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"Whenever a doctor can not do good, he must be kept from doing harm" Hippocrates

Hippocrates of Cos lived between 450 BCE to 380 BCE. He was a physician, and the writings of the Corpus Hippocraticum provided a wealth of information on biomedical methodology and offered one of the first reflective codes of professional ethics. The way most professions try to deal with this sort of problem and the legitimate problems that arise during practice is to create codes of conduct and structures of accreditation. The most famous of these in the biomedical tradition is: The Oath of Hippocrates.

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Congratulations

Barind Medical College Journal

I am very much glad to know that the Academic council of Barind Medical College has decided to publish a medical journal. Undoubtedly it is a challenge for a new medical college like Barind Medical college but still some courageous renowned medical personalities of the college have accepted this challenge not only for the first publication but also to bring this Publication to the academic and scientific progress. Many research activities have been initiated to pave the way of medical education.

I congratulate the Editors and publishers who have taken this challenge of publishing the journal. I also wish success and popularity of this Journal.

Lastly, I want to assure the honorable members who have taken the initiative to publish the journal, of my whole hearted and total co operations to fulfill their dream.

Md. Shamsuddin
Managing Director
Barind Medical College

The Golden Journey of Barind Medical College

"The vernal wood, the blended mode, the balmy tender dawn
The sweaty timber, with natural green, and beauty of its own.
The piece of cloud, hath closed about, the brightness of the sun
The murmur under moon and star hath gone beyond the man..."

Md. Meherullah

In such a moment, the likeminded medical intellectuals of Rajshahi conceived the basic theme, and dreamt of a pioneering Medical College with highest academic insight since inception. The teachers were seated in a breezy-wintery morning & had the cup of frothy coffee before them. Everybody choose the poem when someone stormed in post about its necessity in respect to the medical study and addressed the questions where to undertake graduation from or how many have the quality & desire to be true, empathetic & erudite medical professionals and importantly how many of them are designed for Have-nots?

The nidus for establishing a medical college was initiated in an interaction in between Md. Shahriar Alam, MP, the past & founder chairman, Barind Medical College, a noble Politician with outstanding personality and Prof. Md. Rafiqul Alam with expressing their unexpressed desire and unexplored vision. Hitherto, it was shared with Prof. Dr. A.B. Siddiqui, Prof. Dr. Sujit Kumar Bhadra, Prof. Dr. B. K. Dam, Prof. Dr. Merina Khanom, Prof. Dr. Md. Fakrul Islam and the author and agreed to an issue of establishing a Medical College & Hospital.

On that conception it finds its way to come into light which is a reality of long nourished dreams. Barind Medical College Hospital (BMCH) starts her journey with 50 students with a team of eminent teachers of different disciplines of medical sciences assisted by efficient staff in a rented building at Luxmipur headed by renowned pediatrician in the country as a founder principal Prof. A.B. Siddique in 2011. Soon after it's starting a feeling of deep pain and incompleteness, beating our mind, how early this can be set up in our own campus. Finally, it happened in to being within nine months which was a golden memorable day for the management, teachers, staff and the students. This challenging job was only possible by strong stand, firm decision, untiring efforts, soft motivational behavior and convincing attitude of, who is our guardian, the respected Managing director Md. Shamsuddin. In this regards we recognize and acknowledge the contribution, who did this commendable job possible - he is Major Mollah Hafizur Rahman, Ex-DIG. With all the efforts, contribution of Muhammad A. Quayum is to be mentioned with gratitude.

As the time drifted away, the esteemed BMCH has spread her olive branches on to her stage, has covered to all corners of Medical areas of academic and clinical services and thus spread its flavor & fragrance to her disciplined disciples, efficient management, Principal, teachers, doctors and staff. Now, the students number increases to 90 in the session 2013-14 and runs smoothly as a silvery & golden gem in Rajshahi, Bangladesh. That is not the end - the inner urge always triggers to do something more. Medicine is an ever changing science which broaden knowledge and skill and changes the concept of treatment and management by research and clinical experience. To cope up with these need a media through which information may be updated.

Meanwhile, the BMCH has attained a position in academic and health care that, to boost her image further, the necessity of publication of a Medical Journal is strongly perceived. Keeping this idea, Academic council constituted the Editorial Board for publishing Journal named of Barind Medical College Journal (BMCJ). To the many persons who have already helped us I express sincere thanks. I owe enormous debt to Prof. Dr. M. Manzurul Haque and Dr. Md. Anayet Ullah for the privilege and honor given me however for writing few words in the very first issue of the journal.

It is needless to mention the person, who inspired co-operated and helped in all respects to come to such position and he is our honorable past & founder chairman, Md. Shahriar Alam, honorable State Minister, Ministry of Foreign Affairs, Peoples' Republic of Bangladesh. I apologize to all, if I forget to mention the contribution of anyone inadvertently.

Professor Gopal Chandra Sarker
Barind Medical College

How to write a scientific paper for publishing in medical journal

M Manzurul Haque

Bangladesh, the eighth most populous country in the world with about 153 million people, has recently been applauded as an exceptional health performer.¹ As far as medical education is concerned, it can be very clearly perceived and appreciated that Bangladesh is achieving adequately in the academic arena as well. With the emergence of new medical journals, young researchers are inspired to undertake their work seriously and focus on publishing the findings. Conducting scientific research is only the beginning of the erudition of discovery. To make the results of research accessible to other professionals and the scientific community, it must be written well and published in a standard medical journal. It is important for the academic career of the researcher as well.

Writing for publication in a medical journal is a difficult task. A good medical literature is meant to be a piece of elite writing with the content well balanced in being informative, comprehensive and at the same time comfortable for the readers. This is definitely a tricky job. The most difficult task is being able to engage the reader's interest and communicate succinctly. Not all who look at a medical journal are going to read even one article in it. A writer must know, therefore, what makes the paper interesting for the readers. However the reality is that a reader would usually refer to a scientific literature for information and not entertainment. All these facts actually makes writing for a medical journal more complex than anything.

The basic principles of scientific writing are brevity, clarity, validity and simple mode of presentation. Writing a good scientific paper requires both creative energy and quiet reflective efforts engaging a considerable amount of author's time.

The range of medical writings encompasses conference presentations like abstracts, oral presentations, poster presentations etc. and journal articles like original articles, review articles, systematic review and meta analyses, current concept reviews, case reports, clinical suggestions and innovative technical practices etc. When the presentation is well conceived, before writing the manuscript, the target journal should be chosen. Each journal has its own

Before starting writing and manuscript preparation young authors should better consult with the checklists or guidelines that are available on the International Committee of Medical Journal Editors (ICMJE) website (<http://www.icmje.org/>). The PRISMA checklist was developed for use when performing a meta analyses or systematic review.² A randomized controlled trial can be reported by the CONSORT guidelines.³ The STARD checklist may be used for designing a diagnostic accuracy study.⁴ To express the improvement of quality of health care in a community, one may use the SQUIRE guidelines.⁵ Protocols for different clinical trials can be designed following guidelines from SPIRIT statement.⁶ Observational studies in epidemiology can be designed through STROBE guidelines.⁷

It may be helpful to follow the IMRaD format for writing scientific manuscripts. This acronym stands for the sections contained within the article: Introduction, Methods, Results, and Discussion. Apart from this, article also includes Title, Abstract, Keywords, Acknowledgements, and References which again may be remembered by acronym TAKAR. So to prepare a paper for publication the components should be sequenced as Title, Author, Abstract and keywords, Introduction, Material and Method, Results, Discussion, Conclusion, References and Acknowledgements. The use of graphic/figure representation of data and important procedures or exercises can be considered. Tables should be able to stand alone and be completely understandable at a quick glance. Many formats for graphic presentation are acceptable, including graphs, charts, tables, and pictures or videos. Plagiarism should be strictly and deliberately avoided. It is important to cite any and all information sources used in the article.

Writing a scientific article may appear intimidating and frustrating. But the various parts of a scientific article are explained well and guidelines are given in different easily accessible sources. With time and patience, a young author can write a scientific article and get it published. And when one article is accepted and published it should be celebrated thoroughly to be remembered that the writing for standard medical journals makes a difference in some way.

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Implications of new TSH reference range on infertile Bangladeshi women.

Gopa Sarker,^a Md. Anayet Ullah,^b Hasina Akhter^c

Abstract

Background: For over a decade there has been considerable debate about the correct reference interval for TSH. Practitioners are divided, unfortunately they could not reach a unanimous decision. More recently, researchers have been looking the implications of the new TSH reference range (0.3 to 3.0 mIU/L).

Objective: To explore the implications of the newer TSH reference range recommended by AACE and NACB, USA among the infertile women in Bangladesh. **Methods:** This was a cross-sectional descriptive type of study conducted at Gynaecology & Obstetrics Out Patient Department (OPD) of Rajshahi Medical College Hospital (RMCH), Bangladesh. The sample size was 94. Data on clinical presentations, biochemical and ultrasonographic findings were collected by a preformed Data Collection Sheet. Serum hormone assay TSH, T₃, T₄, and prolactin (PRL) were done in Centre for Nuclear Medicine and Ultrasound (CNMU), Rajshahi, Bangladesh. Data were analyzed in a computer using SPSS for windows. Descriptive analytical techniques involving frequency distribution, computation of percentage etc. were done. **Results:** A total of 94 infertile women, new reference range of TSH identified 10 (10.6%) women having clinical hypothyroidism, 8 (80.0%) of them were identified as same by old reference range. New reference range identified 28 (29.8%) infertile women having subclinical hypothyroidism. But old reference range identified 25 (89.3%) of them as euthyroid. Out of 94 infertile women, Old reference range identified 83 (88.3%) women as euthyroid but it was reduced to 56 (59.6%) in new reference range polycystic ovary syndrome (PCOS) was identified as a most common (25; 26.6%) cause of infertility among the present study subjects. But if the new TSH reference range was followed instead of the old then majority of the PCOS accompanied with subclinical hypothyroidism. **Conclusion:** New TSH reference range has a significant implication on Bangladeshi infertile women. Further studies are needed to observe the treatment outcomes of subclinical hypothyroid infertile women identified by application of the new TSH reference range.

Keywords: new TSH reference range, hypothyroidism, infertility.

