%), HRS6 (3.8%), and lower in IRS1 (7.5%), IRS2 (16.9). Males were higher in all scores compared to females (figure 7). TIA is present with higher prevalence in older ages over sixty years especially with multiple high scores. This result showed that TIA affecting older ages and usually come with or as result of other risk factors forming multiple risks associated with strokes especially in higher scores.



(Figure 7) Showing transient ischemic attack (TIA) & CSRC score

Prior Stroke (PS) (embolic or hemorrhagic) & the classification score

Prior stroke prevalence was 9.7%, males 48.9% and 51.1% females. PS found in all risk scores especially high score grades, HRS3 (26.5%), HRS4 (23.9%), HRS5 (15%), IRS2 (18.4%) and lower prevalence in IRS1 (10%), (figure 8). Females were more among intermediate score and males dominated in higher scores. Prevalence of PS is higher in older ages than forty years old. This result showed that PS usually complicated with other risk factors to form multiple pattern in higher scores.



(Figure 8) Shows prior stroke (embolic or hemorrhagic) & CHADS2 score

DISCUSSION

This is the first time such big study of assessing risk factors of stroke have been done in North Africa (North West of Libya), among Tripoli population; and it founded that stroke is a very common and important public health problem among study population.

A past systematic literature review done in Arab countries[5], and other different studies in Africa & Middle East[8], showed high prevalence of stroke among North African population.

In North Africa (Libya) Reports of research institutes 2001[9], and reports from CDC-WHO 2009[7], revealed that stroke is associated with multiple risk factors. That was also confirmed with the results of our present study.

This present study confirmed that mainly age, hypertension and diabetics, CHF, prior stroke and TIA were major stroke risk factors in North Africa, where in a systematic review including studies in Arab countries (Saudi Arabia, Qatar, Libya, Kuwait, Jordan, United Arab Emirates, Bahrain, Tunisia, Iraq, and Sudan)[5], North Africa[8], and Libya[7] showed that stroke is strongly associated with age, hypertension, DM, obesity and smoking.

Our results showed that stroke can be occurred at any age but the prevalence was increased by age specially over 40 years old, and this finding was also confirmed by other study in Africa[7,8].

Despite the proven utility of the CHADS2 score and other risk stratification approaches in patients with nonvalvular atrial fibrillation, most ischemic strokes (85%) occur in individuals without known atrial fibrillation[10] which encourages us to use the score among community population not having AF. Moreover, epidemiologic studies have shown that hypertension and DM is the most important determinants of stroke risk, and that each component of the CHADS2 score is independently associated with cerebrovascular events in the general population[11]. Nonetheless, to our knowledge, there are no studies investigating the utility of this score for estimating the risk of a cerebrovascular event in general publics without known atrial fibrillation.

This study which used CHADS2 score among community population without AF in North Africa was not odd or unique as this it has been used to classify the risk factors of stroke elsewhere in the world[1,4]. More ever Morillas P et al., 2014[1], showed that CHADS2 score is proved, essential and useful tool to estimating stroke risks in patients with hypertension without presence of AF.

Our study used this score which is usually used as clinical predictor of stroke, in patients with nonvavular AF[12], because its simple rule that easy to remember and to apply in clinical practice and also it has been validated by several studies as that conducted by Ruiz Ortı´z et al., 2008[13].

This study confirms that age, hypertension and DM are major stroke risk factors among North African, moreover, epidemiological studies elsewhere in the world, have shown that hypertension is the most important determinant of stroke risks, and major component of CHADS2 score which is independently associated with cerebral events in general populations[1].

Present study shown that among total population surveyed, 68.7% were having risk factors of stroke where in other studies in North Africa, a Libyan CDC and WHO reported a much higher prevalence (99.8%) of their study population had risk factors[7].

Our results showed that CHADS2 score is the first time used in North Africa but WHO report 2009 did classify strokes in North Africa into two grades, low grade (1-2FR) and High grade (3-5RF)[7], our study classified stroke according to CHADS2 score which divided into Low score (Zero RF), intermediate score (1-2RF) and high score (3-6RF).

Present results confirmed that the intermediate score (1-2RF) was dominated more than other scores (56%), compared to high score (3-6RF)(44%). This is also dominated in age groups; as in 16-49 (76% for 1-2 RF, 33% for 3-6RF), and in 50->80 (51.1% 1-2RF, 48.5% 3-6RF). Also the intermediate score is dominated

among sex, males (55.2% 1-2RF, 44.8% 3-6RF) and females (57.1% 1-2RF, 42.9% 3-6RF).

WHO report in North Africa showed reverse to our results, where high grade (3-5RF) was dominated (57%) than low grade (1-2RF) (42.4%), and this also dominated over sex and age groups, Males (37.3% 1-2RF, 62.7% 3-5RF), females (47.8% 1-2RF, 52.2 3-5RF), in 25-44 age group (21.9% 1-2RF, 51.2% 3-5RF) and in 45-64 age group (21.9% 1-2RF, 78% 3-5RF)[7].

Our finding of dominating intermediate score (1-2RF) more than CHADS2 high score (3-6RF), was not comparable with published CHADS2 rates in AF patients studies where shown domination of high scores of 5-6RF more than the moderate CHADS2 scores of 1-2RF[4]. Our explanation for this is that patients with AF will have a complex of risk factors and multiple medical complications which can be associated with stroke compared to general public with less risk factors. This study showed that CHADS2 score is very simple and useful to be used to classify stroke in North Africa where it used for the first time for such purpose.

This score although used in general public living in the community without the presence of AF but still giving valid classification of the risk factors of stroke among such population.

CONCLUSION

This study confirms that stroke is a major and important public health problem and causing death in North Africa. Results showed that more than 44.6% of study population had only one or two risk factors of stroke constitute intermediate scores (IRS1 & 2), and mostly is associated with HT, DM or age over seventy years old. All classification scores are mostly affected by age, gender, HT, DM and to lesser extent by other risk factors like CHF, TIA and prior stroke. Hypertension and DM found in all age groups, and mostly with intermediate CHADS2 scores (IRS1 & 2), especially in age groups between 40 and 60 years old, and mostly presented each one alone or together associated with strokes and to lesser extent forming multiple risk groups in higher CHADS score.

Other risk factors like CHF, TIA & PS usually presented with multiple pattern in higher CHADS2 score (HRS 3-6) among older ages >60 years old.

Our observations confirm that CHADS2 & CSRC predication of stroke is very good, simple and useful method to classify the grades of risk factors among North African.

STUDY LIMITATION

This is descriptive cross section study which seen each individual in the study only once without follow up or treatment mentoring as its designed to predict prevalence rates and classification of risk factors.

RECOMMENDATION

To conduct future studies which depend on medical and laboratory investigation with follow up & treatment monitoring of stroke.

