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From the Desk of Editor-in-Chief

We are delighted to inform that the Volume 6, Number 1 of the Dhaka Central International Medical College Journal (DCIMCJ) is going to be published very soon. In this issue we have added a new section, Medical Quiz: Images. We are grateful to Almighty Allah. We are sending the complimentary copies of the journal to the libraries of most of the medical college and other medical institutions in Bangladesh. Already our journal has been approved by Bangladesh Medical & Dental Council (BMDC). We invite the doctors of medical colleges and institutes to submit their research articles to the journal committee for publication. We accept both hard & soft copies of the articles. We go through the papers and if necessary, communicate the authors. We also thank all the authors for giving us opportunity to publish their research papers in this journal. We have tried our best to avoid erroneous information. We like to add here that DCIMC Journal and its editorial board accept no liability for any inaccurate and misleading information, opinion and statements. It is the responsibility of the individual author (s). We have mentioned the instruction for the authors in this issue. We request the contributing authors to follow the instructions for their manuscripts. We appreciate our chairman, editors, members and advisors for their encouragement and also appreciate the contributors and reviewers for their participation. Last of all we welcome valuable suggestion, opinion, advice and constructive criticisms for improvement of the quality of the journal.



Prof. Bidhu Bhushan Das
Editor-in- Chief

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Editor-in-Chief,
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2/1, Ring Road, Shyamoli,
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A manuscript number will be mailed to the corresponding author within two working days. The cover letter should include the corresponding author`s full address and telephone / fax numbers and should be in an e-mail message sent to the editor, with the file, whose name should begin with the first author`s surname attachments or triplicate Hard copy with a soft copy.

Article types:

Five types of manuscripts may be submitted:

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It will be preferably written invited only and usually covers a single topic of contemporary interest.

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These should describe new and carefully confirmed findings, and experimental procedures should be given in sufficient detail for others to verify the work. The length of a full paper should be the minimum required to describe and interpret the work clearly.

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This should cover uncommon and /or interesting cases with appropriate confirmation process.

Review process:
All manuscripts are initially screened by editor and sent to selective reviewer. Decisions will be made as rapidly as possible, and the journal strives to return reviewers comments to authors within 3 week. The editorial board will re-review manuscripts that are accepted pending revision. The DCIMCJ editorial board will try to publish the manuscript as early as possible fulfilling all the rigorous journal needs.

I. A. Preparing manuscript for submission to DCIMCJ Editors and reviewers spend many hours reading manuscripts that are easy to read and edit. Much of the information in this journal`s Instructions to Authors is designed to accomplish that goal in ways that meet each journal`s particular editorial needs. The following information provides guidance in preparing manuscripts for this journal.

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2. Margin should be 5 cm for the header and 2.5 cm for the remainder.
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4. Each of the following section should begin separate page :
   - Title page
   - Summary/abstract
   - Text
   - Acknowledgement
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Page should be numbered consecutively at the upper right hand corner of each page beginning from the title page

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- The text of observational and experimental articles is usually (but not necessarily) divided into the following section: Introduction, Methods, Results, and Discussion. This so-called "IMRAD" structure is a direct reflection of the process of scientific discovery.

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- Double-spacing all portions of the manuscript- including the title page, abstract, text, acknowledgments, references, individual tables, and legends- and generous margins make it possible for editors and reviewers to edit the textline by line and add coments and queries directly on the paper copy.
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Research reports frequently omit important information. Reporting guidelines have been developed for a number of study designs that DCIMC journals ask authors to follow. Authors should consult the information for Authors of this journal. The general requirements listed in the next section relate to reporting essential elements for all study designs. Authors are encouraged also to consult reporting guidelines relevant to their specific research design. A good source of reporting guidelines in the EQUATOR network (http: //www.equator-network.org/home/) or CONSORT network (http://www.consort-statement. org).

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The editor reserves the right to style and if necessary, shorten the material accepted for publication and to determine the priority and time of publication

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DCIMCJ

Editorial

DCIMCJ 2019 January;6(1):14-16

Human Organ Transplantation Act in Bangladesh

Nomany BMS[1], Gani MO[2] , Islam SF[3], Alom MR[4], Khan IA[5]

Introduction:

A person can't donate his/her organ of the body on his/her own desire. Organ reception and donation are controlled under the law of respective country. If this regulation is not there, there is every chance of illegal business of organ donation (organ trading) and it is happening so also in many where. In 1999 organ donation act was formulated 1st time in Bangladesh. It was edited further in last 2018. Everybody should understand this issue in the light of this act.

Who can donate kidney? Any person can donate his /her organ to a close relative who needs the organ transplantation. Organ can be donated immediately after the death of a person according to his/ her advance directive to a related or non-related patient. But no person can sell his/her organ. The donor should be mentally sound and it also to be made sure that after donation of the organ the donor's health will not be in danger. Organ selling is prohibited both in the religion and by the constitution.

What are the common organs can be donated? Usually about 10 organs can be donated. For example- Kidney, Heart, lung, liver, pancreas, intestine, cornea, skin, bone and bone marrow.

1. Dr. Bakhtiare Md. Shoeb Nomany, Associate Professor of Medicine (Nephrology wing), Dhaka Central international Medical College.

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When can organs be donated? Organs can be donated by an alive person (live donation) and also after death (cadaveric donation).

Who can receive the organ? Legally organ is donated to the close relatives. According to organ donation act no. 5 of 1999 and act no. 1 of 2018, close relative means 26 category of relatives. For example- Parents, siblings, off springs, spouse, 1st order uncle and aunts, grandparents, grandchildren, 1st order cousins. Organs can't be donated to other than these relationships. Why? Because this unrelated organ donation encourages bad business of organ donation. Exceptionally these restrictions of related donation is not important for cornea, skin or bone marrow donation.

What will be age limit of organ donor? Any person of age between 18-65 years can donate organ. But in case of regenerative tissue donation (for example-liver) , and if donor and recipients are blood related siblings, or transplantation of cornea, skin, bone marrow, this age limit is not applicable.

Can anybody be ineligible for donation of any organ? Yes. For example –

1. If the donor's age is less than 18 or above 65 years. Because below 18 years of age a person can't give consent and above 65 years of age usually a person would have co morbidities.

2. If the functional capability of donating organ is in question. For example- A diabetic and hypertensive patient with mild kidney disease can't donate kidney because he may need kidney transplantation in future.

3. If a person is infected with hepatitis virus/HIV.

4. Cancer patient. But in the initial stage of skin and brain cancer, patient can donate kidney or other organs.

5. A person declared ineligible by medical board for organ transplantation.

6. If the person is mentally incompetent.

What is the age limit of organ recipient? Any person can receive organ within age of 2-70 years. But preferred age group is 15-50 years. There is no age limit for cornea and skin recipient.

Can anybody become ineligible for receiving organ? Yes. For example-

1. If the recipient's age is less than 1 year or more than 70 years.

2. If a person is affected with disease which can make the transplantation non successful. (Example- A cancer patient or an untreated infective patient.