Introduction

Thyroid hormones are essential for normal growth, sexual development and reproductive function. Both hypothyroidism and hyperthyroidism are associated with a variety of changes in reproductive functions including delayed onset of puberty, menstrual disorders, anovulatory cycles and reproductive wastage when pregnancy is achieved.^{1,2} Thus thyroid dysfunctions may have a great impact on fertility in females.³ Thyroid dysfunction particularly hypothyroidism is a well documented, but often overlooked, factor in female infertility.⁴

Thyroid dysfunction, both hyperthyroidism and hypothyroidism can be easily detected by assessing TSH levels in the blood. Low TSH level (< 0.5 mIU/L) accompanied by high T₃ (> 3.54 nmol/L) and T₄ (> 173 nmol/L) levels indicate hyperthyroidism. Hypothyroidism may be either subclinical or overt. A slight increase in TSH levels with normal T₃ and T₄ indicates subclinical hypothyroidism whereas high TSH level accompanied by low T₃ (< 1.1 nmol/L) and T₄ (< 54 nmol/L) levels indicate clinical hypothyroidism.⁵ Conventionally TSH reference range used to be from 0.5 to 5 mIU/L.⁶ But in late 2002, the National Academy of Clinical Biochemistry (NACB), USA issued new guidelines for the diagnosis and monitoring of thyroid disease.⁷ In the guidelines, the NACB reported that the current TSH reference range (0.5 to 5 mIU/L) was too wide and actually included people with thyroid disease. When more sensitive screening was done, which excluded people with thyroid disease, 95 percent of the

population tested actually had a TSH level between 0.4 and 2.5 mIU/L. As a result, the NACB recommended reducing the reference range to that. Meaning, anything below or above that could be a sign of thyroid disease. The NACB guidelines led to a recommendation in January 2003 by the American Association of Clinical Endocrinologists (AACE), calling for doctors to "consider treatment for patients who test outside the boundaries of a narrower margin based on a target TSH level of 0.3 to 3.0 mIU/L". The statement also said: "AACE believes the new range will result in proper diagnosis for millions of Americans who suffer from a mild thyroid disorder, but have gone untreated until now".⁸

For over a decade there has been considerable debate about the correct reference interval for TSH. Practitioners are divided, unfortunately they could not reach a unanimous decision. More recently, researchers have looked at an important question: If the normal TSH range is narrowed, as has been recommended by AACE and NACB, what are the implications?⁹ Dr. Vahab Fatourehchi and fellow researchers estimated that if the range was narrowed according to the AACE recommendations, the total number of people with thyroid disease in America would expand from approximately 5 percent of the population to an estimated 20% of the population, with most of the added patient population falling in the hypothyroid category. This represents a dramatic increase in the number of thyroid patients nationwide, from an estimated 15

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To get the answer of such type of question is also very important in case of infertility in Bangladesh because infertility rate is approximately 15% in Bangladesh, which is the highest among all South Asian countries.²² In this study researchers intended to explore the implication of the new TSH reference range recommended by MAC and IAC, USA among the infertile women in Bangladesh.

Methods

This was a cross-sectional descriptive type of study conducted at Gynaecology & Obstetrics Out Patient Department (OPD) of Rajshahi Medical College Hospital (RMC), Bangladesh. All the infertile women attending at the OPD of RMC for seeking fertility treatment constituted the study population. A total of 94 infertile women attended at the OPD were included in this study. The women who were with any renal or cardiac diseases, those already on treatment for thyroid disorders or hypernatremia, or whose male partner identified as infertile were excluded from the study. Before selecting the women, informed written consent was taken from each of them.

Data were collected by a preformed Data Collection Sheet (DCS). The DCS was designed to record clinical, biochemical and ultrasonographic findings. The information were recorded from the patients' treatment slips, investigation reports, interview with the patients and consultation with the concerned doctors if necessary. Serum hormone assay TSH, T3 and T4, ultrasound were done in Centre for Nuclear Medicine and Ultrasound (CNMU), Rajshahi, Bangladesh.

Data were entered in the computer and processed using SPSS for windows. Descriptive statistical techniques involving frequency distribution, computation of percentage etc. were applied.

Results

On the basis of old reference range, 8 (8.5%) of the study subjects were suffered from clinical hypothyroidism, only 33.2% of the women were suffered from subclinical hypothyroidism and the rest 58.3% of the women were euthyroid. On the other hand, On the basis of new reference range, 12 (12.6%) of the infertile women had clinical

hypothyroidism, 28 (29.8%) of the women had subclinical hypothyroidism and 58 (61.6%) were euthyroid. None of the study subjects were suffered from hyperthyroidism per individual and new reference range (Figure 1).

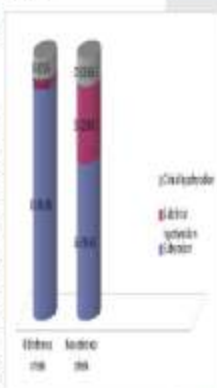


Figure 1: Comparison of thyroid status between old and new reference range

A total of 94 infertile women, new reference range of TSH identified 12 (12.6%) women having clinical hypothyroidism, 8 (8.5%) of them were identified as same by old reference range. New reference range identified 28 (29.8%) infertile women having subclinical hypothyroidism. But old reference range identified 25 (26.7%) of them as euthyroid. Out of 94 infertile, Old reference range identified 58 (61.6%) women as euthyroid but it was reduced to 56 (59.6%) in new reference range (Table 1).

Table 1: Cross table of status of hypothyroidism by old and new reference

Old Reference Range	New Reference Range			Total N (%)
	Clinical hypothyroidism N (%)	Subclinical hypothyroidism N (%)	Euthyroid N (%)	
Clinical hypothyroidism N (%)	8 (8.5)	1 (1)	1 (1)	10 (10.6)
Subclinical hypothyroidism N (%)	8 (8.5)	20 (21.2)	1 (1)	29 (30.7)
Euthyroid N (%)	1 (1)	20 (21.2)	56 (59.6)	77 (81.3)
Total N (%)	17 (18)	21 (22.4)	57 (60.4)	95 (100)

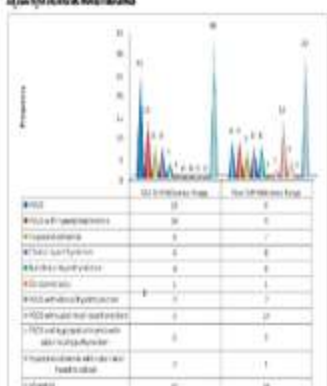


Figure 2: Cases of infertility

If conventional TSH reference range was followed, PCOS was identified as a cause of infertility among the highest number (25; 26.6%) of the present study subjects. The second highest (14; 14.9%) cause of infertility was PCOS with hyperprolactinemia. In case of 4 (4.3%) infertile women, subclinical hypothyroidism was identified as a cause of their infertility. A major number (34; 36.2%) of the women had unexplained infertility. Instead of that, if the new TSH reference range was followed then PCOS was also identified as the highest cause but majority of them accompanied with subclinical hypothyroidism. In case of 30 infertile women, a cause could not be identified (Figure 2)

Discussion

Until November 2002, doctors had relied on a normal TSH level ranging from 0.5 to 5.0 mIU/L to diagnose and treat patients with a thyroid disorder who tested outside the boundaries of that range. Now AACE encourages doctors to consider treatment for patients who test outside the boundaries of a narrower margin based on a target TSH level of 0.3 to 3.0 mIU/L. AACE believes the new range will result in proper diagnosis for millions of Americans who suffer from a mild thyroid disorder, but have gone untreated until now.⁷ But such proposals have been met with substantial critique.^{14,15} There is a great debate about the upper limit of the new reference range but there is no debate about the lower limit of the new TSH reference range because the lower limits of both the reference ranges, old and new are very close. The strongest argument in favor of lowering the upper limit of normal for the serum TSH level is the higher level of antithyroid antibodies detected in persons with a serum TSH level between 3.0 and 5.0 mIU/L and the higher rate of progression to clinical thyroid disease.¹⁶ After exclusion of persons with goiter, antithyroid antibodies, and a family history of thyroid disease, the mean serum TSH is 1.5 mIU/L. The serum TSH distribution curve is not Gaussian; there is a tail end at the upper limits of normal. If the distribution is extrapolated to be Gaussian, then the upper limit for the 97.5th percentile will be 2.5 mIU/L.¹⁶ The argument against lowering the upper limit of normal for TSH values is that 22 to 28 million more Americans would be diagnosed with hypothyroidism without any clinical or therapeutic benefit from this diagnosis.¹⁷ The present study data also showed that decreasing the upper limit of the TSH reference range to 3.0 mIU/L resulted in more than a 3-fold increase in diagnosis of hypothyroidism among the infertile women in a tertiary medical hospital, Rajshahi Medical College. The present study suggested that new reference range was more effective to detect the mild/subclinical hypothyroidism. In this study, new reference range identified 89.5% more subclinical hypothyroid patients who were previously marked as euthyroid by old reference range.

Infertility can be caused by many different things. For 15-50% of couples, a cause cannot be identified.¹⁷⁻¹⁹ In the present study 36.2% of infertile women have unexplained infertility, if conventional TSH reference range was followed. Instead of that, if the new TSH reference range was followed then it is reduced to 31.9%.

Polycystic ovary syndrome (PCOS) is the most common hormonal disorders among women of reproductive age, and is a leading cause of infertility.² It was also the most common cause of infertility identified in this study. PCOS is a fairly common condition with hypothyroidism, especially subclinical hypothyroidism. Newer research has shown that women with PCOS are four times more likely to also have Hashimoto's Disease (autoimmune thyroiditis).² In this study, according to the new TSH reference range, more than 48% of the women with PCOS having also subclinical/mild hypothyroidism.

PCOS and hypothyroidism have many symptoms in common, such as "anovulation" i.e. menstruation without releasing an oocyte (egg cell). Other symptoms the two conditions share are: insulin resistance, blood sugar problems leading to diabetes, high cholesterol levels, heavy periods, weight gain (obesity), hair loss and ovarian cysts. Some suggest this is the cause of PCOS.²¹ Many suspect hypothyroidism is related to PCOS, ovarian enlargement and cyst formation. A recent study investigated this hypothesis among the women having PCOS and hypothyroidism with increased ovarian volume and bilateral multicystic ovaries. When thyroid hormone replacement therapy was initiated, in addition to stabilizing thyroid hormone levels, ovarian cysts regressed and ovarian volume was reduced.² Recent studies suggested that the patients who were erroneously diagnosed with PCOS when they really had hypothyroidism.^{21,22}

Hyperprolactinemia has been reported to be an important cause of infertility.²³ The present study also identified hyperprolactinemia as an important cause of infertility. Subclinical hypothyroidism can cause anovulation directly or by causing elevation in prolactin (PRL). Many infertile women with clinical or subclinical hypothyroidism had associated hyperprolactinemia due to increased production of thyrotropin releasing hormone (TRH) in ovulatory dysfunction.^{23,24} In this study, according to the new TSH reference range, 27.27% of the women with hyperprolactinemia having also hypothyroidism. It has been recommended that in the presence of raised PRL, the treatment should be first given to correct the hypothyroidism before evaluating other causes of raised PRL.²⁵⁻²⁸ This study suggested that the new TSH reference range facilitates to accept the

hypotheses discussed above regarding the PCOS and hyperprolactinaemia among the infertile women and open a new window for the treatment of infertility.

"The adverse health outcome for individuals with TSH levels between 3.0 and 5.0 is progression to overt hypothyroidism. Levothyroxine treatment would clearly prevent that outcome, but at what price?" However, it must be asked, why is preventing progression to overt hypothyroidism not a desired health objective, given that overt hypothyroidism most definitely can contribute to obesity, heart disease, infertility, depression and host of other health problems? Prevention of disease is a major focus of much of today's medicine, with exercise, diet and medications to prevent heart disease, obesity, stroke, and many other conditions. Some of these preventative approaches, particularly drug therapies, come with some risk factors, but the risks are presented along with benefits, so patients can make an informed choice. Even if there is a small risk to treatment of subclinical hypothyroidism (and the existence of such a risk is a theory, not a proven fact) then why is this same approach not used for thyroid patients, who could be given the opportunity to prevent overt hypothyroidism, realizing that the prevention also comes with some risk?²⁴

There is huge debate about narrowing the normal range of TSH. Practitioners are divided about this issue. Opponents of the new range argue against treatment for subclinical thyroid problems because they are concerned about risks of subclinical hyperthyroidism due to overtreatment.²⁵ Allies of the new reference range argue, however, that there is an equivalent risk of under treatment, and that all of these risks can be minimized by educating doctors about the desirable TSH target and teaching them how to use various dosages to reach those targets in patients.²⁶

However, over diagnosis and treatment of hypothyroidism is more justifiable than under treatment specially in case of infertility. Infertile women might take risk of over treatment for conception.