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THE SCOPE OF THROMBOLYTIC THERAPY AMONG ST SEGMENT ELEVATION MYOCARDIAL INFARCTION IN MISURATA CENTRAL HOSPITAL

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ABSTRACT

Little is known about thrombolytic therapy patterns in patients with ST-elevation myocardial infarction (STEMI) in Libya. The objective of this study is to analyze the use of thrombolytic therapy in patients with ST-Elevation Myocardial Infarction (STEMI) in Misurata Central Hospital. The study includes 73 patients diagnosed with STEMI, from hospital admission to discharge, from a total of 125 patients with acute myocardial infraction admitted to Misurata Central Hospital cardiology care unit between January and December of 2009. RESULTS of the 73 patients with STEMI, 52% (n=38) were thrombolysed with Streptokinase, Alteplase, and Tenecteplase. 14% of eligible STEMI patients did not receive reperfusion therapy. The age of patients varied from 31 to 80 years of age, with a median age of 55.9 years, a majority of 84% being male. The overall median symptom onset- to hospital presentation was 4 hours in thrombolytic recipient patients and 20 hours in non recipient patients. The median door to needle time was 34 minutes. Poor left ventricular ejection fraction was less than 30% and reported more in non-thrombolytic recipient patients. Thrombolytic recipient patients were less likely to develop left ventricular failure. The global in-hospital mortality rate for STEMI patients in 2009 was 8%. Thrombolytic therapy is the only form of reperfusion strategy in Misurata. There was inappropriately long symptom-onset to hospital presentation as well as door- to needle times. Thrombolytic agents improve morbidity but early mortality was relatively high, which needs further exploration.

KEY WORDS: Acute coronary syndrome, STEMI, thrombolytic agents, efficacy, mortality, Misurata

INTRODUCTION

Acute myocardial infarction is the result of a ruptured atherosclerotic plaque, causing thrombosis and occlusion of a coronary artery[(1)].

Major attention has been focused on reperfusion therapy, which helps to restore coronary patency in acute ST- segment elevation myocardial infarction (STEMI) that leads to the preservation of left ventricular function and improves survival[(2)].

Current acute reperfusion therapy is available, either with primary percutaneous coronary intervention (PPCI) or with thrombolytic therapy (TT)[(3)].

The preferred option is primary percutaneous coronary intervention (PPCI) especially in those with acute ST-segment elevation myocardial infarction (STEMI) patients, patients who otherwise would receive no reperfusion, those with a bleeding risk, or those likely to have a poor result from fibrinolysis[(4)].

Unfortunately, the majority of countries do not have PPCI capability[(5)].

Misurata Central Hospital is a non invasive hospital that does not have a PPCI facility or the ability to transport patients for PPCI within the recommended time window (90-120 minute). Therefore TT remains the only reperfusion strategy in the hospital.

Several thrombolytic agents are currently being used that differ with respect to fibrin affinity, fibrin specificity, method of administration, allergic reactions and multiple other parameters[(6,7)].

In Libya, little is known about the use of various thrombolytic agents as well as their impact on morbidity and mortality.

The aim of the study is to clarify the extent of use of thrombolytic agents, to estimate the probability of timely administration of thrombolytic agents (factors associated with prolonged delay) and to assess the effect of these agents in regards to a 7-day in hospital mortality rate, complications and post AMI left ventricular functions among patients with STEMI in Misurata Central Hospital.

PATIENTS AND METHODS

In this retrospective hospital based study we reviewed the charts of all consecutive patients with a final principle discharge diagnosis of AMI, including both patients with and without ST-segment elevation who were admitted and treated in Misurata Central Hospital cardiology care unit from January to December 2009. In order to be included in the analysis patients must have presented with symptoms suggestive of myocardial ischemia and an ST-segment elevation of at least 1mm or more, contiguous electrogram leads or new LBBB. Non Libyan patients were excluded. Data was gathered regarding the age, sex, duration of AMI

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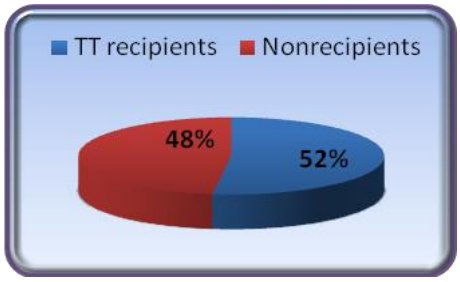
symptoms, eligibility for thrombolysis, timely administration of thrombolytic agent (door-to-needle time), ECHO-Cardiography (estimated within 24 hour of AMI event: post infarction wall motion, LVEF: normal >50%, mild to moderate impairment 31-50%, and severe impairment <30%), complications, and outcome of each patient. Any information that could not be obtained was given a designation of unknown. The information was then analyzed.

RESULT

A total of 125 consecutive patients admitted to Misurata Central Hospital during one year period 2009 with AMI, 73 patients (58%) suffered STEMI and were included in the study. Thrombolysis was applied in 38 patients (52%) (figure 1).



(Figure 1) Frequency of TT among STEMI patients

Demographic and clinical characteristics for TT recipient and non recipient patients are outlined (table 1).

(Table 1) Clinical characteristics of patients with STEMI

Characteristic	TT recipients n=38	Non recipients n=35
Age, yr, median(range)	55.9 (31-80)	61.9 (31-95)
Sex, male, %	84%	66%
Duration of AMI symptoms, hr	4hr	20hr
AMI involving ant wall, %	68%	49%
Cardiogenic shock	5%	0%

The overall median age was 55.9 (34-80) in TT recipient patients while 61.9 (31-95)in non recipient patients with majority being males, (84%) in TT recipient patients and (66%) in non-recipient patients. The overall median symptom onset to-presentation was 4 hrs in TT recipient patients and 20 hours in non-recipient patients. 68% of TT recipient patients the site of MI was involving the Anterior wall. 5% of TT recipient patients presented with cardiogenic shock.

Out of 73 patients, 18 patients did not have complete data on time of symptom onset to hospital arrival, thus we were able to analyze the duration of chest pain for 55 patients. 27% of patients presented to the hospital after 12 hrs (table 2).

(Table 2) Duration of chest pain

	n	%
180 min	17	31%
360 min	23	42%
> 12 hr	15	27%

In 29 TT recipient patients, door to needle (DTN) time was reported. The overall median door to needle time was 34 min and 66% of patients DTN time was within the recommended time (table 3).

(Table 3) Time to reperfusion therapy and factors independently associated with timely administration of TT

Variable	TT. N=29
DTN, min, median	34
DTN, administrated with in recommended time, %	66%
DTN, among patients received Alteplase, min, median	34
DTN, among patients received Tenecteplase, min, median	30
DTN, among patients received Streptokinase, min, median	90

(Table 4) presents eligibility and contraindication for TT, out of 73 patients, 35 patient (48%) did not receive TT. 7 patients was excluded because unknown chest pain duration and complete data set were available for 28 patients. We determine eligibility for TT used on American college of cardiology / American heart association (ACC/AHA) guide line, eligible patient were defined as having all indication for TT and no contraindication.

(Table 4) Eligibility and contraindication for TT

Factor	No	%
Spontaneous reperfusion	2	7%
Late presentation chest pain >12hr	15	54%
Bleeding risk	1	4%
age≥75	2	7%
LBBB	2	7%
Absent ischemic character	2	7%
Looks eligible patients	4	14%

This study revealed that 15 patients (54%) with long symptom –onset to hospital presentation time and 4 patient (14%) of eligible STEMI patient did not receive any reperfusion therapy. Echo- estimation for left ventricular function was reported in 66 patient, from our data TT recipients had median LVEF % of 56% vs. 54% for non recipients. Table 5.While poor left ventricular ejection fraction (LVEF) less than 30% observed more in non TT recipient than TT recipient patient (13% vs. 6% ; p=0.0002).

TT recipients less likely to develop LVF (3% vs. 14%, P =<0.01) but were more likely to exhibit ventricular arrhythmia (11% vs. 9%, P= NS) which may indicate the higher rate of reperfusion (reperfusion arrhythmia) (table 5).

