The Journal of BIRDEM is a peer reviewed Journal. It is published twice (January and July) in a year. It accepts original article, review articles and case reports. Complimentary copies of the journal are sent to libraries of all medical and other relevant academic institutions in the country and selected institutions abroad.

While every effort is always made by the Editorial Board and the members of the Journal Committee to avoid inaccurate or misleading information appearing in the Journal of BIRDEM, information within the individual article are the responsibility of its author(s). The Journal of BIRDEM, its Editorial Board and Journal Committee accept no liability whatsoever for the consequences of any such inaccurate and misleading information, opinion or statement.
INFORMATION FOR AUTHORS

BIRDEM MEDICAL JOURNAL agrees to accept manuscript prepared in accordance with the ‘Uniform Requirements Submitted to the Biomedical Journals’ Published in the New England Journal of Medicine 1991;324: 424-8.

Aims and scope:
BIRDEM is going to publish 6 monthly journal based on clinical and laboratory based research in Bangladesh. It will try to feature the best clinical and laboratory based research on various disciplines of medical science for medical scientists to share experiences which will help others to render better patient care. Conditions for submission of manuscript:

- All manuscripts are subject to peer-review.
- Manuscripts are received with the understanding that they are not under simultaneous consideration by any other publication.
- Submission of a manuscript for publication implies the transfer of the copyright from the author to the publisher upon acceptance. Accepted manuscripts become the permanent property of reproduced by any means in whole or in part without the written consent of the publisher.
- It is the author’s responsibility to obtain permission to reproduce illustrations, tables etc. from other publication.

Ethical aspects:

- Any manuscript that includes table, illustration or photograph that have been published earlier should accompany a letter of permission for re-publication from the author(s) of the publication and editor/publisher of the Journal where it was published earlier.
- Permission of the patients and/or their families to reproduce photographs of the patients where identity is not disguised should be sent with the manuscript.

Preparation of manuscript:
Criteria:

- a) Manuscript should be written in English and type on one side of A4 size white paper.
- b) Double spacing should be used throughout.
- c) Margin should be 5 cm for the header and 2.5 cm for the remainder.
- d) Style should be that of modified Vancouver.
- e) Each of the following section should begin on separate page:
  - Title page
  - Summary/abstract
  - Text
  - Acknowledgement
  - References
  - Tables and legends
- f) Pages should be numbered consecutively at the lower right hand cover of each page beginning with the title page

Tile Page:
The title page should contain:

- Title of the article (should be concise, informative and self-explanatory)
- Name of each author with highest academic degree
- Name of the department and institute where the work was carried out
- Name and address of the author to whom correspondence regarding manuscript to be made.
- Name and address of the author to whom request for reprint should be addressed

The summary/abstract of the manuscript:

- Should be informative
- Should be limited to less than 200 words
- Should be suitable for use by abstracting journals and include data on the problem, materials and method, results and conclusion
- Should emphasize mainly on new and important aspects of the study
- Should contain only approved abbreviations

Introduction:
Should include:

- Nature and purpose of the study
- Rationale of the study/observation
- Strictly pertinent references
- Brief review of the subject except excepting data and conclusion

Materials and method:
Should be very clear and describe:

- The selection criteria of the study population including controls (if, any)
- The methods and the apparatus used in the research.
- The procedure of the study in such a detail so that other worker can reproduce the results.
- Previously published methods (if applicable) with appropriate citations.

Result:
Should be:

- Presented in Logical sequence in the text, tables and illustrations.
- Described without comment
- Supplemented by concise textual description of the data presented in table and figures where it is necessary

Table:
Following principles should be followed:

- Tables should be simple, self-explanatory and supplement, not duplicate the text
- Each table should have a title and typed in double space in separate sheet.
They should be numbered consecutively with roman numerical in order of text. Page number should be in the lower right corner.

If abbreviations are to be used, they should be explained in footnotes.

Illustrations:

- All illustrations must be numbered and cited in the text.
- Print photograph of each illustration should be submitted.
- Figure number, title of manuscript, name of corresponding author and arrow indicating the top should be typed on a sticky label and affixed on the back of each illustration.
- Original drawings, graphs, charts and letters should be prepared on an illustration board or high grade white drawing paper by an experienced medical illustrator.

Figures and photographs:

- Should be use only where data cannot be expressed in any other form.
- Should be on mounted glossy print in sharp focus, 12.7 x 17.3 cms in size.
- Should bear number, title of manuscript, name of corresponding author and arrow indicating the top on a sticky table and affixed on the back of each illustration.

Legend:

- Must be typed in a separate sheet of paper.
- Photomicrographs should indicate the magnification, internal scale and the method of staining.

Units:

- All scientific units should be expressed in System International (SI) units.
- All drugs should be mentioned in their generic form. The commercial name may however be used within brackets.

Discussion:

The discussion section should reflect:

- The authors’ comment on the results and to relate them to those of other authors.
- The relevance to experimental research or clinical practice.
- Well-founded arguments

References:

This section of the manuscript

- Should be numbered consecutively in the order in which they are mentioned in the text.
- Should be identified in the text by superscript in Arabic numerical.
- Should use the form of references adopted by US National Library of Medicine and used in Index Medicine and used in Index medicins.

Acknowledgements:

Individuals, organizations or bodies may be acknowledged in the article and may include:

- Name (or a list) of funding bodies.
- Name of the organization(s) and individual(s) with their consent.

Manuscript submission:

Manuscript should be submitted to the Executive Editor and must be accompanied by a covering letter and following inclusions:

a) A statement that the manuscript has been read, approved and signed by all author.

b) If the article is a whole or part of the dissertation or thesis submitted for diploma/degree, it should be mentioned in detail. In this case the name of the investigator and guide must be specifically mentioned.

Submissions must be in triplicates with four sets of illustrations. Text must be additionally submitted in a CD.

Editing and peer review:

All submitted manuscripts are subject to scrutiny by the Editor-in-chief or any member of the Editorial Board. Manuscripts containing materials without sufficient scientific value and of a priority issue, or not fulfilling the requirement for publication may be rejected or it may be sent back to the author(s) for resubmission with necessary modifications to suit one of the submissions with necessary modifications to suit one of the submission categories. Manuscripts fulfilling the requirements and found suitable for consideration are sent for peer review. Articles found suitable for publication by the reviewer, may need revision/modifications before being finally accepted. Editorial Board finally decides upon the publishability of the reviewed and revision/modifications submission. Proof of accepted manuscript may be sent to the author, and should be corrected and sent to the editorial office within one week. All accepted manuscripts are edited according to the journal’s style.

Reprints for the author(s):

Copies of each published article will be provided to the corresponding author free of cost. Additional reprints may be obtained by prior request.

Communication for manuscript submission:

Communication information for all correspondence is always printed in the title page of the journal. Any additional information or any other inquiry relating to submission of the article the Executive Editor or the Journal office may be contacted.

Copyright:

No part of the materials published in this journal may be reproduced, stored in a retrieval system or transmitted in any form or by any means electronic, mechanical, photocopying, recording or otherwise without the prior written permission of the publisher.

Reprints of any article in the Journal will be available from the publisher.

Subscription:

Annual subscription
Local BDT 200/-
Overseas $ 20/-

Should be sent to: Executive Editor: BIRDEM Medical Journal
BIRDEM, Room No. 1116
122, Kazi Nazrul Islam Avenue, Tel: 9661551-60
E-mail: nahar@dab-bd.org, web: birdem.med.j.org
# BIRDEM MEDICAL JOURNAL

**Vol. 1, No. 1, Page 1-58**  
**July 2011**

## CONTENTS

### EDITORIAL

- BIRDEM: Inception and evolution.  
- Dengue: A Seasonal fever (Moushumi jar)  

### ORIGINAL ARTICLES

- Clinical and Biochemical Assessment of Hypogonadism in Type 2 Diabetic Men  
  Talukder SK, Afsana F, Latif ZA, Pathan F, Ashrafuzzaman SM, Khan SJ, Habib SH, Saha S  
- The Incidence, Predisposing Factors, Complications and Outcome of Preeclampsia in Diabetic Pregnancy  
  Jesmin S, Jahan S, Khan MI, Sultana N, Jerin J, Habib SH, Paul D  
- Clinical Spectrum and Management of Diabetic Ketoacidosis: Experience in A Tertiary Care Hospital  
- Prevalence of Metabolic Syndrome among Obese Children and Adolescents  

### REVIEW ARTICLES

- Overview on Obesity - A Review  
  Ashrafuzzaman SM  
- Extensively Drug-Resistant (XDR) Tuberculosis: A Review  
  Ahmed JU, Musa AKM, Hossain D, Rahim MA, Shaheen AKM, Uddin KN  

### CASE REPORTS

- A Case Report On Peripartum Cardiomyopathy  
  Safider AMB, Mir SA, Miah BM, Tamanna RJ, Mohibullah AKM  
- Kawasaki Disease - A Rare Presentation in a Bangladeshi Infant- A Case Report  
- Surgical Management of Calcific Metamorphosis of Pulp:  A Case Report  
  Kulsum U, Farzana F  
- Granulomatous Hepatitis: A Rare Case Report  
  Amin AA, Mondal SK, Ullah ME  

### IMAGES IN MEDICAL PRACTICE

### LETTERS TO THE EDITOR

### BIRDEM NEWS

### FROM THE DESK OF THE EXECUTIVE EDITOR

### NAME OF THE REVIEWERS OF ARTICLES IN THIS ISSUE
EDITORIAL

BIRDEM: Inception & Evolution

Diabetic association of Bangladesh (DAB) is the symbol of a success story of the devoted visionary- late national professor Dr. Md Ibrahim, starting in 1956. BIRDEM (Bangladesh Institute of Research & Rehabilitation in Diabetes, Endocrine and Metabolic disorders). Though an icon, it is one of the seven enterprises of - DAB, now BADAS-(Bangladesh Diabetic Samity).

It was started in a semi permanent space of 35.5 sq meters at Segun Bagicha, Dhaka with one man and two to three associates. From the day of inception it has three themes - to serve diabetic and related patients, a good laboratory service and authentic research, which are still continuing.

In 1957 DAB had 39 registered patients. Now BIRDEM has around 500000 registered patients (Diabetics-4,34,753, IGT- 37,860, GDM-641). The hospital first started with only 18 beds in 1957. Now BIRDEM general hospital has become a multidisciplinary tertiary care hospital with 600 bed including 110 free beds where treatment is provided 100% free of cost, to keep the motto of Prof. Ibrahim that “no diabetic should die unfed, unemployed, untreated even if he is poor”. It is the best referral centre of the country for care of patients with diabetes mellitus, it’s complications and co morbidities.

In 1980 BIRDEM was shifted from Segun Bagicha to the present Shahbagh complex. Initially the OPD started in 3 storied building and the hospital moved to this site in 1984. Subsequently through successive revised plans and extension it came to the present state of 16 storied complex through generous support of different government. In 1982 it was recognized as WHO collaboration centre for developing community oriented services, education, training and research for prevention and control of diabetes mellitus.

Starting in 1987, BIRDEM Academy has produced so many (Ph.D, MS, MD, M.Phil) experts who are serving both nationally and internationally. It has been running 18 regular postgraduate courses, certificate courses for graduate diabetes practitioners (DLP), Emergency health care (BLS, ACLS). It also run diabetic educator course and nursing update course.

The hospital is equipped with modern facilities for haemodialysis and organ transplants. So far 89 successful living related donor kidney transplants and two successful liver transplants have been done at BIRDEM.

It also has a state of the art ICU service, a Special care baby unit (SCABU) and Physiotherapy centres. It has 24 hr emergency service for all disciplines of medical sciences with available laboratory services.

BIRDEM has the largest OPD facilities for diabetics in the world, handling 3000 patients everyday on average. It also has OPD treatment follow up fascilities for both diabetics and non diabetics patients in supraspecialities of Pediatrics, surgery, Gynae and Obstetrics and Medicine. It has specialized infertility centre, foot care centre and day care centre for Gastroenterology, haemato-oncology. It also runs Obesity clinic, PCOS clinic, Rheumatology clinic and liver clinic. Recently it has expanded it’s facility by opening BIRDEM-2 at Segun Bagicha with help of the Ministry for Women and Children Affairs, exclusively for women and children.

To encourage learning, BIRDEM library is open for 14 hours everyday and has a wide array of books, magazines, journals, periodicals and internet browsing and printing facilities.

Other facilities like the auditorium, canteen, mosque all are within the premises.

BIRDEM is run by formidable service rule. Each employee has his own ID number and health card, all of them enjoying free health facilities. There are a number of associations like Officers Welfare Association, Employee’s Welfare association, Teacher’s association, Young diabetic welfare association, Non-diabetic patient welfare association. All are recognized bodies of ministry of social welfare.
BIRDEM, the pioneer of non-government health care facilities of the country, the unspoken monument to the great son of the soil Prof. Dr. Md. Ibrahim is serving the nation for nearly seven decades keeping it’s motto “I am obliged for giving me the opportunity to serve you” to the suffering humans.

Dengue: A seasonal fever (Moushumi jar)
The first outbreak of dengue fever (Dhaka fever) was documented in 1964 in Dhaka. The first outbreak of dengue hemorrhagic fever (DHF) occurred in mid 2000. Aedes egypti mosquito was identified as the main vector responsible and in Chittagong aedes albopictus was also identified as potential vector. The maximum transmission period is from July to September. The number of mosquito increases after rainfall, because they breed in containers that hold clean water for more than five days. Higher temperature shortens the incubation time for the virus and humid weather increases the biting activity of mosquito.

A National guideline for clinical management of dengue has been developed, based on the established WHO guidelines and distributed among medical officers of the country.

Countries that reported less than 1% of the total case are Bhutan, Nepal and Timore Leste. Maldives and Bangladesh reported about 1% of the cases. India, Myanmar and Sri Lanka reported 6% each. Thailand 23% and Indonesia 57% cases in South east Asia region (SEARO) of WHO.

Ensuring adequate fluid intake is the mainstay of treatment. Whole thing is so far directed to prevention and personal protection from mosquito is important. Killing of mosquito and its larva is utmost necessity.

Development of birth control pill for female mosquito is an approach on the way. Malaysia is considering releasing genetically modified mosquitoes designed to combat aedes mosquito. Australian scientist are trying to modify mosquitoes by introducing bacteria in them so that female Aedis could not harbour dengue virus.

Dengue vaccine is on the way. In Thailand it has so far been tried on mice and monkeys. It will come into market in 2015. Antiviral drug using protease inhibitors are being thought by researcher.
Clinical and Biochemical Assessment of Hypogonadism in Type 2 Diabetic Men

TALUKDER SK\textsuperscript{a}, AFSANA F\textsuperscript{b}, LATIF ZA\textsuperscript{b}, PATHAN F\textsuperscript{b}, ASHRAFUZZAMAN SM\textsuperscript{b}, KHAN SJ\textsuperscript{c}, HABIB SH\textsuperscript{d}, SAHA S\textsuperscript{d}

Abstract

Aim: The aim of the study was to assess the prevalence of clinical hypogonadism in type 2 diabetic men based on clinical features and available biochemical measures. Materials and Methods: In this study carried out in a tertiary level hospital, serum concentration of total testosterone was measured in 170 type 2 diabetic (mean age 44.9±7.9 years) subjects who have erectile dysfunction or other features of hypogonadism. Results: The mean total testosterone concentration in type 2 diabetic men was 14.4±5.6 nmol/l. Fifty nine of 170 (34.7%) type 2 diabetic subjects had low serum testosterone levels (d"12 nmol/L). Luteinizing hormone (LH) and follicle stimulating hormone (FSH) concentrations in type 2 diabetic men were inappropriately low with a very high prevalence of hypogonadotropic hypogonadism. BMI and waist circumference were both negatively correlated with testosterone levels, with the association being stronger for waist circumference. HbA\textsubscript{1C} level also reveal a negative association with sexual dysfunction and hypogonadotropic hypogonadism among type 2 diabetic men. Metabolic syndrome is also associated with the low serum testosterone levels in the study subjects. Conclusions: This study reveals that serum total testosterone levels are lower in diabetic men with signs/symptoms of hypogonadism. Hypogonadotropic hypogonadism is frequent in diabetic hypogondal population. There is an association between poor glycaemic control and hypogonadism in male diabetic persons.

Key Words: Hypogonadism; Metabolic syndrome; Diabetes Mellitus.

Introduction

Type 2 diabetes is the predominant form of diabetes worldwide, accounting for 90% of cases globally.\textsuperscript{1,2} Asian Indians have surprisingly higher prevalence of type 2 diabetes compared to Caucasians. Excessive insulin resistance in Asian Indians compared to Caucasians may be one of the contributing factors. This difference in the degree of insulin resistance may be explained by either an environmental or a genetic factor or by combination of both.\textsuperscript{3-10} Diabetes mellitus is a medical condition which is often associated with male sexual dysfunction. Erectile dysfunction (ED) is estimated to occur in 28-75% of diabetic males and its prevalence appears to increase with age & duration of diabetes.\textsuperscript{11-14} The etiology of ED in type 2 diabetes is often multifactorial and include poor metabolic control, diabetes-induced micro-and macrovascular alterations, autonomic neuropathy, hypogonadism, or a combination of all these factors.\textsuperscript{15-17} Type 2 diabetes, which is not an autoimmune disorder is also associated with other endocrine diseases, in particular hypogonadism in men. Androgen deficiency has recently come to the forefront of the medical literature after being ignored for decades. Important associations are being developed and confirmed in the literature between androgen deficiency and metabolic disorders. More specifically, there is an important health impact related to metabolic syndrome (MetS), insulin resistance (IR), type 2 diabetes and ultimately vascular disease and erectile dysfunction (ED). Low concentrations of testosterone are linked with IR and implicated in hyperglycaemia, hypertension, dyslipidaemia, and an increased risk of vascular disease.\textsuperscript{18-23} Insulin resistance is an important feature of type 2 diabetes. It is being increasingly recognized that low...
testosterone levels in men are associated with reduced insulin sensitivity and type 2 diabetes. Serum testosterone levels are lower in a large number of Japanese patients with type 2 diabetes when compared with healthy men and suggested that testosterone supplementation in hypogonadal men could decrease IR and atherosclerosis. These observations suggest that androgen deficiency plays a central role in the various pathologies encompassing the components of MetS including type 2 diabetes, IR, obesity and ED.

Various guidelines for the diagnosis of hypogonadism are available. Joint guidelines for the diagnosis and treatment of men with late onset hypogonadism—testosterone deficiency associated with aging have been produced by the International Society for the Study of the Aging male (ISSAM) and the European Association for Urology (EAU). They recommend that, a total testosterone < 8 nmol/L in the presence of symptoms requires substitution and >12 nmol/L does not. In symptomatic men with a total testosterone between 8 and 12 nmol/L trials of therapy can be considered. Both the American Association of clinical Endocrinology and the Endocrine Society recommend that the diagnosis of hypogonadism should based on low serum testosterone levels and signs / symptoms.