The findings of this study suggested that if the conventional TSH range are narrowed, as has been recommended by AACE and NACB, there are some implications in both practice and further research in infertility in Bangladesh. There are minimum effect to detect hyperthyroidism but increased 3 fold hypothyroidism particularly mild/subclinical. Idiopathic causes of infertility are reduced. During the treatment of infertility, practitioners should first consider the hypothyroidism then PCOS and hyperprolactinemia. Further studies are recommended to observe the treatment benefits of subclinical hypothyroid infertile women considering the risks with a very close supervision.

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A comparative study of lung functions in rice mill workers and non dust producing industrial workers

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Abstract

Background: Rice mill workers are potentially exposed to organic and inorganic dusts and synthetic chemicals mainly moldy hey or grain dust and silica that may have adverse effects on respiratory health.

Objective: To determine the effect of rice mill exposure on lung function. **Methods:** This was a cross-sectional comparative type of study conducted among the rice-mill workers and workers other than dust producing industry in Rajshahi, Bangladesh. In this study 300 rice mill workers as exposed group (B) and 100 workers other than dust producing industry as controls (A) were selected purposively. Data were collected by a pre-tested partially structured interview schedule designed to record the background characteristics of the workers and their lung function test results. **Results:** Of a total 300 rice mill exposed workers, 286 (95.3%) workers had impaired lung function (FVC <80% and or FEV₁ <80%). On the other hand out of 100 non rice mill exposed workers, only 14 (14.0%) workers had impaired lung function. Rice mill workers had a 32.53 (95% confidence interval (CI) 9.93-106.50) fold greater risk to impair their lung function than the workers worked other than rice mill. **Conclusion:** Rice mill workers should be advised to use tight facemasks during working hours as a routine and maximum necessary measures to control air pollution should be taken. And they should have periodic clinical and spirometric evaluation and those showing significant impairment in ventilatory functions should be advised to work in other non dust producing industries.

Key words: rice mill workers, lung function tests.

Introduction

Functions of the lungs are absorption and elimination of O₂ and CO₂ in and or out from the lungs. By respiration the term is generally used, external respiration, the absorption of O₂ and elimination of CO₂, and internal respiration, the utilization of O₂ and production of CO₂ by cells.¹ Forced vital capacity (FVC), Forced expiratory volume in 1st second (FEV₁), Forced expiratory volume in 1st second/ Forced vital capacity% (FEV₁/FVC%) and Peak expiratory flow rate (PEFR) are done to assess the different functions which reflect performance of it.^{2,3}

Nowadays, the significance of occupational hazards and need for protecting the health of industrial workers has been well recognized. Occupational pulmonary diseases are more widespread and more disabling than any other group of occupational diseases. The lung with its extensive surface area, high blood flow and thin alveolar epithelium is an important site of contact with substance in environment. The inhalation of dusts over a period of time leads to proliferation and fibrotic changes in lungs.^{4,5}

Rice mill workers, who are involved in husking process, are directly exposed to enormous dust particles. They are potentially exposed to organic and inorganic dusts and synthetic chemicals mainly moldy hey or grain dust and silica that may have adverse effects on respiratory health. They might face impaired lung function due to long term exposure to dust. Several reports have suggested that unprotected dust exposure in the paddy husking process may lead to chronic bronchitis, dyspnoea, wheezing, sinusitis, eosinophilia, asthma, COPD, chest tightness, nasal bleeding, nasal catarrh etc.^{6,7}

The pulmonary function tests have opened a new era towards scientific approach in diagnosis, prognosis and management of pulmonary disorders by the early recognition of their alteration in industry workers like rice mill workers who are constantly exposed to various dust pollutants and to institute protective and preventive measures to minimize the hazards of exposure to polluted environment.⁸ This study intended to determine the effect of rice mill exposure on lung function in Rajshahi district and recommend the concerned authority to take necessary measures to reduce the problem.

Methods

This was a cross-sectional comparative type of study conducted in the department of Physiology, Rajshahi Medical College among the Rice-mills workers and workers other than dust producing industry in Sopura Industrial area of Rajshahi City Corporation, Rajshahi from July 2010 to June 2011. Total 400 industrial workers were selected purposively as sample units. Of the 400 industrial workers, 300 were rice mill workers (exposed group or group B) and 100 were workers other than dust producing industry (control group or group A). A pre-tested partially structured interview schedule was used to collect data from the workers. The interview schedule was designed to record the background information (i.e. gender, age, weight, height and calculated BMI) of the workers and their lung function test results. The workers were firstly interviewed and then lung function tests viz forced vital capacity (FVC), forced expiratory volume in 1st second (FEV₁) and peak expiratory flow rate (PEFR) were determined by Spirometer maintaining proper procedures and steps. Verbal/written informed consent from the authorities of the industries and workers were obtained.

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Data were entered in the computer and processed using SPSS for windows. Descriptive statistics such as frequency distribution, computation of percentage etc. were applied. Chi-square and Student's t-test were applied to observe the homogeneity between exposed and non-exposed group and the difference of lung function parameters between the two groups, and the association of participants' characteristics with their lung function status. Multiple logistic regression analysis was used to determine the independent effects of participants' characteristics on lung function.

Results

A total of 300 rice mill exposed workers, 151 (50.3%) workers were male and 149 (49.7%) were female. Among the rice mill non-exposed workers, the percentages of male and female were 70.0% and 30.0% respectively. The mean age and BMI of exposed group were 30.47 years and 20.8 respectively. On the other hand, those of control group were 38.49 years and 22.0 respectively. These background characteristics of the exposed and control groups were significantly differed from each other (Table 1).

Table 1. Background characteristics of the exposed and control groups.

Group	Gender		Age (year)	BMI (Kg/m ²)
	Male N (%)	Female N (%)		
Exposed group (n=300)	151 (50.3)	149 (49.7)	30.47 ± 9.32	20.8 ± 2.26
Control group (n=100)	70 (70.0)	30 (30.0)	38.49 ± 7.23	22.0 ± 1.92
Test statistic (t/x ²) value, df	11.73, 1		7.85, 398	4.76, 398
P value	<0.001		<0.0001	<0.0001

In the control group, the mean values of FVC, FEV₁ and PEFR were 3.72±2.13, 3.45±2.24 and 20.85±43.19 respectively. These lung function indexes were significantly lower among the exposed group (Table 2).

Table-2: Comparison of lung function parameters between control and exposed group. (Control group =100 and Exposed group =300)

Parameter	Control group	Exposed group	Test statistic	P value
	Mean ± SD	Mean ± SD	T value, df	
PVC (Litre)	3.72 ± 2.13	1.93 ± 1.12	-10.8, 398	0.000
FEV ₁ (litre)	3.45 ± 2.24	1.80 ± 0.85	-10.72, 398	0.000
PEFR (Litre/sec)	5.41 ± 3.55	4.33 ± 1.76	-3.98, 398	0.000

Of a total 300 rice mill exposed workers, 286 (95.3%) workers had impaired lung function (FVC <80% and or FEV₁ <80%). On the other hand out of 100 non rice mill exposed workers, only 14(14.0%) workers had impaired lung function. Exposure to rice mill, gender, age and BMI of the industrial workers were identified as significant

correlates of their lung function status. A total of 300 rice mill workers, majority (95.3%) workers had impaired lung function. Among the non rice mill workers, it was only 14.0% (Table 3).

Table 3 Association of participants' background characteristics with their lung function status.

Factor	Status of lung function		Chi-square value	P Value
	Normal	Impaired		
Exposure to rice mill			264.8	0.000
Exposed (n=300)	14(4.7)	286(95.3)		
Non exposed (n=100)	86(86.0)	14(14.0)		
Gender			4.12	0.042
Male (n=221)	64(29.0)	157(71.0)		
Female (n=79)	36(20.1)	43(79.9)		
Age			47.26	0.000
Up to 30 years (n=207)	22(10.6)	185(89.4)		
>30 years (n=193)	78(40.4)	115(59.6)		
BMI			23.06	0.000
<18.5 (n=38)	0 (0.0)	38(100.0)		
18.5-24.9 (n=341)	100 (29.3)	241(70.7)		
>24.9 (n=21)	0 (0.0)	21(100.0)		

Rice mill workers had a 32.53 (95% confidence interval (CI) 9.93-106.50) fold greater risk to impair their lung function than the workers worked other than rice mill (Table 4). More than 79.0% of the female and 71.0% of the male workers had impaired lung function. The prevalence of impaired lung function among the younger (aged up to 30 years) workers was remarkably higher (29.8%) than the workers older than 30 years (Table 3). Younger age also showed significant log odds [11.18 (95% CI 3.36-37.21)] in comparison to older age (Table 4) to reduce the lung function. All of the workers having under and overweight had impaired lung function. It was 70.7% among the normal weight workers (Table 3). Gender and BMI were not identified as significant determinants of lung function (Table 4).

Table 4 Multiple logistic regression analysis: effects of rice mill exposure, age, gender and body mass index (BMI) on lung function.

Variable	Adjusted odds ratio [95% confidence interval (CI)]	P Value
Exposure to rice mill		0.000
Exposed	32.53 (9.93-106.50)	
Non exposed*	1.00	
Gender		0.060
Male*	1.00	
Female	.395 (0.150-1.041)	
Age		0.000
Up to 30 years	11.18 (3.36-37.21)	
>30 years*	1.00	
BMI		1.00
<18.5*	1.00	
18.5-24.9	0.09 (0.00-0.96)	
>24.9	2.69 (0.00-4.78)	

Discussion

In the present study the cases and controls were not matched for their background characteristics i.e. gender, age and BMI and the analysis suggested that case and control were heterogeneous groups. So, though bivariate analysis in this study suggested, exposure to rice mill dust was associated with impaired lung function, it did not insure the independent effect of exposure to rice husk on lung function, but multivariate

analysis suggested that exposure to rice mill dust impaired lung function.

The advent of pulmonary function tests have opened a new era towards the scientific approach in diagnosis, prognosis and management of bronchopulmonary disorders.⁹ Many studies have been done in relation to pulmonary functions both in normal subjects and in workers exposed to different occupation dust hazards.³⁻¹¹ The results of these studies are indicating that workers of different dust industries are prone to respiratory dysfunctions while working in them. The present study findings suggested that with a progressive trend towards industrialization, like others workers of dust generating industries, there is also a definite increase in occupational lung diseases in rice mill workers.

In this study FVC, FEV1 and PEFR were significantly reduced in rice mill workers than that of the controls. It indicated that study subjects had both obstructive and restrictive type of lung impairment. This reduced FVC may be due to much more changes to the bronchil and elastic component of lungs resulting in restrictive type of lung impairment.¹² Decreased FEV1 indicated that exposure to dust causes early obstructive pulmonary impairment, which further increases with increase in number of years of exposure.¹³ This may be due to release of air borne endotoxin which may cause inflammatory reaction in the bronchopulmonary system.¹⁴ Reduced PEFR is probably due to hypertrophy of mucosal cells due to irritation by grain dust and smoke resulting in the increased secretion of mucous and formation of mucosal plugs which cause obstruction to the exhaled air.¹⁵

Decreased in various lung function parameters in rice mill workers may be due to exposure to industrial dust, poor ventilation, non-use of face masks and lack of proper exhaust facility.¹⁶ This exposure to industrial dust causes occupational air way obstruction which occurs due to chronic bronchitis occurring due to chronic irritation of air ways.¹⁷

Thus in concluding it can be seen that spirometric parameters in rice mill workers showed lower values than in the corresponding control subjects. The difference is statistically significant indicating that the air pollution at work site accelerated decline in lung functions. So workers should have periodical clinical and spirometric evaluation and those showing significant impairment in ventilatory functions should be readjusted in other sections of the industry where exposure to industrial dust is negligible. Workers should be advised to use tight facemasks during working hours as a routine and maximum necessary measures to control air pollution.