(Table 5) ECHO estimation LV function

	TT recipients	Non recipients	P value
LVEF, median, %	56%	54%	NS
Normal LVEF >50%	71%	64%	NS
mild to moderate LVEF30-49%	23%	23%	NS
poor LVEF<30%	6%	13%	0.0002

The global in-hospital mortality for STEMI patients throughout the study period, regardless of whether reperfusion was carried out or not, was 8%. The effect of thrombolytic therapy on mortality is also shown in (table 6).

(Table 6) In-hospital mortality rate and complication regarding TT

	TT recipients	Non recipients	P value
In hospital MR	11%	6%	NS
LVF	3%	14%	0.0075
CC	5%	0%	0.0037
Vent. Arrhythmia	11%	9%	NS

DISCUSSION

The present study is the first one to review STEMI patients in our city. The registry of Myocardial infarction is important to reveal the extent of this condition in our area and could contribute to the optimal use of reperfusion therapies, with the ultimate goal of reducing mortality[8].

The main findings from this study are STEMI patients in our city are predominantly male reperfusion done only by use of thrombolytic therapy in 52% of cases.

There was inappropriately long symptom, onset to hospital presentation time, the overall median symptom-onset to hospital for TT recipient patients was 4 hours which is inappropriately long compared to 89 and 120 minutes in emergency medical services (EMS) transported and self transported patients respectively in the NCDR registry[9]. This long delay may reflect poor use of emergency medical service in our country. Increased delay times to restoration of coronary flow are associated with increased infarction size, increased risk of subsequent congestive heart failure and higher mortality[10].

The overall median door-to-needle time in this study was 34 minutes which is longer compared to 29 and 30 minutes seen in the NCDR and GRACE registry respectively[9,10]. The reasonable cause for this delay that thrombolytic therapy administered only by cardiology service unit in intensive care unit rather than emergency room. The guide line recommended optimal door-to-needle time of less than 30 minutes, was achieved in 66% which is reasonable result compared to 45%, 64% and 66% in the GRACE, Euro Heart survey ACS-III and the UK MINAP registry, respectively[10-12]. Nearly 14% of patients with STEMI who present within 12 hours and are candidates for thrombolytic therapy according to current guide lines, did in fact receive no such therapy.

This result appear to be less than reported in Brasil and Middle East, (35% and 21%) respectively [13, 14]. In this study Cardiogenic shock was not present limitation for TT use and two patient with Cardiogenic shock received TNK, in spite poor outcome; incomplete lyses in the infarct related artery and high frequency of multi vessel disease in patient with Cardiogenic shock may limit the efficacy of TT[15].

One other observation from our data relates to the poor left ventricular ejection fraction less than 30% was more in non TT recipient than TT recipient patients (13% vs. 6%, p=0.0002). and occurrence of left ventricular failure was more in non TT recipient.

This is similar to Schoming, et al[16] study which showed that patients who received TT regimen have a slightly higher global ejection fraction.

There is a curvilinear correlation between left ventricular ejection fraction and morbidity has been demonstrated for patient in both the pre thrombolytic and thrombolytic eras[17].

The global in hospital mortality for STEMI was 8% which is comparable with that reported from European and international multicenter studies (6-8%)[18-20].

A finding that needs further exploration is the relatively high mortality in TT recipient patients, which was 11% when compared with 5.7-6% reported in previous registries[21-24].

This is could be explained by occurrences of ventricular arrhythmia or by use of streptokinase. GUSTO-1 trial[25] demonstrated the superiority of alteplse over streptokinase regarding mortality. The mortality benefit seen from newer thrombolytic agents suggests that there should be a change in pattern of thrombolytic agents[20].

CONCLUSION

Just over 50% of patients suffered STEMI, were thrombolysed with Streptokinase, Alteplase and Tenecteplase. Thrombolytic therapy is the only form of reperfusion strategy in Misurata. There was inappropriately long symptom-onset to hospital presentation as well door to needle time. Thrombolytic agents improve morbidity but early mortality was relatively high, that need further exploration.

RECOMENDATION

At a national level, mortality in STEMI patients could be reduced through the following actions. First, it is important for authorities and organizations to monitor continuously the profile of STEMI patients. Second, it is very important to reduce the percentage of patients receiving no reperfusion therapy at all. Third, fibrinolysis should be administered as early as possible and ideally in pre-hospital phase[4]. Fourth, more high risk patients should be treated with primary percutaneous coronary intervention (PPCI), so the facility for that program should be established.

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DECISION-MAKING FOR USE OF INJECTABLE CONTRACEPTIVES IN ALEXANDRIA, EGYPT: A COMPARATIVE STUDY

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ABSTRACT

Injectable contraceptives are considered one of the modern methods that help in the rapid increase of the prevalence of family planning methods all over the world. In the past few years their use has increased considerably. To identify the potential factors affecting the decision to use injectable contraceptives in Alexandria, Egypt. A cross-sectional study was carried out in 26 family planning clinics affiliated to the Ministry of Health (MOH), Alexandria, Egypt. The study was conducted for seven months during October 2006 - April 2007. Alexandria has seven health districts; each district was represented by one clinic selected randomly from each type of the following 4 types of facilities: rural units, urban maternal and child health centers, hospitals, and health offices. They were selected by using the multistage stratified random sample technique. Totally 26 clinics were selected as two districts had no rural units. The sample size was 790 clients. All clients (new acceptors, current users, continuers and discontinuers of all methods) were interviewed using two predesigned questionnaire. The use of all methods was affected by the positive attitude of the husband towards the use of contraceptive methods. Refusal of husbands to use methods led to the covert use of injectable contraceptives in only 2.3% of clients. Nearly all current users discussed family planning with their husbands and, nearly 75% of wives expected that their husbands would discuss use freely. A higher proportion of new users expected refusal of use of family planning methods by their husbands than current users (25% versus 5.4%). None of new users expected their husbands would be aggressive during the discussion or to refuse discussion from the start. A considerable proportion of new users of injectable contraceptives changed to other methods after being counseled by health providers. Service providers (physicians and leaflets) were not the main source of information; they represented only 6% of information sources. The main sources of knowledge about the injectables were friends and peers (65%) and television (29%). The main rumor heard about injectables was that they cause infertility (56.9%) followed by causing breast tumors (10.8 %). Decision to use injectable contraceptives depends not only on women acceptability of the method but also on husbands' and health providers' attitudes and beliefs, as well as friends' opinion about injectables and also on rumors.

KEY WORDS: injectable contraceptives; decision-making; use; Alexandria

INTRODUCTION

Egypt has the world's largest Arab population, at 92 million, according to the Central Agency for Public Mobilization and Statistics (CAPMAS, 2012)[(1)]. Contraceptive prevalence in Egypt reached its highest value of 60.3% in 2008; the injectable dominated changes in modern method use, accounting for 50% or more of the change in use of all modern methods[(2)]. In Egypt, the most commonly used modern methods are intrauterine contraceptive devices (IUD), pills and then injectables. Intrauterine device use stands at 36% of modern methods users, representing a skewed contraceptive method mix[(3)]. Injectable contraceptives use has significantly increased in the past few years from 0.5% to 21.1% among ever users of family planning methods[(4)], the percentage of spacers who use injectables grew from 1% to 5%; for limiters, the figure rose from 1% to 13% of all method use[(5)].

Several factors influence the use of injectables including their acceptability to women, which is affected by knowledge. Perceptions and experiences of health providers can affect the decision to use injectables through counseling sessions and dependent on the type of information given to clients. Method availability, including method cost, access to services and method choice, can affect choice of method and continuation of use[(6)].