Signs and symptoms of low testosterone levels in adults, are decreased energy level, reduced or loss of libido, diminished spontaneous erectile function, depression, poor concentration and memory, hot flushes or sweats, and infertility. The clinical signs of hypogonadism are usually only manifest in the more overt cases and include fine wrinkling of facial skin, eunuchoid body habitus, loss of secondary sexual hair, decreased lean body mass, increased body fat, decrease testicular volume, gynaecomastia and osteoporosis.

Current evidence shows that there is a significant proportion of men with type 2 diabetes who have hypogonadism. Although, androgen status in diabetic men is not routinely considered by the majority of medical practitioners, symptomatic patients should be considered to measure serum testosterone levels. The present study was designed to assess hypogonadism in type 2 diabetic men, referred to Endocrine Department, BIRDEM. The general objective of the study was to identify the clinical hypogonadism, based on signs / symptoms and biochemical measures available, in type 2 diabetic Bangladeshi men. The specific objectives of the study were to find out the type of hypogonadism in type 2 diabetic subjects and to find association between low testosterone level and glycaemic status in type 2 diabetic subjects.

Materials and Methods

The study was conducted in the Dept. of Endocrinology, Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh during the period of may 2008- April 2009. It was a cross sectional study.

Inclusion Criteria

• Men with type 2 diabetes
• Age 20-55 years
• Presence of signs /symptoms that are suggestive of hypogonadism

Exclusion Criteria:

• Patients already receiving hormone replacement therapy
• Endocrine disorders other than DM
• Patients receiving any medications that may alter gonadal function
• Surgical interventions likely to impair sexual function
• Patients with liver, renal and severe heart failure
• Acute infections

Study Subjects:

Study subjects were selected purposively about 450 patients was interviewed at outdoor and indoor department of Endocrinology, BIRDEM. After taking brief history, preliminary selection was done on the basis of signs/ symptoms of hypogonadism and exclusion of other systemic illnesses. 350 patients were enlisted their name after primary selection. History taken and clinical examination performed with a pre-structured questionnaire. Next morning following an overnight (10-12 hours) fast blood sample was collected. One hundred and seventy subjects were attended and investigated properly. A diagnosis of hypogonadism was made if anybody had symptoms/ signs of hypogonadism and total testosterone < 12 nmol/L. In a patient with low testosterone level LH, FSH, Prolactin and SHBG were measured for further assessment.
Anthropometric measurements and other physical examinations:
Standing height and weight was measured using appropriate scales. Body mass index (BMI) of the subjects were calculated using the formula: BMI = Weight (kg)/(Height in meter)². Waist circumference was measured to the nearest 0.5 cm with a soft nonelastic measuring tape. The tape was snug, but not so tight as to cause skin indentation or pinching. Horizontal arm span (between the out spread middle fingertips with the patient standing against a flat backboard) was measured to the nearest 0.5 cm. Lower segment was measured from the top of the symphysis pubis vertically to the floor with the subject standing straight. Then the upper segment was determined by subtracting the lower segment from the standing height measurement noted above. Breast staging was done according to Marshal and Tanner stages of breast development. After proper exposure of the subjects, pattern of pubic hair was seen and the stage of pubic hair was determined by marshal and Tanner staging. Testicular volume was estimated with the Prader Orchidometer. The fully stretched dorsal penile length was measured in the flaccid state from the pubopenile skin junction to the tip of the glans. Subjects were requested to fast at least 10 hours and fasting venous blood sample (10 ml) was collected between 8.00-9.00 A.M.

Statistical analysis:
Statistical analysis was performed using SPSS software for Windows Version 11.5. All data were expressed as mean with 95% confidence interval and percentage (%) as appropriate.

Results and Observations
A total of 170 diabetic subjects were studied.
Clinical and biochemical characteristics of study subjects.
Age (years) mean±SD was 44.9±7.9. Weight (kg) mean ±SD was 66.8±9.7. BMI (kg/m²) mean ±SD was 24.6±2.9. Mean±SD of waist circumference (cm) was 91.6±7.6 Mean±SD of systolic blood pressure (mmHg) and diastolic blood pressure (mmHg) were 120.9±13.6 and 79.4±7.7. Right and left testicular volume (ml) mean ±SD were 19.5±4.4 and 20.0±4.2. Fasting blood glucose (mmol/l), mean±SD was 7.7±2.3 Mean ±SD cholesterol (mg/dl), TG (mg/dl), LDL (mg/dl) were 185.3±34.9, 193.2±80.8, 114.0±32.6. Mean ±SD of HDL (mg/dl) was 32.6±5.4.
Serum total testosterone (nmol/L) mean±SD was 14.4±5.6. Mean±SD of serum SHBG (nmol/L), LH (mIU/l), FSH (mIU/ml), prolaction (mIU/ml) were 36.0±16.5, 6.8±5.3, 8.0±6.9, 193.0±87.9
Maximum numbers (39.4%) of the subjects were found in the age group of 40–49 years One hundred and thirty one (77.0%) subjects had history of regular exercise (at least 3 days a week). Alcohol consumption was very limited. History of diminished nocturnal erection was found in 166 (97.6%) subjects. Decreased libido was found in 65(38.2%).Fourteen (8.2%) subjects gave history of sub-fertility.

<p>| Table I |
| Background characteristics of study subjects |</p>
<table>
<thead>
<tr>
<th>n</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>5</td>
</tr>
<tr>
<td>30-39</td>
<td>38</td>
</tr>
<tr>
<td>40-49</td>
<td>67</td>
</tr>
<tr>
<td>≥ 50</td>
<td>60</td>
</tr>
<tr>
<td>Exercise</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>131</td>
</tr>
<tr>
<td>No</td>
<td>39</td>
</tr>
<tr>
<td>Smoking</td>
<td></td>
</tr>
<tr>
<td>Smoker</td>
<td>79</td>
</tr>
<tr>
<td>Non smoker</td>
<td>91</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>10</td>
</tr>
<tr>
<td>No</td>
<td>160</td>
</tr>
<tr>
<td>Diminished nocturnal erection</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>166</td>
</tr>
<tr>
<td>No</td>
<td>4</td>
</tr>
<tr>
<td>Libido</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>105</td>
</tr>
<tr>
<td>Decreased</td>
<td>65</td>
</tr>
<tr>
<td>Sub fertility</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>14</td>
</tr>
<tr>
<td>No</td>
<td>156</td>
</tr>
<tr>
<td>Testosterone</td>
<td></td>
</tr>
<tr>
<td>&lt; 8 nmol/l</td>
<td>29</td>
</tr>
<tr>
<td>8 –12 nmol/l</td>
<td>30</td>
</tr>
<tr>
<td>&gt;12 nmol/l</td>
<td>111</td>
</tr>
</tbody>
</table>
Frequency of hypogonadism according to low serum total testosterone (≤12 nmol/L)

Subjects were divided into hypogonadal (serum total testosterone ≤12 nmol/L) and eugonadal (serum total testosterone >12 nmol/L) according to serum total testosterone level. Out of which 59 (34.7%) had hypogonadism. Hypogonadism was classified according to LH concentration (<50% of normal range was classified as lower level). In this way hypogonadotropic hypogonadism was found in 34 (57.6%). Normogonadotropic hypogonadism and hypergonadotropic hypogonadism was found 17 (28.8%) and 8 (13.6%) respectively. In this observation hypogonadotropic hypogonadism was found more in study subjects.

Comparison of clinical and biochemical characteristic of study subjects with normal or low total testosterone.

Age (years) as mean±SD of hypogonadal (low total testosterone) and eugonadal (normal total testosterone) study subjects were 43.9±7.4 and 45.5±8.1 respectively and did not different significantly (p=0.223). Duration of diabetes (years) in hypogonadal and eugonadal subjects were 5.2±4.4 and 6.1±5.1 respectively, not significantly (p=0.227) different. BMI (kg/m²), waist circumference (cm) were 24.8±2.9, 93.1±6.9 in hypogonadal subjects and 24.5±2.8, 90.7±7.9 in eugonadal subjects respectively. Right sided testicular volume (ml) was significantly (p=0.023) different in two groups; 19.0±4.7 vs 20.6±3.8 in hypogonadal vs eugonadal subjects respectively. Left sided testicular volume (ml) was 18.1±5.1 and 20.3±3.8 respectively, there was also significant (p=0.002) difference in two groups. In hypogonadal subjects HbA₁C level was found significantly (p=0.001) higher than the eugonadal subjects [8.9±1.6 and 7.8±1.3 respectively]. Among the four components of lipid profile, serum TG (mg/dl) was significantly (p=0.031) different in two groups. [211.1±81.5 vs 183.5±79.0 in hypogonadal vs eugonadal subjects]. Mean±SD of cholesterol, LDL, HDL were 192.4±36.8, 117.8±31.9, 32.1±5.4 in hypogonadal subjects and 181.6±33.5, 112.0±29.8, 32.8±5.4 in eugonadal subjects respectively. Serum total testosterone (nmol/l) as mean ±SD in hypogonadal subjects was 9.5±1.8, whereas in eugonadal subjects was 18.6±4.1. Serum SHBG (nmol/l), and prolactin (mIU/ml) level were not significantly different between the hypogonadal and eugonadal subjects. Serum LH and FSH (mIU/ml) was significantly (p=0.001, p=0.020) lower in hypogonadal subjects than the eugonadal subjects.

In this study, there was significant difference in testicular volume, HbA₁C level, serum TG, total testosterone, and LH , FSH level between the hypogoadal and eugonadal subjects.

Table II

Comparison of clinical and biochemical characteristic of subjects with normal (eugonadal) or low (hypogonadal) total testosterone.

<table>
<thead>
<tr>
<th></th>
<th>Hypogonadal (≤12 nmol/l)</th>
<th>Eugonadal (&gt;12 nmol/l)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=59)</td>
<td>Mean ±SD</td>
<td>Mean ±SD</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>43.9 ±7.4</td>
<td>45.5 ±8.1</td>
<td>0.223 NS</td>
</tr>
<tr>
<td>Duration of diabetes</td>
<td>5.2 ±4.4</td>
<td>6.1 ±5.1</td>
<td>0.227 NS</td>
</tr>
<tr>
<td>(years)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>24.8 ±2.9</td>
<td>24.5 ±2.8</td>
<td>0.491 NS</td>
</tr>
<tr>
<td>Waist circumference</td>
<td>93.1 ±6.9</td>
<td>90.7 ±7.9</td>
<td>0.055 NS</td>
</tr>
<tr>
<td>(cm)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Testicular vol Rt(ml)</td>
<td>19.0 ±4.7</td>
<td>20.6 ±3.8</td>
<td>0.023 S</td>
</tr>
<tr>
<td>Testicular vol LT(ml)</td>
<td>18.1 ±5.1</td>
<td>20.3 ±3.8</td>
<td>0.002 S</td>
</tr>
<tr>
<td>HbA₁C (%)</td>
<td>8.9 ±1.6</td>
<td>7.8 ±1.3</td>
<td>0.001 S</td>
</tr>
<tr>
<td>Cholesterol (mmol/l)</td>
<td>4.98 ±0.95</td>
<td>4.70 ±0.86</td>
<td>0.054 NS</td>
</tr>
<tr>
<td>TG(mmol/l)</td>
<td>2.38 ±0.92</td>
<td>2.07 ±0.90</td>
<td>0.031 S</td>
</tr>
<tr>
<td>LDL(mmol/l)</td>
<td>3.05 ±0.83</td>
<td>2.90 ±0.77</td>
<td>0.241 NS</td>
</tr>
<tr>
<td>HDL(mmol/l)</td>
<td>0.83 ±0.13</td>
<td>0.85 ±0.13</td>
<td>0.374 NS</td>
</tr>
<tr>
<td>Total testosterone</td>
<td>9.5 ±1.8</td>
<td>18.6 ±4.1</td>
<td>0.001 S</td>
</tr>
<tr>
<td>(nmol/l)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SHBG (nmol/l)</td>
<td>35.8 ±14.8</td>
<td>36.2 ±17.7</td>
<td>0.894 NS</td>
</tr>
<tr>
<td>LH (mIU/ml)</td>
<td>4.6 ±4.4</td>
<td>8.6 ±6.6</td>
<td>0.001 S</td>
</tr>
<tr>
<td>FSH (mIU/ml)</td>
<td>7.1 ±5.2</td>
<td>12.2 ±11.9</td>
<td>0.020 S</td>
</tr>
<tr>
<td>Prolactin (mIU/ml)</td>
<td>198.8 ±89.6</td>
<td>183.7 ±85.3</td>
<td>0.418 NS</td>
</tr>
</tbody>
</table>
Past medical history of study subjects
Past history of hypertension was found 33.9% and 24.5% of hypogonadal and eugonadal subjects respectively. Previous history of coronary artery disease (CAD) was found 2.7% of eugonadal subjects. Both hypertension and CAD were found 1.8% of eugonadal subjects. But in majority of the subjects (66.1% of hypogonadal and 70.9% eugonadal), no significant past illness was found.

Distribution of hypogonadism among the study subjects according to different age groups
Maximum subjects were found 40-49 years age group. Fifty or more than 50 age group were 17(28.8%) and 20-29 years age group was 1(1.7%).

Association of low testosterone levels with clinical variables in study subjects (n=170)
BMI >25(kg/m²) was found in 32(54.2%) hypogonadal subjects and 47(42.3%) eugonadal subjects. Waist circumference WC e" 90 cm was found in 53(89.8%) hypogonadal subjects and 71(64.0%) eugonadal subjects. Hypertension was found in 28(47.5%) hypogonadal subjects and 44(39.6%) eugonadal subjects. History of smoking was found in 23(39.0%) hypogonadal subjects and 56(50.5%) eugonadal subjects. History of regular exercise was found in 47(79.7%) hypogonadal and 84(75.7%) eugonadal subjects. History of alcohol ingestion was found in 5(8.5%) hypogonadal and 23(20.7%) eugonadal subjects. Sensory neuropathy was found in 8(13.6%) hypogonadal and 23(20.7%) eugonadal subjects.

Table III
Association of low testosterone levels with clinical variables in study subjects (n=170)

<table>
<thead>
<tr>
<th></th>
<th>Hypogonadal (n=59)</th>
<th>Eugonadal (n=111)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &gt;25 (kg/m²)</td>
<td>32 54.2</td>
<td>47 42.3</td>
<td>0.138 NS</td>
</tr>
<tr>
<td>WC e&quot; 90 cm</td>
<td>53 89.8</td>
<td>71 64.0</td>
<td>0.001 S</td>
</tr>
<tr>
<td>Hypertension</td>
<td>28 47.5</td>
<td>44 39.6</td>
<td>0.326 NS</td>
</tr>
<tr>
<td>Smoking</td>
<td>23 39.0</td>
<td>56 50.5</td>
<td>0.153 NS</td>
</tr>
<tr>
<td>Exercise</td>
<td>47 79.7</td>
<td>84 75.7</td>
<td>0.556 NS</td>
</tr>
<tr>
<td>Alcohol intake</td>
<td>5 8.5</td>
<td>5 4.5</td>
<td>0.236 NS</td>
</tr>
<tr>
<td>Sensory neuropathy</td>
<td>8 13.6</td>
<td>23 20.7</td>
<td>0.249 NS</td>
</tr>
</tbody>
</table>

Metabolic syndrome was present in 52 (88.1%) and 67(60.4%) in hypogonadal and eugonadal subjects. The difference was statistically significant (p=0.001) in between the hypogonadal and eugonadal subjects.

Relationship of glycaemic status (HbA₁C) to distribution of hypogonadism in study subjects
In diabetic hypogonadal subjects (n=59), 13(22.0%) had good glycaemic status (HbA₁C <7%) and 46 (88.0%) had poor glycaemic status (HbA₁C >7%). HbA₁C 7.1-8% was found in 15(25.4%), 8.1-9% was found in 12(20.3%), 9.1-10% was found in 9(15.3%) and >10% was found in 10(16.9%) of hypogonadal subjects. This study showed higher percentage of hypogonadal subjects had poor glycaemic control.

Correlation of BMI, waist circumference and with HbA₁C total testosterone
Total testosterone was correlated inversely with BMI and waist circumference in study subjects. Total testosterone was negatively correlated with HbA₁C level in study subjects.
Discussion

Previous studies showed that about one third of type 2 diabetic men have low serum testosterone levels, but these studies had not correlated this value with symptoms. The present study clearly shows that there is a high prevalence of symptomatic hypogonadism in men with type 2 diabetes. In the Baltimore longitudinal study on aging and 28% of men aged > 40, 50, 60 and 70 years, respectively, had serum total testosterone levels below the normal range. In the present study, the mean total testosterone levels in diabetic men were also progressively lower in higher age groups. The frequencies of hypogonadal symptoms were similar in all age-groups of low testosterone in the present study and supported the similar results found in a previous study.

Gonadotropin Concentrations were not elevated in most of the hypogonadal subjects of type 2 diabetes in present study, and thus the primary defect in these patients would appear to be either in the pituitary gland or hypothalamus. In fact, the LH and FSH levels were significantly lower in the hypogonadal group than the eugonadal group. To rule out the possibility that the cause of hypogonadotropic hypogonadism was a pituitary lesion, MRI of pituitary and perisellar region was done in 15 randomly selected hypogonadal subjects. None of the MRIs showed pituitary or hypothalamic abnormalities. Previously in a study, it was similarly found high prevalence of hypogonadotropic hypogonadism in type 2 diabetes.

In this study, testosterone level is inversely correlated with waist circumference and BMI. A Possible explanation for this is the hypogonadal obesity cycle. Essentially, visceral adipocytes have a high activity of the enzyme aromatase which converts testosterone to estrogen. Testosterone inhibits the enzyme lipoprotein lipase, which takes up free fatty acids into adipocytes. Lower levels of testosterone result in increased triglyceride levels in adipocytes, which promote further adipocyte proliferation and hence higher aromatase activity. In this study, it was also shown that serum total testosterone negatively correlated with HbA1C level. This observation may suggest relation of hypogonadism to poor glycaemic control.

Serum testosterone levels have been reported to be lower in men with hypertension. But the present study did not show a significant association between testosterone levels and history of hypertension. Similarly, this study found no significant association between testosterone levels and smoking. The majority of cross-sectional studies have shown that low testosterone levels are associated with a pro-atherogenic lipid profile high total and LDL cholesterol and triglycerides (TG) and low HDL cholesterol. In this study, high TG and low HDL were found more in hypogonadal subjects than the eugonadal subjects, but the total cholesterol and LDL cholesterol did not vary between the two groups.

In this study, higher prevalence of metabolic syndrome (according to IDF criteria) was found among the hypogonadal subjects. Different components of metabolic syndrome were also significantly higher among the hypogonadal subjects than the eugonadal subjects. These observations suggest that androgen deficiency plays a central role in the various pathologies encompassing the components of metS including central obesity, insulin resistance, hyperglycaemia, dyslipidaemia and hypertension.

Conclusion:

This study reveals that serum total testosterone levels are lower in diabetic men with signs/symptoms of hypogonadism. Hypogonadotropic hypogonadism is frequent in diabetic hypogonadal population. There is an association between poor glycaemic control and hypogonadism in male diabetic persons.

Acknowledgement

We are thankful to all the study participants and Department of Endocrinology for their kind support throughout the study period.

Disclosure:

We did not get any type of financial support from anywhere at home or abroad.