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Bio-social factors of the mothers and birth weight of their newborns in a tertiary hospital, Bangladesh

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Abstract

Background: Low Birth Weight (LBW) is one of the major problems of children in Bangladesh. LBW can be prevented by looking into its associated factors. **Objective:** To explore the bio-social factors of the mothers and its relationship with the birth weight of their new born babies. **Methods:** This cross sectional type of descriptive study was conducted among the mothers, who delivered their babies at the Rajshahi Medical College Hospital. The sample size was 298. Data were collected from the respondents by face to face interview through a partially structured questionnaire. Data analysis involved simple descriptive as well as analytical techniques including chi-square and Fisher's Exact test. **Results:** A total of 298 newborns, only 6.6% had birth weight < 2500 grms. Prevalence of LBW among the anaemic mothers and mothers having body weight < 45 kgs in 3rd trimester were significantly higher than that of non anaemic mothers ($P=0.039$) and the mothers of body weight = 45 kg ($P=0.002$). **Conclusion:** Prevention of Maternal malnutrition and anaemia may reduce the incidence of LBW in Bangladesh.

Key words: LBW, bio-social factors, Bangladesh.

Introduction

The birth weight is a reliable indicator of foetal wellbeing and maturity.¹ The birth weight of a newborn baby is probably the single most important factor that affects its survival and quality of life.^{2,3} The common causes of low birth weight (LBW) are maternal malnutrition, obstetric or medical complications associated with pregnancy, congenital malformations of the foetus and socio-economic factors like heavy work during pregnancy, pregnancy in quick succession or pregnancy at a very young age. Genetic and geographic factors are also related to LBW.⁴ There is a correlation between low socio-economic status and LBW.⁵ In developing countries maternal malnutrition, anaemia and short birth intervals commonly cause LBW babies.⁶ Mothers' weight in pregnancy is associated with birth weight variation.⁶ Mean birth weight of babies is less in underweight mothers than that of mothers weighing above 100 lbs (45.4 kgs).⁷ In one study it was shown that 51.2% of LBW babies were born to mothers weighing 40 kgs and below. In another study, it was observed that low level of maternal education and paternal unemployment were important determinants of LBW. LBW is one of the major problems of children in Bangladesh.⁸ Maximum morbidity and mortality of neonates are related to LBW. LBW can be prevented by looking into the risk factors.⁹

As the prevalence of LBW is one of the most important health indices, it is important to know the prevalence and risk factors for LBW. The aim of this study was to determine the prevalence of LBW and some of its risk factors specially maternal risk factors in Bangladesh. It was hoped that the results of this study could help the health authorities by informing about the maternal risk factors for LBW thereby to reduce its prevalence.

Methods

This cross-sectional type of descriptive study was

carried out among the mothers, who delivered a singleton full-term normal newborns in the Department of Obstetrics of Rajshahi Medical College Hospital in the year 2011. The sample size of the study was 298, which was selected purposively. Data were collected from the respondents by face to face interview through a partially structured questionnaire. The questionnaire was designed to record maternal age, educational status, monthly family income, anaemic status and body weight, and birth weight of the newborns. The weight of the mothers were measured by bath room weight machine to the nearest 100 gm. Birthweights of the apparently full-term (based on the date of the last menstrual period) normal newborns were measured just after separation from the placenta by the Detecto-type baby weight machine to the nearest 10 gm. A pregnant women having haemoglobin levels <11 g/dl was considered as anaemic. Data were analyzed in computer by using SPSS/PC+ for windows. Data analysis involved simple descriptive as well as analytical techniques including chi-square and Fisher's Exact test.

Results

Out of 298 newborns, 93.4% newborns had birth weight = 2.5 Kg and the rest only 6.6% had birth weight < 2.5 Kg, i.e.; they were LBW babies (Fig. 1).

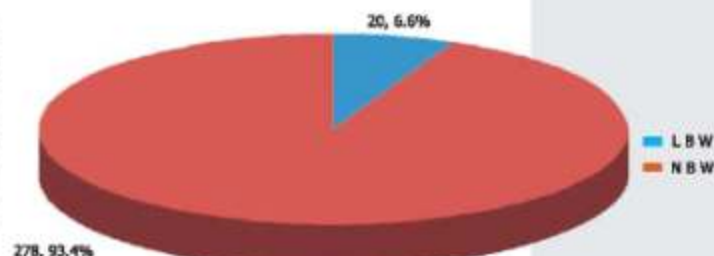


Figure 1 : Birth weight status of the babies

A total of 298 pregnant mothers, 75.2% mothers were in the 20-35 years age group, 15.1% were in group >35 years and 9.7% in group <20 years. The mean age of the mothers was 23.80 ± 4.18 years. The prevalence of LBW among the mothers of < 20 years, 20-35 years and >35 years age groups were 10.3%, 5.4% and 11.1% respectively. Age of the mothers was not significantly associated with LBW. Majority (60.4%) of the mothers did not complete their primary education (up to Class V). The rest of the mothers (39.6%) completed their primary level education. Prevalences of LBW among the mothers of different educational levels were not remarkably differed from each other. More than 92% of the mothers had monthly family income TK 12000.00 or less. Only 7.72% of the mothers had family income more than Tk.12000. The average monthly family income was $Taka\ 6460.53 \pm 8424.49$. Monthly family income of the mother was not significantly associated with LBW. Forty three percent of the mothers were anaemic. Prevalence of LBW among the anaemic mothers was significantly higher than that of non anaemic mothers ($P=0.039$). Out of 298 mothers, 83.2% mothers had body weight ≥ 45 Kg and the rest (16.8%) mothers had body weight < 45 Kg. Prevalences of LBW among the mothers of body weight < 45 Kg and ≥ 45 Kg were 18.0% and 4.4% respectively. Prevalence of LBW was statistically associated with the body weight of the mothers ($P=0.002$). The age, educational status and monthly family income were not statistically associated with the prevalence of LBW (Table 1)

Table-1: Mothers' biosocial factors and low birth weight.

Mother's biosocial factor	Status of birth weight		P-value
	Low birth weight N (%)	Normal birth weight N (%)	
Age			
< 20 years	3 (10.3)	26 (89.7)	0.264**
20-35 years	12 (5.4)	212 (94.6)	
>35 years	5 (11.1)	40 (88.9)	
Educational status			
Below class V	12 (6.67)	168 (93.33)	0.572*
Class V or above	8 (6.78)	110 (93.22)	
Family Income			
Up to taka 12000	20 (7.27)	255 (92.73)	0.246**
Taka 12001 +	0 (0.0)	23 (100.0)	
Anaemia			
No anaemia	7 (4.12)	163 (95.88)	0.039*
Anaemia	13 (10.15)	115 (89.85)	
Body weight			
> 45 Kg	9 (18.0)	41 (82.0)	0.002**
≥ 45 Kg	11 (4.43)	237 (95.57)	

*Chi-square test applied, **Fisher's Exact test

Discussion

One of the nutritional goals of the 1990 World Summit for Children was to reduce the prevalence of LBW to less than 10% by the year 2000 needless to say, LBW remains a formidable challenge for the 21st century for the developing countries like Bangladesh¹⁶. But the different studies¹¹⁻²⁴ in the last few decades indicated that Bangladesh achieved a remarkable

progress to overcome this challenge. The prevalence of LBW declined from 50% to 20% as well as the mean birth weight increased from 2.48 to 2.66 kgs in Bangladesh. The present study findings were also consistent with this trend.

Although in this study age of the mothers was not significantly associated with the LBW, but the mothers who were young (<20 years) or old (>35 years) are more likely to birth LBW infants than those aged 20-35 years. It corresponds with the findings of Ahmed et. al.¹⁵ and Eisner et al.¹⁶ This fact reflected both biological immunity in case of mothers below 20 years of age and consequences of aging in elderly women may be due decline hormonal activities, which may occur after the age of 35 years.

Anaemia in pregnancy is a common problem and 50% of the pregnant women in developing countries are suffering from anaemia.¹⁷ The present study findings also agreed with this. In a study in Pakistan, Badshah et al.¹⁸ observed that the anaemic mothers were at risk to deliver LBW babies compared to non anaemic mothers. The results of a study in Ahmedabad, India by Mavalankar et al.¹⁹ were also consistent with Badshah et al.¹⁸ with reference to the effect of maternal anaemia on low birth weight. Lone et al.²⁰ In a multivariate analysis of their study population showed that the risk of low birth weight babies in the anaemic population was 1.9 times higher (95% CI 1.0-3.4) than non-anaemic mothers. The results of this present study were also consistent with the above mentioned studies, showing that the majority of anaemic mothers gave birth to LBW babies, with a significant difference ($p=0.039$) from the non anaemic group.

Maternal weight <45 kgs in 3rd trimester of pregnancy is an important risk factor of LBW.²¹ The prevalence of low birthweight (LBW) is higher in Asia than elsewhere,²² because about 60% of women in South Asia and 40% in South-East Asia are underweight (<45 kg).²³ In this present study low birth weight was also significantly associated with maternal pre-delivery body weight ≤ 45 kg.

LBW is probably the main reason why over 50% of the children in South Asia are underweight.²⁴ The adverse consequences of LBW continue to be manifested during childhood, and are passed on to the next generation when women, who have been chronically undernourished in their past, become pregnant. LBW and subsequent stunting are caused by undernutrition and other health problems, rather than by racial or ethnic differences. So, Improvements in maternal nutrition and health can increase birthweight and prevent LBW in the developing countries like Bangladesh.

The present study findings suggested anaemia and body weight <45 kgs in 3rd trimester, are predominant bio-social factors associated with LBW. Thus, more care on mother (maternal) nutrition and prevention of anaemia may prevent LBW in Bangladesh.

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Frailty among the elderly rural people of Bangladesh

Zoha Mohammad Meherwar Hossain

Abstract:

Background: Frailty is a multidimensional geriatric syndrome resulted as the loss of reserves that gives rise to vulnerability. Measurement of frailty is useful at a health care policy level as well as clinically. **Objective:** To estimate the prevalence of frailty among the elderly population in a rural community of Bangladesh. **Methods:** This was a cross-sectional type of descriptive study carried out in a rural area of Bangladesh. All the people aged ≥ 65 years of the village constituted the study population. A total of 174 elderly people available at their houses during data collection were included in this study. Data were collected by face to face interview with the help of a semi-structured questionnaire. The questionnaire was designed to record the age, gender and frailty status of the participants. Frailty status was measured by a valid and reliable Frailty scale. Descriptive analytical techniques involving frequency distribution, computation of percentage etc. were applied. Chi-square test was applied to find out the association of frailty status with age and gender of the participants. **Results:** Out of 174 elderly people, 161 (92.53%) people were found to be frail. Women had significantly higher occurrence of frailty (97.59%) than men (87.91%). Advancement of age showed no significant change in the result. **Conclusion:** A detailed and extensive study should be planned in the national level to reveal the actual situation of the elderly people and specific policy should be taken by the government to take proper care of this population group. All the concerning agencies should also be aware of the situation.