3. If a medical board declares a patient ineligible for receiving organ.

Can any specialized or renal hospital transplant kidney? No non-government hospital can transplant organ without permission of the government. A hospital can transplant organ only with the permission of the government after full filling the pre requisites for organ transplantation. The hospital license will be withheld if this rule is violated. Any specialized unit of government hospital can transplant human organ without prior permission of the government.

What are the penalties for illegal organ transplantation? According to Bangladesh Organ Transplantation act no. 5 of 1999 and act no. 1 of 2018 -

1. If anybody intentionally identifies a non-relative donor as a relative, for example – fake siblings or fake spouse and if anybody influences or threatens to provide such wrong information, the person will be penalized for minimum 2 years of rigorous imprisonment or minimum 5 lacs BDT or both punishments for violation or assisting the violation of the laws.

2. Any person commits or assists to commit the crime other than mentioned above; the person will be penalized for minimum 3 years of rigorous imprisonment or minimum 10 lacks BDT or both punishments.

3. The registration of the treating physicians or surgeons will be cancelled by BMDC if he/she commits such crime under this act.

4. If such crime is committed in any hospital the permission of organ transplantation will be cancelled and financial penalty will be given. In this situation owner, director or manager will be accused for such crime until they prove that the crime happened beyond their knowledge or they tried their best for not to occur such crime.

What are the hospitals of Bangladesh doing organ transplantation legally? legally the following hospitals are doing organ transplantation: Kidney foundation, CKDU, NIKDU, BSMMU, BIRDEM, and some other hospitals. These hospitals are following rules strictly.

Can any dead person donate an organ like alive person? Yes. It is possible. The rules in this respect are:

1. The person should give advance directive before death for cadaveric donation.

2. If the person couldn't give such advance directive for organ donation before death, after brain death any legal successor can give written permission for collection of organ. The person's

organ can be collected after the declaration of the brain death by the hospital if any legal successor gives written consent. Here legal successor means spouse, major son, major off springs, major siblings and other major blood related relatives. In this situation the name of the successor mentioned 1st in the list will be preferred than major other relatives.

3. After brain death a person without a valid legal successor within 24 hours, the administrative authority of hospital can give consent for collection of organ for donation.

4. After the brain death of a person without available legal successor, the related deputy commissioner of the district can give consent only for cornea and skin collection for transplantation.

Conclusion:

There are plenty of patient of CKD. To keep them alive there are only 2 ways until today. First one is dialysis and the second one is kidney transplantation. Single kidney transplantation can save a person, also can save a family as well. Besides, a kidney donor can be a living legend. Unfortunately there is scarcity of kidney donor in respect to expected kidney recipients number. There is a problem of tissue matching and the persons wanted to donate kidney may suffer from other diseases. So cadaveric kidney transplantation is the realistic approach for current time. For this, intensive national awareness of kidney donation is important. It is very easier in this digital era. Just a good initiative is important now.

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Original Article

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Ocular Fundus Abnormalities in Pre-dialytic Chronic Kidney Disease Patients

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Summary: **Chronic kidney disease (CKD) has been associated with many other chronic conditions, like anaemia, cardiovascular disease, etc. In some recent studies it is shown that, several types of ocular fundus abnormalities has been associated with CKD. A cross sectional observational study was carried out in 100 CKD patients. Out of them 43 (43%) patients had ocular fundus abnormalities. Among the participants, 54(54%) were male and 36(36%) were female. Of them 27(62.8%) male and 16 (37.2%) female showed ocular fundus abnormality. We also found that, Low haemoglobin level was very strongly associated with development of retinopathy. The average haemoglobin level in patients with retinopathy was very significantly lower ($p < 0.0001$) than that of patients without retinopathy. Proteinuria was also associated with retinopathy. Urinary total protein (UTP) in patient with retinopathy was significantly higher ($p < 0.05$) than patient without retinopathy. High serum creatinine level and high serum cholesterol level were also associated with development of retinal abnormalities. Among the 43 patients with ocular fundus abnormality, 38 (88.37%) patients showed any type of hypertensive retinopathy and 13 (30.23%) patients shows any type of diabetic retinopathy. 8(18.6%) patients had both hypertensive and diabetic changes. Maculopathy was seen in 11 (25.58%) patients, of them, 3(6.98%) were associated with hypertensive retinopathy and 8(18.6%) were diabetic maculopathy. Optic atrophy was seen in 2(4.6%) patients and drusen like retinal deposit was seen in 2(4.6%) patients. In 13 patients with diabetic retinopathy. 8(61.54%) patients had non-prolifeartive background diabetic retinopathy, 2 (15.38%) patients had pre-proliferative diabetic retinopathy and 3(23.7%) patients showed vision threatening proliferative diabetic retinopathy with neovascularisation. 8(61.54%) patients showed diabetic maculopathy. Optic atrophy was seen in 1 (7.69%) patient with diabetic retinopathy. It was observed that retinopathy was significantly ($p < 0.001$) higher in advanced stages of CKD than in early stages. Six patients of the total 43 patients with retinopathy were presented with vision threatening reninal abnormalities. 3 of them had optic disc swelling and 3 had proliferative diabetic retinopathy with maculopathy, and needed for urgent ophthalmological consultation.**

Keywords: Fundoscopy, fundal abnormality, chronic kidney disease (CKD)

Introduction:

Chronic kidney disease (CKD) is an irreversible and progressive process. It affects 10- 16% of the adult population in Asia, Australia, Europe and the United States[1]. According to Rashid et al in Bangladesh, about 18-20% patients are suffering from CKD[2] . CKD has been associated with many other chronic conditions, like anaemia, cardiovascular disease, bone and mineral disorder, dyslipidaemia, poor nutritional status, cognitive function, etc[3]. In some recent studies it is shown that, several types of ocular fundus abnormalities has been associated with CKD such as microvascular retinopathy, diabetic retinopathy, macular degeneration, retinal hemorrhage, and calcification[4,5].Important ocular finding related to renal insufficiency are cataracts, conjunctival calcification, lid edema, conjunctival pallor, and xanthalasma, of them the later is associated with increased serum lipids. Corneal and

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conjunctival calcification may occur due to secondary hyperparathyroidism. Inflammatory reactions of conjunctiva and episclera is associated with a sudden, marked rise in serum calcium[6,7]. Conjunctival degenerative changes e.g. pinguecula are frequently seen in CKD. Recurrent subconjuctival hemorrhage can occur due to sclerosed conjunctival vessels secondary to HTN[8]. Rubeosis iridis and neovascular glaucoma occur due the posterior segment pathology.

Deterioration of vision in CKD is due to worsening of hypertensive or diabetic retinopathy, ischemic optic neuropathy, central retinal vein occlusion and cortical blindness. By the ESRD, 80.0% of patients will have developed secondary HTN[9] Ocular abnormality may be directly due to HTN, uremia and anemia. Some are related to the causes leading to CKD. Some effects are due to haemodialysis.