There is no conflict of interest.

References

Clinical and Biochemical Assessment of Hypogonadism in Type 2 Diabetic Men


The Incidence, Predisposing Factors, Complications and Outcome of Preeclampsia in Diabetic Pregnancy

JESMIN S\textsuperscript{a}, JAHAN S\textsuperscript{a}, KHAN M I\textsuperscript{a}, SULTANA N\textsuperscript{a}, JERIN J\textsuperscript{a}, HABIB SH\textsuperscript{b}, PAUL DC

Abstract

Introduction: Preeclampsia is a serious complication of pregnancy and common cause of fetal and maternal morbidity as well as mortality worldwide. In diabetic women, the chance of preeclampsia is increased. The incidence of preeclampsia in diabetic pregnancy is approximately 10 to 15 percent, which is associated with poor glycaemic control. Aim: This study was carried out to find the predisposing factors related to preeclampsia and determine the complications of preeclampsia in diabetic pregnancy and also the impact of preeclampsia in infants born to diabetic mothers. Methods: This prospective study was carried out at the Bangladesh Institute of Research and Rehabilitation in Diabetics, Endocrine and Metabolic Disorders (BIRDEM), Dhaka. The patient population consisted of 80 diabetic pregnant women who attended or admitted to BIRDEM hospital during the study period. The women were divided into groups: 50 pregnant diabetic women with preeclampsia were taken as case. 30 pregnant diabetic women without preeclampsia were taken as control. Diagnosis of preeclampsia was made on the basis of the criteria of the Committee on Terminology of the American College of Obstetrician and Gynecologist. Results: Preterm delivery (<37 weeks gestation) was higher among study group (64%) compared to control (33.3%) women. Term delivery was 36.0 vs 66.7 percent among case and control women, respectively. The distribution is statistically significant ($P<0.01$). 35 percent of Caesarean section was done due to fetal distress in the study group and in control group it was 20 percent. In study group, 22.5 percent Caesarean sections were done due to impending eclampsia and eclampsia, 705 percent due to accidental haemorrhage and 5 percent due to IUGR. Maternal complication in study and control subjects. In the case group, maximum number of the women (16%) showed signs of impending eclampsia, while among control women, maximum number (10%) developed postpartum haemorrhage (PPH). 48 percent neonates were of low birth weight and in controls it was 13.3 percent. Both hyperbilirubinaemia (40%) and hypoglycaemia (30%) were more in study group than controls (16.66% and 20%, respectively). Perinatal outcome among study group and controls. Neonatal survival was 82.0 percent in study group and 86.7 percent in control group. Comparison of Perinatal outcome between the groups is not statistically significant. Most of the perinatal mortality was due to prematurity (8%) and intrauterine death (6%). In control group, most of the perinatal deaths were due to congenital anomalies (6.6%). Conclusion: The higher incidence among study group may be, in part, the result of more preterm birth or shortened gestational duration because early delivery is a consequence of preeclampsia. The higher rate in associated with preeclampsia was due to increased incidence of IUD and prematurity.

Key Words: Incidence, Predisposing Factors, Complications, Preeclampsia, Diabetic Pregnancy

(BirDEM Med J 2011; 1(1): 10-14)
protein in urine) which leads to serious complications if not treated promptly. The incidence of preeclampsia in diabetic pregnancy is approximately 10 to 15 percent, which is associated with poor glycaemic control. Proper antenatal check-up and early diagnosis of preeclampsia in diabetic women, prompt treatment and strict control of blood sugar may reduce the complications of diabetic preeclampsia.

This study was carried out to find the predisposing factors related to preeclampsia and determine the complications of preeclampsia in diabetic pregnancy and also the impact of preeclampsia in infants born to diabetic mothers.

Materials and Methods:
This prospective study was carried out at the Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka. The Patient population consisted of 80 diabetic pregnant women who attended or admitted to BIRDEM hospital during the study period. The women were divided into groups:

- 50 pregnant diabetic women with preeclampsia were taken as case.
- 30 pregnant diabetic women without preeclampsia were taken as control.

The inclusion criteria for the case were as follows; Gestational proteinuric hypertension, Patients with increased systolic blood pressure of ≥ 30 mmHg or diastolic ≥15 mmHg over a baseline blood pressure after 20 weeks of gestation, Blood Pressure of ≥140/90 mmHg at least on two measurements taken 6 hours apart after 20 weeks of pregnancy if prior blood pressure is not known, Preconception diabetic women, Gestational diabetic women.

The exclusion criteria for the case were as follows; History of Gestational hypertension without proteinuria, Diabetes and Preeclampsia toxaemia (PET) with other systemic disease like congestive cardiac failure, chronic liver disease, endocrinopathy and autoimmune disease.

Method:
Diagnosis of preeclampsia was made on the basis of the criteria of the Committee on Terminology of the American College of Obstetrician and Gynecologist. Blood pressure measurement was taken with the patient in sitting position with right in a roughly horizontal position at heart level. Blood pressure measurement was done every two weeks from 28 to 36 weeks and weekly from 36 weeks gestation up to delivery.

Serial measurement of serum uric acid, creatinine and blood urea levels were done. Diagnosis of gestational diabetes was madder on the basis of WHO criteria.

The diabetic patients were managed with dietary regulation and intensified by subcutaneous insulin therapy with goals to maintain fasting blood glucose level at <105 mg/dl and postprandial glucose <140 mg/dl.

Statistical Analysis:
Relevant data of each of the study subjects were recorded on a predesigned data collection sheet. Data were compiled and appropriate statistical analyses were done using computer based software, Statistical Package for Social Science (SPSS).

Results:
Table I shows that 12.0 percent study group and 6.7 percent control subjects had Oligohydramnios, 6.0 percent case and 13.3 percent control subjects had polyhydramnios and 82.0 percent case and 80.0 percent control subjects had adequate volume of liquor amnii. Liquor volume did not show any statistical difference between the two groups.

<table>
<thead>
<tr>
<th>Liquor amnii</th>
<th>Case (n=50)</th>
<th>Control (n=30)</th>
<th>P valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Oligohydramnios</td>
<td>6 (12.0)</td>
<td>2 (6.7)</td>
<td></td>
</tr>
<tr>
<td>Polyhydramnios</td>
<td>3 (6.0)</td>
<td>4 (13.3)</td>
<td>0.428 NS</td>
</tr>
<tr>
<td>Adequate</td>
<td>41 (82.0)</td>
<td>24 (80.0)</td>
<td></td>
</tr>
</tbody>
</table>

aChi-square test, NSNot significant
In study group, 80 percent and in control group, 66.7 percent were delivered by LUCS which is statistically significant (P<0.001) and 20.0 percent in study group and 33.3 percent in control group had normal vaginal delivery which is statistically significant (P<0.01).

**Table II**

<table>
<thead>
<tr>
<th>Mode of Delivery</th>
<th>Case</th>
<th>Control</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUCS (Lower Uterine Caesarean Section)</td>
<td>40 (80.0)</td>
<td>20 (66.7)</td>
<td>0.000***</td>
</tr>
<tr>
<td>NVD (Normal Vaginal Delivery)</td>
<td>10 (20.0)</td>
<td>10 (33.3)</td>
<td>0.002**</td>
</tr>
</tbody>
</table>

*Z-test, **Significant at P<0.01, ***Significant at P<0.001

Table III shows that preterm delivery (<37 weeks gestation) was higher among study group (64%) compared to control (33.3%) women. Term delivery was 36.0 vs 66.7 percent among case and control women, respectively. The distribution is statistically significant (P<0.01).

**Table III**

| Incidence of preterm delivery in study and control subjects: |
|------------------|------|---------|----------|
| Delivery         | Case | Control | P value* |
|                  | (n=50) | (n=30) |          |
| Preterm          | 32 (64.0) | 10 (33.3) | <0.01** |
| Term             | 18 (36.0) | 20 (66.7) |          |

*Chi-square test, **Moderately Significant

Table IV shows that 35 percent of Caesarean section was done due to fetal distress in the study group and in control group it was 20 percent. In study group, 22.5 percent Caesarean sections were done due to impending eclampsia and eclampsia, 705 percent due to accidental haemorrhage and 5 percent due to IUGR.

**Table IV**

| Indication of Caesarean section among study group and control subjects |
|------------------|------|---------|----------|
| Indications      | Case | Control | P value* |
|                  | (n=40) | (n=20) |          |
| Impending eclampsia | 8 (20.0) | 0 |          |
| Eclampsia        | 1 (2.5) | 0 |          |
| Fetal distress   | 14 (35.0) | 4 (20.0) |          |
| History of previous | 4 (10.0) | 3 (15.0) |          |
| Caesarean section | 8 (20.0) | 0 |          |
| Failed induction | 4 (10.0) | 5 (25.0) |          |
| Malpresentation  | 2 (5.0) | 2 (10.0) |          |
| Accidental haemorrhage | 3 (7.5) | 0 |          |
| IUGR             | 2 (5.0) | 0 |          |
| Bad obstetric history | 2 (5.0) | 2 (10.0) |          |
| Macrosomia       | 0 | 4 (20.0) |          |

Table V shows maternal complication in study and control subjects. In the case group, maximum number of the women (16%) showed signs of impending eclampsia, while among control women, maximum number (10%) developed postpartum haemorrhage (PPH).

**Table V**

| Maternal Complication in study group and control subjects |
|------------------|------|---------|----------|
| Complications    | Case | Control | P value* |
|                  | (n=50) | (n=30) |          |
| Impending eclampsia | 8 (16.0) | - |          |
| Eclampsia        | 1 (2.0) | - |          |
| Accidental haemorrhage | 3 (6.0) | 1 (3.3) |          |
| DIC              | 2 (4.0) | - |          |
| Cerebrovascular accident | 0 | - |          |
| HELLP syndrome   | 6 (6.0) | - |          |
| PPH              | 2 (4.0) | 3 (10.0) |          |
| Wound infection  | 3 (6.0) | 2 (6.6) |          |

Table VI shows 48 percent neonates were of low birth weight and in controls it was 13.3 percent. Both hyperbilirubinaemia (40%) and hypoglycaemia (30%) were more in study group than controls (16.66% and 20%, respectively).
Table VI

Perinatal morbidity in study group and control subjects

<table>
<thead>
<tr>
<th>Morbidity</th>
<th>Case (n=50)</th>
<th>Control (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Low birth weight</td>
<td>24 (48.0)</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Intrauterine growth retardation (IUGR)</td>
<td>8 (16.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Birth asphyxia</td>
<td>6 (12.0)</td>
<td>2 (6.6)</td>
</tr>
<tr>
<td>Respiratory distress syndrome (RDS)</td>
<td>7 (14.0)</td>
<td>2 (6.6)</td>
</tr>
<tr>
<td>Hyperbilirubinaemia</td>
<td>20 (40.0)</td>
<td>5 (16.6)</td>
</tr>
<tr>
<td>Hypoglycaemia</td>
<td>15 (30.0)</td>
<td>6 (20.0)</td>
</tr>
<tr>
<td>Septicaemia</td>
<td>3 (6.0)</td>
<td>0</td>
</tr>
<tr>
<td>Congenital anomaly</td>
<td>3 (6.0)</td>
<td>1 (6.6)</td>
</tr>
</tbody>
</table>

Table VII shows perinatal outcome among study group and controls. Neonatal survival was 82.0 percent in study group and 86.7 percent in control group. Comparison of Perinatal outcome between the groups is not statistically significant.

Table VII

Neonatal outcome in study group and control subjects

<table>
<thead>
<tr>
<th>Perinatal outcome</th>
<th>Case (n=50)</th>
<th>Control (n=30)</th>
<th>P value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
<td></td>
</tr>
<tr>
<td>Survived</td>
<td>41 (82.0)</td>
<td>26 (86.7)</td>
<td>0.584 NS</td>
</tr>
<tr>
<td>Expired</td>
<td>9 (18.0)</td>
<td>4 (13.3)</td>
<td></td>
</tr>
</tbody>
</table>

\(^a\)Chi-square test,
NSNot significant

Here shows that in the study group, most of the perinatal mortality was due to prematurity (8%) and intrauterine death (6%). In control group, most of the perinatal deaths were due to congenital anomalies (6.6%).

Table VIII

Causes of Perinatal mortality

<table>
<thead>
<tr>
<th>Causes</th>
<th>Case (n=50)</th>
<th>Control (n=30)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
</tr>
<tr>
<td>Congenital anomaly</td>
<td>2 (4.0)</td>
<td>2 (6.6)</td>
</tr>
<tr>
<td>Intrauterine death</td>
<td>3 (6.0)</td>
<td>1 (3.3)</td>
</tr>
<tr>
<td>Prematurity</td>
<td>4 (8.0)</td>
<td>1 (3.3)</td>
</tr>
</tbody>
</table>

Discussion:
Preeclampsia is a serious complication of pregnancy. Diabetes and pregnancy may affect each other over a range of interaction from conception to delivery and possibly even later. Pregnant women with diabetes have an increased risk of developing preeclampsia. The incidence of preeclampsia in diabetic patients in this study was 10.82 %, which correlates with that Garner et al\(^3\) (9.9%) and Arias\(^2\) (10-15%). The vascular endothelial dysfunction associated with diabetes mellitus may contribute to the increased incidence of preeclampsia among diabetic women\(^5\).

Thirty- four percent cases had family history of hypertension, which is nearly similar to the findings of Hossain\(^4\) (39%). The rate of preeclampsia increases significantly with the increase in severity of diabetes. Several studies have reported an association between maternal glycaemic control and adverse outcome, such as preeclampsia, preterm delivery etc\(^6\). In this study, 64 percent cases had poor glycaemic control, mostly in their half of pregnancy, which may be due to late diagnosis.

Significantly more women delivered by Caesarean section in the study group (80%) than in the control group (66.6%) (P<0.001). The higher incidence is mostly due to early termination of pregnancy due to maternal and fetal complications. The rate Caesarean section in control group was 66.6 percent, which is similar to the findings of Khatun\(^7\) (65%), but higher than reported by Rokshana\(^8\) (57.45%).

The diabetic women with preeclampsia have a significant higher rate of preterm deliveries. In this study, the rate of preterm (<37 week gestation) was 64 percent, which is slightly higher than Sibai et al\(^6\) (57%). In diabetic pregnancy without preeclampsia (control), preterm delivery was 33.3 percent and according to Sibai et al, it was 2704 percent. Other complications found in study group were impending eclampsia (16%), eclampsia (2%), DIC (4%), HELLP syndrome (6%), accidental haemorrhage (6%) which was due to associated preeclampsia. Wound infection occurred possibly due to uncontrolled blood sugar.

The neonates of mother with preeclampsia (study group), in addition to having the threats associated with prematurity, are often compromised as a result of uteroplacental insufficiency. Marker of such chronic intrauterine comprise include intrauterine growth
retardation (IUGR) and oligohydramnios. In this study, in the control group, the incidence of IUGR was 3.3 percent which coincides with the findings of Sibai et al 6 (5.4%). It may be due to poor control of hypertension and associated in controlled blood sugar.

In the present study, oligohydramnios was present in 12 percent cases. It may be due to associated IUGR and placental insufficiency. In control group, oligohydramnios was present in 6.7% women and polyhydramnios in 13.3 percent cases, which coincides with the study of Rokshana 8 (12.77%).

Mother with preeclampsia usually has low-birth-weight babies. In this study, among control subjects, 13.3 percent had low-birth-weight babies, and in study subjects, the rate was 48 percent.

In the study group, 30 percent neonates developed hypoglycaemia, percent hyperbilirubinaemia, 12 percent RDS, 14 percent birth asphyxia and 6 percent septicaemia. In control group, 16.6 percent neonate’s developed hyperbilirubinaemia, 20 percent developed hypoglycaemia and 6.6 percent each developed RDS and asphyxia. The higher incidence in study group may be due to prematurity. Because of hepatic insufficiency, hyperbilirubinaemia may occur in preterm babies. RDS and birth asphyxia are common complications of preterm birth. Septicaemia may occur to less protective passive immunity 9.

Congenital anomalies occurred in study group in 4 percent and in control group in 6.6 percent, which is almost similar to the findings by Rokshana 8 (4.6%). Incidence of IUD in study group is slightly higher (6%) than control group (3.3%). In present study, perinatal mortality rate was 18 percent in study group and 13.2 percent in control group, which is similar to the findings of Khatun 7 (14.29%).

Conclusion:
The higher incidence among study group may be, in part be, in part, the result of more preterm birth or shortened gestational duration because early delivery is a consequence of preeclampsia. The higher rate in associated with preeclampsia was due to increased incidence of IUD and prematurity.

References:
Clinical Spectrum and Management of Diabetic Ketoacidosis: Experience in A Tertiary Care Hospital

RAHIM MAa, UDDIN KNa, ZAMAN Sc, MUSA AKMd, RAHMAN MRc, HOSSAIN MDf, AHMED AKMSg, AHMED JUa, SAMAD T, HAQUE HF, DEWAN Pg, SARKER RSCg, DASTIDAR Sh

Abstract

Background: Diabetic ketoacidosis (DKA) is an acute metabolic complication of diabetes mellitus (DM). It may be the presenting feature in type 1 DM, but more commonly it complicates previously diagnosed diabetic patients, both type 1 and type 2. If not recognized early and treated in a judicious way the outcome is often fatal.

Objectives: The objectives of this study was to see the common presenting features of DKA, their precipitating causes, patterns of electrolyte imbalance, treatment requirement in early hours and to see the outcome.

Materials and methods: This cross sectional study was done in BIRDEM General Hospital on fifty adult patients who presented with DKA over a period of nine months (January 2007 to September 2007).

Results: Total number of patients were 50, male were 24 and female were 26 (M:F =12:13). Mean age was 27.6 ± 3.7 years. The incidence of DKA was more in known diabetic patients (32, 64%), in comparison with new cases (18, 36%). Frequency was more in poor village people (31, 62%). Vomiting (24, 48%) was the most frequent complaint, followed by fever (19, 38%), nausea (16, 32%), abdominal pain (14, 28%), weakness (13, 26%), polyuria (12, 24%) and polydypsia (8, 16%). Infection (18, 36%) was the most common precipitating cause, closely followed by inadherence to insulin therapy (17, 34%). In 12 (24%) cases no cause could be identified. Glycaemic control was poor, HbA1c was >7% in 98% cases. Severe acidosis (pH < 7) was less common (4, 8%) and gross electrolyte imbalance was uncommon but all patients required potassium supplementation in course of treatment. Neutrophilic leukocytosis was present in 44 (88%) cases, irrespective of presence of infection. Mortality was low (3, 6%).

Conclusion: Diagnosis and treatment of DKA is not difficult if recognized early. So, high index of suspicion is necessary, particularly in previously undiagnosed cases.

Key wards: Diabetic Ketoacidosis, Diabetes Mellitus.