Key words: frailty, elderly rural people, Bangladesh.

Introduction

Frailty is a term widely used to denote a multidimensional geriatric syndrome resulted as the loss of reserves (energy, physical ability, cognition, health) that gives rise to vulnerability.¹ It seems to be a valid construct, but the exact definition is still not so clear. According to Rockwood et al. there are many operational definitions, which typically are rules-based²; for example, a person may be considered as frail if three or more symptoms (of unintentional weight loss, feeling exhausted, weak grip strength, slow walking speed and low physical activity) are present.³ Rules-based definitions often are derived from multiple regression analysis and cannot be reliable cent per cent, for example: in requiring combinations of factors that might not apply to an individual case. Summing the number of impairments is another way to define frailty. Thus there are so many different scales to measure frailty and it means only the situation that the term 'frailty' is still an obscure one and also its components are not yet clear and unanimous to all. A reliable operational definition and classification of frailty was suggested by Canadian Study on Health and Aging which was used in this study, that depends upon clinical judgment to interpret the results of history-taking and clinical examination.⁴

The ability to measure frailty is useful at a health care policy level as well as clinically: information about frailty helps program planners by identifying the range of services that might be required and the anticipated need for them. The frailty stratification clinically helps for planning and management of the patients' risk of death and need for institutional care. As the scales are mainly intended to stratify risk, the ability to predict adverse outcomes serves a common goal. In the Canadian Study on Health and Aging three

approaches were worked there. First, like other groups, they developed a rules-based definition of frailty. Later, they developed a method of counting a patient's clinical deficits (identified by the clinical symptoms and signs, but mainly by the assessment of the old person him/herself or by the care-giver of the person). And finally, they described their third approach which has been used here in this paper: the derivation and validation of the Clinical Frailty Scale, a measure of frailty based on clinical judgment.⁴ Rockwood et al. also carried out their study in the same way.² This approach is valid and reliable as seen in their studies.

As the size of the geriatric population is increasing in course of time, the burden of the national economy is also increasing. Hypothetically the elderly people in our country are largely devoid of any work that affects to the economic growth of our country. But there is lack of information regarding the frailty status of the elderly people in our country. So no proper planning is possible yet to be designed to take proper care of them. In this study the researcher attempted to explore the frailty status of the elderly people in a rural community of Bangladesh.

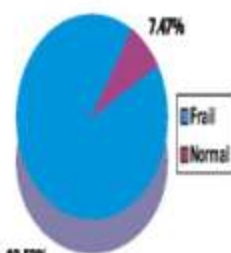
Methods

This was a cross sectional descriptive type of study conducted in a village, Kendra-Guchchha Gram of Puthia Upazilla, Rajshahi, Bangladesh. All the people aged ≥ 65 years of the village constituted the study population. A total of 174 elderly people available at their houses during data collection were included in this study. Data were collected by face to face interview with the help of a semi-structured questionnaire. Frailty was measured by a valid and reliable Frailty scale.⁴ The interpretation has been simplified in the way that the frailty positive and negative persons were categorised only by 'Frail' and 'Normal' or 'Not Frail' groups, not doing the minute

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92.53%

Figure 1: Frailty status of the elderly people.

scaling of them, as the sample size was not very large. Data were entered in the computer and processed using SPSS for windows. Descriptive analytical techniques involving frequency distribution, computation of percentage etc. were applied. Chi-square and Fisher's exact test were applied to find out the association of frailty status with age and gender of the participants.

Result

More than 92% of the elderly people were found as frail (Figure 1). Out of 174 elderly people, 91 (52.30%) were male and 83 (47.70%) were female. The proportions of frail among males and females were 87.91% and 97.59% respectively. The females were significantly more frail than the males ($p < 0.05$) (Table 1).

Table 1: Gender differentiation of frailty among the elderly people

Frailty conditions	Male N (%)	Female N (%)	Total N (%)
Frail	80 (87.91)	81 (97.59)	161 (92.53)
Not Frail (Normal)	11 (12.09)	2 (2.41)	13 (7.47)
Total	91 (52.30)	83 (47.70)	174 (100.00)

$$\chi^2 = 5.88, df = 1, p < 0.05$$

Of the total 174 elderly people, 146 (83.91%) people were in the age-group of 65 to 74 years and the rest 28 (16.09%) were in the age-group of 75 years and above. Of the 146 elderly people in the age-group of 65 to 74 years, 135 (92.47%) were found to be frail and the rest 11 (7.53%) were not frail or normal. In the age-group of 75 years and above, out of 28 elderly people, 26 (92.86%) were frail and the rest 2 (7.14%) were not frail or normal. Frailty was not significantly associated with age (Table 2).

Table 2: Frailty among different age-groups

Age Group (In Years)	Frail N (%)	Not frail N (%)	Total N (%)
65-74	135 (92.47)	11 (7.53)	146 (83.91)
75 and above	26 (92.86)	2 (7.14)	28 (16.09)
Total	161 (92.33)	13 (7.47)	174 (100.00)

$$\text{Fisher's exact test value} = 0.942, df = 1, p > 0.05$$

Discussion

The occurrence of frailty among the elderly people was found very high in this study (92.53%). This result differs a lot from the study by Fried et al. where the prevalence of frailty was found to be 7-16%, reported in community-dwelling older adults of African American origin.⁸ It was found to be 14.1% in a Mexican study by Casale-Marín et al.⁴ Colford et al. stated that reported prevalence of frailty varies enormously in different communities (range 4.0-59.1%).¹ In other studies, the prevalence of frailty among the community-dwelling people was seen as 6.9% by Fried et al. and 5.3% by Steinman et al. in USA.⁹ In the Japanese community, Kobayashi et al. found prevalence of frailty among the Japanese old women to be 23%.¹⁰ Rechat et al. showed in their study that in the community of Sydney in Australia, 50% of the subjects were robust, the rest were not (3.4% were frail and 46.6% were pre-frail).³ None of these results was as high as that in this study.

Santos-Eggimann et al. found in the population of 10 European countries, frail (4.1%) and prefrail (37.4%) were in total 41.5%.¹¹ In the Nepalese community, Chalise found the functional limitation of the elderly 65 plus population to be 12.8 per cent.¹² In Rotterdam study of the Netherlands, Lahousse et al. showed out of 2,833 respondents, 163 (5.8%) elderly people were frail, and 1,464 (51.3%) were intermediate frail.¹³ Summing up the frail and intermediate frail, the total percentage goes up to 57.1%, much higher than the other European countries but still very less than the present study.

Curcio and his colleagues' study showed in a rural area in the Andes Mountains, the prevalence of frailty was only 12.2% and they demanded it was similar to that reported in other populations in the Latin American region.¹⁴ Result of this study differs a lot with the result of Runzer-Colmenares et al. who conducted their study in the Peruvian community and found that out of 311 participants, only 78 (25.1%) were not frail, i.e. the rest 74.9% fell in the groups of frail and pre-frail.¹⁵ A similar result was found in a southern state of Brazil by Oliveira, who studied upon 99 subjects aged 65 or older in Rio Grande do Sul state and there were only 4% people classified as non-frail.¹⁶ Result of this study is very much similar to the present study. But Duarte et al. found prevalence of pre-frail was 45.9% and frailty was 12.9% in the Brazilian urban community.¹⁷ Comparing the prevalence of frailty in the different communities of the world, it is clear that the prevalence of frailty is much more higher in this country.

Result of this study is very much similar to all other studies in case of gender distribution of frailty. This study showed that occurrence of frailty was higher in female (97.59%) than in male (87.91%). This fact of higher prevalence of frailty among the women was also supported by Fried et al.⁹ Gu et al. also stated that women are frailer than men at all ages.¹⁸

Regarding age-distribution of frailty, this study showed no difference in the occurrence of frailty with the advancement of age. The studies by Lahousse et al.¹³ Gu et al.¹⁸ Saum et al.¹⁹ and Nishi et al.²⁰ showed the fact that occurrence of frailty increased with the advancement of age, contrary to this study. This disagreement of the present study findings with the others might be due to small number of respondents in the present study. A well designed study with a large sample size is necessary for further evaluation.

Conclusion

The occurrence of frailty among the elderly rural population of our country is very much high. This condition is not hopeful for the development of a country. If proper medical and social care would be taken, this group of population can contribute to the economic growth of the country. They can also lead a socially and economically productive healthy life. Unfortunately, special and specific care for the elderly people has not yet been established in our society. So a detailed and extensive study should be planned in the national level to reveal the actual situation of the elderly people and specific policy should be taken by the government to take proper care of this population group. All the concerning agencies should also be aware of the situation.

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Laparoscopic orchiopexy for the nonpalpable testis: 3 years experience.

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Abstract

Background: We evaluated the safety and efficacy of laparoscopic orchiopexy in management of nonpalpable intra-abdominal testis and studied the outcomes. Here, 3 years experience is being reported. **Methods:** Laparoscopic Orchiopexy was performed on 28 children (32 testicular units) for non-palpable intra-abdominal testis between 2010 and 2012. We retrospectively reviewed the medical records. The mean age was 3.4 years (range, 2.5 -11 years). Of the 28 patients, 18 (64.3%) were on the right, 6 (21.4%) were on the left and 4 (14.3%) were bilateral. The mean follow-up period was 14.8 months (range, 3-36 months). Testicular viability and orchioepexy positioning were evaluated within 1 month and beyond 3 months. **Results:** Thirty one testes were descended successfully by laparoscopy. The average operative time was 41.5 ± 3.8 min. Primary laparoscopic orchiopexy done in 26 testes. Three of unilateral and 2 of bilateral testicular units underwent one-stage Fowler-Stephens Orchiopexy. One patient needed laparoscopic orchiectomy. At follow-up (mean 14.8 months), one testis atrophied and needed orchiectomy. Testicular survival rate was 96.8% (30/31) and all of the testes maintained an adequate size. Twenty six (83.9%, 26/31) are in an acceptable scrotal position and 4 testes (12.9%, 4/31) are mid to high in the scrotum without atrophy. There was no recurrent inguinal hernia. **Conclusions:** Laparoscopic orchiopexy is successful for a nonpalpable intra-abdominal testis with a high testicular survival rate. The low incidence of complications and high success rate underscore the feasibility of this procedure.

Key words: Non palpable testis, Laparoscopic Orchiopexy, Children.

INTRODUCTION

Undescended testis (UDT) is one of the common clinical disorders of childhood, occurring in approximately 3% of full-term newborns, 21% of premature newborns, and 0.8-4% of 1-year-old boys.¹⁻³ In the eight week of intrauterine life, the testes develops in the abdominal cavity, and descend through inguinal canal to the scrotum in the third trimester.⁴ In 80% of cases of UDT, a testis is palpable in the groin, and in 90% of these boys, it is associated with hernia. In these cases, conventional open orchiopexy has been accepted as a standard treatment. In 20% of cases, testis is nonpalpable and among them 20% is absent on exploration.⁵ Due to increased risk of malignant transformation and infertility,^{6,7} it is important to determine the presence or absence of testis. Accurate preoperative localization of nonpalpable testes has been difficult. CT scan, although noninvasive, is unable to localize such testes and carries risk of radiation.⁸ Sonography and MRI are noninvasive but USG is poor in localizing the nonpalpable testes and the value of

laparoscopy has been proved to have the most important role both in diagnostic and treatment of undescended testis.^{9,10} Since 1976 when Cortesi and associates first described laparoscopic diagnosis of a nonpalpable testis,¹⁰ this method for diagnosing a nonpalpable testis has been established as the most reliable one. Since 1992 when the first laparoscopic orchiopexy was reported by Jordan et al.,¹¹ laparoscopic orchiopexy has obtained wide popularity with technological advances. The final goals of orchiopexy are to keep the testes viable in optimal position within the scrotum. We aimed to evaluate the safety and efficacy of laparoscopic orchiopexy in management of nonpalpable intra-abdominal testis in our settings. It was carried out after gaining experience in laparoscopic cholecystectomy, laparoscopic appendectomy and laparoscopic herniotomy. A three years experience on testicular positing in Rajshahi Medical College Hospital is being reported performed by retrospective review of patient records.