Injectable contraceptives are considered one of the modern methods that helped in the rapid increase in the use of family planning methods all over the world. They are the fourth most popular method worldwide after female sterilization, intrauterine devices and oral contraceptives. They have recently become more popular in Africa and lower-income Latin American countries[(7)]. For some women, these contraceptives are attractive because they are easy to use covertly[(8)]. In Sub-Saharan Africa, injectables are the most popular method, chosen by 38% of women using modern methods. In 2009, use of injectables in Africa stood at 6.8%, double the global average of 3.5%. In Asia,

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Latin America and the Caribbean, over 40% of married contraceptive users rely on injectables[7].

Depo-Provera (depot-medroxy progesterone acetate DMPA) is the most commonly used injectable in the United States[9]. It is a convenient, discreet and low-maintenance method, and is ideal for patients with contraindications to estrogen use and certain medical conditions. In addition, there are many non-contraceptive benefits to Depo-Provera use. Side effects with this method include irregular bleeding, breast tenderness and weight gain[10]. In addition, the impact on bone mineral density should be taken into consideration when prescribing the method, especially for adolescents (age group 15-19)[11].

According to the Demographic and Health Survey (DHS), the unmet need for family planning in Egypt was 14%[12]. Unwanted pregnancies remain high in many low- and middle-income countries, suggesting that many factors could be driving contraceptive use. One of these factors involves disagreement between husbands and wives about method use and family size[13].

Understanding factors affecting the decision to use injectable contraceptives with regard to client characteristics and why women prefer some contraceptive methods over others, husbands' roles and providers' perceptions of the use of injectable contraceptives can be useful for strengthening family planning programs; having a broad range of methods available is a key element of family planning service quality. It also raises the overall level of contraceptive use[14,15]. The aim of this study is to identify potential factors associated with the decision to use injectables by women living in Alexandria, Egypt.

MATERIALS AND METHODS

Study design

A cross-sectional study was carried out in the family planning clinics of the Ministry of Health and Population (MOHP) in Alexandria.

Study sample

A total of 790 females, who attended the family planning clinics, were included in the present analysis. The following four types of health facilities were included: 1) Urban Health Centers (UHCs), Family Health Units (FHUs)/Maternal and Child Health Centers (MCHCs), 2) Health Offices (HOs), 3) Rural Health Units (RHUs) and 4) Ministry of Health Hospitals (MOHHs). Alexandria has seven health districts. Using the multistage stratified random sample technique, each of the seven health districts was represented by one clinic selected randomly from each type of these facilities. Thus, a total of 26 clinics were included (because El-Gomrouk and West districts have no rural units). A sample of 790 users was recruited from these clinics.

Data collection

The researcher spent 26 weeks in collecting the data. One week was spent in each of the selected clinics, during the morning working hours between eight a.m. and one p.m. All clients (new acceptors, continuers and discontinuers of all methods) who could be approached by the researchers and accepted to participate were included in the study and interviewed at the clinic exit. Each exit interview took about 20 minutes. In crowded clinics, up to ten clients were interviewed daily. Data collection was completed within seven months in 2006-2007.

A structured interview was undertaken, using two predesigned questionnaires, one for first-time users of contraceptives (n=169) and a second for current users (n=621). The content of the questionnaire varied according to type of user and included: a) Socio-demographic data (age, wife and husband education levels, income sufficiency, number of living children, age of youngest child and opinion on the ideal number of children in the family), b) Communication between husband and wife; this was elaborated through discussion of family planning with husbands and relatives, attitudes of husbands towards family planning and wives' roles in decision-making, c) Covert use of contraceptives, including the main motives behind decisions to use contraceptives covertly and the reactions of wives and husbands if side effects rose, d) Role of counseling in decision-making, including reasons for choosing injectables, sources of information, expectations about use, rumors about injectables, decisions taken after counseling and reasons for changing opinions. Clients who admitted covert use of contraceptives (n=18) were further interviewed in in-depth interviews. Each interview lasted between 25 and 30 minutes.

Ethical considerations

Permission to conduct the research was obtained from the Under-secretary of Health in the Alexandria Directorate. Necessary approvals from every district's general director and managers of family planning units at district level were obtained. The protocol was approved by the Ethics Committee of the High Institute of Public Health. Verbal consent was obtained from each client before conducting interviews.

Statistical analysis

The SPSS Program version 11.5 (SPS Inc. Chicago, Illinois, USA) was used for processing the quantitative data (data coding, entry analysis and tabulation). Data was summarized using mean and standard deviation. Chi squared test was used to test the differences in categorical data at the level of significance <0.05.

RESULTS

A total of 790 participants of family planning clients were interviewed. This sample included 169 new users and 621current users of contraceptive methods. (Table 1) displays the socio-demographic characteristics affecting the decision to use injectable contraceptives. Compared with women who used other contraceptive

methods, injectable users were significantly older, less educated (both husbands and wives), and having bigger family size (P<0.05).

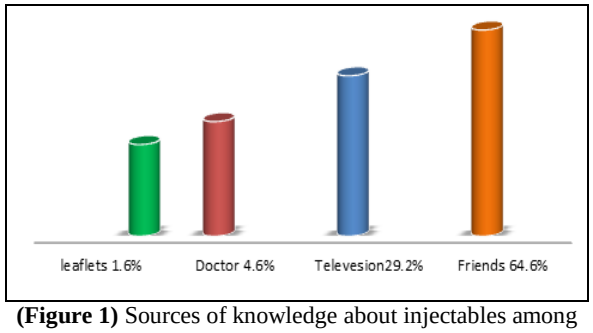
Table (1) Socio-demographic characteristics affect the choice to use injectable contraceptives of clients attending family planning clinics, Alexandria

Women's socio-demographic variables	Injectables Users(N=226)		Users of other methods(N=564)		Total (n=790)		Chi^2 P Value
	No.	%	No.	%	No.	%	
1-Age:							
<20	4	1.8	12	2.1	16	2.0	
20	82	36.3	276	48.9	358	45.4	.00*
30	97	42.9	211	37.5	308	38.9	
40+	43	19.0	65	11.5	108	13.7	
2- Education of clients							
• Illiterate, read and write	146	64.6	288	51.1	434	54.9	
• Primary education	14	6.2	37	6.6	51	6.5	
• Preparatory education	13	5.8	64	11.3	77	9.8	.01*
• Secondary education	47	20.8	133	23.6	180	22.8	
• University education	6	2.7	42	7.4	48	6.0	
3- Education of Husband							
• Illiterate ,read and write	144	63.7	260	46.1	404	51.2	
• Primary education	17	7.5	53	9.4	70	8.9	.01*
• Preparatory education	16	7.1	67	11.9	83	10.5	
• Secondary education	40	17.7	139	24.6	179	22.6	
• University education	9	4.0	45	8.0	54	6.8	
4- Income sufficiency							
• Always in debt	66	29.2	135	23.9	201	25.42	.39
• Sometimes in debt	57	25.2	132	23.4	189	23.9	
• Sufficient	76	33.6	219	38.8	295	37.4	
5- Number of children							
1	28	12.4	119	21.1	147	18.6	
2	63	27.9	189	33.5	252	31.9	.00*
3	74	32.7	160	28.4	234	29.6	
4+	61	27.0	96	17.0	157	19.9	
6- Age of youngest child(years)							
<2 years	82	36.3	336	59.6	418	418	
2-4	59	26.1	91	16.1	150	150	.00*
4+	85	37.6	137	24.3	222	222	

(Table 2) shows the decision-making and husband's attitude towards family planning use by new users and current users. The decision to adopt injectable contraceptives was made jointly by the woman and her husband. Most of the clients discussed using family planning methods with husband alone (69.9% and 72.3% of new and current users respectively). The majority of husbands discussed family planning smoothly with the wives (92.0%) and agreed to the use from the first discussion approving wives' rights to choose the method . Only 2.3% of all husbands didn't agree to the use of the contraceptive method (their wives were covert users).