Hypertensive retinopathic changes are particularly severe in renal failure. This has been attributed to the effects of retained nitrogen products. Accelerated hypertension can result in optic disc edema[10].

Blindness due to proliferative retinopathy or maculopathy is approximately five times more common in diabetic patients with nephropathy compared with normoalbuminuric patients[11].

To the best of our knowledge, the relationship between CKD and ocular fundus abnormalities has never been explored in Bangladeshi Population. For this we have enrolled 100 CKD patients to find out the status and pattern of ocular fundal abnormalities.

Operational definition:

Definition of chronic kidney disease and staging:

CKD is defined as abnormalities of kidney structure or function, present for >3 months.

Stages of CKD:

- Stage 1: normal eGFR ≥ 90 mL/min per 1.73 m^2
- Stage 2: eGFR between 60 to 89 mL/min per 1.73 m^2 (mildly decreased)
- Stage 3a: eGFR between 45 to 59 mL/min per 1.73 m^2 (Mildly to moderately decreased)
- Stage 3b: eGFR between 30 to 44 mL/min per 1.73 m^2 (Moderately to severely decreased)
- Stage 4: eGFR between 15 to 29 mL/min per 1.73 m^2 (Severely decreased).
- Stage 5: eGFR of < 15 mL/min per 1.73 m^2 (Kidney failure).

Hypertension[12]:

According to 'The Eighth Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure, the goal of target blood pressure:

	Target systolic blood pressure	Target diastolic blood pressure
Age ≥ 60 years	<150 mm of Hg	< 90 mm of Hg
Age < 60 years	<140 mm of Hg	< 90 mm of Hg
Age ≥18 years with chronic kidney disease (CKD)	<140 mm of Hg	< 90 mm of Hg
Age ≥18years with diabetes	<140 mm of Hg	< 90 mm of Hg

Diabetes[13]:

- FPG ≥ 126 mg/dL (7.0 mmol/L). Fasting is defined as no caloric intake for at least 8 h. OR
- 2 hours plasma glucose ≥ 200mg/dL (11.1mmol/L) during an OGTT. The test should be performed as described by the WHO, using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water. OR
- In a patient with classic symptoms of hyperglycemia or hyperglycemic crisis, a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L).

Results of fundus examination were evaluated as:

Retinopathy defined as vascular pathology as a result of diabetes, hypertension or other conditions. The presence of retinal microaneurysms only, dot and blot and/or flame hemorrhages only, hemorrhages and/or microaneurysms, cotton-wool spots, hard exudates, intraretinal microvascular abnormalities, venous beading, arteriovenous nipping, new vessels on the disc and elsewhere, and pre-retinal and vitreous hemorrhages was defined as retinopathy.

Arteriolar narrowing and arteriovenous nipping were also defined as retinopathy. Macular degeneration suggested by large drusen and pigmentary changes. Other fundus pathology, such as other macular abnormalities and optic nerve atrophy. "Any ocular fundus pathology" was defined by the presence of at least one of fundus abnormalities mentioned above[14].

Methodology:

Study design: This was a cross-sectional observational study.

Place of study: Department of Nephrology, Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh.

Period of study: April, 2012 to March, 2014.

Study population: Total 100 pre-dialytic chronic kidney disease (CKD) patients admitted in Department of Nephrology, BSMMU, Dhaka, according to inclusion criteria.

1. Selection criteria:

Inclusion criteria: Patients with following criteria were included in this study:

i. All adult patients (>18 years) admitted in Dept. of nephrology, BSMMU, with CKD.
ii. Sex: both sexes.
iii. Patients with all stages of CKD.

Exclusion criteria:

i. Patient with clinical picture or investigations suggesting acute kidney injury (AKI).
ii. Patient on maintenance haemodialysis.
iii. Patient with renal transplant.
iv. Patient with cataract.

Ethical issue:

a. Approval to perform the study was taken from Ethical Committee, Bangabandhu Sheikh Mujib Medical University, Dhaka.

b. All participating individual were thoroughly briefed about nature, purpose implications of the study as well as entire spectrum of benefit and risks.

c. Informed written consent was taken from each study subjects.

Preparation of questionnaire:

In this study a questionnaire was designed with a view to collect data from patient who was enrolled in the study. Relevant information from history, physical findings and later laboratory investigation was recorded in pre-designed data sheet.

According to the e-GFR, patients were grouped into different stages of CKD according to KDIGO, 2012 guidelines.

Then the patients were assessed with routine laboratory investigations (CBC, urine R/M/E), renal function tests (blood urea, serum creatinine, serum calcium, serum inorganic phosphate ctc) with some other specific laboratory tests (UTP, FBS, 2 HAB, serum fasting lipid profile, serum total protein, serum albumin) as per data sheet. Renal USG was done to measure kidney size and to see any structural abnormality.

Finally patients were undergone for color fundoscopy photograph of both eyes in department of Ophthalmology, BSMMU . Photograph was taken after dilation with 0.5% tropicamide. One image of each eye using a KOWA 7 (Canon, Tokyo, Japan) retinal camera. After that the color fundus photograph was of each patient was assessed by an ophthalmologist in department of ophthalmology, BSMMU and comment was given.

Observations and Results:

To evaluate the rate and pattern of ocular fundus abnormality in CKD patients of different stages in our country, we have evaluated 100 patients (male 64 and female 36) over a period of two years Studysubjects are divided into two groups:

Group-A: occcular fundus abnormality present.

Group-B: occcular fundus abnormality absent.

Table-I: Status of ocular fundus abnormality in the study patients

	Frequency	Percentage
Total study patients	100	
Ocular fundal abnormality Present (Group-A)	43	43%
Ocular fundal abnormality absent(Group-B)	57	57%

Table –I shows the status of ocular fusdus abnormalities among the 100 CKD patients. Out of them, 43 (43%) patients have ocular fundus abnormalities. The rest 57 (57%) patients showed no ocular fundus abnormalities.

Table-II. Basic data of the study patients

Parameters	**Group A (n=43)**	**Group B (n=57)**	**P value**
Age (years)			
Mean±SD	45.56±13.79	37.46±14.46	0.006**
Range	20.00-73.00	16.00-71.00	
	No. (%)	No. (%)	
<40	14 (32.6)	34 (59.6)	
40-59	19 (44.2)	17 (29.8)	0.022*
≥60	10 (23.3)	6 (10.5)	
Sex			0.827ns
Male	27 (62.8)	37 (64.9)	
Female	16 (37.2)	20 (35.1)	
BMI (kg/m^2)			
Mean±SD	21.97±3.53	21.76±2.93	0.740ns
Range	15.55-34.63	15.20-30.61	
	No. (%)	No. (%)	
<26.00	39 (90.7)	53 (93.0)	
26.00-29.99	3 (7.0)	3 (5.3)	0.917ns
30.00-39.99	1 (2.3)	1 (1.8)	
Systolic blood pressure (mmHg)			
Mean±SD	141.40±23.46	128.77±19.94	0.005**
Range	90.00-200.00	90.00-170.00	
Diastolic blood pressure (mmHg)			
Mean±SD	87.56±11.72	81.40±11.75	0.011*
Range	60.00-120.00	60.00-100.00	

Unpaired Student's 't' test/Chi-square test
ns = Not significant
* = Significant (P<0.05)
** = Highly Significant (P<0.01)

Table-II shows the basic data of the study patients. Among the 100 study patients, 64 were male and 36 were female. In male patients, 27(62.8%) and in female 16 (37.2%) showed ocular fundus abnormality. Male and female showed no significant difference (p=0.827) in development of ocular fundus abnormality.