Methods

We reviewed pre and postoperative medical records including clinical results and complications of 28 patients (32 testicular units) who underwent laparoscopic orchiopexy for a non-palpable intra-abdominal testis between January 2010 and December 2012 in the department of pediatric surgery, Rajshahi Medical College Hospital. Data were collected by using a data collection sheet. The data collection sheet was designed to record the information regarding age of the patients, affected side, location of the testis at the time of laparoscopy, operation performed, operative time, complications and the surgeon who performed the surgery. The age of the children when undergoing the laparoscopic orchiopexy ranged from 2.5 to 11 years, with a mean age of 3.4 years. Initially, diagnostic laparoscopy is performed under general anesthesia to locate the testis, distance from the internal ring and presence of hernia, if any.

The testicle was classified as peeping (at the internal inguinal ring (IIR)) or low (within 3 cm from the IIR) or high (> 3 cm from the IIR); primary laparoscopic orchiopexy (PLO) was performed if peeping or low, one-or two-staged Fowler- Stephens laparoscopic orchiopexy (FSLO) if high, or PLO if atrophic.

All patients were followed up post-operatively at 1 month and 3 months thereafter for a mean post-operative follow-up of 14.8 months with highest up to 36 months and findings noted included: surgical site infections, post-operative testicular location, and testicular size, measured at the time of surgery and compared to the normal contralateral testis on follow-up.

Data were entered in the computer and processed using SPSS for windows. Descriptive techniques involving frequency distribution, computation of percentage etc. were applied.

Surgical procedure

All laparoscopic orchiopexy were done under general anesthesia. A stab incision was made in umbilicus through which a Veress needle was inserted and CO₂ was insufflated at a pressure of 10-12 mmHg. A 5 mm laparoscopy port was inserted after enlarging the umbilical stab incision. This port was restricted for the use of a laparoscope with an attached camera that was connected to a television monitor. On

the location and volume of testes, the length of vas deferens and vessels, the presence of a patent processus vaginalis, and presence of inguinal hernia were determined. Two additional 3 mm working port were inserted at the lateral border of the rectus muscle in each flank under visual control in order to facilitate the laparoscopic dissection. The port on the side of UDT was placed at a higher level than the umbilicus and in case of bilateral UDT both ports were placed higher. The child was then placed in Trendelenburg position and the operating table tilted away from the side of the UDT. Further procedure depended upon whether or not the testes were present and their size.

When the testes were found and seemed suitable size, laparoscopic orchiopexy was performed (Figur-1). The gubernaculum of the testes was transected and the dissection was performed alongside the testicular vessels, carefully teasing all the bands with good visual control. Mobilization was carried out up to the aorta and left renal vein or the aorta and venacava depending on the side involved. The vas deferens was also mobilized retaining its blood supply in the adjacent tissue (Figur-2). Practically mobilization of the testis is enough when the testis easily reaches the opposite deep ring. Through a



Figure-1: laparoscopic view of UDT

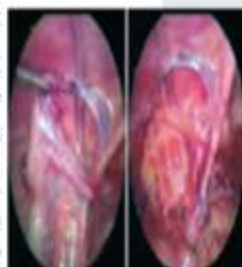


Figure-2: Laparoscopic dissection of UDT

made in the scrotum, tip of a long curved artery forceps was guided cephalad in to the peritoneal cavity just medial to the inferior epigastric vessels. Grasping the gubernaculum, the testes were delivered in to the scrotal wound, making sure that there was no twist on

the testicular vessels (Figur-3). The testes were then secured in the extra dartos pouch and the scrotal wound closed with vicryl. After adequate mobilization when the length is not sufficient testicular vessels



Figure 3: Dartos pouch in orchidopexy.

are dissected after proper coagulation (Figur-4). In case of atrophied or severely hypoplastic, it was removed after diathermy of testicular vessels and vas deferens. The laparoscopy ended in all cases with deflation of peritoneum, suturing of the laparoscopy ports using Vicryl.



Figure 4: Laparoscopic dissection of testis.

Result
By analyzing the diagnostic laparoscopic findings of

the 28 UOT patients, 18 (64.3%) were on the right, 6 (21.4%) were on the left and the rest 4 (14.3%) were bilateral. Of 32, 23 (65.6%) testicular units were located within 3 cm of the IIR among them 1 (3.1%) testicle was found atrophied, 5 (15.6%) testicular units (3 of unilateral and 2 of bilateral) were more than 3 cm from the IIR, and 6 (18.8%) testicular units were peeping testes.

Diagnostic laparoscopy was successful in localization in each of the 28 patients. Thirty one testes of the 28 patients were descended successfully by laparoscopic orchidopexy. Initially we took significantly longer time for the first 11 patients than the next 17 patients. The mean operative time was 41.5 ± 3.8 min. Five high testicular units (> 3 cm from the IIR) underwent 1-stage FSO (2 of unilateral and 2 of bilateral). No testicular units underwent 2-stage Fowler-Stephens orchidopexy in this series. The remaining 26 low testicular units (within 3 cm from the IIR) underwent FSO without division of any vessels. One patient needs laparoscopic orchiectomy as it was atrophied.

The clinical results within 1 month after the laparoscopic orchidopexy. One testis becomes atrophy and 30 testicular units survived, giving a testicular survival rate (TSR) of 96.8%. At the end of the follow-up (mean 14.8 months), the rest 30 (96.8%) testes maintained an adequate size, 26 (83.3%) testes were low in an acceptable scrotal position and 4 testes (12.9%) were mid to high in the scrotum without atrophy or recurrent inguinal hernia (Table 1).

Table 1: Patient's outcome

Age (months)	Testicular survival (%)	Orchidopexy (%)	Position of testis		Hernia (%)
			Low (%)	Mid/high (%)	
10	5 (100)	0 (0)	5 (100)	0 (0)	0 (0)
11-15	1 (100)	0 (0)	1 (100)	0 (0)	0 (0)
16-20	1 (100)	0 (0)	1 (100)	0 (0)	0 (0)
21-25	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

DISCUSSION

The experience of laparoscopic cholecystectomy, laparoscopic appendectomy and laparoscopic herniotomy has opened the door of laparoscopic management of UOT. Laparoscopy has been established as a very useful diagnostic tool in the management of children with non palpable testes.¹² The findings of this study also suggest that laparoscopy is a reliable way to locate the site of impalpable testis.

Cryptorchidism is the most common disorder of male sexual differentiation and affect about 0.04%-4% of male and 20% of these are non palpable.¹³ Important long-term sequelae include infertility and testicular tumors. Orchidopexy is thought to decrease the incidence of infertility and allow early detection of tumor. The ideal age of orchidopexy is as early as 6 months. Orchidopexy is recommended at between 6 and 12 months of age as histological damage is thought to occur if delayed.¹⁴ The age of the children in this study were several fold higher than the optimal age of laparoscopic orchidopexy. It may be due to lack of awareness and poor socioeconomic status of the parents. The people of Bangladesh should be aware about the optimal age for the management of non palpable UOT.

Traditional surgical option of non palpable undescended testes includes a staged orchidopexy,¹⁵ orchiectomy or microvascular auto-transplantation.¹⁶ With increasing experience in the usages finer resolution equipment and smaller (pediatric) laparoscopes, a laparoscopic orchidopexy has been shown to be feasible, easier and more effective.¹⁷ In this study a complete

testes. Because of high degree of magnification, laparoscopy gives excellent visualization of testicular vessels up to the origin from the aorta and drainage in to the renal vein and inferior vena cava respectively. All adhesion to the testicular vessels can be divided with precision. A total 28 patients, incidence of intra-abdominal non palpable UDT was higher in right side. It is in conformity with recently published data.¹⁷

Samadi et al. conducted PLO in 70.5% and FSLO in 29.5% of a total of 203 testicular units and reported a success rate of 95%, which was higher than the 76% success rate of open surgery.¹⁸ Lindgren et al. did a 6-month clinical follow-up after laparoscopic orchiopexy and reported a success rate of 93%.¹⁹ Lintula et al. reported a success rate of 88% for 19 testicular units undergoing laparoscopic orchiopexy and a success rate of 82% for 18 testicular units receiving open surgery, highlighting the excellent surgical outcomes of the laparoscopic orchiopexy.²⁰ In this series, 14.8 months after the laparoscopic orchiopexy, the TSR was 96.8% and the rate of fixation in the lower scrotum was 83.9%. These outcomes are similar with those reported studies,¹⁸⁻²⁰ and the successful results in this study confirm the clinical significance of laparoscopic orchiopexy for a non palpable intra-abdominal testis. One-stage FSLO was performed in 5 testicular units and success rate was 80%. Chang and Franco performed FSLO in 48 testicular units and reported that the success rate of one-stage FSLO was 94.3%.²¹ Comparing with the findings of these studies, the success rate of the FSLO in the present study was relatively unsatisfactory, it might be due to small number of cases. Improved results are expected in the near future after accumulating experience with FSLO for non palpable intra-abdominal testis.

In case of non palpable UDT, the reported rate of orchidectomy seems to vary between 14%² and 48%.¹⁶ In this series, the orchidectomy rate is 6.25%. Our decision at the time of laparoscopy to carry out orchidectomy was supported by subsequent histopathological result.

CONCLUSIONS

Laparoscopic Orchiopexy certainly avoids a groin or laparotomy incision. It is safe and effective to manage a non palpable intra-abdominal testis. It should be a method of choice for a non palpable intra-abdominal testis.

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Middle East Respiratory Syndrome Coronavirus (MERS-CoV): Global alert and response

Shahanara Begum

ABSTRACT

Middle East Respiratory Syndrome Coronavirus (MERS-CoV) is a newly emerging respiratory virus with a high case fatality rate among identified cases. The virus is thought to cause a severe disease in patients with underlying co-morbidities. The identification of asymptomatic patients and mild cases among family and healthcare workers contacts of confirmed cases indicates a wider spectrum of clinical manifestation of the disease. The majority of patients presented with fever (98%), fever with cough (83%), and shortness of breath (72%). The understanding of the epidemiology and clinical presentation of the disease is increasing overtime.

Key words: MERS-CoV, Human Coronavirus-EMC, Dipeptidyl peptidase 4 (DPP4)

INTRODUCTION

Coronaviruses are RNA viruses which usually cause mild upper respiratory illnesses. The emergence of SARS (Severe Acute Respiratory Syndrome) MERS (Middle East Respiratory Syndrome) has focused global attention on the clinical significance of coronaviruses. Since mid-2012, a novel coronavirus was found to cause severe disease in humans. The virus was recently named Middle East Respiratory Syndrome Coronavirus (MERS-CoV) 1. Other terms that have been used to describe this virus include novel Coronavirus (nCoV) and human Coronavirus-EMC (for Erasmus Medical Center).