(Figure 1) shows that the main sources of knowledge about the method came from friends or neighbors, then from television Knowledge from doctors or leaflets represented small proportion.

(Table 3) shows the methods desired before counseling and those used after counseling. Nearly a quarter of new acceptors attending family planning clinics who initially desired to use injectable contraceptives changed their decision and shifted to other methods after being counseled by service provider



(Figure 1) Sources of knowledge about injectables among new acceptors

(Table 2) Decision-making and husband's attitude to family planning use by type of clients attending family planning clinics in Alexandria

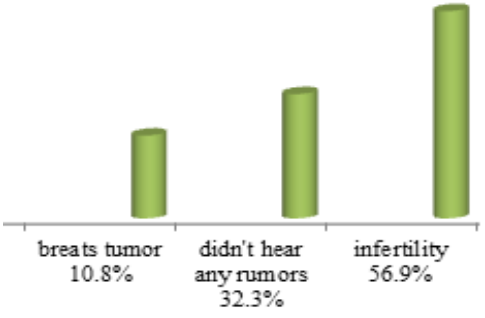
Decision-making and husband's attitude to contraceptive use	New users		Current users		Total	
	No.	%	No.	%	No.	%
1-Discuss family planning with anyone						
• Yes	169	100.0	621	100.0	790	100.0
• No	0	0.0	0	0.0	0	0.0
2-With whom:						
• Husband only	118	69.9	449	72.3	567	71.8
• Mother, sister and husband	41	24.3	112	18.1	153	19.3
• Neighbor, friends, and husband	8	4.7	29	4.7	37	4.7
• Husband and mother in law	0	0.0	28	4.5	28	3.6
• Someone other than husband	2	1.1	3	0.4	5	0.6
-Husband attitude to discussing family planning in general; Discuss smoothly:						
• Yes	161	95.3	566	91.1	727	92.0
• No	8	4.7	55	8.9	63	8.0
-Frequency of discussions (with husband)						
• Once or twice	161	95.3	565	91.0	726	91.9
• Many times	6	3.5	53	8.5	59	7.5
• Didn't discuss at all	2	1.2	3	0.5	5	0.6
Husband agreement to use family planning method						
• Agree to use a method	167	98.8	605	97.4	772	97.7
• Not agree to the use	2	1.2	16	2.6	18	2.3

(Table 3) Distribution of new acceptors attending family planning clinics after counseling, Alexandria

Method	Initially desired method before counseling		No change in preferred method		Switch to other choices	
	No.	%	No.	%	No.	%
• IUD	109	53.7	109	100.0	-	-
• Injectables	65	32.0	50	76.9	15	23.1
• Pills	22	10.8	22	100.0	-	-
• Implants	6	2.9	6	100.0	-	-
• Condoms	1	0.6	1	100.0	-	-
Total	203†	100.0	188	92.6	15	7.4

†These 203 included 169 users who did not previously use any method plus 34 clients who were currently using methods, but switching to other methods at the time of the interview.

(Figure 2) shows the rumors about side-effects of injectable contraceptives. The main rumor heard about injectables was that they cause infertility (56.9%). The second rumor was that they cause breast tumors (stated by 10.8 % of new acceptors of injectables) and 32.3% didn't hear any rumors.



(Figure 2) Rumors about injectable contraceptives

DISCUSSION

All over the world the contraceptive decision follows a fixed pattern based on a couple's demographic situation, educational level and religious beliefs than on characteristics of the contraceptive methods[16]. The current study was implemented to investigate the factors affecting the decision to use injectable contraceptive in Alexandria to increase our understanding of the contextual variables behind method choice and covert use of injectable contraceptives. Contraceptive use is determined mainly by reproductive status, the combined impact of, age, parity, and future child wish. A considerable proportion of injectable users was of older age group and had larger family size than other contraceptive methods users. A possible explanation is that injectable users usually use them as a long-acting method for limiting rather than for spacing. Illiteracy was more among injectable users than other methods

users; also income insufficiency was more among injectable users than other methods users. These results agree with other reports from developing countries like Kenya[17], where injectable use increases consistently with declining educational attainment, it also increases with the living number of children. Studies from Pakistan revealed that users of injectables were generally poor and illiterate[18]. On the other hand, in Jordan a study agreed with all the above determinants except for education where it found that education was less likely to influence contraceptive use[19].

Husband-wife communication is another important factor that affects the decision making about the use of family planning method. In many developing countries discussions about sexual matters are taboo for men as well as for women and couples may be afraid to raise the topic of contraception especially at the beginning of their marriage. In Malaysia, a report mentioned that there was 2.8 time increase use of family planning methods among couples who had good communication than those couples with poor communication[20]. In Nepal, a study indicated that husband-wife communication and wife perceptions of her husband approval of family planning were the strongest predictors of current use[21]. In the present study, the majority of husbands discussed family planning smoothly with their wives and agreed to the use from first discussion. Also the good communication between husbands and wives and agreement to use contraceptive methods affected positively the methods use. This study showed that husbands have a very strong role in the decision-making to use family planning methods as nearly all wives stated that they will not use a method without husband agreement about this particular method even if the husband implicitly accepts family planning. It also showed that even those who admitted readiness to use a contraceptive method without husbands' knowledge, when came to practice, some of them refrain from covert use, as only a small percent of our sample resorted to covert use. The main causes of covert use were economic, health and limiting. A study in Mali mentioned the same order of causes [22]. The estimated rate of covert use in Sub-Saharan African countries was 6-12%[23] while in the present study covert use represented only 2.3% of the sample, which might be due the high approval of husbands of family planning. This indicates high levels of agreement between couples regarding decision to choose and use contraceptive methods. In Egypt as a whole, there is a high rate of acceptance of family planning, which is largely due to the intense use of mass media to disseminate family planning massages as well as the increasing participation of religious leaders in efforts declaring that Islam approves family planning. In addition, many husbands as a result of the progressively increasing economic pressures became less resistant to the concept of small families.

Reasons for choosing injectable contraceptives were: very low failure rate, reversibility, long term option, independence of intercourse and users' memory, ease to use and privacy[24]. Also convenience of use was one of the main causes of injectable use among first-time contraceptive users[25]. The decision to use injectable contraceptives by new users in the present study was affected by many factors including, their knowledge about the injectable contraceptives advantages and disadvantages. The main advantages included, high effectiveness, long action, less side effects, covert use and the ease to use. The main disadvantages of injectable contraceptives stated by current users in the present study were, menstrual problems including amenorrhea, irregular periods and bleeding, followed by medical problems and the desire for longer acting methods.