The mean (±SD) age of group-A (Ocular fundus abnormality present) was 45.56 ±13.79, and that of group- B (Ocular fundus abnormality absent) was 37.46 ±14.46. So the difference is not significant between these two groups (p = 0.827).

The mean (±SD) BMI of the patients with retinopathy (group-A) was 21.97±3.53 kg/m², and without retinopathy (group-B) was 21.76±2.93 kg/m² and the difference is not significant (p=0.740).

The mean (±SD) systolic blood pressure in retinopathy positive group-A was found, 141.40±23.46 (mm of Hg), and that of group-B, where the patients have no retinopathy, was 128.77±19.94 (mm of Hg) and shows significant difference (p = 0.005).

The mean (±SD) diastolic blood pressure in group-A was found 141.40±23.46 (mm of Hg), and that of group-B was 128.77±19.94 (mm of Hg) and the difference is highly significant (p = 0.005).

Table-III Laboratory investigation findings of the study patients

Parameters	Group A (n=43)	Group B (n=57)	P value
Haemoglobin (g/dl)			
Mean±SD	9.51±1.82	11.16±2.39	0.0001***
Range	5.80-15.10	6.70-18.90	
	No. (%)	No. (%)	
[a]≥12.0/11.5 (Male/Female)	3 (7.0)	21 (36.8)	0.001**
<12.0/<11.5 (Male/Female)	40 (93.0)	36 (63.2)	
Urinary total protein (g/24h)			
Mean±SD	2.47±2.06	4.16±3.25	0.003**
Range	0.59-10.40	0.18-12.60	
	No. (%)	No. (%)	
[a]≤0.3	0	1 (1.8)	1.000ns
>0.3	43 (100.0)	56 (98.2)	
Serum creatinine (µmol/L)			
Mean±SD	422.57±256.73	196.52±161.55	0.0001***
Range	84.00-1228.00	62.00-961.10	
	No. (%)	No. (%)	
[a]60-120	4 (9.3)	28 (49.1)	0.0001***
>120	39 (90.7)	29 (50.9)	
Serum cholesterol (mmol/L)			
Mean±SD	5.75±2.69	8.18±3.28	0.0001***
Range	2.40-13.70	2.30-14.70	
	No. (%)	No. (%)	
[a]3.3-6.3	21 (48.8)	12 (21.1)	0.003**
>6.3	22 (51.2)	45 (78.9)	
Triglyceride (mmol/L)			
Mean±SD	3.05±1.76	2.95±1.47	0.761ns
Range	1.20-8.30	1.20-7.60	
	No. (%)	No. (%)	
[a]<2.3	25 (58.1)	26 (45.6)	0.215ns
≥2.3	18 (41.9)	31 (54.4)	
Dyslipidaemia			
	No. (%)	No. (%)	
Positive TG≥2.3/SChol >6.3)	29 (67.4)	47 (82.5)	0.082ns
Negative (TG<2.3/SChol≤6.3)	14 (32.6)	10 (17.5)	

[a]Normal value

Unpaired Student's 't' test/Chi-square test/Fisher's Exact test

ns = Not significant

** = Significant (P<0.01)

*** = highly Significant (P<0.001)

Table-III: shows the laboratory investigations findings among the two groups. The mean (±SD) haemoglobin level of patient with retinopathy (group-A) was 9.51±1.82 g/dl, and that of patients without retinopathy (group B) was 11.16±2.39 g/dl. The difference is highly significant (p =0.0001).

It was observed that, the mean (±SD) urinary total protein (UTP) in patient with retinopathy (group-A) was 2.47±2.06 g/24 hour, and in patients without retinopathy was 4.16±3.25 g/24 hour (p=0.003).

The mean (±SD) serum creatinine of patient with retinopathy was observed 422.57±256.73 µmol/L, and in patients without retinopathy was 196.52±161.55 µmol/L. The difference was highly significant (p=0.0001).

The mean (±SD) cholesterol level of group-A and group-B were 5.75±2.69 mmol/L and 8.18±3.28 mmol/L respectively (p=0.0001). The mean (±SD) triglyceride level of group-A and group-B was 3.05±1.76 mmol/L and 2.95±1.47 mmol/L, (p = 0.761).

Table-IV: Basic data of patients based on CKD stages

Parameters	**Stage 4-5 (n=49)**	**Stage 1-3 (n=51)**	**P value**
Age (years)			
Mean±SD	46.65±13.71	35.45±13.53	0.0001***
Range	20.00-73.00	16.00-65.00	
BMI (kg/m^2)			
Mean±SD	21.59±3.16	22.11±3.22	0.416^{ns}
Range	15.20-29.43	15.62-34.63	
Systolic blood pressure (mmHg)			
Mean±SD	142.65±21.48	126.08±20.13	0.0001***
Range	100.00-200.00	90.00-180.00	
Diastolic blood pressure (mmHg)			
Mean±SD	87.76±11.18	80.49±11.93	0.002**
Range	60.00-120.00	60.00-100.00	
Haemoglobin (g/dl)			
Mean±SD	9.33±1.44	11.53±2.48	0.0001***
Range	6.30-12.90	5.80-18.90	
Urinary total protein (g/24h)			
Mean±SD	2.30±1.62	4.53±3.43	0.0001***
Range	0.18-8.78	0.40-12.60	
Serum cholesterol (mmol/L)			
Mean±SD	5.66±2.44	8.56±3.33	0.0001***
Range	2.40-11.90	2.30-14.70	
Triglyceride (mmol/L)			
Mean±SD	2.76±1.46	3.22±1.70	0.149^{ns}
Range	1.20-6.70	1.20-8.30	

Unpaired Student's 't' test
ns = Not significant
** = Significant (P<0.01), *** = Highly Significant (P<0.001)

Table – IV shows basic and laboratory data of patients based on CKD stage. Here it was observed that, the mean (±SD) age of patients in CKD stages 4-5 was 46.65±13.71 years and 35.45±13.53 in CKD stages1-3.

The mean (±SD) in CKD stages 4-5 was 21.59±3.16 kg/m² and 22.11±3.22 kg/m² in CKD stages 1-3.