Introduction

Diabetic ketoacidosis is a medical emergency. It may be the presenting feature of type 1 diabetes, but more frequently it occurs in established diabetic patients- both type 1 and type 2. The cardinal biochemical features of diabetic ketoacidosis are hyperglycaemia, hyperketonaemia and metabolic acidosis. Alberti’s definition describes ‘severe uncontrolled diabetes requiring emergency treatment with insulin and intravenous fluids with a blood ketone body (acetoacetate and 3-hydroxybutyrate) concentration of greater than 5 m.mol per litre’. For practical purpose, diagnostic criteria often includes a plasma bicarbonate concentration of 15 m.mol per litre or less with significant ketosis (urine ketostix reaction at least ++ or plasma ketostix reaction + or more) in a patient with high blood glucose. American Diabetic Association (ADA) has given a guideline of assessing severity of diabetic ketoacidosis and it’s differentiation from hyperglycaemic hyperosmolar state (HHS).
The presence of no or near no insulin is the critical underlying defect in the pathogenesis of DKA coupled with increased quantity of counter regulatory hormones. Insulin deficiency leads to hyperglycaemia, which in turn causes osmotic diuresis and dehydration. Withdrawal of insulin from insulin dependent patients lead to an early rise of plasma glucagon resulting in increased fat metabolism and production of ketone bodies. As hyperglycaemia and ketoacidosis develop, dehydration and acidosis stimulate the release of catecholamines and cortisol, leading to a vicious circle in which worsening metabolic decompensation stimulates further secretion of catabolic hormones. In moderate DKA, average 6 litres of fluid, 500 m.mol Na, 400 m.mol Cl and 350 m.mol K are lost.

Most patients present with polyuria, polydipsia, nausea, vomiting, generalized weakness and weight loss. Abdominal pain is a recognized feature, particularly in children. Patients are frequently dehydrated, hypotensive, tachycardic and dyspneic. Ultimately they become comatose. Features of infection may be present. Precipitating causes of diabetic ketoacidosis include infection 30%, errors in management 15%, newly diagnosed diabetes 10%, other identifiable medical disease 5% and in 40% cases no cause is found. Drugs e.g. corticosteroids, thiazides and sympathomimetics are often the culprits.

The diagnosis of diabetic ketoacidosis is simple if it is considered in the differentials. A urine sample showing marked glycosuria and ketonuria or an undiluted plasma sample giving a strongly positive result in nitroprusside test for acetoacetate is sufficient for diagnosis. These common tests are often not done and there occurs delay in diagnosis. Differential diagnoses include hyperglycaemic hyperosmolar state, lactic acidosis, other causes of metabolic acidosis like uraemia, salicylates, methanol, ethylene glycol poisoning etc.

Investigations include plasma glucose, blood urea, serum creatinine, serum electrolytes, serum osmolality, urinalysis, urine or plasma ketones and arterial blood gas analysis. Bacterial cultures of urine, blood, throat swabs and chest X-ray are often required.

Successful treatment of DKA requires correction of dehydration, hyperglycaemia, electrolyte imbalance, identification of precipitating cause and its treatment and above all frequent monitoring. Use of flow chart documenting clinical status (blood pressure, intake-output chart and level of consciousness, if necessary), blood glucose, electrolytes and anion gap is recommended.

The common complications of DKA and its treatment are hypoglycaemia, hypokalaemia and hyperglycaemia. Cerebral oedema is a rare but fatal complication, occurring in 0.7-1.0% children with DKA with mortality rate >70%, with only 7-14% patients recovering without permanent morbidity. Hypoxemia and rarely noncardiogenic pulmonary oedema may complicate treatment of DKA. Thromboembolic complications, DIC and rarely rhinocerebral mucormycosis can occur in diabetic patients with ketoacidosis.

The average mortality rate for ketoadicosis in developed countries is currently estimated 5-10%, although reported rates vary greatly. Mortality is greatly higher in less specialized centers and in elderly population.

Many cases of DKA can be prevented by better access to medical care, proper education and effective communication with the health care provider during an intercurrent illness.

Materials and methods
This cross sectional study was done in the Department of Medicine, BIRDEM General Hospital, Dhaka. Data were collected from fifty hospitalized patients with a diagnosis of DKA who were admitted and managed in general medical wards. The study period was nine months (January 2007 to September 2007). All adult patients aged 18 years and above with a diagnosis of DKA, whether previously known diabetic or newly diagnosed case were included in the study. Patients having other causes of acidosis like chronic kidney disease (CKD), those who required transfer to Critical Care Units for treatment and those who were below the age of 18 years were excluded from the study.

Results
Total number of cases were 50, male were 24 and female were 26, M:F ratio was 12:13. Mean age was 27.6 ± 3.7 years. Thirty one (62%) patients came from villages and 19 (38%) patients were from urban and sub-urban areas. Most (47, 94%) of the patients were from family of low income group. Eighteen patients (36%) were detected as diabetic first time at this admission (new case) and 32 (64%) patients were known diabetic (old case).
Among the 32 known diabetic patients, 24 (75%) patients were on insulin, 7 (21.88%) patients were on oral anti-diabetic agents (OAD), and 1 (3.13%) patient was on medical nutrition therapy (MNT). (Figure 1)

The common presenting features were vomiting (26, 52%), fever (19, 38%), nausea (16, 32%), abdominal pain (14, 28%) (including epigastric pain in 4 cases, suprapubic pain in 3 cases, right hypochondriac pain in 2 cases and non-specific pain in 5 cases), polyuria (12, 24%) and polydipsia (8, 16%). Other features were relatively less common. Five (10%) patients had diabetic foot (2 cases had gangrene of one or more toes, 2 cases had abscess on dorsum of foot and 1 case had infection of amputated stump of leg) and 1(2%) patient had cellulitis and thrombophlebitis involving fore arm. Out of 50 cases, 4 (8%) cases had repeated history of hospitalization with DKA.

All patients had hyperglycaemia (Figure 2), almost all 49 (98%) had HbA1C > 7%.(Table I)

Thirty seven (74%) patients had +++ acetonuria and 13 (26%) patients had ++ acetonuria at the time of admission. In a significant number of patients acetonuria persisted for a longer time compared with clinical and biochemical improvement of the patients evidenced by pH and bicarbonate levels. Thirty (60%) patients had moderate metabolic acidosis, 16 (32%) had mild metabolic acidosis and 4(8%) patients had severe metabolic acidosis (ADA criteria). (Figure 3)

Infection was the commonest (18, 36%) precipitating cause, followed by inadherence to insulin therapy (17, 34%). Pancreatitis precipitated DKA in 3 (6%) cases, and in 12 (24%) cases no cause was identified. (Figure 4)

Most of the patients had normal Na and K levels at presentation and only three (6%) patients had severe hyponatraemia and hypokalaemia (Table II). All patients developed hypokalaemia within twelve hours of admission during the process of correction of metabolic acidosis with treatment (with intravenous fluids and insulin) and in all patients IV replacement of potassium was given.

Six (12%) patients had normal total white cell count (4000-11000/cmm of blood), in 17(34%) cases white cell count was between 11000-15000/cmm of blood and in 27 (54%) cases total white cell count was > 15000/ cmm of blood, though infection was present only in 18(36%) cases.

During the first 24 hours of in-hospital treatment, each patient required, on an average of 4.12 litres of intravenous fluids, 60 m.mol of potassium and 72 units of insulin.

Most patients (47, 94%) recovered from the acute crisis and only 3 (6%) patients expired within 48 hours of admission.
Table-II

<table>
<thead>
<tr>
<th>Serum sodium (m.mol/L)</th>
<th>Number of Patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;120</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>121-125</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>126-130</td>
<td>9</td>
<td>18</td>
</tr>
<tr>
<td>131-135</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>136-140</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>141-145</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>146-150</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>&gt;150</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Serum potassium (m.mol/L)</th>
<th>Number of Patients</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;3</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>3-4.5</td>
<td>20</td>
<td>40</td>
</tr>
<tr>
<td>4.6-6</td>
<td>21</td>
<td>42</td>
</tr>
<tr>
<td>&gt;6</td>
<td>6</td>
<td>12</td>
</tr>
</tbody>
</table>

Discussion

This study was done to see the common presenting features of diabetic ketoacidosis, their precipitating causes, the glycaemic control of these patients, electrolyte disturbances at presentation and their correction in first 24 hours and the outcome in BIRDEM General Hospital, a tertiary care hospital. The study was carried out on hospitalized adult patients aged 18 years and above. Total number of patients were 50. Among them, 32 (64%) patients were already diagnosed as diabetic and 18 (36%) patients were diagnosed diabetic first time during this admission. There was slight female predominance, female : male ratio was 13:12. Most patients were from villages and many were of lower socio-economic group. Female: male ratio in Denmark was 7.2 : 5.7. In a study in Taipei, it was found that 67% DKA patients were female. In a small series of paediatric patients in India, female: male ratio was 1:2.

Surprisingly, the typical features of polyuria, polydipsia and weight loss which are the predominant features of DKA, were relatively less common than nausea, vomiting and abdominal pain. Vomiting (24, 48%) was the most frequent symptom. Features of infection e.g. fever, cough, urinary symptoms and diabetic foot infection were also common.

Infection (18, 36%) was the commonest precipitating cause in this study. In 17 (34%) cases DKA was precipitated by omission or error in insulin management. In 12 (24%) cases no cause was found and pancreatitis precipitated DKA in 3 (6%) cases. In different studies, it was found that infection and drug non-compliance were the most common precipitating causes and these two collectively comprised 70-90% causes. In a study in Nairobi, 34% cases were precipitated by omitting insulin, 23.4% cases had infection. Non-compliance was the most common cause in Korea, whereas in another study in Pakistan, infection precipitated DKA in 63% cases of type 2 diabetes mellitus.

Of the 50 cases studied, 30 (60%) had moderate metabolic acidosis, 16 (32%) had mild metabolic acidosis. The remaining 4 (8%) cases had severe metabolic acidosis. Most patients had grossly elevated HbA1c, 24 (48%) cases had HbA1c > 8.5%, 16 (32%) cases had HbA1c > 10%. In a study in Nairobi, >90% patients had HbA1c >8%.

In this study, most patients with mild to moderate acidosis did not have gross electrolyte imbalance. Most had normal or slightly low Na+ levels, high normal or slightly elevated K+ levels. Similar results were found in a study in Pakistan. Three patients had severe
hyponatraemia and hypokalaemia, but after initiation of treatment with intravenous fluid and insulin, all patients developed hypokalaemia requiring intravenous correction. In a National Survey of Denmark, similar observation was found.

Most patients had grossly elevated blood sugar levels and ++ or more ketonuria on urine ketostix test. Patients were found to have ketonuria for longer period in comparison with their clinical and biochemical improvement evidenced by pH and HCO3⁻ levels. Similar observation was reported in a small study in India.

Forty four (88%) patients had neutrophilic leukocytosis. Among these 44 patients, only 18 patients had infection. In another study, >65% patients had leucocytosis and in 55% patient there was no infection.

The outcome, in terms of in-hospital mortality (in general medical wards), was quiet satisfactory. Only 3 (6%) patients expired within 48 hours of admission and these patients had severe acidosis with gross hyponatraemia and hypokalaemia at presentation. Among them, two patients were treated initially in less specialized hospitals, one had acute pancreatitis, one patient was grossly neglected diabetes mellitus and had history of repeated admissions with DKA. All other patients recovered. In the UK, in-hospital mortality rate was upto 14% because of variations in management and various other factors, in Denmark it was 4% and in Korea, in-hospital mortality was 11.8%. In Nairobi, 29.8% patients expired in hospital within 48 hours of admission.

**Conclusion**

In this cross-sectional observational study of fifty adult diabetic ketoacidosis patients (treated in general medical wards) in BIRDEM General Hospital, it was found that DKA occurred more commonly in known diabetic patients who were non-compliant to insulin treatment or who had had infection. New cases were not uncommon. Polyuria, polydypsia, vomiting, abdominal pain and infection were common features. The glycaemic control in these patients was poor. Severe metabolic acidosis was less common. In mild to moderate acidosis, gross electrolyte disturbances were infrequent but hypokalaemia developed after initiation of treatment. Leukocytosis was common, even in absence of infection and ketonuria persisted with treatment in spite of clinical and biochemical improvement. The overall outcome was comparable with developed countries. (The only limitation of the study was that, those patients who required treatment in Critical Care Units were not included in this study).

**Acknowledgement**

I am indebted to Professor Mohammad Omar Faruq, Head of Critical Care Medicine of BIRDEM General Hospital for many valuable suggestions and comments in the process of preparation of this manuscript.

**References**


Prevalence of Metabolic Syndrome among Obese Children and Adolescents

MOHSIN F, BAKI A, NAHAR J, AKHTAR S, BEGUM T, AZAD K, NAHAR N

Abstract:
Objectives: The prevalence and magnitude of childhood obesity are increasing dramatically. The study was undertaken to see the prevalence of metabolic syndrome among children and adolescents with obesity, attending the Pediatric Endocrine OPD, BIRDEM.

Methods: A cross sectional study was conducted from January 2006 to December 2008 among obese children and adolescents (6-18 years) attending Paediatric endocrine out patient department of BIRDEM. Children with any other endocrine disorder, dysmorphism/syndrome were excluded. Obesity was defined as BMI<95th percentile for age and sex using CDC growth chart. Children underwent two-hour oral glucose tolerance test, anthropometric and blood pressure measurement. Fasting serum insulin and lipid profile were measured. Impaired glucose tolerance (IGT) was defined as fasting plasma glucose (FPG) <7 mmol/L and 2 hr post glucose load <7.8 mmol/L and >11.1 mmol/L. Metabolic syndrome was identified if 3 or more of following criteria were met: BMI > 97th percentile for age and sex, high triglyceride (TGe"150 mg/dl), low high-density lipoprotein cholesterol (HDL cholesterol<40mg/dl), Systolic or diastolic blood pressure>95th percentile for age and sex, IGT.

Results: A total of 161 children presented with obesity. Male to female ratio was 1.3:1. Mean age was 10.3±2.5 years. Metabolic syndrome was identified in 36.6% subjects (59 out of 161, twentyfive male and 34 female). Higher BMI and hip circumference, systolic and diastolic hypertension, high TG, low HDL cholesterol and IGT were significantly associated with metabolic syndrome.

Conclusions: The prevalence of metabolic syndrome is high among obese children and adolescents. Factors contributing towards obesity needs to be identified and strategies should be planned for prevention and management of this health problem.

Key Words: Obesity, Children, Adolescent, Metabolic syndrome

Introduction:
The prevalence of childhood obesity has risen several times in past few decades in developed as well as developing countries. Urbanization, unhealthy diets and increased sedentary lifestyles have contributed to the increased prevalence of childhood obesity, particularly in developing countries. The prevalence of obesity was found to be 17.9% and that of overweight was 23.6% among affluent school children and adolescents in Dhaka. Childhood obesity is associated with several metabolic and endocrine derangements including hyperinsulinaemia, glucose intolerance, hypertension and dislipidaemia that predispose individuals to early development of cardiovascular disease and type 2 diabetes mellitus (T2DM). The clustering of these cardiovascular and metabolic risk factors have been identified as metabolic syndrome. The prevalence of metabolic syndrome varied from 28.7% to 50% in various studies among obese children and adolescents. We have found a high rate of Impaired glucose tolerance (IGT) and dislipidaemia in obese children and adolescents. Limited data is
available from our country on metabolic syndrome in children and adolescents and hence the present study was conducted to see the prevalence of metabolic syndrome among obese children and adolescents.

**Methods:**
A cross-sectional study was conducted from January 2006 to December 2008 among children and adolescents attending Paediatric endocrine outpatient Department (OPD) of BIRDEM with the complaints of excessive weight gain.

Obese children and adolescents aged 6-18 years were included in the study. Children with any other endocrine disorder, dysmorphism/syndrome were excluded. History was obtained from all subjects and physical examination was performed. Blood pressure was measured using appropriate sized cuff encircling at least 2/3rd of upper arm. Anthropometric measurement of weight, standing height, waist and hip circumference were taken. Weight was measured using a bathroom scale to the nearest 100 gram. Standing height was measured with stadiometer and measurement was done to nearest 0.1 cm. The waist circumference was measured at the level midway between the lower rib margin and iliac crest, at the level of umbilicus with the child breathing out gently. The hip circumference was measured at the maximum width over the buttocks at the level of the greater trochanter with a plastic measuring tape. The body mass index (BMI) was calculated as weight in kilogram (Kg) divided by square of the height in meter. Obesity was defined as BMI > 95th percentile for age and sex using CDC growth chart. Hypertension was defined as BPE”95th percentile for age and sex. Metabolic syndrome (MT) was identified if 3 or more of following criteria were met: BMI > 97th percentile, high TG, low HDL cholesterol, Systolic or diastolic blood pressure > 95th percentile, IGT. Data were analysed using SPSS software (version 12). Student T test and Chi-Square test was performed when applicable. P value of < 0.05 was considered significant. Descriptive statistics were reported as mean (±SD).

**Results:**
A total of 161 children presented with obesity. Male to female ratio was 1.3:1. Mean age was 10.3±2.5 years. Metabolic syndrome was identified in 36.6% of subjects (59 out of 161). There was a female predominance with 34 female and 25 male (female to male ratio 1.36:1). Clinical and biochemical data of children with metabolic syndrome (Group 1) and without metabolic syndrome (group 2) are shown in table 1. While comparing the clinical phenotype and biochemical data of obese children and adolescents with metabolic syndrome (group 1) and without metabolic syndrome (group 2) BMI, hip circumference, systolic blood pressure, diastolic blood pressure, Blood glucose at 2 hour of OGTT and triglyceride was found significantly higher among the former group. HDL cholesterol was lower in group 1 compared to that of group 2. Fasting serum insulin was measured in 34 subjects. Mean serum insulin level was not significantly different among the two groups. Mean insulin-resistance index (Ins-resistance index) was higher in the former group, although it was not statistically significant. The clinical and metabolic profile of children and adolescents of both groups are shown in Table 1.
Among the 59 children and adolescents with metabolic syndrome BMI >97th percentile was found in 51 (86.4%), low HDL-Cholesterol in 44 (74.5%), high TG in 41 (69.4%), IGT in 19 (32.2%), diastolic hypertension in 18 (30.5%) and systolic hypertension in 16 (27.1%) of subjects. Fig I shows the frequency of various components of metabolic syndrome.

On Chi-square analysis BMI >97th percentile (p=0.01), high TG (p=0.000), low HDL cholesterol (p=0.000), IGT (p=0.000), Systolic hypertension (p=0.008) and diastolic hypertension (p=0.02) were significantly associated with metabolic syndrome. No association was found with family history of diabetes, presence of high cholesterol and high LDL cholesterol (Table II).