The Egyptian Demographic and Health Survey (DHS, 2005), showed that knowledge about family planning was universal among currently married women in Egypt, and that television is the main source of information[26]. In the present study neighbors and friends were the main source of knowledge and information about injectables, followed by television, and minority from doctors and leaflets. First time users usually receive incomplete information about their desired methods. Appropriate counseling should provide unbiased information, and correct any misbelieves and rumors. More than 25% of women using methods other than injectables in the present sample did not know any advantage of injectables. Also, nearly half of current users of injectables did not know any disadvantage of injectable. This is in agreement with the results of DHS[26] where most women mentioned that they had not received sufficient information to make informed choice. Research all over the world consistently documented poor quality of counseling in general and inadequacy of information provided on side effects in particular[14,27,28]. In the present study, nearly a quarter of the new acceptors who decided to use the injectables had changed their decision after counseling and hence changed to other methods. Also more than 66% of them heard rumors about injectable entailing causing infertility and breast cancer which may contribute to the change in their decision to use them.

Limitations

Our study has a number of limitations that warrant mention. We have interviewed users of contraceptive methods only, although the decision to use contraceptive methods is shared by many parties including women, husbands, family members, peers and health care providers. Information about the decision to use injectable contraceptives was addressed from the women points of view only. We encountered some difficulty to discuss the husbands' roles and their points of view directly to explore their attitude about using family planning methods.

Also, the health providers' role is important their knowledge and experience about the different methods can deeply affect the decision to use the methods through advices given during the counseling sessions. In this study there was no direct exploration of health

providers' beliefs and knowledge about the injectable contraceptives.

CONCLUSION AND RECOMMENDATIONS

The decision to use injectable contraceptives is affected by many factors including, age of the users, educational status and communication between husband and wife, income and knowledge about injectable contraceptives. In the present study users were older, less educated than other methods users and communication between husbands and wives was good. Husband refusal to use the method was minimal where only 2.3 % of users resorted to covert use. Knowledge about injectable contraceptives was mainly from friends and neighbors; this draws attention to the importance of peer education and word of mouth in attracting more new clients to use injectables. Many rumors are associated with the use of injectables such as infertility and breast cancer. Counseling should emphasize on giving sufficient unbiased information on side effects and actively counteracting myths and correcting misperceptions about injectable contraceptives. Couple counseling rather than women-only counseling should be encouraged. Service providers should be instructed to avoid steering clients away from methods that might otherwise be suitable for them.

RECOMMENDATIONS

Research should be directed towards providing useful, sound information and knowledge about injectables advantages, disadvantages and side effects by the use of media (mainly television) and peer education. Addressing couples' communication and providers' perceptions can help in improving the use of injectable contraceptives.

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ASTHMA MIMICS
(ACUTE RESPIRATORY FAILURE CAUSED BY GIANT RETROSTERNAL NONTOXIC GOITER)

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Summary

A 70 years old Libyan lady complaining of dyspnea and was treated as bronchial asthma for 3 years. She was admitted to the medical ward; as her condition worsened recently; where she re-evaluated and diagnosed as acute respiratory failure caused by giant retrosternal nontoxic goiter.

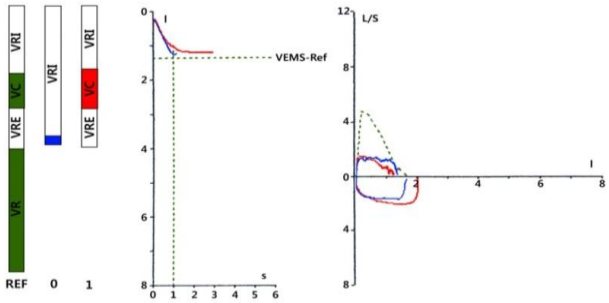
INTRODUCTION

Retrosternal goiter (RSG) is defined as a goiter in which the thyroid mass has descended the plane of the thoracic inlet or if more than 50% of the thyroid mass is located below the thoracic inlet. Due to the variety of definitions the percentage of RSG varies from 2% to 20% of all patients undergoing thyroidectomy[1,2]. It accounts for 3-12% of mediastinal masses[3]. The symptoms are usually caused by compression of the adjacent structures including the trachea, esophagus, and superior vena cava[1,4,5]. This condition has a clinical importance as it presents a diagnostic dilemma with its compressive symptoms and operative difficulty.

CASE REPORT

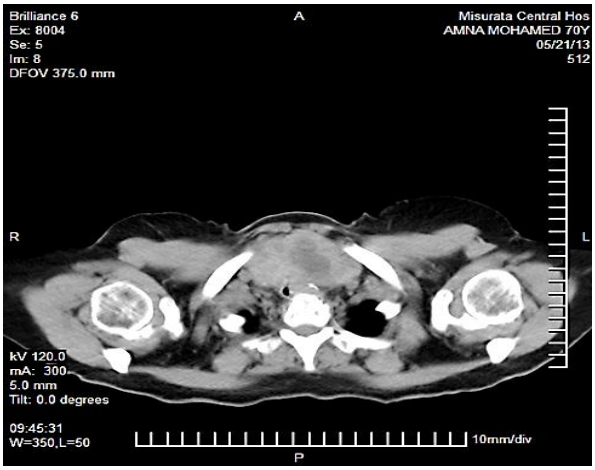
A 70 years old lady was presented to the emergency room complaining of shortness of breath. She had any difficulty in breathing for 3 years and was diagnosed and treated previously as a bronchial asthma. She did not improve with medications and began to experience orthopenea and referred for admission to the medical ward for further management. She had been investigated by spirometer as part of work up for bronchial asthma. She did not notice any swelling in the neck and not show symptoms of hypo or hyperthyroidism. On examination she was dyspenic, tachypenic and orthopenic, with blood pressure of 200/100 mmHg, visible JVP pulse and audible strider. However, there was a small diffused swelling in the anterior aspect of the neck which moved with swallowing. The trachea was shifted to the right side. By percussion, there was dullness over the sternum and all laboratory parameters were within normal limits. Furthermore; flow-volume loops revealed flattened top and bottom loops so that configuration approaches that of rectangle which indicates a fixed obstruction of upper airway as shown in (figure 1).

Ultrasound and CT scan of the neck revealing a retosternal mass, that showed the thyroid gland as a large heterogeneous ill-defined multinodular lesion measured ≈ 92 x 60 x 40 mm with mixed density due to calcification and necrosis.



(Figure 1) flow-volume loops

The lesion causes compression of the trachea and right shift, with retrosternal extension that reach up to level of T3 vertebrae as shown in (figure 2). Fine needle aspiration cytology revealed a follicular adenoma.



(Figure 2-a)

A significant variability regarding the clinical presentation and the surgical management of RSG has found during review of literature which can be explained to some extent by the different definitions employed. RSG is classified as primary accounting for less than 1% and derive from ectopic thyroid tissue in the mediastinum[1,4]; or secondary RSG which account for 99% it is characterized by the downward growth of cervical thyroid tissue into the thoracic inlet[1,4], and continue

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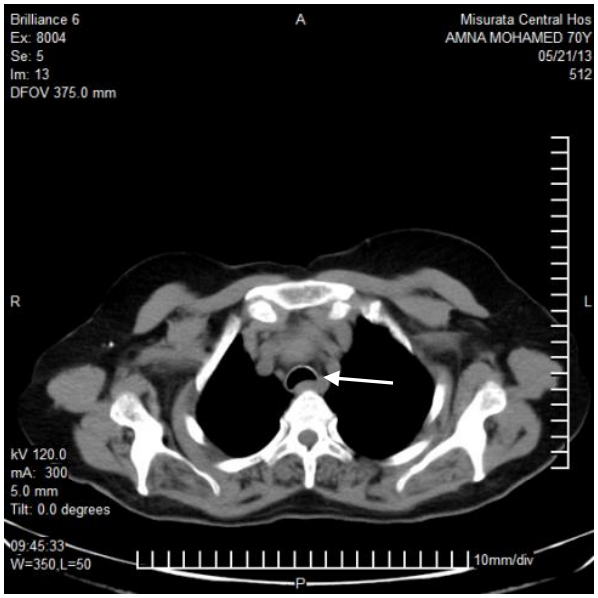
to receive blood supply form the superior and inferior thyroid arteries[1].