The mean (±SD) systolic blood pressure in CKD stages 4-5 was 142.65±21.48 mm of Hg and 126.08±20.13 mm of Hg in CKD stages 1-3. The difference is significant. (p=0.0001).

The mean(±SD) diastolic blood pressure in CKD stages 4-5 was 87.76±11.18 mm of Hg and 80.49±11.93 mm of Hg in CKD stages 1-3. The p value is 0.002.

The mean (±SD) haemoglobin level in CKD stages 4-5 was 9.33±1.44 g/dl and 11.53±2.48 g/dl in CKD stages 1-3. The result is significantly different (p=0.0001).

The mean (±SD) urinary total protein (UTP) level in CKD stages 4-5 was 2.30±1.62 g/24 hour, and 4.53±3.43 g/24 hour in CKD stages 1-3. The p value was 0.149.

The mean (±SD) serum cholesterol level in CKD stages 4-5 was 5.66±2.44 mmol/L, and 8.56±3.33mmol/L in CKD stages 1-3. The difference is significant. (p=0.0001).

The mean (±SD) serum triglyceride level in CKD stages 4-5 was 2.76±1.46 mmol/L, and 3.22±1.70 mmol/L in CKD stages 1-3. It shows no significant difference (p=0.0001).

Table - V: Causes of CKD among the study patients

Causes of CKD	Frequency	Percentage (%)	Ocular fundal abnormality n (%)
Total CKD patients	100		
Glomerulonephritis	58	58%	17 (29.3%)
Diabetes mellitus	21	21%	13(61.9%)
Others			
Obstructive uropathy	7	7%	3(61.9%)
Hypertension	5	5%	5(100%)
ADPKD	3	3%	3(100%)
Alport's syndrome	1	1%	1(100%)
Analgesic nephropathy	1	1%	0
Ethanol poisoning	1	1%	1(100%)
Unclassified	3	3%	0

*CKD = Chronic kidney disease
*ADPKD = Autosomal dominant polycystic kidney disease

Table - V shows the causes of CKD among the study patients. The cause of CKD in 58 patients was glomerulonephritis. Diabetes mellitus was the cause of CKD in 21 patients. The other causes were obstructive uropathy (n=7), hypertension (n=5), ADPKD (n=3), Alport's syndrome (1%), analgesic nephropathy (1%), and ethanol poisoning (1%). In 3 patients, no cause of CKD was found.

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It was observed that, 17 (29.3%) patients with glomerulonephritis, 13(61.9%) patients with diabetes, 3(61.9%) patients of obstructive uropathy, 5(100%) patients with hypertensive nephrosclerosis, 3(100%) patients with ADPKD , 1(100%) patient with Alport's syndrome, 1(100%) patient with ethanol poisoning showed ocular fundus abnormality.

Table-VI: Different types of ocular fundus abnormality (n=43)

Types of ocular fundus abnormality	**Frequency**	**% among total patients**	**% among fudus abnormality**
Total study patients	100		
Ocular fundus abnormality	43		
Only hypertensive retinopathy	30	30%	69.76%
Only diabetic retinopathy	05	5%	11.6%
Mixed hypertensive and diabetic retinopathy	08	8%	18.6%
Maculopathy	11	11%	25.58%
Optic atrophy	02	2%	4.6%
Retinal deposit	02	2%	4.6%

**Some participants have more than one finding.

Table – VI shows different types of ocular fundus abnormalities. Among the 43 (43%) patients with retinal abnormality, 30(69.76%) subjects showed only hypertensive retinopathy and 5(11.6%) subjects showed only diabetic retinopathy. Mixed hypertensive and diabetic retinopathy was found in 8(18.6%) subjects. Maculopathy was seen in 11 (25.58%) subjects. Optic atrophy was seen in 2(4.6%) subjects and drusen like retinal deposit was seen in 2(4.6%) subjects.

Table-VII: Different types of hypertensive retinopathy

Types of hypertensive	**Frequency**	**% among retinopathy**	**% among *HTN retinopathy**
Total study patients	100		
Total retinopathy	43		
Only hypertensive retinopathy	30	69.76%	78.95%
Grade-I hypertensive retinopathy	04	9.3%	10.52%
Grade-II hypertensive retinopathy	20	46.51%	52.63%
Grade-III hypertensive retinopathy	11	25.58%	28.95%
Grade-IV hypertensive retinopathy	03	6.98%	7.89%
Hypertensive retinopathy with maculopathy	03	6.98%	7.89%
Hypertensive retinopathy with Optic disc swelling	03	6.98%	7.89%
Hypertensive retinopathy with optic atrophy	01	2.32%	2.63%

*HTN = hypertensive

**Some participants have more than one finding.

Table-VII shows the different types of hypertensive retinopathy. Among the 43 study patients with retinal abnormality, only hypertensive retinopathy was seen in 30 (69.76%) patients. Grade - I hypertensive retinopathy was seen in 4(9.3%), grade – II hypertensive retinopathy was seen in 20(46.51%) patients, grade-III was in 11(25.58%) and grade – IV was seen in 3(6.98%). Maculopathy associated with hypertensive retinopathy was seen in 3(6.98%) patients. Only 1(2.63%) patient with hypertensive retinopathy showed optic atrophy.

Table-VIII: Different types of diabetic retinopathy.

Types of diabetic retinopathy	**Frequency**	**% among total retinopathy**	**% among diabetic retinopathy**
Total study patients	100		
Total retinopathy	43		
Diabetic retinopathy	13	30.23%	
Only diabetic retinopathy	05	11.63%	38.46%
Both diabetic and hypertensive retinopathy	08	18.6%	61.54%
Background non-proliferative diabetic retinopathy	08	18.6%	61.54%
Pre-proliferative diabetic retinopathy	02	4.65%	15.38%
Proliferative diabetic retinopathy	03	6.98%	23.06%
Diabetic retinopathy with maculopathy	08	18.6%	61.54%
Diabetic retinopathy with optic atrophy	01	2.32%	7.69%

**Some participants have more than one finding.

Table -VIII shows the different types of diabetic retinopathy. Among the total 43 patients with retinal abnormalities, diabetic retinopathy was seen in 13 (30.23%) patients. Background non-proliferative diabetic retinopathy was seen in 8 (61.54%) patients. Pre-proliferative diabetic retinopathy was observed in 2(15.38%) patients and proliferative diabetic retinopathy was observed in 3(23.7%) patients. Diabetic maculopathy was seen in 8(61.54%) patients. And only 1(7.69%) patient with diabetic retinopathy showed optic atrophy.

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Table-IX: Types/pattern of ocular fundal abnormalities in the study subjects (n=43)

Types of diabetic retinopathy	Frequency	% among total patients	% among total retinopathy
Total study patients	100		
Total retinopathy	43		
A-V nipping	34	34%	79%
Retinal Haemorrhage	26	26%	60.46%
Soft exudate	14	14%	32.55%
Hard exudate	13	13%	30.23%
Microaneurysm	13	13%	30.23%
Maculopathy	11	11%	25.58%
Neovascularization	03	3%	6.98%
Papilloedema	03	3%	6.98%
Optic atrophy	02	2%	4.65%
Retinal deposit	02	2%	4.65 %

**Some participants have more than one finding.

A-V nipping = Arterio-venous nipping.