Table I

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Group 1</th>
<th>Group 2</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(Yrs)</td>
<td>10.56(±1.95)</td>
<td>10.40(±2.63)</td>
<td>0.73</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>60.15(±14.77)</td>
<td>56.07(±16.17)</td>
<td>0.14</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>143.48(±12.27)</td>
<td>142.68(±14.84)</td>
<td>0.74</td>
</tr>
<tr>
<td>BMI kg/m²</td>
<td>29.02(±3.76)</td>
<td>27.46(±3.74)</td>
<td>0.02</td>
</tr>
<tr>
<td>Waist (cm)</td>
<td>87.80(±9.81)</td>
<td>85.41(±10.33)</td>
<td>0.25</td>
</tr>
<tr>
<td>Hip (cm)</td>
<td>96.66(±10.63)</td>
<td>91.36(±11.12)</td>
<td>0.02</td>
</tr>
<tr>
<td>Waist/hip</td>
<td>0.90(±0.05)</td>
<td>0.93(±0.09)</td>
<td>0.06</td>
</tr>
<tr>
<td>Systolic BP (mm of Hg)</td>
<td>114.79(±13.02)</td>
<td>107.58(±14.58)</td>
<td>0.005</td>
</tr>
<tr>
<td>Diastolic BP (mm of Hg)</td>
<td>74.93(±10.11)</td>
<td>68.98(±9.53)</td>
<td>0.001</td>
</tr>
<tr>
<td>Fasting Plasma glucose (mmol/l)</td>
<td>4.85(±0.59)</td>
<td>4.76(±0.63)</td>
<td>0.41</td>
</tr>
<tr>
<td>Plasma glucose at 2 hr of OGTT (mmol/l)</td>
<td>7.26(±1.27)</td>
<td>6.73(±1.26)</td>
<td>0.02</td>
</tr>
<tr>
<td>Insulin (µU/ml)</td>
<td>22.05(±8.68)</td>
<td>21.91(±15.35)</td>
<td>0.97</td>
</tr>
<tr>
<td>Ins-resistance index</td>
<td>4.72(±1.94)</td>
<td>3.84(±2.24)</td>
<td>0.27</td>
</tr>
<tr>
<td>TG (mg/dl)</td>
<td>200.89(±83.96)</td>
<td>131.03(±55.08)</td>
<td>0.00</td>
</tr>
<tr>
<td>Cholesterol (mg/dl)</td>
<td>182.14(±36.05)</td>
<td>181.91(±41.88)</td>
<td>0.97</td>
</tr>
<tr>
<td>LDL cholesterol (mg/dl)</td>
<td>106.31(±32.89)</td>
<td>112.06(±39.40)</td>
<td>0.39</td>
</tr>
<tr>
<td>HDL cholesterol (mg/dl)</td>
<td>35.75(±7.43)</td>
<td>42.34(±9.86)</td>
<td>0.00</td>
</tr>
</tbody>
</table>

Table II

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>With Met S, n=59 n (%)</th>
<th>Without Met S, n=102 n (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI &gt;97th percentile</td>
<td>51(86.44)</td>
<td>71(69.64)</td>
<td>0.01</td>
</tr>
<tr>
<td>High triglyceride level</td>
<td>41(69.49)</td>
<td>23(22.54%)</td>
<td>0.000</td>
</tr>
<tr>
<td>High total cholesterol</td>
<td>17 (28.81)</td>
<td>26 (25.49%)</td>
<td>0.64</td>
</tr>
<tr>
<td>Low HDL cholesterol</td>
<td>44 (74.57)</td>
<td>35 (34.31)</td>
<td>0.000</td>
</tr>
<tr>
<td>High LDL cholesterol</td>
<td>13(22.03)</td>
<td>24(23.52)</td>
<td>0.82</td>
</tr>
<tr>
<td>Family H/O diabetes present</td>
<td>32(54.23)</td>
<td>46(45.09)</td>
<td>0.48</td>
</tr>
<tr>
<td>IGT present</td>
<td>19(32.20)</td>
<td>8(7.84)</td>
<td>0.000</td>
</tr>
<tr>
<td>Systolic hypertension present</td>
<td>16(27.11)</td>
<td>11(10.78)</td>
<td>0.008</td>
</tr>
<tr>
<td>Diastolic hypertension present</td>
<td>18(30.50)</td>
<td>16(15.68)</td>
<td>0.02</td>
</tr>
</tbody>
</table>
Discussion:
In our study the prevalence of metabolic syndrome in obese children and adolescence is 36.6%. This is comparable with the figures of 28.7% to 37.5% reported in other studies carried out among obese children and adolescents.\(^7,17,18\) In one study in USA the prevalence of metabolic syndrome increased with the severity of obesity, it was 38.7% in moderately obese subjects (a BMI z-score of 2 to 2.5) and reached 49.7% in severely obese subjects (a BMI z-score above 2.5).\(^9\)

The metabolic syndrome in adults is defined as a Cluster of cardiovascular and diabetes risk factors including abdominal obesity (expressed by waist circumference), dyslipidaemia, glucose intolerance and hypertension.\(^3\) There are a range of published metabolic syndrome definition in paediatrics \(^7-9,17,19\) and the result of study on metabolic syndrome in children and adolescent can vary with the criteria used to define metabolic syndrome. We have adopted the criteria from Weiss et al \(^9\) where obesity was defined on the basis of BMI instead of waist circumference. Waist circumference and waist hip ratio are difficult to interpret in children as body proportion changes during childhood and adolescents. We have slightly modified the criteria for abnormal TG and HDL cholesterol level. A TG level of more than 95th percentile and HDL cholesterol level of less than 5th percentile for their population was designated as abnormal by Weiss. In our study a TG \(>150\) mg/dl and HDL cholesterol <40 mg/dl was taken as abnormal as used by others in case of children and adolescents.\(^14\)

In our study BMI was significantly higher in children with metabolic syndrome as found in other studies.\(^7,9,20\) Metabolic syndrome was more frequent in female than males, which does not agree with the data reported in other studies of similar age.\(^7-9\) A study carried out among adult population in Bangladesh has found higher prevalence of metabolic syndrome in females using International Diabetes Foundation (IDF) criteria.\(^21\) We did not find age, family history of diabetes to be associated with metabolic syndrome in agreement with Cook et al.\(^7\) In the present study the waist-hip ratio in obese children in all age group was more than 0.9 indicating abdominal adiposity. Waist-hip ratio is an excellent predictor of abnormalities of lipids and glucose metabolism in the adult population and similar correlation have been made for paediatric obesity.\(^22\) A ratio greater than 0.8 in women and 0.9 in men is associated with an increased risk of insulin resistance and associated disease.\(^23\) Several studies have shown that waist circumference more than 90th percentile are more likely to have multiple risk factors.\(^7,18,24-26\) In our study we have not found any association of waist circumference and waist hip ratio with metabolic syndrome. Surprisingly hip circumference was higher in children with metabolic syndrome. We have found similar association of hip circumference with IGT in our previous study.\(^10\) This can be due to racial difference in fat distribution but needs further studies to comment. Moreover body proportion normally changes with age and may vary among different races and ethnic groups.

We found IGT, high triglyceride, systolic and diastolic hypertension and low HDL cholesterol to be associated with risk of metabolic syndrome as found in other studies.\(^9,18\) This is expected as these are components of metabolic syndrome. Insulin resistance index were higher in subjects with metabolic syndrome compared to those without metabolic syndrome but did not reach statistical significance. This may be due to the fact that serum level of insulin could be measured in a small number of subjects. Various studies among obese children and adolescents have found higher insulin resistance index to be important risk factor for metabolic syndrome.\(^9,18\)

The present study has certain limitations. It was a cross-sectional, clinic based study. Only obese children were included and it was not a case-control study. Risk factors for obesity were not identified. The prevalence of metabolic syndrome as found in our study can vary depending on various criteria used while defining paediatric metabolic syndrome.

We have found a high rate of metabolic syndrome in our obese subjects. Lifestyle modification can lead to reduction in the incidence of metabolic syndrome.\(^27,28,29\) Obesity is of critical importance in the development of metabolic syndrome and needs to be prevented in childhood.

References:


Overview on Obesity - A Review
ASHRAFUZZAMAN SM

Abstract
Obesity is a global health problem including Bangladesh resulting in major morbidity and premature death. The causes of this epidemic are complex and multifactorial, but fundamentally lead to an excess calorie intake over energy expenditure. Modern lifestyles, incorporating altered eating patterns, access to cheap, highly palatable, energy-dense yet nutritionally poor foods, sedentary habits and labor-saving devices, have hugely accelerated the problem during last few years. Till date safe and efficacious drug therapies remains unmet. The two drugs for the long-term treatment of obesity, Orlistat and Sibutramine, provide only modest weight-loss benefits and are associated with high attrition rates owing to side effects. Currently neuroendocrine control of energy homeostasis and major pharmacological treatments for obesity in the pipeline. The discovery of leptin and other gut hormones as major neuroendocrine regulators of bodyweight is leading the way to the development of attractive therapeutic approaches to the long-term manipulation of energy homeostasis in favor of appetite reduction and weight loss. It is hoped that this may be associated with a relative paucity of central or unexpected side effects. The rest of this article will concentrate on these therapeutic strategies. Still shortcomings of medical treatment encouraged the Barriatric surgery specially for morbid obese subjects. Though many advantages are ascribed including remission and improvement of Type 2 diabetes mellitus, long term metabolic and nutritional effects still remains questionable. Comparative data among different procedures of Barriatric surgery are also insufficient.

Introduction:
Obesity has become one of the most important public health problems in the worldwide. Bangladesh is not an exception. In all ages obesity is increasing. Due increase in prevalence of obesity, the complications and co morbidities of obesity also increasing. Obesity means excess of body fat, overweight means weight more than Normal. The body mass index (BMI) is the accepted standard measure of overweight and obesity for children two years of age and older. Body mass index provides a guideline for weight in relation to height and is equal to the body weight divided by the height squared (Weight in Kg/Ht in M²). For Children and adolescent other measures of obesity, including weight-for-height and measures of regional fat distribution (eg, waist circumference and waist-to-hip ratio) may be considered. As children approach adulthood, the 85th and 95th percentile BMI for age and sex are approximately 25 and 30, the thresholds for overweight and obesity in adults respectively.

A growing consensus supports the following definitions for children between 2 and 20 years of age:

- **Underweight** — BMI <5th percentile for age and sex.
- **Normal weight** — BMI between the 5th and 85th percentile for age and sex.
- **Overweight** — BMI between the 85th and 95th percentile for age and sex.
- **Obese** — BMI ≥95th percentile for age and sex.
- **Severe obesity** — BMI ≥120 percent of the 95th percentile values, OR a BMI ≥35. This corresponds to approximately the 99th percentile, or BMI z-score ≥2.33.
Prevalence and trends — The prevalence of obesity among school-aged children (6 to 11 years) and adolescents (12 to 19 years) in the United States dramatically increased between 1976-1980 and 2007-2008 (from 6.5 to 19.6 percent in children, and from 5.0 to 18.1 percent in adolescents). The prevalence of obesity also doubled for preschool-aged children (2 to 5 years) from 5 percent in 1976-1980 to 10.4 percent in 2007-2008. Among infants and toddlers, the prevalence of high weight for recumbent length was 9.5 percent in 2007-2008. In a study in 2006, Bangladesh has a prevalence of School Children 27.7% (6-9 years).

Etiology: It is very complex and multifactorial, still not well understood. The possible factors that may contribute to the obesity are given below:

**Environmental** (increasing trends in glycemic index of foods, sugar-containing beverages, larger portion sizes for prepared foods, fast food service, diminishing family presence at meals, decreasing structured physical activity, shortened sleep duration, and changes in elements of the built environment (eg, availability of sidewalks and playgrounds)

Television
Video games
Sleep
Medication

**Virus:** Preliminary evidence suggests the possibility that obesity can be triggered or exacerbated by exposure to a virus. Adenovirus 36 increases body fat in several animal models.

**Genetic:** Genetic factors play a permissive role and interact with environmental factors to produce obesity. Studies suggest that heritable factors are responsible for 30 to 50 percent of the variation in adiposity, but most of the genetic polymorphisms responsible have not yet been isolated. A few specific syndromes and single-gene defects which are linked to obesity in childhood have been identified.

**Metabolic programming:** There is increasing evidence to support a role for “metabolic programming” in the development of obesity. Metabolic programming refers to the concept that environmental and nutritional influences during critical periods in development, particularly during gestation, can have permanent effects on an individual’s predisposition to obesity and metabolic disease.

**Endocrine diseases:** Endocrine causes of obesity are identified in less than 1 percent of children and adolescents with obesity.

**Nutrition during gestation and Early in life:** Individuals born small for gestational age (SGA) or large for gestational age (LGA) have higher rates of insulin resistance during childhood, even after controlling for obesity status. Similarly, many population-based studies confirm an association between birth-weight (reflecting fetal nutrition) and later diabetes, heart disease, insulin resistance, and obesity.

**Maternal endocrine factors:** Younger age of the mother at menarche was an independent predictor of the child’s obesity status, after adjustment for the maternal obesity status as well as socioeconomic factors.
Complications and Co morbidities:
Endocrine co morbidities of obesity include impaired glucose tolerance, diabetes mellitus, hyperandrogenism, and abnormalities in growth and puberty. Obesity in children and adolescents may be accompanied by accelerated linear growth and bone age. Overweight has been associated with early onset of sexual maturation in girls. However, this relationship is inconsistent. In contrast, obesity in boys may be associated with delayed onset of sexual maturation. HTN Dyslipidemia Other CV risk like MI, ACS may be associated with Obesity. Obesity is also associated with spectrum of NAFLD. Increased prevalence is noted with obesity of some GI or breast cancer. Pulmonary (Obstructive Sleep Apnea), Orthopedic (Osteoarthritis) and psychological (Depression) co morbidity also increases with obesity. Benign intracranial Hypertension may also occur. Dermatological problems (intertrigo, furunculosis, cyst lipoma) also may increase with increased weight.

Treatment: As many of our obese patients are Type 2 diabetic I shall focus more in the management of Obesity with type 2 diabetes. The challenges of weight loss in diabetes are some OAD gain weight (Sulfonylurea, TZD), some of them cannot do adequate exercise, some may use antidepressants, some time Calorie restriction may cause Hypoglycemia. The role of Endocrinologist is from front line as a member of the team, starting with to find any secondary cause of Obesity. Weight loss for management as well as prevention of type 2 diabetes. Endocrinologists’ are the leader of medically directed weight loss programme. They will also take care of Pre and Post operative Barriatric surgery patient. Starting from self directed weight loss patient will require commercial community based behavioral programme for weight loss. Then comes medically managed structured programme with low calorie diet and Pharmacotherapy. Finally comes the question of Barriatric Surgery and Long term medial management. Many recommendations are there more acceptable is to start with 1200-1500 Kcal if < 250 Pounds and 1500-1800 Kcal if ≥250 Pounds. ≤ 30 % Calorie should come from fat. Gradually building > 175 Mins/week physical activity should be done.

For pharmacotherapy available drugs are Orlistat, Phentermine Diethylpropion. Sibutramine is Withdrawal from the market due to CV toxicity. Three newer agents are before FDA but none is approved. Orcaserin, Contrave (Buprepiion+Naltrexon), Qnexa (Topiramate+Phentermine) etc may have side-effect like cardiac, Congenital Malformation (Cleft plate etc). Other molecules yet to be approved are Phendimetrazine, Benzephetamine, Mazindol etc. Tips for managing patients with Orlistat is to discuss about mechanism of action and Bowel leak. Start 120 mg before each meal and reduce fat intake. Metamucil may reduce bowel symptoms. Longer time gives more benefit but may shows vitamin deficiency. So it’s better to use Multivitamin concomitantly. Patient can achieve 5-8 % weight loss in 4-6 months. It lowers waist circumference, LDL & Triglyceride and increases HDL. Phentermine is FDA approved for short term. It should be used with low calorie diet and acts by appetite reduction. It may cause restlessness, tachycardia, insomnia increased BP etc. Weight loss may be 4-5 % in six months. But long term weight maintenance is challenging. Some may need Barriatric surgery with BMI > 40 or >35 with Co morbidities. Type 2 Diabetes usually improved by Metabolic parameters and some may cures.

References:
5. William J Klish. Definition; epidemiology; and etiology of obesity in children and adolescents Up To Date. Vol 19.1


Abstract:
Extensively drug-resistant (XDR) tuberculosis is defined as disease caused by Mycobacterium tuberculosis with resistance to at least isoniazid and rifampicin, any fluoroquinolone, and at least one of three injectable second-line drugs (amikacin, capreomycin, or kanamycin). This definition in immensely valuable for more uniform surveillance in varied international settings. The prevalence of tuberculosis drug resistance has risen to the highest rate ever recorded. Although the gold standard for drug-susceptibility testing has been the agar proportion method; due to it’s time consumption, more sensitive, specific and rapid diagnostic tests are required. It is difficult to differentiate XDR tuberculosis from non-XDR tuberculosis clinically, although the former is associated with greater morbidity and mortality. The treatment of XDR tuberculosis should include agents to which the organism is susceptible, and should continue for a minimum of 18—24 months. However, treatment continues to be limited in tuberculosis-endemic countries largely because of weaknesses in national tuberculosis health-care models. The ultimate strategy to control drug-resistant tuberculosis is one that implements a comprehensive approach incorporating innovation from the political, social, economic, and scientific realms.

Key words: Extensively drug-resistant (XDR) tuberculosis, Mycobacterium tuberculosis

Introduction:
Extensively drug-resistant (XDR) tuberculosis has received substantial attention since the initial report of an association of XDR-TB with extremely high mortality in patients co-infected with M. tuberculosis and HIV in a rural area of South Africa in the year 2006.1 XDR strains of M. tuberculosis have now been identified in at least 49 countries around the globe.2 From the advent of tuberculosis chemotherapy in the 1940s, hints of resistance were evident. When Selman Waksman accepted the Nobel Prize in 1952 for his laboratory’s discovery of streptomycin, he claimed the drug would lead the path to the elimination of “The Great White Plague”.3, 4 Such statements were premature - strains of streptomycin-resistant Mycobacterium tuberculosis were found within months of the drug’s widespread use.5 The classic 1948 British Medical Research Council (BMRC) trial that investigated the efficacy of streptomycin monotherapy showed that most patients who were treated with the drug developed resistant strains.6 As the tuberculosis chemotherapy era evolved, increasing cases of drug resistance continued to occur mainly as a result of inadequate regimens and non-adherence to therapy. Researchers initially suspected that these resistant organisms had reduced fitness and thus could be classified as being less virulent.7, 8 This assumption was reversed in the 1990s with the rise in multidrug-resistant (MDR) tuberculosis—ie, M tuberculosis resistant to at least rifampicin plus isoniazid.9 Substantial attention was focused upon New York City (NY, USA) where a virulent and transmissible strain had spread among immunocompromised populations.10, 11 Awareness of tuberculosis drug resistance was refocused with a study presented in August, 2006, at the XVI International AIDS Conference in Toronto, Canada, which described an epidemic of XDR tuberculosis in a rural hospital in KwaZulu-Natal Province, South Africa.12

Definition of XDR tuberculosis:
The term XDR tuberculosis was first developed by the US Centers for Disease Control and Prevention (CDC) in March, 2005.13 It came to public focus in October, 2005, at the 36th Union World Conference on Lung Health in Paris, France.14, 15 The original definition...
was proposed in March, 2006, in CDC’s Morbidity and Mortality Weekly Report, defining it as M tuberculosis with resistance to at least isoniazid and rifampicin among the first-line tuberculosis drugs and resistance to at least three of the six main classes of second-line drugs (aminoglycosides, polypeptides, fluoroquinolones, thioamides, cycloserine, and aminosalicylic acid). This definition was subsequently revised in October, 2006, during the first meeting of the WHO Global XDR-TB Task Force. The classification, which continues to be accepted, requires resistance of M tuberculosis to at least isoniazid and rifampicin, any fluoroquinolone, and at least one of three injectable second-line drugs (capreomycin, kanamycin or amikacin). The revision was made to facilitate reproducibility of drug-susceptibility testing and to focus attention on drugs accessible in resource-limited settings. Moreover, the classification has also been shown to have value in its ability to predict poorer outcomes.