This virus was initially identified in September 2012 from samples obtained from a Saudi Arabian patient who developed a severe acute respiratory infection and later had acute renal failure and ultimately died 2. The virus was subsequently reported as a cause of pneumonia in additional cases from Saudi Arabia, Qatar and United Arab Emirates 3, 4. The initial cases from Saudi Arabia occurred before the Al-Hasa outbreak in April-May 2013. The majority of these cases occurred in patients with underlying comorbidities. As of September 19, 2013, globally, the World Health Organization (WHO) recorded 132 laboratory-confirmed cases of infection with MERS-CoV, including 58 deaths 5. A major resurgence of MERS-CoV cases during April 2014 expanded the geographic distribution of confirmed MERS-CoV cases to include countries in Asia (Malaysia, Bangladesh) and North America and several additional countries the Middle East (Yemen, Egypt) and Europe (Greece) 6. Moreover, as of June 16, 2014, 249 of 701 patients (36%) with laboratory-confirmed MERS-CoV infection reported to the WHO have died 7.

In addition to humans, MERS-CoV has been found in camels in Qatar, Oman, Egypt and Saudi Arabia, and a bat in Saudi Arabia. Camels in several other countries have also tested positive for antibodies to MERS-CoV, indicating that the camels were previously infected with MERS-CoV or a closely related virus. It may be that people became infected after contact with camels, although more information is needed to figure out the possible role that camels, bats, and other animals may play in the transmission of MERS-CoV 8. It is likely that camels serve as the source of infection

to human for MERS-CoV. Researchers investigated a case of human infection with Middle East respiratory syndrome coronavirus (MERS-CoV) after exposure to infected camels 9. Analysis of the whole human-derived virus and 15% of the camel-derived virus sequence yielded nucleotide polymorphism signatures suggestive of cross-species transmission. Camels may act as a direct source of human MERS-CoV infection.

The first-ever case of MERS infection was detected in Bangladesh 15th June, 2014. The Institute of the Epidemiology, Disease Control and Research (IEDCR) diagnosed a Bangladeshi expatriate living in the US with MERS corona virus after examining samples. The 53-year-old Bangladeshi returned home from New York via Abu Dhabi airport. He was admitted to the hospital with syndromes of fever, cough and respiratory problems. The National Rapid Response Team of the IEDCR kept those who came in close contact with the patient under observation, said a Directorate General of Health Services release (UNB).

The most urgent needs include detailed outbreak investigations, understanding how humans become infected from animal or environmental source(s) through case-control studies, identifying risk factors for infection in health care settings, and enhancing community studies and surveillance for community-acquired pneumonia 10.

VIROLOGY

MERS-CoV is a betacoronavirus, different from the other human betacoronaviruses (severe acute respiratory syndrome coronavirus, OC43, and HKU1) but closely related to several bat coronaviruses 11. Dipeptidyl peptidase 4 (DPP4), which is present on the surfaces of human nonciliated bronchial epithelial cells, is a functional receptor for MERS-CoV. Expression of human and bat DPP4 in nonsusceptible cells enables infection by MERS-CoV. The DPP4 protein displays high amino acid sequence conservation across different species, including the sequence that was obtained from bat cells. In a cell line susceptibility study, MERS-CoV infected several human cell lines, including lower respiratory, kidney, intestinal, and liver cells, as well as histiocytes.

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The range of tissue tropism *in vitro* was broader than that for any other known human coronavirus. MERS-CoV can also infect nonhuman primate, porcine, bat, civet, and rabbit cell lines¹².

Genetic analysis

In an analysis of the full or partial genomes of MERS-CoV obtained from 21 patients with MERS-CoV infection in Saudi Arabia between June 2012 and June 2013, there was sufficient heterogeneity to support multiple separate animal-to-human transfers¹³. Moreover, even within a hospital outbreak in Al-Hasa, Saudi Arabia, there was evidence of more than one virus introduction. By estimating the evolutionary rate of the virus, the authors concluded that MERS-CoV emerged around July 2011.

SEROLOGY

The Top of form Serologic studies have shown low prevalence of MERS-CoV antibodies in humans in Saudi Arabia. In 130 blood donors sampled during 2012 in Jeddah, Saudi Arabia, and 226 slaughterhouse workers sampled in October 2012 in Jeddah and Makkah, Saudi Arabia, eight reactive sera were observed using a screening immunofluorescence assay, but on further testing, the antibodies were found to be specific for other established human coronaviruses, not MERS-CoV¹⁴. Two further serologic studies were conducted in the Eastern Province of Saudi Arabia: one was of 158 pediatric sera obtained before the MERS-CoV outbreak was recognized, and the second was of 110 plasma samples from adult male blood donors in December 2012. No MERS-CoV antibody-positive samples were found¹⁵.

TRANSMISSION

Bats

Coronaviruses are recognised causes of mild respiratory tract infections in humans, first identified in the 1960s¹⁶. These large RNA viruses affect a wide range of animals including domestic and companion animals and bats¹⁷. Limited surveillance data show that bats host the greatest diversity of coronaviruses, varying by region and species¹⁸, suggesting that they may be the natural reservoir. Studies performed in Europe, Africa, and Asia, including the Middle East, have shown that coronavirus RNA sequences are found frequently in bat fecal samples and that some of these sequences are closely related to MERS-CoV sequences. In a study from Saudi Arabia, 823 fecal and rectal swab samples were collected from bats, and using a PCR assay, many coronavirus sequences were found¹⁹. Most were unrelated to MERS-CoV, but notably, one 190 nucleotide sequence in the RNA-dependent RNA polymerase (RdRp) gene was amplified that had 100 percent identity with a MERS-CoV isolate cloned from the index patient with MERS-CoV infection; the sequence was detected from a fecal pellet of a *Taphozous perforatus* bat captured from a site near the home of the patient. MERS-CoV grows readily in several bat-derived cell lines²⁰. Although

bats might be a reservoir of MERS-CoV, it is unlikely that they are the immediate source for most human cases because human contact with bats is uncommon. Camels

The strongest evidence of camel-to-human transmission of MERS-CoV comes from a study in Saudi Arabia in which MERS-CoV was isolated from a man with fatal infection and from one of his camels; full-genome sequencing demonstrated that the viruses isolated from the man and his camel were identical²¹. There are also substantial data add to recent findings showing high similarity of MERS-CoVs carried by humans and camels²², supporting the hypothesis that human MERS-CoV infection may be acquired directly from camels. Given the synchronized parturition pattern of dromedary camels, with birthing in the winter months, an increase of epizootic activity might be expected after some latency during the first half of each year²³.

Human-to-human transmission

The case clusters in the United Kingdom, Tunisia, Italy, and in healthcare facilities in Saudi Arabia and France strongly suggest that human-to-human transmission occurs²⁴. The number of contacts infected by individuals with confirmed infections, however, appears to be limited. Secondary cases have tended to be milder than primary cases, and many secondary cases have been reported to be asymptomatic. The majority of cases in the spring of 2014 in Saudi Arabia were acquired through human-to-human transmission in healthcare settings, likely due at least in part to systemic weaknesses in infection control. Possible modes of transmission may include droplet and contact transmission²⁵.

CLINICAL MANIFESTATIONS

In an outbreak of MERS-CoV in Saudi Arabia that resulted in laboratory-confirmed MERS-CoV in 23 individuals, the median incubation period was found as 5.2 days. In one secondary case that occurred in a patient in France who shared a room with an infected patient, the incubation period was estimated at 9 to 12 days²⁶. The WHO and the United States Centers for Disease Control and Prevention (CDC) recommend that an evaluation for MERS-CoV be considered in individuals with a syndrome of MERS who returned from travel to the Arabian peninsula or neighboring countries within the past 14 days²⁷. Most patients with MERS-CoV infection have been severely ill with pneumonia and acute respiratory distress syndrome, and some have had acute kidney injury. Other clinical manifestations that have been reported are gastrointestinal symptoms (anorexia, nausea, vomiting, abdominal pain, and diarrhea), pericarditis, and disseminated intravascular coagulation²⁸. As of late September 2013, 27 of 130 patients (21%) have had mild or no symptoms. A few reports have described individuals with a mild respiratory illness not requiring hospitalization²⁹. Several individuals with

asymptomatic infection have been identified among contacts of patients with symptomatic infection.

It remains unclear whether persons with specific conditions are disproportionately infected with MERS-CoV or have more severe disease. In a study of 47 patients with MERS-CoV infection in Saudi Arabia, 45 (96%) had underlying comorbidities, including diabetes mellitus (68%), hypertension (34%), chronic cardiac disease (28%), and chronic kidney disease (49%). One patient was receiving long-term immunosuppressive therapy with glucocorticoids 30.

DIAGNOSIS

The United States Centers for Disease Control and Prevention (CDC) recommends that lower respiratory tract specimens should be the first priority for collection and real-time reverse-transcriptase polymerase chain reaction (rRT-PCR) testing, since rRT-PCR testing of lower respiratory specimens appears to be more sensitive for detection of MERS-CoV than testing of upper respiratory tract specimens 31. Given the potential severity of MERS-CoV infections, the risk for human-to-human transmission, and the limited data about the sensitivity of each diagnostic test, researchers suggest that multiple specimens should be collected from different sites and at different times to increase the likelihood of detecting MERS-CoV 13. Several serological assays have been developed for the detection of MERS-CoV antibodies, including immunofluorescence and a protein microarray assay 32. The CDC has developed a two-stage approach, which uses an enzyme-linked immunosorbent assay (ELISA) for screening followed by an indirect immunofluorescence test or microneutralization test for confirmation. Any positive test by a single serological assay should be confirmed with a neutralization assay.

TREATMENT

As with other coronaviruses, no antiviral agents are recommended for the treatment of MERS-CoV infection. In cell culture and animal experiments, combination therapy with interferon (IFN)-alpha-2b and ribavirin appears promising 33. In a study in which MERS-CoV was grown in two different cell lines, high concentrations of interferon-alpha-2b or ribavirin were required to inhibit viral replication. However, when used in combination at lower concentrations, IFN-alpha-2b and ribavirin resulted in a comparable reduction in viral replication as high concentrations of either agent alone. Other experimental therapies being investigated include convalescent plasma, monoclonal antibodies, and inhibition of the main viral protease 34.

PREVENTION

Infection control

The World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC) have issued recommendations for the prevention and control of MERS-CoV infections in healthcare settings 35. The WHO recommends that standard and droplet precautions be used when caring for patients with acute respiratory tract infections. Contact precautions and eye protection should be added when caring for probable or confirmed cases of

MERS-CoV infection. Airborne precautions should be used when performing aerosol-generating procedures. The CDC recommends the use of standard, contact, and airborne precautions for the management of hospitalized patients with known or suspected MERS-CoV infection 36.

Avoiding camels

The individuals at high risk of severe disease, such as immunocompromised hosts and those with diabetes, chronic lung disease, or preexisting renal failure, take precautions when visiting farms, camel pens, or market environments where camels are present 37. These measures include avoiding contact with camels, practicing good hand hygiene, avoiding drinking raw camel milk, avoiding eating meat that has not been cooked thoroughly, and avoiding eating food that may be contaminated with animal secretions or products unless they are properly washed, peeled, or cooked. Unless protected, people should avoid contact with any animal that has been confirmed positive for MERS-CoV until subsequent tests have confirmed that the animal is free of the virus.