Table-IX: shows types of fundal abnormalities of the study subjects. Total 43 patients showed ocular fundal abnormalities. Among them, A-V nipping was found in 34(79%) patients. Retinal haemorrhage was found in 26(60.46%) patients. Soft exudate was found in 14(32.55%) patients and hard exudates in 13 (30.23%) patients.

Microaneurysm was found in 13(30.23%) patients. Maculopathy in 11(25.58%) patients, neovascularisation in 3(6.98%), papilloedema in 3(6.98%), optic atrophy in 2(4.65%), and retinal deposit in 2(4.65%) patients.

It also observed that retinopathy was significantly (p =0.0001) increased with reduction of eGFR.

Table-XI. Retinal abnormalities in different stages of CKD (n=43)

Parameters	n	CKD Stage 1-3 No. (%)	CKD Stage 4 No. (%)	CKD Stage 5 No. (%)
Retinal abnormality	43	12 (27.9)	11 (25.58)	20 (46.51)
Only hypertensive retinopathy	30	7 (23.3)	8 (26.66)	15 (50)
Only diabetic retinopathy	5	1 (20)	2 (40)	2 (40)
Mixed hypertensive and diabetic retinopathy	8	2 (25)	2 (25)	4 (50)
A-V nipping	34	6 (17.65)	8 (23.53)	20 (58.82)
Retinal haemorrhage	26	8 (30.76)	3 (11.54)	15 (57.7)
Maculopathy	11	2 (18.2)	3 (27.27)	6 (54.5)
Microaneurysam	13	5 (38.5)	3 (23.07)	5 (38.5)
Papilloedema	3	1 (33.3)	0 (0)	2 (66.7)
Preproliferative diabetic retinopathy	2	1 (50)	0 (0)	1 (50)
Proliferative diabetic retinopathy	3	1 (33.3)	0 (0)	2 (66.7)
Optic atrophy	2	0 (0)	1 (50)	1 (50)
Background diabetic retinopathy	8	3 (37.5)	2 (25)	3 (37.5)

**Some participants have more than one finding.

Table – XI shows retinal abnormalities in different stages of CKD. Among the 43 patients with retinal abnormalities, 27.9% (n = 12) was in CKD stage 1-3, 25.58% (n=11) in CKD stage-4 and 46.51% (n = 20) were in CKD stage V. 50% (n = 19) of the hypertensive retinopathy was in CKD stage V. In patients with diabetic retinopathy, 38.5% (n=5) patient was in both CKD stage-1 to 3 and CKD stage -5, and 23.07% (n=3) was in CKD stage -4.

Discussion:

Chronic kidney disease (CKD) affects different organs of the body including eye. To find out the ocular fundus abnormalities in CKD patients, we evaluated one hundred admitted patients in dept of Nephrology, BSMMU, who fulfilled the inclusion criteria.

A recent study by Grunwald et al showed that among 1904 CKD patients in the United States, the overall prevalence of ocular fundus pathology was as high as 45%[15].

Bixia et al, also did similar study among Chinese population. In that cross-sectional study of the Chinese population, the prevalence of overall ocular fundus pathology was found to be 32% of patients with CKD, and was significantly higher than that of patients without CKD[14].

In this study, out of 100 CKD patients, 43 (43%) patients showed ocular fundus abnormality. Therefore this finding has got similarity with studies mentioned.

In a cross-sectional study in Singapore, both retinal arteriolar diameters and retinopathy was found to be independently associated with presence of CKD[16].

In a CRIC (Chronic Renal Insufficiency Cohort) by Grunwald et al[15] showed that male sex have significantly higher retinopathy than female. (Male =48.10%, female= 42.15%, p<0.05). In our study, 64 (64%) patients were male and 36(36%) were female. Among the male patients, 27 (62.8%) and among the female 16(37.2) showed ocular fundus abnormality. So there is no significant statistical difference between male and female (p=0.827) in development of retinopathy.

In two different studies by Tien et al.[14] and another by Grunwald et al.[15], both observed retinopathy was high in older age group.In this series, the mean (±SD) age of retinopathy positive and retinopathy negative patients were 45.56±13.79 years and 37.46±14.46 years and p=0.006. So our finding is similar with their result.

Bixia et al showed significantly high BMI in patients with retinopathy. Another study by Grunwald et al showed significantly low BMI in patients with retinopathy. In this study, BMI showed no significant difference between retinopathy positive and retinopathy negative patients (p=0.740) in our study. So relation of BMI with retinopathy remains unexplained[14,15].

In a study by Bixia et al[14] both systolic and diastolic blood pressure were significantly higher in patients with retinopathy than those who had no retinopathy.

In the current study, the mean (±SD) systolic blood pressure in CKD stages 4-5 was 142.65±21.48 mm of Hg and 126.08±20.13 mm of Hg in CKD stages 1-3. So it was significantly higher in patients with retinopathy (p=0.0001). The mean (±SD) diastolic blood pressure in CKD stages 4-5 was 87.76±11.18 mm of Hg and 80.49±11.93 mm of Hg in CKD stages 1-3, which was also significantly high in patients with retinopathy (p=0.002). So similar result was observed between the current and previous study.

In the present study, low hemoglobin level was strongly associated with development of retinopathy. The hemoglobin level in retinopathy positive group was 9.51±1.82 g/dl, and retinopathy negative group was 11.16±2.39 g/dl, and the p value was 0.0001, which was highly significant.

Qiao et al in Finland studied on 1691 diabetic patients found that, the diabetic patients with hemoglobin level lower than 12 mg/dl were two times more likely to develop diabetic retinopathy (DR) [17]. Davis et al reported that low hematocrit is a risk factor for development of diabetic retinopathy (DR)[18]. Regarding the effect of anemia on DR, it seems that anemia-induced hypoxia leads to the increased release of vaso-proliferative factors (X factor) and bring about the progression of DR[17].

Proteinuria was found to be independently associated with retinopathy, which further support that both retinopathy and proteinuria are markers of systematic microvascular abnormalities. Furthermore, the association between proteinuria and retinopathy existed among participants without hypertension or diabetes, suggesting that susceptibility to microvascular disease may be caused by mechanisms other than those directly stemming from hypertension or diabetes.[14] We had found, the mean (±SD) urinary total protein (UTP) in patient with retinopathy was (2.47±2.06 g/24 hour) was significantly low (p=0.003) than patient without retinopathy (4.16±3.25 g/24 hour). It may be due to sclerosis of renal vasculature in advanced stages of CKD. We founded 2 patients with glomerulonephritis. They were normotensive and non-diabetic, but both had retinopathy.