**Epidemiology:**

In the face of rising cases of MDR tuberculosis, WHO and the International Union Against Tuberculosis and Lung Diseases (IUATLD) established the Global Project on Anti-tuberculosis Drug Resistance Surveillance in the early 1990s. One of the most important outcomes of the project was the formation of an international quality assurance programme supervised by supranational reference laboratories (SRLs). There are currently 26 SRLs that assist over 100 national laboratories in six continents by standardizing culture and drug-susceptibility techniques. To determine the rate of XDR tuberculosis, CDC and WHO assessed 17,690 M tuberculosis isolates collected by 25 SRLs from 2000—2004. The study found that 20% of the isolates met MDR-tuberculosis criteria and 2% were classifiable as XDR tuberculosis. Population-based assessment showed that 4%, 15%, and 19% of XDR-tuberculosis cases were obtained from the USA, South Korea, and Latvia, respectively.

In a rural hospital in Tugela Ferry, KwaZulu-Natal Province, South Africa, 1539 individuals were tested for tuberculosis from January, 2005, to March, 2006, 542 had at least one culture that was positive for M tuberculosis. Of these 542 patients with confirmed tuberculosis, 53 had XDR tuberculosis. Factors that have fuelled this South African epidemic include ineffective tuberculosis treatment in the context of a high prevalence of HIV, lack of proper diagnostic testing, and poor infection control practices.

The occurrence of MDR tuberculosis has reached its highest level, with cases reported in a record 49 countries. In South Africa, Tomsk Oblast (Russian Federation), and Estonia—all countries with a high burden of tuberculosis—5.7%, 6.6%, and 23.7% of all MDR-tuberculosis cases were XDR, respectively.

![Figure: Countries with XDR-tuberculosis cases in December, 2006, and June, 2008](image-url)
According to ICDDR, B report, MDR surveillance is continuing at Shyamoli TB clinic, Dhaka, Bangladesh in collaboration with National TB control programme (NTP). In their observation, out of 657 isolates, multidrug resistance was observed in 5.5% isolates. It was significantly higher among persons who received tuberculosis treatment for one month. (15.4% vs 3.0%)

**Mechanisms of resistance and fitness in XDR tuberculosis:**

The basis of tuberculosis drug resistance is the selection of bacterial mutants with innate resistance to chemotherapy.24, 25 Epidemics of drug-resistant disease can be generated by three interrelated mechanisms: (1) conversion of wildtype pan-susceptible strains to drug-resistant strains during treatment (acquired resistance); (2) increasing development of resistance in drug-resistant strains because of inappropriate chemotherapy (amplified resistance); and (3) transmission of drug-resistant cases (transmitted resistance).26

Acquired and amplified drug resistances are the primary means by which tuberculosis drug-resistant strains have been generated. However, the key determinant that has led to the exponential rise in XDR-tuberculosis cases is likely to have been transmitted resistance. The role of transmitted resistance can be elucidated by noting the clonal strains evident in tuberculosis outbreaks. The MDR-tuberculosis outbreak in the early 1990s in New York City, fuelled by the HIV epidemic and urban settings, was primarily associated with a clinically virulent strain of Beijing/W genotype.27 Moreover, 39 (85%) of 46 isolated XDR-tuberculosis strains in the Tugela Ferry outbreak in South Africa belonged to the KwaZulu-Natal (KZN) genotypic family of strains.21 The transmission of drug-resistant tuberculosis largely depends on the virulence of the mutated organism.28-30

**Diagnostic tests for XDR tuberculosis:**

The gold standard for drug-susceptibility testing has been the agar proportion method on Lowenstein-Jensen medium and Middlebrook 7H11 agar.31 But, there are several disadvantages. The reproducibility and accuracy of drug-susceptibility testing for second-line antituberculosis drugs remains questionable. The technique can take up to 4—8 weeks for finalized results. Thus, the inability to detect drug resistance rapidly could increase the likelihood of an isolate developing resistance through ineffective chemotherapy,32 likelihood of transmission of resistant strains and the potential to produce clusters of secondary infections.33 Line-probe hybridization assays in conjunction with nucleic-acid amplification offer a promising route to rapid identification of isoniazid and rifampicin resistance and are currently being studied by the WHO SRLs.35

Other molecular methods that could be used in the detection of drug-resistant tuberculosis strains include the molecular beacon assay, luciferase mycobacteriophage strategy, dideoxy fingerprinting, direct sequencing of PCR products, and heteroduplex analysis. These methods are generally described as providing results rapidly and being highly sensitive. However, they are also labour intensive and costly compared with the agar proportion method.

One particular form of testing that has received much attention because of its potential application in resource-limited settings is the microscopic-observation drug-susceptibility (MODS) assay. A median time of only 7 days (IQR 6—8 days) is needed for both disease identification and drug-susceptibility testing.36

**Clinical course of XDR tuberculosis:**

MDR tuberculosis is associated with a high mortality in individuals with HIV or other immunosuppressive conditions.37 The even poorer clinical outcomes associated with XDR tuberculosis was initially documented in the first CDC report of the disease in 2006.13 During 1993—2002, patients with XDR tuberculosis were 64% more likely to die during treatment than patients with MDR tuberculosis.10, 13 An appreciation for the substantial morbidity and mortality associated with co-infection with XDR tuberculosis and HIV was heightened by the findings in KwaZulu-Natal.21 Fifty two (98%) of 53 patients with XDR tuberculosis died during the study period. Forty four (83%) of the 53 XDR-tuberculosis patients agreed to HIV testing and all tested positive for co-infection. The first published case reports of XDR tuberculosis in India noted that among 54 HIV-positive patients, 4 (33%) of 12 diagnosed MDR tuberculosis cases were reclassified as XDR tuberculosis after drug-susceptibility testing.37 All the patients with XDR tuberculosis died within 2-6 months of diagnosis. A recent study from South Korea described the clinical
outcomes of 43 HIV-uninfected patients with XDR tuberculosis. Treatment failure, defined as a lack of culture conversion, was noted in 19 (44%) patients with XDR tuberculosis compared with 46 (27%) non-XDR-tuberculosis patients. Moreover, the mortality was 14% in those with XDR tuberculosis and 8% in those with MDR tuberculosis. A five-fold increase in the risk of death in patients with XDR tuberculosis was seen in a study done in Germany and Italy. XDR-tuberculosis patients required longer hospital stays and longer treatment durations, mainly because of clinical complications (ie, sputum conversion).

**Treatment of XDR tuberculosis:**
The principles of treatment for MDR-TB and for XDR-TB are the same. Treatment requires extensive chemotherapy for up to two years. Second-line drugs are more toxic than the standard anti-TB regimen and can cause a range of serious side-effects including hepatitis, depression and hallucinations. Patients are often hospitalised for longer periods, in isolation. In addition, second-line drugs are extremely expensive compared with the cost of drugs for standard TB treatment.

Strategies to treat drug-resistant tuberculosis can be categorized as either standardized or individualised. Standardized regimens are determined on representative drug-resistance surveillance data of specific regions. Individualized regimens are more specific in that they take into account previous antituberculosis treatments and drug-susceptibility testing of the particular isolate. XDR tuberculosis requires individualized treatment given the inability of standardized regimens to accurately address both first-line and second-line treatment resistance. Individualized regimens are also the only reliable means by which the amplification of drug resistance may be avoided. Unfortunately, the difficulty in performing drug-susceptibility testing in many resource-limited countries has led to long-term use of inadequate empiric regimens that could lead to further acquired resistance.

The length of treatment for XDR tuberculosis has not been firmly established and is often based on individual clinical presentations. Key factors determining treatment duration include cost, drug availability, toxicity, bactericidal capacity, clinical improvement, and patient adherence. Typical MDR-tuberculosis regimens can consist of up to five drugs, and WHO recommends their use for a minimum of 18 months of treatment after culture conversion to negative. Treatment of XDR tuberculosis should include agents that the strain of M tuberculosis has proven to be susceptible to. Any first-line agent to which the isolate has shown to be susceptible, and any appropriate second-line drugs should be used to achieve a regimen with a minimum of four to five effective medications. Treatment with this regimen should be continued for a minimum of 18—24 months.

**Grouping of anti-tubercular drugs:**

<table>
<thead>
<tr>
<th>Grouping</th>
<th>Drugs (Abbreviation)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 - First-line oral antituberculosis agents</td>
<td>Isoniazid (H); Rifampicin (R); Ethambutol (E); Pyrazinamide (Z)</td>
</tr>
<tr>
<td>Group 2 - Injectable antituberculosis agents</td>
<td>Streptomycin (S); Kanamycin (Km); Amikacin (Am); Capreomycin (Cm); Viomycin (Vi)</td>
</tr>
<tr>
<td>Group 3 - Fluoroquinolones</td>
<td>Ciprofloxacin (Cfx); Ofloxacin (Ofx); Levofloxacin (Lfx); Moxifloxacin (Mfx); Gatifloxacin (Gfx)</td>
</tr>
<tr>
<td>Group 4 - Oral bacteriostatic second-line antituberculosis agents</td>
<td>Ethionamide (Eto); Prothionamide (Pto); Cycloserine (Cs); Terizidone (Trd); Raminosalicylic acid (PAS); Thioacetazone (Th)</td>
</tr>
<tr>
<td>Group 5 - Antituberculosis agents efficacy (not recommended by WHO for routine use in MDR TB3 patients)</td>
<td>Clofazimine (Cfz); Amoxicillin/Clavulanate (Amx/ with unclear Clv); Clarithromycin (Clr); Linezolid (Lzd)</td>
</tr>
</tbody>
</table>
A possible treatment regimen is as follows: The treatment is divided into 2 phases: An initial phase of 6 months, which is extended to 9 months if the sputum culture is positive at 4th month; to be followed by a continuation phase of minimum 18 months. Sputum smear examination should be conducted monthly during initial phase and quarterly during continuation phase. Sputum culture should be done at least at 4, 6, 12, 18, 24th month.

A study in the Tomsk oblast of Russia, reported that 14 out of 29 (48.3%) patients with XDR-TB successfully completed treatment.49 In Hong Kong the overall treatment success rate of XDR tuberculosis compared to MDR tuberculosis is 38% vs 63%.

Surgical treatment should also be considered if clinically significant parenchymal lung disease is localized and high-grade resistance is present.50 Bilateral disease can also be approached surgically but requires multiple, staged resections. Cure rates of MDR tuberculosis can be greater than 90% with post-surgical chemotherapy.51

In view of the multiple drug cross-resistance patterns, new antituberculosis drugs with novel mechanisms of action are necessary if XDR tuberculosis is to be successfully treated. Future treatment also requires development of drugs with minimal adverse events. Ideally, such agents would not have pharmacological interactions with antiretroviral drugs commonly used to treat HIV. Promising new compounds with high potency against M tuberculosis include a diarylquinoline compound (R207910, also called TMC207) and two nitroimidazole compounds (PA-824 and OPC-67683).52-54 Moreover, tuberculosis vaccines are currently being tested which might serve as immunotherapeutic agents to accompany tuberculosis drug regimens.55

Prevention:
A multifaceted approach is advocated to address the XDR-tuberculosis epidemic. The WHO Global XDR-TB Task Force initially established comprehensive recommendations in 2006 after recognizing the impact of the disease.56


- Develop programme management and treatment guidelines of XDR tuberculosis in high and low HIV prevalence settings
- Strengthen laboratory diagnostic services to ensure rapid and accurate drug-susceptibility testing
- Reducing transmission in health-care settings and other high-risk areas to improve infection control
- Increase disease surveillance efforts to accurately assess epidemiological trends
- Enhance educational advocacy and research funding to encourage development of new drugs and diagnostics
- Improve global tuberculosis control by enhancing the testing and care of HIV-infected populations

Conclusion:
The rising prevalence of XDR tuberculosis has brought a resurgence of interest in drug-resistant tuberculosis. Because of a confluence of several epidemiological factors—such as the HIV pandemic and inadequate case detection and treatment completion—virulent XDR-tuberculosis strains have been increasingly reported worldwide. The development of highly sensitive and rapid laboratory tests for tuberculosis diagnosis also remains an area worthy of further investigative efforts. Immediate action can be implemented through the use of currently available strategies such as enhanced HIV detection and treatment, improved tuberculosis diagnostics (ie, MODS and line-probe hybridisation assays), effective infection control policies (ie, isolation, natural ventilation, and respiratory masks), and increasing local advocacy/research efforts

References:
A Case Report On Peripartum Cardiomyopathy
SAFDER AMB\textsuperscript{a}, MIR SA\textsuperscript{b}, MIAH BM\textsuperscript{c}, TAMANNA RJ\textsuperscript{d}, MOHIBULLAH AKM\textsuperscript{e}

Abstract:
A 32 year-old primigravida with gestational diabetes & subclinical hypothyroidism on replacement therapy and no previous cardiac problem, developed features of shock few hours after elective caesarian section at term, in the absence of any chest pain or palpitation. Following resuscitation she developed features of acute left ventricular failure. ECG showed nonspecific T changes, chest x-ray revealed enlarged cardiac shadow with pulmonary congestion, arterial blood gas analysis was normal with supplemental oxygen. Serial cardiac markers were normal & serum d-Dimer was negative. Echocardiogram revealed dilatation of all cardiac chambers with global hypokinesia & severe left ventricular (LV) systolic dysfunction. She was diagnosed as a case of peripartum cardiomyopathy and treated conservatively with medications. Her condition improved dramatically & she became symptom-free by the 5\textsuperscript{th} post-operative day (POD) and subsequently discharged on 9\textsuperscript{th} POD. Follow-up echocardiogram after 6 weeks revealed regional wall motion abnormality, normal chamber dimensions and fair LV systolic function.

Key words: cardiomyopathy, Pericardium

Introduction:
Peripartum cardiomyopathy (PPCM) is a rare but potentially fatal disease which presents with symptoms of heart failure primarily due to left ventricular (LV) systolic dysfunction presenting in the last part (mean 32-38 weeks) of pregnancy and up to 5-6 months post delivery\textsuperscript{1,5}. It is clinically very similar to other forms of non-ischemic dilated cardiomyopathy except for its unique relationship with pregnancy\textsuperscript{1,2} and the higher likelihood for full recovery in almost half of the cases\textsuperscript{3}. However it can still result in chronic disability and ultimately death in relatively young women in their reproductive years. This emphasizes the need for a thorough understanding of PPCM, so that the early diagnosis & institution of effective multi-disciplinary management can influence patient’s long term prognosis.

Case Report
Mrs. X, a 32 year-old primigravida from old town, Dhaka, with history of amenorrhoea for 37\textsuperscript{+}2 weeks, got admitted in BIRDEM Hospital for elective lower segment caesarian section (LSCS). Her pregnancy period was uneventful. She had regular antenatal check-up & was properly immunized as per schedule. She was diagnosed of having gestational diabetes mellitus (GDM) & subclinical hypothyroidism in the early part of pregnancy on the basis of OGTT & thyroid function tests. There was no past history of any major illness. She was getting levothyroxine, iron, folic acid and calcium supplements. Her blood sugar was well controlled with dietary & nutritional measures alone. She was a homemaker with sedentary life style & came from an upper middle-class family. Both her parents were alive & suffering from diabetes. Prior to conception her menstrual history was normal.

At the time of admission, she was mildly anemic with normal vital parameters. There was no edema or cyanosis. Bed side urine test was normal. Abdomen was distended due to gravid uterus with fundal height corresponding 35 weeks of gestation; fetal movement was present. Fetal heart sounds were audible. Other systemic examinations were unremarkable. Investigations done prior to operation revealed
hemoglobin 8.9 gm% with normal total and differential count of WBC. Both fasting & post-prandial blood glucose levels were normal as well as total protein, serum albumin levels and renal function tests. Serum TSH was within normal range & USG revealed single live fetus with gestational age corresponding to 34 weeks.

She underwent LSCS two days following admission under spinal anesthesia. Bleeding during LSCS was average. Three hours later, in the post-operative ward, she suddenly developed shock with cold clammy extremities, feeble pulse & non-recordable BP. There was no associated chest pain or palpitation. ECG revealed sinus tachycardia with nonspecific T changes. Abdomen was soft with contracted uterus, dressing was dry. Per vaginal bleeding was average.

Initial bed side 2-D, m-mode echocardiogram revealed global hypokinesia with dilatation of all 4 chambers & severe LV systolic dysfunction (EF-30%). Pulmonary trunk including the main branches was normal in dimension. Follow-up echocardiogram with color doppler study on the next day revealed global hypokinesia, dilated left ventricle, severe LV systolic dysfunction (EF-30%), grade ¼ PR, with trivial MR.
Her general conditions improved on conservative management with oxygen supplementation, frusemide (initially parenteral), digoxin, spironolactone, trimetazidine, fluid and salt restriction. The patient gradually improved and in the fifth post-operative day became symptom-free. She was finally diagnosed as a case of – Cardiogenic shock & acute left ventricular failure due to peripartum cardiomyopathy (PPCM), Status post LSCS, GDM & subclinical Hypothyroidism. She was discharged on the 9th post-operative day with oral frusemide, spironolactone, losartan potassium, digoxin, calcium, iron, folic acid & vitamin supplements. She was properly counseled about contraception, time for future pregnancy & risk of recurrence of PPCM & was asked to come for follow-up after 6 weeks. Follow-up echocardiogram at that time revealed mild anteroseptal wall hypokinesia with fair LV systolic function (EF-50%) and normal dimension of cardiac chambers.

**Discussion**

Peripartum cardiomyopathy (PPCM) is an infrequent but critical disorder in which a destabilized heart is diagnosed within the last months of pregnancy or early puerperium and often complicating obstetrics as well as anesthetic management. Usually, it occurs early in the postpartum period, with about 45% in the first week and 75% within the first month\(^1\). It is largely a diagnosis of exclusion. Other causes of heart disease must be ruled out first before making a diagnosis of PPCM. It is then diagnosed in previously healthy women presenting with symptoms of heart failure and evidence of decreased LV systolic function from late pregnancy to early puerperium.

A relationship between pregnancy and dilated cardiomyopathy was first noted in 1870 when Virchow and Porak first reported autopsy evidence of myocardial degeneration in patients who died in the puerperium\(^6\). In 1937 Gouley et al\(^7\) described the clinical and pathologic features of seven pregnant patients who had severe and often fatal heart failure. The incidence of PPCM was one case per 1,374 live births in an Indian study\(^8\). PPCM occurs in 1 in 3,000 to 1 in 4,000 pregnancies in the United States\(^9\). In South Africa, the reported incidence is higher (1: 1,000 live births)\(^10\). A much higher incidence of 1:300 live births has been reported from Haiti\(^11\) and an extremely high rate of 1% has been described in Nigeria\(^12\). Higher rates in developing countries may be due to variations in local cultural as well as puerperal practices, ecological factors, environmental influence, diagnostic criteria and reporting pattern used\(^13\).