(Figure 2-b)

(Figure 2) CT scan of neck (arrow indicates compressed deviated trachea)

DISCUSSION

Majority of these goiters (85 - 90%) are mostly situated in the anterior mediastinum, and can be unilateral or bilateral, growing cross the midline, the others are located in the posterior mediastinum[1,2,4]. Patients with RSG are generally presented in their fifth and sixth decades of life and have a female predominance; female/male ratio 3:1[1,6]. While 15 to 50% of patients are asymptomatic[6]. The most important presented symptoms result from mediastinal compression[7] and especially from tracheal compression. The majority of them (68.8%) present with dyspnea or asthma like symptoms as was the presented case. Patients may also present by neck mass (75%), hoarseness of voice (37.5%), dysphagia (31.3%), strider/wheezing 19%, or superior vena cava obstruction (6.25%)[8]. It is reported that up to (25 - 33%) of patients with giant goiters have upper airway obstruction symptoms, and (10%) of these patients require emergency airway intubation[9]. In fact that, the upper airway obstruction indicating prompt intervention for an enlarged thyroid gland is rare condition; the incidence of benign nodular goiters causing upper airway obstruction is not well defined varying between 0.8% and 31% in different studies[10,11]. It was suggested that several reasons have been responsible for the acute obstruction of the upper airway in benign nodular goiter. Additionally; retrosternal localization of the enlarged gland in relatively small space is mostly associated with tracheal compression and displacement, leading to varying degrees of dyspnea. It predisposes, but does not cause, obstruction and the exact cause of obstruction in such patient who already has a compressed airway is not clear. Upper respiratory tract infections, chronic obstructive pulmonary disease, and bleeding into a cystic component of the enlarged gland might have contributed to this acute event[12]. It is also reported that recognizable changes in lung function occur when the cross-sectional area of the airway has been reduced by more than 50%[10]. In fact, despite these contributing factors, they thought that the main reason for the acute presentation is the time delay between diagnosis and operation[12]. This impairment can easily develop into upper airway obstruction when these factors are considered. The differential diagnosis of acute dyspnea and upper airway obstruction must be considered including bronchial carcinoma, thymomas, dermoid cysts, or lymphomas. Similarly to the presented case Nandwani et al. reported a case in which upper airway obstruction and dyspnea were confused with asthma, they used a flow-volume loop serving to aid in the diagnosis and monitoring of suspected airway obstruction[13]. Similar findings were reported by Thusoo et al. who support the idea that flow-volume loops provide an added advantage over conventional radiology alone in the detection of upper airway obstruction[14]. CT scan was considered the gold-standard preoperative radiological investigation[15]. As it more clearly demonstrated the tracheal obstruction and retrosternal component; CT scan also provides more information for the differential diagnosis of mediastinal masses that can also cause upper airway obstruction[16]. On the other hand; the standard post-anterior and lateral chest X-rays are considered the most single valuable diagnostic tools with regard to the study of intrathoracic goiters as these radiographs can provide valuable information about the compression of the trachea[17]. Surgical treatment is indicated for RSG causing upper airway obstruction; this was the case as the studied patient had total thyroidectomy through collar incision. Post-operative our patient was in good general health, without any respiratory symptom after cessation of all anti-asthma treatment which she was receiving for 3 years.

CONCLUSION

Prognosis in RSG is very good if diagnosed and treated in the proper time.

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EVALUATION OF UNDERGRADUATE MEDICAL STUDENT

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With the change in the medical curriculum and teaching modalities there also a need for effective methods to assess the candidate with emphasis on clinical competence and skills as well as knowledge. It is the responsibility of every physician to pass his knowledge to the next generation, and so examinations have been set to test what the candidate have been leant and their ability to practise medicine safely. Examinations cannot be hundred percent ideal to test any candidate. It is the most commonly used method of assessment all over the world. Most of the discussions and many studies are now carried out to find the proper way of examination.

FUNCTIONS OF THE EXAMINATIONS

1-They have an educational function as they drive the student learning, the majority of students would study according to what they would be tested on, and they read only when they are going to set an exam.

2-Examination also gives a guarantee to the society that the graduates are safe doctors [(1)].

Students qualified from the medical colleges differ from students qualified from other colleges. They should be thoroughly evaluated to obtain a safe medical practitioner, having at least the basic knowledge to practise medical profession and able to deal with the patients, especially the urgent cases. It seems that it is not easy to found an ideal way to examine the medical students; especially it is harder because they should be able express their knowledge and communicate with the others.

Students are of different levels, in the exam, it is not only to the decide that the student able to pass the exam or not, grading of the students levels is very essential, some students are interested only to be qualified. Other are working hardly to be distinctive in their knowledge and performing the skills, they are brilliant not interested to pass the exam only, they are able also to interpretate and communicate with the others to reach an accurate clinical diagnosis.

The examination is not to test the memorisation (to present what has been told) of the candidate only, it should test also the intelligence (to think and link some points that are not teached).

All candidates should be save and carry no risk of danger to the patients to pass the exam. First of all they should be honest. Safety is a broad term that involves; not doing harm to the patient, able to serve the patient in a scientific way, doing minimum interventions that leads to the diagnosis, consult the other at any time they face a difficulty, never do wrong, stopping and cessation to proceed their management whenever not possible to continue because of lack of knowledge.

Evaluation of undergraduate candidate usually involves theoretical and practical parts. There are different ways to evaluate each of them. For the exam to be eligible, each candidate should get a certain percent of the total marks, so for each candidate to pass the exam he or she should get the pass mark in each section as well as the pass mark in all sections collected to each other. The exam and the scoring system should include the identification of the source of the knowledge; spoon-fed from the teacher, sheets, recommended books, journals, internet, ect. Another point to be considered during the exam; is our candidate safe to the patient, and he or she is able to pass the exam without fatal mistakes?

The theoretical part of the exam tests the basic and essential knowledge needed to pass the other parts of the exam. In this part of examination the candidate is exposed to several questions, scoring is done according to the total performance. This part of exam should cover the whole subject. Questions should be; direct and indirect, not only test the amount of knowledge but also should test the intelligence of the candidates. Unlike the clinical exams the theoretical exams are not vital, gives minimum ideas about the skills and practical hints, they assess the basic knowledge more accurate. This can be done by different ways or the combination of them, namely; choosing the most correct answer from multiple choice questions (MCQs), selection of the true and false statements, filling of spaces, matching of related paragraphs and essay questions. The best evaluation that includes all of them. The questions should cover the whole subject; more frequent questions should cover the common and urgent diseases.

The drawback of the theoretical exam includes:

-Fatal mistakes are not recognised.

-The ability of the candidate to communicate verbally with the others is not tested.

-The time elapsed from facing the problem to the action is not tested.

-Grading of the essential and less-essential knowledge are not recognised.