In this study, high serum creatinine level was also associated with retinal abnormalities. The mean (±SD) serum creatinine of patient with retinopathy (422.57±256.73 µmol/L) was very significantly higher (p<0.001) than in patients without retinopathy (196.52±161.55 µmol/L). The prospective analysis from the Atherosclerosis Risk in Communities Study by Wong et al and the Cardiovascular Health Study by Edwards et al suggested that, retinal microvascular abnormalities was associated with deteriorating renal function. The possible explanation for the retinopathy-kidney link might be, retinal microvascular abnormalities resulting from diabetes, hypertension, cigarette smoking, inflammation and other process may provide a common pathophysiologic link for the development and progression of CKD[19,20]. Grunwald et al showed that, the prevalence of retinopathy was significantly higher among participants with CKD, compared with participants without CKD[15].

Evaluation of lipid profile showed that, the mean (±SD) cholesterol level of retinopathy positive and retinopathy negative patients were 5.75±2.69 mmol/L and 8.18±3.28 mmol/L respectively, which was higher in patients without retinopathy. It may be due to the maximum glomerulonephritis patients with proteinuria was in the group with no retinopathy.

Serum triglyceride was not associated with development of retinopathy in the present study. The mean (±SD) triglyceride level of group-A and group-B was 3.05±1.76 mmol/L and 2.95±1.47 mmol/L, and not statistically significant (p=0.761). In a study by Tien and Josef et al. retinopathy was associated with high cholesterol levels and higher triglyceride levels[21].

In a study by Rajeev Deva and Mohamad Afzal et al the main causes of CKD in 150 study patients were due to diabetes (54, 36%). then glomerulonephritis (38, 25%); hypertension/renovascular disease (26, 17%); reflux or other structural malformations (8, 5%); polycystic kidney disease (7, 5%); cancer, trauma, and nephrotoxic agents (9, 6%); or unknown causes (8, 5%)[22].

In current study, the main cause was glomerulonephritis (58%, n =58), then diabetes (21%, n =21). The other causes are obstructive uropathy (7%, n=7), hypertension (5%, n =5), ADPKD (3%, n=3), Alport's syndrome (1%), analgesic nephropathy (1%), and ethanol poisoning (1%). In 3 patients, we could not found any cause of CKD.

We had found, 43 patients showed retinal abnormality. Of them 30(69.76%) patients showed only hypertensive retinopathy and 5 (11.6%) patients showed only diabetic retinopathy. 8(18.6%) patients had both hypertensive and diabetic changes on their ocular color fundal examination. Optic atrophy was seen in 2(4.6%) patients and drusen like retinal deposit was seen in 2(4.6%) patients.

Among the 38 (88.37%) patients with hypertensive retinopathy, the most common abnormality we had found was grade-II hypertensive retinopathy (21, 55.26%). Then grade-III (10, 26.31%) and grade-I hypertensive retinopathy (4, 10.52%). The least we found was grade–IV hypertensive retinopathy (3, 7.89%). Soft exudates, which was due to hypertensive retinopathy was found in 32.55% (n = 14) patients. Maculopathy was seen in 7.89% (n=3) patients. Only 1 patient with hypertensive retinopathy showed optic atrophy.

Of the 13 patients, 38.46% (n=5) with diabetic retinopathy, and 61.54% (n=8) patients showed combination of both diabetic and hypertensive retinopathy in their fundal photograph. Majority of them, about 61.54% (n=8), had non-proliferative background diabetic retinopathy. 15.38% (n=02) patients showed pre-proliferative diabetic retinopathy and 230.7% (n=03) patients showed vision threatening proliferative diabetic retinopathy with neovascularisation. Hard exudates, which was due to diabetic retinopathy was found in 30.23% (n = 13) patients.

Microaneurysm , which was the hallmark of diabetic retinopathy was found in 30.23% (n = 13) patients. More than half of the patients 61.54% (n=8), showed diabetic maculopathy. Optic atrophy was seen in 7.69% (n=1) patients with diabetic retinopathy.

In a study by Rajeev et al 41 (41 of 149, 28%) patients with CKD stages 3 to 5 had a moderate-severe diabetic retinopathy, compared with 16 (11%) patients with CKD stages 1 to 2 (OR 3.18, CI 1.69 to 5.98, $P < 0.001$). In addition, diabetic retinopathy became more common as renal function deteriorated in CKD stages 3 to 5 ($P < 0.001$). But they did not found any difference in level of hemoglobin A1c in patients with diabetic retinopathy with CKD stages 3 to 5 compared with CKD stages 1 to 2 (7.9 ± 1.81 and 8.5 ± 2.34%, respectively, P = 0.30) They also found proliferative diabetic retinopathy (PDR) were more common in CKD stages 3 to 5 than CKD stages 1 to 2 (18 of 149, 12% compared with 2 of 150, 1%, OR 10.17, CI 2.32 to 44.65, P = 0.001) and similarly became more common as renal function deteriorated ($P < 0.001$). In the present study, diabetic retinopathy in CKD stage 1-3 and CKD stage 4-5 had no significant statistical difference (p=1.0)[22].

Maculopathy in current study was seen in 11 (25.58%) patients, of them, 3(6.98%) were associated with hypertensive retinopathy and 8(18.6%) were diabetic maculopathy. In a study, it was observed that macular degeneration was increased in patients with CKD stages 3 to 5 compared with patients with CKD stages 1 to 2. They had seen 62 (62 of 140, 44%) patients with CKD stages 3 to 5 had these changes compared with 43 (43 of 148, 29%) patients with CKD stages 1 to 2 (OR 1.94, CI 1.19 to 3.16, P = 0.010)[22].

The study by Grunwald and Alexander et al observed that, lower eGFR was associated with a much higher incidence of fundus pathology. The percentage of participants with any eye pathology was 60% in those with eGFR <30 and 35% in participants with eGFR ≥50[15].

In the current study, it was observed that, the mean (±SD) eGFR of patients with retinopathy positive was 22.98±18.16 ml/min per 1.73 $m^{2,}$ which was significantly lower ($p < 0.001$) than those who do not have retinopathy (50.69±24.95 ml/min per 1.73 $m^{2)}$. It also showed that retinopathy was significantly (p=0.0001) higher in advanced stages of CKD than in early stages. So low eGFR was a risk factor for development of retinopathy as retinopathy significantly increases with decreasing eGFR.

Conclusion:

Our study suggests that, ocular fundus abnormality is common among the study populations. Hypertensive retinopathy, non- proliferative diabetic retinopathy, vision threatening proliferative diabetic retinopathy, maculopathy is not uncommon in CKD patients.