Risk factors favoring development and recurrence of PPCM include the following: 1) advanced maternal age (>30 years), 2) multiparity, 3) Afro-American race, 4) twin pregnancy, 5) pre-eclampsia, 6) gestational hypertension, 7) chronic hypertension, 8) obesity, 9) prolonged use of tocolytics (\(\alpha_2\) stimulants e.g. terbutaline). PPCM is still regarded as a disease of unknown etiology. However there are several hypotheses like selenium deficiency, inflammatory pathology leading to myocarditis (viral infection or auto-immune response to released fetal antigen). Recent evidence in an animal (mice) model suggests a role for a 16 kDa prolactin derivative produced by proteolytic cleavage of prolactin secondary to unbalanced oxidative stress present during late pregnancy and early puerperium\(^14\)-\(^15\). In certain cultures where the incidence of PPCM is high, certain cultural practices performed during the puerperium such as consuming lake salt or rock salt (known as ‘kanwa’ which has a particularly high sodium content) to promote the flow of breast milk and the heating of the body by sitting on a clay bed with a fire
beneath to keep warm (a belief felt to ward off infection) have both been suggested as contributory factors in its development as well16-17.

Presentation of PPCM is similar to that of patients presenting with Left ventricular failure due to other causes. The clinical presentation is most often dyspnea (90%), tachycardia (62%), and edema (60%)18. Some case studies also cite unusual presentations, including multiple thromboembolic events19 and acute hypoxia20. The classical symptoms of heart failure can be masked - especially in obese women. Onset occurs one month prior to delivery and up to five months after delivery. However, the majority of women present postpartum. Possible complications include thromboembolism, arrhythmias, organ failure, obstetric & perinatal complications (premature delivery, small for date and low birth weight babies, intrauterine growth retardation and fetal deaths). PPCM is largely a diagnosis of exclusion. Other causes of heart disease such as congenital heart disease or acquired conditions that is, myocardial infarction causing LV dysfunction, pulmonary hypertension or valvular heart disease must be ruled out first before making a diagnosis of PPCM. The diagnosis of PPCM poses many challenges, as many women in the last month of normal pregnancy experience similar symptoms to that of early heart failure, such as shortness of breath on exertion, nocturnal dyspnea and cough, fatigue, palpitations and pedal edema, making differentiation difficult.

Original diagnostic criteria for PPCM were developed by Demakis et al in 19715. They did not include echocardiographic findings because echocardiography was not readily available at that time. In 1999, echocardiographic criteria21 were incorporated in a new definition. Diagnostic criteria for PPCM include:

- Onset of heart failure in last month of pregnancy to 5-6 months post partum.
- Without any other demonstrable cause of heart failure.
- Absence of any heart disease before pregnancy.
- Echocardiography criteria to include
  - An ejection fraction <45%, fractional shortening <30% or both, and
  - End-diastolic dimension (LVIDd) >2.7 cm/m2 body surface area.

The most common and confusing differential diagnosis of PPCM is Idiopathic Dilated Cardiomyopathy (IDCM). Though PPCM is identical to IDCM in several ways, most researchers now accept PPCM as a distinct entity for the following reasons22-23:

- PPCM occurs at a younger age and is generally associated with better prognosis.
- The incidence of PPCM is higher than IDCM.
- PPCM occurs mostly postpartum (78 - 93%), whereas IDCM usually manifests by the second trimester.
- PPCM exclusively affects pregnant women and recurrent PPCM is seen to manifest again in the peripartum period.
- Varying types of hemodynamic patterns are seen in PPCM compared to IDCM.
- Unique sets of antigen and antibodies against myocardium are seen in PPCM compared to IDCM patients.
- The incidence of myocarditis is higher in PPCM than in IDCM.
- Heart size returns to normal after delivery in a greater percentage of PPCM patients compared to IDCM.
- Contrary to IDCM, PPCM may lead to rapid worsening of clinical condition.

All patients should have routine blood tests to exclude anemia, electrolyte disturbance, and kidney, liver and thyroid dysfunction, inflammatory markers, a septic screen and viral serology. Cardiac markers such as troponins and CK-MB are not helpful alone in reaching a diagnosis. Radiological signs of heart failure such as cardiomegaly, pulmonary congestion and pleural effusion may be found on chest x-ray. ECG may show sinus tachycardia or other arrhythmias such as atrial fibrillation, atrial flutter, ventricular tachycardia, intraventricular block pattern, nonspecific ST-T changes and LV hypertrophy pattern. Moreover, the ECG may demonstrate no significant changes24. Echocardiography confirms ventricular failure with increased left ventricular end-diastolic dimensions and decreased ejection fraction (LVEF) and differentiates PPCM from other causes of heart failure, such as valve disease, etc. Invasive evaluation, such as cardiac
catheterization or endomyocardial biopsy, is often unnecessary for diagnosis or treatment. Coronary angiography is not routinely indicated, as coronary arteries are usually normal in PPCM. The role of endomyocardial biopsy in the diagnosis of PPCM is controversial. It is not routinely recommended, because of its limited availability, higher complication rate & low specificity. The pathology identified on endomyocardial biopsy is often nonspecific.

The treatment for peripartum cardiomyopathy is similar to that for other nonischemic dilated cardiomyopathies; however, consideration must also be given for the fetus. Non-pharmacological therapy includes low sodium diet (<4 gm/day), fluid restriction (<2 L/day) and modest daily exercise (i.e., walking).

The cornerstone of optimal oral pharmacologic therapy for cardiomyopathy begins with afterload reduction with use of angiotensin converting enzyme inhibitors (ACEI) or angiotensin II receptor blockers (ARB). Unfortunately, pregnancy is a contraindication to the use of ACEI and likely the ARB as well. In this circumstance, the combination of hydralazine and nitroglycerin or amlodipine can be safely used in pregnancy to provide needed afterload reduction. Preload reduction can be accomplished with diuretics and low-dose oral nitrates. In pregnancy diuretics must be used with caution to avoid dehydration. Oral inotropic therapy is provided by digoxin. Furthermore, the deleterious effects of excessive sympathetic nervous system activation may be blocked and reversed with low-dose ß-blockers. In the treatment of acutely ill or highly symptomatic patients, intravenous preload and afterload reducing agents (nitroprusside, nitroglycerin) or inotropic agents (dobutamine, dopamine, milrinone) should be considered. Intravenous nitroglycerin, dobutamine, dopamine, and milrinone can be used in pregnant patients if medically necessary. Invasive hemodynamic monitoring is often used to guide the acute phase of this therapy. As there is a high incidence in thromboembolism in this population, anticoagulation with either heparin or warfarin should be strongly considered. However warfarin should be avoided during pregnancy as it can cause birth defects.

Cardiac transplantation offers a final yet very viable alternative for patients with peripartum cardiomyopathy who do not improve or who continue to deteriorate with medical management. Due to limited availability of donor hearts, it may become necessary to support the patient with an intra aortic balloon pump (IABP) or ventricular assist device (VAD) as a bridge to transplant.

No specific treatment has been identified to significantly alter the morbidity of PPCM. Small trials have reported benefits of pentoxifylline, intravenous immunoglobulin, and bromocriptine. Pentoxifylline decreased TNFá levels and increased EF in patients with PPCM25. Intravenous immunoglobulin (IVIG) improved EF compared to standard treatment in one small retrospective study of 6 cases compared to 11 controls26. Case reports of recovery from PPCM with bromocriptine treatment have been described27-29.

There are several possible outcomes in PPCM. Some women remain stable for long periods, while others get worse slowly. Others get worse very quickly and may be candidates for a heart transplant. The death rate may be as high as 25-50%. The prognosis is poor in patients with persistent cardiomyopathy. Subsequent pregnancies are often associated with recurrence of left ventricular systolic dysfunction. The risk of recurrence in women who have completely recovered LV function after their previous pregnancy is lower than previously believed. Ideally, every woman planning a future pregnancy should have echocardiography performed, and, even if it is normal, they ought to have dobutamine stress echocardiography as well. Women with a full recovery of LV function on both echocardiography and dobutamine stress test can be advised that the risks of major complications are relatively low. Women with persistent LV dysfunction are advised not to pursue further pregnancies.

Conclusion

PPCM is an uncommon but potentially life threatening cardiac failure of undetermined etiology taking place in late pregnancy or early on in puerperium. Thromboembolism and cardiac arrhythmia are common complications. Diagnosis of PPCM should essentially include echocardiographic substantiation of left ventricular dysfunction. Treatment is generally the same as for heart failure with left ventricular systolic dysfunction with some possible exceptions because of the risks of certain drugs to the unborn child. In resistant cases, management with immunosuppressive drugs, immunoglobulin and pentoxifylline can be thought of.
For those who do not improve with conventional medical therapy, have persistent cardiomegaly, or have moderate to severe mitral regurgitation, referral to a cardiac transplant center should be considered. In the presence of persistent heart failure, further pregnancy is not recommended. If inevitable, subsequent pregnancy in patients with enhanced cardiac function should be managed in a multidisciplinary unit. Prognosis is linked to recovery of ventricular dysfunction.

References
Kawasaki Disease - A Rare Presentation in a Bangladeshi Infant- A Case Report

AKHTER S, ISLAM SMS, ISLAM N, BAKI A, AHMED A, NAHAR J, ZABEEN B, MOHSEN F, NAHAR N

Abstract

A three month old exclusively breast fed, immunized, male baby having presented with high continued fever for 5 days. There was no clue to any infection. It was treated as viral fever. As soon as Kawasaki Disease was suspected, on about 12th day of fever, appropriate treatment was started. The baby developed multiple coronary artery aneurysms, large pericardial effusion and a rare complication, right brachial artery thrombosis resulting in pulselessness and subsequently dry gangrene of right hand and forearm.

Introduction

Kawasaki disease (KD) is an acute, self limiting vasculitis of unknown origin. The incidence is increasing worldwide. It commonly affects children less than 5 years, but it is rarely seen in infants of less than 3 months age. KD is characterized by high continued fever of 5 days or longer duration, bilateral non-exudative conjunctivitis, erythema of lips and mouth, changes in extremities, polymorphous exanthema and cervical lymphadenopathy. Coronary arterial ectasia or aneurysms occur in about 20% of untreated patients and may cause ischemic heart disease or sudden death in 2% of patients. Although it can occur among all age groups, the under five children have the highest incidence of Kawasaki disease; little is known about its incidence or prevalence in Bangladeshi children. Diagnosis of Kawasaki disease is challenging in young infants because of its rarity, as well as for its frequently incomplete presentations. Coronary complication is a common association of KD, and it also complicates incomplete KD. As in many other developing countries, Kawasaki disease is not very commonly reported in Bangladesh. Because of under reporting of this disease, KD often does not come as a differential diagnosis in our physician’s mind. Milder cases are readily missed.

The aim of this case report is to create awareness that Kawasaki disease is not absent in this country, and may be, its incidence is rising as most investigators believe it is related to, if not caused by an infectious disease. This disease should be kept in mind as a differential diagnosis in otherwise unexplained high continued fever in infants and young children, especially those aged less than 5 years, as early diagnosis and treatment of such cases may be life saving.

Case Report

A three month, appropriately immunized exclusively breastfed male baby with dark complexion presented with history of 5 days fever, which was high grade and continued, maximum recorded temperature was >105°F. His palms, soles, lips and tongue were red with blanching rash over trunk and limbs; conjunctivae were injected without any discharge. There was no history of contact with any febrile patient. He had been taking breast milk well and bowels and bladder moved normally. Complete blood count (CBC) and blood for culture & sensitivity were sent. Blood reports excluded bacterial cause of fever. Though no focus of infection was found, a third generation oral cephalosporin was started for a benefit of doubt. About the 5th day of fever, the baby developed loose stools, which was doubted to

Effusion was tapped. The baby died following amputation of the limb - probably of a major adverse cardiac event.

Early diagnosis and appropriate treatment according to guidelines on time are essential for saving life of children with Kawasaki disease. Lack of awareness about the disease is a problem in our country.

Key word: Kawasaki Disease; coronary aneurysm; peripheral artery thrombosis, dry gangrene

be side effect of the oral antibiotic. The fever subsided after 12 days. In the mean time, he developed a cool right forearm, increased sweating of forehead and became restless. That was confused with effect of too hot weather. In a few days it was followed by blue-discoloration of the tip of the thumb (Figure 1).

On examination, his right fore-arm was cool, radial and brachial pulses were absent, and there was an indurated area, about 3 cms x 2 cms in size, over distal third of fore-arm (Figure 1). The baby was admitted in Pediatric General Ward of BIRDEM. CBC was sent; it showed thrombocytosis (4, 54,000/cu mm). Aspirin and intravenous immunoglobulin (IVIG) infusion was started within first 24 hours of admission.

Bluish discoloration rapidly spread to involve other fingers, and extended proximally towards elbow. All his four limbs on and off became cold, with simultaneously sweating of fore-head; pulses were rapid and of low volume, and heart sounds were muffled. IV Heparin was started; streptokinase was added. In the mean time echocardiography was done which showed multiple large and medium sized aneurysms involving both right and left coronary arteries and major branches, including a giant one in the right coronary (Figure 2).

This baby had pancarditis -there was dilatation of LV, stretching of mitral valve-annulus & moderate mitral regurgitation, and huge pericardial effusion in which the heart was swinging (Figure 2). Heparin was temporarily stopped with a plan for pericardiocentesis.

The baby was immediately transferred to a Cardiac ICU of the city where about 300ml of pericardial fluid was drained by a senior pediatric cardiologist. Close monitoring and treatment were continued. Platelet count progressively went up to 8,00,000/ mm³ in third week. PT & APTT were normal all along. IV Urokinase, Warfarin, Methyl Prednisolone were administered at different times to contain and prevent further thromboembolic complication. Ischemic changes initially progressed proximally in right forearm and then stopped leaving a well circumscribed margin distal to elbow. In several days the right hand and fore-arm became dry and gangrenous With (Figure 3).

His consultant vascular surgeon removed the ischemic limb. Following amputation of the limb, the baby died suddenly on first post operative day- most probably of a major adverse cardiac event.

Fig.-1: Bluish discoloration of tip of fingers and right fore-arm

Fig.-2: Coronary arterial huge aneurism and pericardial effusion

Fig.-3: Dry gangrene in right forearm and hand
Discussion
The baby had his fever started before he completed 3 months of age. Onset of KD before this age is rare. Incomplete presentation often occurs in young infants. Our case, rather, had a typical presentation. The likely reason for delayed diagnosis was that most of the physicians in Bangladesh are more concerned with infectious diseases, and non-contagious illnesses strike our mind rather late. As a result an antibiotic was readily prescribed. Though not frequently reported, KD is not absent in our country. Blue discoloration of fingertips made the physician alert, which is a rare complication of the disease. Our case had thrombocytosis, 454,000/µ mm in the second week, and it went up to 800,000/µ mm in the third week. This progressive thrombocytosis is also supported by previous study. Fever of 5-day or longer duration without any foci and an elevated platelet counts along with relevant clinical features should be treated as a KD. Echo-cardiogram showed multiple aneurysmal dilatations of the coronary arteries, including a giant lesion in the right one. This is the hallmark in diagnosis of KD. Also there were features of cardiac dilatation and regurgitation of mitral valves, and large pericardial effusion- all suggested pancarditis. The baby had developed extensive dry gangrene of right fore-arm. This is a very rare complication; rather a high predictor of mortality. Thrombocytosis is also supported by previous study. 10. The baby was given IVIG within 2 weeks of onset of disease, along with aspirin and methyl prednisolon. But his platelet count did not come down. The baby was a poor responder to IVIG. Both these conditions are associated with worse prognostic signs. He also had a large peripheral artery thrombosis. He was administered with thrombolytics too. The poor response to thrombolytics and not performing a thrombectomy resulted in grave ischemic damage to the right forelimb, the dry gangrene. The sympathetic block to prevent arterial spasm in right upper limb could not be undertaken. All these measures needed a skill that we clearly lacked. The cause of death of this baby was not identified because autopsy of dead bodies is not a routine practice in our country. The baby died on the 1st post operative day. Sudden cardiac death is not uncommon in KD. But in this case exposure to an extra trauma— the amputation, on the background of rather generalized vasculitis and multiple coronary aneurysms likely had caused myocardial infarction due to acute thrombosis and/or rupture of aneurysms.

Conclusion
Clinical diagnosis of KD in infancy requires high index of suspicion. Early diagnosis and treatment are important to prevent coronary artery aneurysms which are significantly more frequent in patients with delayed diagnosis.

Physicians should keep Kawasaki disease as a differential diagnosis in presence of un-explained high continued fever of 5 days or longer duration, and watch for other ‘major clinical features’.

References
Surgical Management of Calcific Metamorphosis of Pulp: A Case Report
KULSUM Ua, FARZANA Fb

Abstract:
A case is reported which states calcific metamorphosis of pulp in a mandibular left lateral incisor and concomitant pulp necrosis of both central incisors for a single trauma. There was a large periapical lesion associated with the teeth. Conventional endodontic treatment was performed on teeth with pulp necrosis, but the canal with calcific metamorphosis could not be negotiated with endodontic files. The periapical lesion was surgically removed and diagnosed as acute periapical abscess on histopathology. During the surgical procedure root apices of calcified tooth as well as other teeth were removed and retrograde cavity was prepared and filled with glass ionomer cement i.e apicectomy was done. The bony defect was filled with calcium hydroxyapatite crystal. Six months later the teeth were asymptomatic and radiological follow-up showed gradual healing of the bony cavity.

Keywords: Retrograde filling, apicectomy, calcific metamorphosis of pulp, calcium hydroxyapatite crystal.

Introduction:
Calcific metamorphosis is defined as a pulpal response to trauma that is characterized by deposition of hard tissue within the root canal space. Initially, calcification is a process involving the reduction in size of the intradental cavities as a result of hard-tissue formation by the cells of the vital pulp; it tends in complete calcification as a result of dentin deposition inside the tooth.

The mechanism of hard tissue formation during calcific metamorphosis is characterized by an osteoid tissue that is produced by the odontoblasts at the periphery of the pulp space or can be produced by undifferentiated pulpal cells that undergo differentiation as a result of the traumatic injury. This results in a simultaneous deposition of a dentin-like tissue along the periphery of the pulp space and within the pulp space proper. These tissues can eventually fuse with one another, producing the radiographic appearance of a root canal space that has become rapidly and completely calcified.

Calcifications of varying extent develop in teeth that have been subjected to luxation trauma. Pulpal necrosis occurs with some major delay in 20% of teeth with radiologically detectable calcifications. Calcifications have been observed in 2.3% of patients following Le Fort I operations; according to other studies, the incidence may be as high as 30%. Further causes that have been described include surgery-related changes in perfusion and in combined surgical and orthodontic treatment. Calcifications in the pulp chamber have also been observed following orthodontic treatment.