In my view any candidate who cannot pass the theoretical part of the exam, should not be allowed to attend the other components of the exam. It is non-logic to allow some body to touch the patient without having suitable basic background knowledge of the subject. This is not only time consuming to the candidate, examiner and the patient; it is also dangerous to the patients.

The oral part of the exam should concentrate mainly on the diagnosis and management of the emergencies and acute cases, to assess how the candidate behave

during emergencies, as those cases are not included in the clinical part of the exam.

The clinical evaluation is very important and essential part of the expected clinician evaluation, candidates should have special personality and behaviours that allow them to be able to explain and convince the others (patients and examinares). In most of the clinical exams there is shortage of cases at all or shortage of the cooperated cases or cases with clear physical finding. So, the contact personal or verbal should be minimized as much as possible between the pre and post exam candidate.

The examiner should be expert enough, actively involved in the teaching and clinical practice. In the clinical evaluation the candidate usually allowed to tack a brief or detailed history (depending on the case), perform general and specific (systemic) examinations. Finally the discussion is opened with the examiner; sometimes the examiner asks questions which are related or not related to the case. In my view the examiner should:

-Allow the candidate to present the case without disturbances.

-Follow the candidate while he is presenting the case (even if the case is known to him).

-Limit the discussion related to the case as much as possible.

-Ask questions related only to the case. It is not recommended to ask about proptosis when discussing a case of cataract.

-Avoid asking direct and theoretical questions (even if they are related to the subject), for example, asking what are the causes of irregular pupil in a patient with dilated fixed pupil.

-Should not ask more specific questions if the candidate not answering more simple and basic questions. If the stages of diabetic retinopathy and the modality of their treatment are unknown to the candidate, there is no need to ask about the different types of laser, the answer is of no value, even if he answering the later without answering the former.

-Evaluate the candidate ability to give a detailed description to the physical sign. In a patient with hazy cornea, it should be fully described (is it oedema or opacity, localized or diffuse, its site, size, shape, margin and density)

-Calculate the wrong answers, they should be considered in the final scoring.

-Document dangerous mistakes (the fatal or that leads to permanent anatomical or functional damage) and report them to the examination committee. According to the discussion with the other examiners, the candidate should not pass the exam even if his or her performance is accepted in the other sections of the exam.

Preparing and conducting a clinical examinations a-has always been a change and huge responsibility for the medical educator, as once the candidate passes the examinations they are licensed to practice medicine.

The clinical evaluation includes:-

1-General evaluation of the candidate; in this part of assessment the following are observed:

-Is the candidate caring the essential basic instruments that help in the clinical evaluation?

- Is he behaving like a medical personal, respecting the staff and other patients?

-The behaviour of the candidate with the examiner.

-The behaviour of the candidate with the patient.

-Is he or she save or harmful to the patient?

-Is he or she confident and systematic?

2-Communication skills: they are learnable, trainable, adaptable tasks, just like any other skill. Communications requires the background skills of presentation, audience, awareness and critical body languages. They are verbal and non verbal. Verbal communication includes words, phrases and voice tone. Non-verbal communication (body language) includes facial expressions, gesture, emotions and body movements, that are used to express and explain some ideas[(2)].

Communications include:

a-Communication with the patient; history tacking is very important step in the clinical evaluation of any patient, we knew that many diseases can be diagnosed by proper history and many diseases can be rolled out also. It is skill to extract from the patient what you need. The examiner should include the following points in the evaluation:

-Is the candidate able to communicate with the patient?

-Is the patient allowed to explain the problem freely?

-Is the candidate able to follow and understand what's the patient telling?

-Is the candidate able to guide the patient?

-Is he able to make an accurate interpretation to what the patient is telling?

-If so, did he ask about other symptoms related to patient presenting symptoms and helpful in reaching a proper diagnosis?

b-Communication with the examiner;

Presentation of the case;

-Is he or she able to present the case to the examiner in a proper way, easily understandable (verbal and written)?

Case discussion; the candidate should be able to discuss the obtained data from the patient, including the history and examination. It is very essential to show to the others your way of thinking, how you correlate your finding to reach a clinical diagnoses, what investigations to do to reach a final diagnosis.

3-Evaluation of the knowledge: In 1990 the psychologist George Miller proposed a frame-work for assessing clinical competence in the form of a pyramid with the lowest part being the knowledge (knows), followed by the competence (knows how), performance (shows) and action (does), i.e. the candidate should know the clinical sign (knows), its pathogenesis (knows how), able to demonstrate it (shows) and capable to map-out the line of management (Does)[(2)].

4-Evaluation of the clinical skills:

-Is the skill performed?
-Is it done in the proper way?
-If so, is the candidate able to discover the physical finding?
-Is he or she able to describe it properly?
-Is the candidate thinks about the other physical finding related to the discovered signs that helps to reach a diagnosis?
-Is the candidate able to correlate all the physical finding with each other and link them with the history of the disease?
-If so, is he able to map out a list of differential diagnosis?

Assessment of the candidate view for the next step; what to do after the clinical examination:

-To start treatment, then investigate.
-To consult somebody or ask for help.
-Refer the case to another centre for better care.
-Ask for some investigation; the candidate should be aware of:

-Choosing a non invasive, less expensive investigations.

-Is the candidate aware about the expected abnormality or just to investigate and then read the result looking for abnormal finding.

In conclusion, it is not an easy job to examine an undergraduate medical student. It becomes more difficult, the number of students is increasing, the time allowed to have a perfect evaluation of each student is limited. We have to look for a method that test the student away from the examiner mode and fulfil the quality control requirements.

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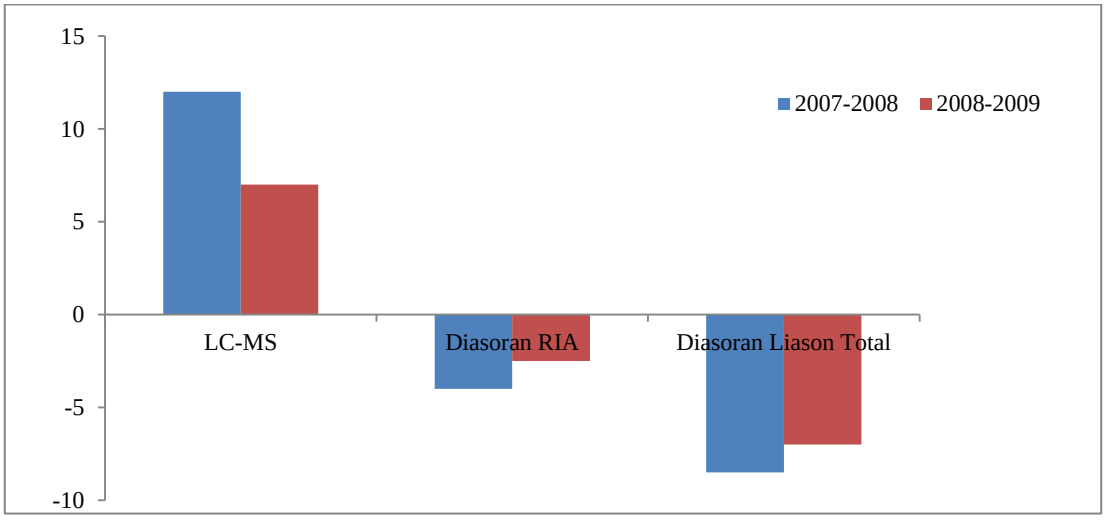

الإصدار الثاني

العدد الأ ول

صيف 2015