Travel recommendations

The WHO recommends that countries outside the affected region maintain a high level of vigilance, especially countries with large numbers of travelers or guest workers returning from the Middle East 38. In May 2014, the United States Centers for Disease Control and Prevention's (CDC's) travel notice was upgraded to a Level 2 Alert, which includes enhanced precautions for travelers to countries in or near the Arabian Peninsula who plan to work in healthcare settings. Such individuals should review the CDC's recommendations for infection control for confirmed or suspected MERS patients before they depart, practice these precautions while in the area, and monitor their health closely during and after their travel.

Vaccine

There is no licensed vaccine for MERS-CoV, although one manufacturer has developed an experimental candidate MERS-CoV vaccine based on the major surface spike protein using recombinant nanoparticle technology. Other candidate vaccines that are being studied include a full-length infectious cDNA clone of the MERS-CoV genome in a bacterial artificial chromosome and a recombinant Modified Vaccine Ankara (MVA) vaccine expressing full-length MERS-CoV spike protein 39.

CONCLUSION

MERS-CoV is closely related to coronaviruses found in bats, suggesting that bats might be a reservoir of MERS-CoV. Camels are likely serve as intermediate hosts for MERS-CoV. The presence of case clusters strongly suggests that human-to-human transmission occurs. There is currently no treatment recommended for coronavirus infections except for supportive care as needed. The emergence of a novel coronavirus with a global threat requires a thorough assessment which is currently being coordinated at international level.

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Leydig Cell Tumor of Ovary in a Pre-Menopausal Woman: A rare case of Virilization.

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Abstract

Background: Leydig cell tumor, a rare type of ovarian steroid cell tumor shows signs of virilization due to overproduction of testosterone. The condition is difficult to identify without histopathological examination. **Methods:** The authors report a case of Leydig cell tumor in a 34-year-old woman who first presented with severe clinical hyperandrogenism and associated complex medical history. **Results:** Investigations revealed markedly raised serum concentrations of total testosterone (680 ng/dL) (Normal reference values 02-45 ng/dL for adult woman), whereas prolactin, luteinizing hormone (LH) and follicle stimulating hormone (FSH), cortisol were all within the normal range. Transabdominal ultrasound and computed tomography (CT) scan of the pelvis and abdomen showed a bulky right ovary, but no other abnormalities. An ovarian source of androgens was suspected and surgery was arranged. The patient underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy. Histopathologically the case was diagnosed as Leydig cell tumor within the right ovary. After surgery, androgen levels returned to normal, and there was regression of the signs of virilization. **Conclusion:** Virilizing Leydig cell tumors usually have a benign behavior, with an excellent prognosis and reversion of symptoms after surgical treatment.

Keywords: Leydig cell tumor, virilization.

INTRODUCTION

Leydig cell tumors account for 0.1% of all ovarian tumors, and are a type of steroid cell tumor¹. These tumors are uncommon but distinctive ovarian tumors of sex cord or stromal origin that often produce steroid hormones. Though polycystic ovary syndrome (PCOS) and nonmalignant androgen excess disorders are common causes of hyperandrogenism, other aetiologies such as ovarian or adrenal tumors have to be excluded. Leydig cell tumors and hilus cell tumors are distinctive functioning ovarian tumors that produce testosterone leading to hyperandrogenism and virilization in women.¹

These typically occur in post menopausal women. The average age is 58 years and almost all patients are over 30 years of age. The usual presentation is with hirsutism or signs of virilization such as acne, hair loss, deepening of voice, a male body contour or hypertrophy of the clitoris. The serum testosterone concentration is elevated in virilized patients, but urinary 17-ketosteroids are generally within normal limits.² Non virilized patients have amenorrhoea or postmenopausal bleeding, depending on their age. Some Leydig cell tumors are found incidentally during surgery for some other condition. The endometrium may

show hyperplasia or even adenocarcinoma, most likely secondary to peripheral conversion of testosterone to estrogen. Symptoms are often present for several years before the diagnosis is made. This is because Leydig cell tumors are usually small and difficult to localize.² The diagnosis can be very difficult because the size of such tumors is often too small to be detected by imaging techniques.³ The diagnostic role and impact on management of ovarian and adrenal venous sampling in women presenting with symptoms and signs of hyperandrogenism has recently been debated.⁴

The authors hereby report an uncommon case of ovarian Leydig cell tumor in a pre-menopausal woman with severe hyperandrogenism and virilization with an attempt to delineate the clinical features and characteristics of this tumor with respect to histological findings.

CASE REPORT

A young woman aged 34 years reported to Rajshahi Medical College Hospital in Gynecology OPD on 20/04/2014 with worsening history of hyperandrogenism and virilization for last 6 months. She was then admitted to Gyne & obstetric department in ward -23, Rajshahi Medical College Hospital, for proper diagnosis and appropriate treatment. She presented with severe facial and body

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hirsutism, male-pattern baldness, receding hairline, and 4 years history of amenorrhoea. She was 2nd para, her last delivery was 6 years back. She had an intra-uterine device in situ as method of contraception. She reported rapid onset of virilization with hirsutism, androgenetic alopecia and deep voice starting one year back. Her medical history was complicated by ischaemic heart disease, hypertension, hypercholesterolaemia, osteoarthritis and anxiety disorder with prominent agoraphobia. She admitted to be a non-smoker and consumed no alcohol.

Physical examination revealed signs of virilization with hirsutism androgenetic alopecia, and deep voice. Her weight was 70 kg and height was 161cm and blood pressure was 130/90mmHg while on medications. Gynecological examination revealed an enlargement of the clitoris and no palpable adnexal masses. She had no features of Cushing syndrome. Initial biochemistry included baseline hormone profile, amenorrhoea work-up including prolactin, estradiol, luteinizing hormone (LH) and follicle stimulating hormone (FSH), total serum testosterone, cortisol, thyroid function tests and liver function tests. Endocrine evaluation revealed hyperandrogenism, with markedly increased total serum testosterone (680 ng/dL) (Normal reference values 02-45 ng/dL for adult woman⁵). Serum levels of luteinizing hormone (LH) and follicle stimulating hormone (FSH) were inappropriately low for a pre-menopausal woman with high levels of estradiol.

Liver function test showed raised cholesterol (9.6mmol/l) and triglyceride (6.1mmol/l), and normal HDL (0.87 mmol/l). Transabdominal ultrasound scan of the pelvis and abdomen showed normal findings, although the right ovary (6.5 x 5.8 x 5.8 cm) was reported as being larger compared with the left ovary (3.2 x 2.9 x 2.8 cm). These findings were confirmed by computed tomography (CT) scan. An ovarian source of clinical and biochemical hyperandrogenism was suspected. The patient was therefore advised to undergo surgery in the form of total abdominal hysterectomy & bilateral salpingo-oophorectomy, and all the specimens were sent to department of pathology, Rajshahi Medical College Hospital for histopathological diagnosis.

(Figure 1). Other parts of the specimen showed no gross abnormality. Histopathological examination in right ovary revealed tumor cells arranged in lobules separated by fibrous septa (Figure-2). The tumor cells were round to polygonal with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli (Figure-3). These findings confirmed the diagnosis of Leydig cell tumor.

The pre-operative elevated androgen levels normalized following surgery. Post-operatively, the clinical signs of hyperandrogenism improved significantly. At 6-month follow-up, the patient remains fit and well, with significantly improved signs of virilization and completely resolved anxiety.

DISCUSSION

Most androgen secreting ovarian tumors are sex cord stromal tumors, which constitute less than 5% of all ovarian neoplasms.⁵ According to the World Health Organization (WHO) histologic classification of ovarian tumors, sex cord stromal tumors can be classified as granulosa stromal cell tumors, Sertoli stromal cell tumors, mixed sex cord stromal tumors and steroid cell tumors.⁶ Steroid cell tumors were also designated as "lipid cell tumors" but this term is not recommended because upto 25% of tumors in this category contain little or no lipid. The term "steroid cell tumor" has been accepted by the WHO because it reflects both the morphological features of the neoplastic cells and their propensity to secrete steroid hormones. Leydig cell tumors are rare ovarian steroid cell neoplasms composed entirely or predominantly of Leydig cells.⁶



Figure 1: A well circumscribed nodular mass with grey yellow glistening surface.

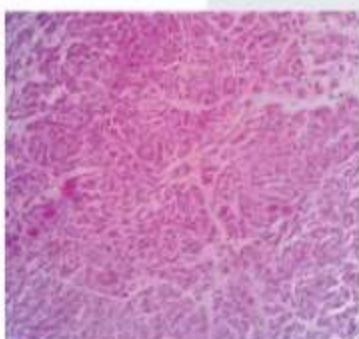


Figure 2: Photomicrograph showing tumor cells arranged in lobules separated by fibrous septa (Haematoxylin and eosin, x 40).

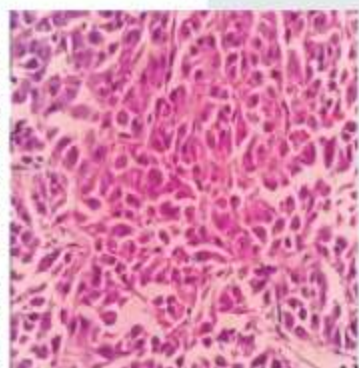


Figure 3: Photomicrograph showing round to polygonal tumor cells with abundant eosinophilic cytoplasm and round nuclei (Haematoxylin and eosin, x 400).

In the hilar zone, the Leydig cells can be normally found in 80% to 85% of the postpubertal ovaries, usually in association with non-myelinated nerve fibres. Hilar Leydig cell tumours arise from these preexisting Leydig cells of the hilus and can extend into the ovarian stroma depending on the size of the tumor. These tumors are generally benign and are usually unilateral.⁷ The stromal-Leydig cell tumors take their origin in the cortex or subcortical region in the ovary from ovarian stromal cells, which have differentiated into Leydig cells. They are very rare benign tumors. Like hilus tumors they also occur in postmenopausal patients and are unilateral.⁷

Though Leydig cell tumors typically occur in post menopausal women in this case the woman was aged 34 years of young lady- a rare case scenario. However unilateral location for this tumor is supported by our case report. These tumors secrete testosterone and occasionally oestrogenic activity may be observed. The androgenic manifestations are milder than those associated with Sertoli-Leydig cell androblastomas and their onset is less abrupt. Oestrogenic manifestations, such as irregular menses or postmenopausal bleeding have also been reported.⁸

The differential diagnosis of the Leydig cell tumors includes ovarian neoplasms containing Leydig cells or luteinized stromal cells. Sertoli-Leydig cell androblastoma occasionally exhibits predominance of Leydig cell component. But presence of Sertoli cells excludes the diagnosis of pure Leydig cell neoplasm. Stromal luteoma is a distinct type of steroid tumors arising in the ovarian stroma which resembles Leydig cell neoplasms.

Androgen producing tumors should be suspected in women with virilizing clinical symptoms and high testosterone levels. Sertoli-Leydig cell tumors are larger and usually found easily on imaging, whereas hilar Leydig cell tumours are smaller and often difficult to find on imaging. If clinical suspicion is high exploratory laparotomy is indicated. It is noteworthy that in this era where sophisticated and expensive histopathological methods including immunohistochemistry are available, this rare and benign tumor can be diagnosed with high accuracy on good quality haematoxylin and eosin stained slides.

Conclusion

This case-report confirms that androgen-secreting ovarian tumors have to be considered amongst other disorders causing virilization in peri-menopausal and reproductive age women. Appropriate diagnostic approach encompassing clinical presentation, conventional biochemical, imaging methods & finally histopathological diagnosis is paramount.

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Competing interests

The authors declare that they have no competing interests.

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M. Manzurul Haque
Editor in chief

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