The clinical picture of calcific metamorphosis has been described by Patterson and Mitchell as a tooth that is darker in hue than the adjacent teeth and exhibits a dark yellow color because of a decrease in translucency from a greater thickness of dentin under the enamel. Pulp testing ceases to have any diagnostic value once the calcification has reached an advanced stage. Radiograph alone can never be used as a basis for determining whether complete calcification has taken place; these teeth always require clinical verification.

The radiographic appearance of calcific metamorphosis is partial or total obliteration of the pulp canal space with a normal periodontal ligament space and intact lamina dura. Complete radiographic obliteration of the root canal space, however, does not necessarily mean the absence of the pulp or canal space; in the majority of the cases there is a root canal space with pulpal tissue. Periapical lesions of endodontic origin are always manifestations of a disease that develops from the

---

a. Dr. Umme Kulsum, BDS, DDS, MS (Cons. Dentistry), Associate Professor, Department of Conservative Dentistry, Dhaka Dental College, Dhaka, Bangladesh
b. Dr. Farhad Farzana, FCPS (Part II) trainee, Department of Conservative Dentistry & Endodontics, Dhaka Dental College & Hospital, Dhaka, Bangladesh

Address of Correspondence: Dr. Umme Kulsum, Associate Professor, Department of Conservative Dentistry, Dhaka Dental College, Dhaka, Bangladesh

Received: May 30, 2011  Accepted: June 30, 2011
presence of microorganisms in the root canal system (or, in rare cases, in the periapical region). Healing can take place only if these bacteria are removed as completely as possible. Therefore, root canal treatment is strongly indicated in a tooth with a partially (apparently) calcified root canal system and apical periodontitis.  

Calcifications completely or partially block and obscure the access into the root canal systems and can hamper preparation, disinfection and obturation. Searching for calcified root canal systems carries an increased risk of perforation. However, if all attempts still fail to result in complete exposure and instrumentation of the root canal system, the clinician should consider root end resection or apicectomy, hemisection or extraction.  

The purpose of this article is to describe a clinical case of calcific metamorphosis of pulp associated with acute periapical abscess treated by apicectomy and retrograde-filling with glass ionomer cement and filling of bony cavity with hydroxyapatite crystal.  

Case Report

A 23 year-old male, named Md. Monirul Islam was referred to the Department of Conservative Dentistry & Endodontics, Dhaka Dental College & Hospital, with pain and swelling in his mandibular left lateral incisor. The patient described recent severe pain over 3 days, but no previous history or any signs or symptoms. He gave a history of trauma about 15 years back. The patient could not recollect about the treatment he received at that time. The medical history was noncontributory. Yellow discoloration on mandibular left central incisor was noticed (Fig-1). Both central incisors and left lateral incisors were sensitive to percussion, but failed to respond to pulp sensitivity testing. The labial gingiva was tender on palpation. A periapical radiograph revealed a large radiolucent area of \((13 \times 8) \text{ mm}^2\) involving apices of the mandibular central incisors and left lateral incisor. Left central incisor showed open apex (not divergent) and the left lateral incisor was calcified (Fig-2). A clinical diagnosis of calcific metamorphosis of pulp in mandibular left lateral incisor, pulp necrosis of mandibular central incisors with chronic periapical abscess was established. Taking into account the canal with calcific metamorphosis and open apices (not divergent) and the periapical radiolucency, the first step of treatment was root canal treatment and the need for apicectomy followed by retrograde filling was in consideration.

Following isolation of the teeth pus was drained through access cavity of both mandibular central incisors. A radiograph was obtained with files inserted in the root canals to establish working length. Both canals were debrided thoroughly and prepared by standardized technique to a size 35 file. Copious irrigation with 1% sodium hypochlorite solution was carried out throughout the procedure. After drying the root canals with paper points, calcium hydroxide was applied and cavity was temporarily sealed with zinc oxide eugenol cement. An access opening was made on the left lateral incisor tooth at the same visit but the root canal could not be negotiated with an endodontic file and EDTA as the canal was calcified. Then decision was made for combined nonsurgical and surgical endodontic treatment.

One week later, the right central incisor tooth was sealed with gutta-percha point and zinc-oxide eugenol cement.
After 7 days, the patient returned and apical surgery was performed to remove a portion of the undebried space and to retroseal the canal. The surgical intervention consisted of apical curettage, apicectomy, root-end preparation and retrofilling.

An intrasulcular incision along with two vertical incisions at each end was made under local anaesthesia, a full thickness flap was retracted, and bone removed to gain access to the lesion and to the apical third of the root. The granulation tissue was removed with the help of surgical curette (Fig-4) and sent for histopathological examination (Fig-5). The lower left central incisor tooth which was with open apices was sealed through and through with gutta-percha point and zinc oxide eugenol sealer followed by coronal sealing. The resection involved the apical 3 mm of the root on both teeth i.e. on calcified canal and open apex, with a bevel of 0 degree angle to the long axis of the tooth, using a high speed diamond fissure bur, followed by finishing with a diamond finishing bur and irrigation with sterile saline.

The root-end was prepared with a round diamond bur 3 mm into root dentine to receive the glass ionomer filling material. The cavity was dried and glass ionomer filling was prepared and placed on to the root-end cavity. The bony cavity was cleaned with normal saline and filled with calcium hydroxyapatite crystal (Fig-6). Sutures were used to close and healing and healing period was uneventful.

Histopathological examination showed fibro edematous infiltration with inflammatory cells suggestive of wall of an abscess.

Fig.-3: Obturation of mandibular right Central incisor.

Fig.-4: Removal of abscess wall with curette

Fig.-5: Tissue for Histopathological examination.

Fig.-6: Hydroxyapatite crystal in the bony cavity.
At 3-month and 6 months follow-up examinations, the patient was asymptomatic and radiographic evidence of gradual healing was confirmed by a decrease in the size of the periapical radiolucency.

**Discussion**

Depending on its severity, injury to the oral cavity can involve all dental tissues. Biological consequences of traumatic luxation injury include pulp necrosis, calcification and root resorption either internal and/or external along with bone resorption. The cause of pulp pathology is infectious products from an infected pulp space or from the periapical area. Microorganism that colonize these areas release their product into the periapical tissue and causes a lesion in the bone. The severity of destruction is dependent on the amount of products as well as the resistance of the host. The inflammatory development might be acute, and leading to a periapical abscess or chronic with sign of a periapical granuloma or cyst. The reported case showed almost all biological consequences of traumatic injury.

Most of the recent literature indicates that endodontic treatment is unnecessary unless the tooth is symptomatic or there is radiographic evidence of pulp necrosis and infection i.e., periapical radiolucency. Signs of pulp necrosis and infection may be seen in a small percentage of calcified canals particularly in which the pulp appears almost totally calcified and in teeth with complete root formation. Assessment of the status of the pulp was difficult since these teeth do not usually respond to thermal sensibility testing. Most, however, do respond to electrical stimulus and therefore the electrical pulp sensibility testing is the desirable method for assessing the status of the pulp in calcified canals. The reported case was non-responsive to thermal sensibility test; electrical sensibility could not be performed because of economical consideration. In the present case, radiographic complete calcific metamorphosis of pulp in a mandibular lateral incisor was associated with a large periapical lesion with concomitant pulp necrosis of both central incisors and thus endodontic treatment was inevitable.

Pulp chamber was flooded with 1% sodium hypochlorite. Canal with calcific metamorphosis was instrumented with fine file, though radiographic interpretation suggested for complete blockage. Ethylenediamine tetraacetic acid (EDTA) solution was used to assist in canal penetration. Surgical Operating Microscope (SOM) for visualization and magnification,
Ultrasonic (US) tip 7 or Laser light 8 for locating and negotiating calcified canal was not chosen because of financial consideration. Symptomatic teeth that exhibit complete calcific metamorphosis radiographically or in which the canals cannot be negotiated must be treated with periradicular surgery. 1

In the present case, all attempts with available facilities failed in negotiation and instrumentation of the calcified canal and decided for apicectomy followed by retrograde filling. Apicectomy and retro-preparation was performed with conventional method. Laser-powered apicectomy and ultrasonic retro-preparation was not chosen because of non-availability and financial consideration.

Periapical surgery is successful in 25.0-99.0% of cases, and success is influenced by many factors including the tooth involved, surgical procedure, complex anatomy of the root canal, quality of root canal filling, apical repair and the length of follow-up.9,10,11 In this case, 3 mm apical resection was performed with 0 bevel. According to Cohen et al. the length of root for resection depends upon the frequency of lateral canals and apical ramifications at the root-end. They found that when 3 mm of apex is resected, the lateral canals are reduced by 93 percent and apical ramifications decreased by 98 per cent. Whereas a root resection of 3 mm at a 0 degree bevel angle eliminates most of the anatomic features that are possible cause of failure. 1

In the present case, retrograde filling was undertaken with glass-ionomer cement, which has been shown to have good apical sealing properties, availability and is less expensive. Though this cement is more sensitive to contamination with saliva and blood unlike expensive MTA, it exhibits satisfactory periapical healing after apical surgery.12

The bony cavity was filled with calcium hydroxyapatite crystal, a non-resorbable alloplastic material as studies showed reduction of the osseous defects greater in hydroxyapatite than curettage only.13

Conclusion: Because of the calcific metamorphosis of pulp and an acute periapical abscess with concomitant pulp necrosis, combined nonsurgical and surgical endodontic therapy was indicated in this case. Follow-up radiograph over 6 months showed marked reduction of size of the radioluency and thereby healing. (Fig: 8-9)

References:
Granulomatous Hepatitis: A Rare Case Report
AMIN AAa, MONDAL SKb, ULLAH MEc

Abstract
Hepatic granulomas are found in about 3 to 10% of liver biopsies. In the liver, granulomas often merely serve as the morphologic clue to some underlying systemic process while liver function is well preserved. In approximately 15% of cases no aetiology can be established despite extensive investigations. Here we report a case of 43 years old lady with history of right upper quadrant pain with occasional fever and vomiting which was attributed to her gall bladder stones. Her liver function tests (LFT), hematological, biochemical test results were normal and all the viral markers were negative. During laparoscopic cholecystectomy, the liver was found to be studded with numerous grayish white small nodules. Liver biopsy was done which revealed non-caseating granulomatous hepatitis.

Key words: Granulomatous hepatitis, liver biopsy

Introduction
Granulomatous hepatitis is a multifactorial infiltrative liver disorder with or without additional hepatic inflammation and fibrosis. The term “granulomatous hepatitis” is often used, but the condition is not a true hepatitis. Epithelioid granulomas have been reported in about 3–10% of unselected liver biopsies1, with numerous underlying aetiologies described. There may be insignificant incidental findings, but more often they reflect clinically relevant disease — usually a systemic disorder rather than primary liver disease. A specific aetiological agent cannot be identified in approximately 15% of cases despite serological, immunological, microbiological, and radiological investigations leading to a diagnosis of ‘idiopathic granulomatous hepatitis’.
A few such patients have a syndrome of recurrent fevers, myalgias, fatigue and other systemic symptoms.

Case report
A 43-year-old diabetic woman was admitted in our hospital with right upper abdominal pain and vomiting with low grade fever and sonographic evidence of gall bladder stone. She had the history of dyspepsia and persistent dull ache in upper abdomen for 3 months. During this period, she also had occasional fever and vomiting. But there were no history of jaundice or any respiratory symptoms and her bowel and bladder habit were also normal. Her past medical history includes pulmonary tuberculosis 1½ years back for which she had received full 6 months course of anti TB chemotherapy.

On examination, her right hypochondrium was slightly tender and liver was palpable about 2 cm from costal margin without any clinical stigmata of chronic liver disease. Murphy’s sign was positive. Her chest was clear, vital signs were normal and there were no other abnormal clinical findings. She was diagnosed as a case of acute on chronic cholecystitis.

Her LFT results were normal. Findings of a full blood examination and urea, electrolytes, sugar and creatinine levels were all within normal limits. Results of serological tests for hepatitis A, B and C were negative. USG of abdomen revealed mild hepatomegaly with cholelithiasis.

We planned for laparoscopic cholecystectomy. During laparoscopy, the liver was found to be enlarged and it’s surface was studded with numerous grayish white small nodules (Fig 1). Gall bladder wall thickness was normal and there was no pericystic adhesion. GB lumen contained multiple small, soft, black stones. Rest of the abdominal organs and the peritoneum looked normal and there was no ascites either. Liver tissue was taken for biopsy.

Histopathology revealed non-caseating granulomatous reaction with aggregates of epithelioid histiocytes and Langhans giant cells. Some of the granulomas are
Granulomatous hepatitis is an uncommon condition with a lengthy list of possible causes. Infectious disorders are the most important (TB, Viral, Parasitic, fungal) and sarcoidosis is common among noninfectious causes. A variety of drugs can be responsible (eg, quinidine, sulfonamides, allopurinol). It may also be found in primary liver disease like primary biliary cirrhosis and autoimmune hepatitis. Other rare causes include non-Hodgkin’s lymphoma, polymyalgia rheumatica, juvenile chronic arthritis, graft versus host disease etc. In some cases no etiology can be established and thus labeled “idiopathic”. These patients are typically middle aged women who have an excellent prognosis.

In the liver, granulomas often incite little or no hepatocellular reaction and merely serve as the morphologic clue to some underlying systemic process; and liver function is well preserved like that in our patient.

In most situations, liver function test results are only mildly deranged, usually with a disproportionate elevation of alkaline phosphatase. Bilirubin levels are typically normal or only mildly elevated, unless concomitant hepatocellular injury coexists.

Histological examination of liver tissue provides crucial information in the differential diagnosis of hepatic granulomas. However, the morphologic pattern is often nonspecific and the diagnosis should be pursued with appropriate studies (eg, cultures, skin tests, laboratory and x-ray studies, and other tissue specimens) which had been done in our patient.

Hepatic granulomas of infective or drug etiology regress completely after appropriate therapy. Without an etiologic diagnosis, it is generally best to follow the patient rather than blindly treat with antibiotics or other therapies. Corticosteroids may be helpful in idiopathic group but should be given only if TB and other infective disorders can confidently be excluded particularly in the endemic area.

In our patient, the biopsy did not show bile duct destruction characteristic of primary biliary cirrhosis, or any evidence of malignancy. The patient was not taking any offending drugs. Histological appearance and distribution of granulomas was not consistent either with the diagnosis of hepatic sarcoidosis or with TB. Ziehl-Neelsen stain for AFB were negative. Moreover, she did not have any constitutional features of TB and her chest was normal along with negative MT test and normal ESR. In most cases, TB involvement of the liver occurs in disseminated TB. However, Negative culture result / PCR on liver biopsy specimen could have confirmed it. Perhaps thereby, our patient fell into the idiopathic category.

Postoperative recovery was uneventful and she was discharged on 2nd POD.

Discussion
Granulomatous hepatitis is an uncommon condition with a lengthy list of possible causes. Infectious disorders are the most important (TB, Viral, Parasitic, fungal) and sarcoidosis is common among noninfectious causes. A variety of drugs can be responsible (eg, quinidine, sulfonamides, allopurinol). It may also be found in primary liver disease like primary biliary cirrhosis and autoimmune hepatitis. Other rare causes include non-Hodgkin’s lymphoma, polymyalgia rheumatica, juvenile chronic arthritis, graft versus host disease etc. In some cases no etiology can be established and thus labelled “idiopathic”. These patients are typically middle aged women who have an excellent prognosis. In the liver, granulomas often incite little or no hepatocellular reaction and merely serve as the morphologic clue to some underlying systemic process; and liver function is well preserved like that in our patient.

In most situations, liver function test results are only mildly deranged, usually with a disproportionate elevation of alkaline phosphatase. Bilirubin levels are typically normal or only mildly elevated, unless concomitant hepatocellular injury coexists.

Histological examination of liver tissue provides crucial information in the differential diagnosis of hepatic granulomas. However, the morphologic pattern is often nonspecific and the diagnosis should be pursued with appropriate studies (eg, cultures, skin tests, laboratory and x-ray studies, and other tissue specimens) which had been done in our patient.

Hepatic granulomas of infective or drug etiology regress completely after appropriate therapy. Without an etiologic diagnosis, it is generally best to follow the patient rather than blindly treat with antibiotics or other therapies. Corticosteroids may be helpful in idiopathic group but should be given only if TB and other infective disorders can confidently be excluded particularly in the endemic area.

In our patient, the biopsy did not show bile duct destruction characteristic of primary biliary cirrhosis, or any evidence of malignancy. The patient was not taking any offending drugs. Histological appearance and distribution of granulomas was not consistent either with the diagnosis of hepatic sarcoidosis or with TB. Ziehl-Neelsen stain for AFB were negative. Moreover, she did not have any constitutional features of TB and her chest was normal along with negative MT test and normal ESR. In most cases, TB involvement of the liver occurs in disseminated TB. However, Negative culture result / PCR on liver biopsy specimen could have confirmed it. Perhaps thereby, our patient fell into the idiopathic category.
Conclusion
A wide variety of underlying conditions can cause granulomatous hepatitis with resulting prognostic and therapeutic implications. The idiopathic subgroup does very well though the exact cause remains undetermined. Steroid therapy is beneficial in some cases but should be given only after excluding potential infective causes.

References
A 43 years old male presented with recurrent convulsion. He had some papular lesion on the face & hand and patch on the forearm; the images of which are given below. A skull x-ray and CT scan of brain was done.

Q. What is the likely diagnosis?
• 2nd unit of BIRDEM (BIRDEM-2) has been inaugurated by Honorable Prime Minister on 29.07.2011. It is a 100 bed hospital. It was financed by Ministry of Women & Child Welfare. It would be run by Bangladesh Diabetic Samity (BADAS).

• 2nd Successful liver transplant was done on 06.08.2011.

• 1st Successful liver transplant in Bangladesh was done at BIRDEM on 03.06.2010.
1st issue of BIRDEM Medical Journal

To have a journal of BIRDEM was long cherished desire. 1st meeting with formation editorial board was held on May 11, 2011 with Professor Nazmun Nahar, Academic Director as Chair. An editorial board was formed.

A final shape was proposed and finalized in two subsequent meeting. It was decided to publish 2 issues (January & July) in each year. Principles of journals was decided. It will primarily entertain the works of BIRDEM staffs but will remain open for all.

This peer reviewed journal will be a valuable collection of different articles of all disciplines. It will publish CME articles, article of researchers of different disciplines. We have already registered web sites (www.birdem.med.j.org). We are trying to disseminate the journal to different web site and databases (HINARI, Free Medical Journal, Bangladesh Publishing Group, Bangla JOL, Google, etc).

Eagerly waiting for your valuable advise and new article.

Prof. Khwaja Nazim Uddin
Executive Editor
BIRDEM Medical Journal
NAME OF THE REVIEWER OF ARTICLES IN THIS ISSUE

(Birdem Med J 2011; 1(1): 58)

Professor Mohammad Omar Faruq
Professor Jalaluddin Ashraful haque
Professor Tahmina Begum
Professor Reza bin Zaid
Dr. Zahurul Alam
Dr. Rwnak jahan Tamanna
Dr. Delwar hossian
Dr. Feroj Amin
Dr. Muhammad Abdur Rahim
Dr. Jamaluddin Ahmed
Bipin Bihari Karmaker