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Original Article

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Preventing Pain on Propofol Injection: A Comparative Study between Fentanyl and Dexamethasone

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Abstract:

Background and aim of study: Propofol is widely used for induction of general anesthesia, although the pain during its injection remains a concern for all anesthesiologists. A number of techniques have been adopted to minimize propofol-induced pain. This placebo-controlled study was conducted to compare the efficacy of fentanyl and dexamethasone in terms of attenuation of propofol-induced pain during induction ofgeneral anesthesia. Materials and methods: Seventy five American Society of Anesthesiologists (ASA) physical status I and II patients undergoing general anesthesia were randomly allocated into three groups. A 20-gauge cannula was inserted into a superficial vein of dorsum of the left hand, and after the occlusion of venous drainage, Group F (fentanyl group), group D (dexamethasone group) and group C (control group) were pretreated with 2 mcg/kg of fentanyl in 10 ml saline, 0.1 mg/kg of dexamethasone in 10 ml saline and 10 ml of saline without any drug, respectively. The occlusion was released after 90 seconds and one-fourth of the total propofol dose was injected into the vein over a period of 5 seconds. During the injection of propofol, patients' pain was assessed and recorded as 0–3, corresponding to no, mild, moderate or severe pain, respectively. Chi squire test was used for the statistical analysis of propofol injection induced pain. For all analysis, differences were considered to be significant at $p<0.05$. Results: The overall incidence of pain on propofol injection was lower in fentanyl group (20%) and dexamethasone group (24%) than in control group (72%) ($P<0.05$). There was no significant difference in the incidence of pain between fentanyl and dexamethasone group ($P>0.05$). Four (16%) and three (12%) patients in control group had moderate and severe pain respectively. Five patients (20%) in fentanyl group, six patients (24%) in dexamethasone group and eleven patients (44%) in control group had mild pain. There was no moderate or severe pain in fentanyl and dexamethasone group. Conclusion: Pre-treatment with intravenous 2 mcg/kg fentanyl is equally effective as intravenous dexamethasone 0.1 mg/kg in preventing propofol injection induced pain and both were better than pretreatment of normal saline.

Keywords: Fentanyl, dexamethasone, pain on propofol injection (POPI)

Introduction:

Pain on injection of propofol (2,6-diisopropyl phenol) is considered to be a problem for the anesthesiologists. The incidence of pain on propofol injection (POPI) is 28% to 90% in adults and 28% to 85% in children[1]. Propofol has been commonly used for induction and maintenance of anesthesia, but pain of propofol injection can be extremely distressing to the patients[2]. The mechanism of pain due to propofol injection has been unclear. Propofol belongs to the group of phenol and can directly irritate the skin, mucous membrane and venous intima and could immediately stimulate nociceptors and free nerve endings[3]. The concentration of propofol in solution is associated with the pain. By its indirect action on the endothelium, it was considered that propofol activates the kallikrein-kinin system and releases bradykinin, through producing venous dilation and hyper permeability, which increases the contact between aqueous phase of propofol and free nerve

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endings, arises in delayed pain within half a minute[4,5]. Pain on injection of propofol may be related to release of local kininogens and that the non-steroidal anti-inflammatory drugs (e.g.ketorolac) may have a role in reducing that pain[6]. Although it is not a serious complication, efforts are assumed to reduce the severity of the pain or discomfort.

Various pharmacological and non-pharmacological interventions have been done for investigation and elimination of propofol-inducedpain[7,-9]. Such as, cooling or diluting the propofol solution, and pretreatment with lignocaine, ephedrine, ondansetron, metoclopramide, nafamostatmesilate, opioids, dexamethasone, hydrocortisone, thiopental, or ketamine[3,7,10-14].

Fentanyl is a short-acting pure opioid agonist commonly used for intraoperative and postoperative analgesia. Also, it has some peripherally mediated analgesic action within the clinical dose range[15].

Recent studies have shown that dexamethasone reduces postoperative pain, nausea and vomiting[16,17]. Propofol releases nitric oxide (NO) from the vessels animal and human models and causes pain in vein[18,-20]. In addition, NO produced by vascular endothelium leading to guanylatecyclase catalyzes the conversion of guanosine triphosphate to guanosine monophosphate which in turn, catalyzes the production of prostaglandin E_2 causing hyperalgesia[20]. The effect of corticosteroids such as dexamethasone has been shown to reduce the production of NO[21,22].

The objective of the present study was to compare the effect of pretreatment with fentanyl, dexamethasone and normal saline as placebo, using the venous occlusion technique for prevention of pain on propofol injection.

Materials and methods:

The study was conducted at Dhaka central international medical college hospital, Dhaka during the period of January to April, 2018. Having obtained the informed consent, 75 patients aged 18–55 years, American Society of Anesthesiologists (ASA) physical status I and II and scheduled for general anesthesia were included in this study. All relevant investigations for GA fitness were done. Patients were randomly allocated into one of the three groups of 25 each. Patients with habituation to analgesics, sedatives or anti-anxiety drugs; allergic diseases or sensitivity to opioids or steroids and infection on the dorsum of their left hands were excluded from the study.

None of the patients was pre-medicated before entering the operation room. After routine monitoring (ECG, noninvasive arterial pressure and pulse oximeter) a 20-gauge cannula was inserted into a superficial vein of the dorsum of left hand and lactated Ringer's solution was infused at 100 ml per hour. After 5 minutes, lactated Ringer's infusion was stopped and the arm with the intravenous (i.v.) line was elevated for 15 seconds for gravity drainage of venous blood. After occluding the venous drainage using a manual blood pressure cuff as tourniquet (pressure inflated to 50 mm Hg) on the upper arm, the patients were pretreated over a period of 10 seconds with one of the pretreatment solutions; 2 mcg/kg of fentanyl diluted to 10 ml (Group F), 0.1 mg of dexamethasone (Group D) or 10 ml of normal saline without any drug as control (Group C). An independent anesthesiologist prepared the solutions and the investigator was blind to the contents of the solutions. After 90 seconds, the occlusion was released and one-fourth of the total calculated dose of propofol was delivered through the i.v. line over a period of 5 seconds. No other analgesics or sedatives were administered before propofol injection. During the injection, the patients were asked standard questions regarding comfort of the injection. A clinician blinded to the group assignment evaluated propofol-induced pain as described. Thereafter, induction of anesthesia was continued by the remainder of the calculated dose of propofol (2 mg/kg) and vecuronium 0.1 mg per kg to facilitate endotracheal intubation.

General anesthesia was maintained with oxygen, nitrous oxide and halothane. After the end of surgery patients were reversed by neostigmine and atropine as usual. Heart rate and mean arterial pressure were recorded as basal, pre-intubation and 1 minute after intubation (post intubation). Within 24 h after the operation, the injection site was checked for pain, edema or allergic reaction by an anesthesiologist who was blinded to group assignment.

Grading of pain:

0= No pain

1=Mild pain (pain reported only in response to questioning without any behavioral signs)

2= Moderate pain (pain reported in response to questioning and accompanied by a behavioral sign or pain reported spontaneously without questioning).

3= Severe pain (strong vocal response or response accompanied by facial grimacing, arm withdrawal or tears).

Statistical analysis:

For comparison of quantitative variables between the three groups, the ANOVA test and for qualitative variables the Chi-squared test was used. The statistically significant level was $P<0.05$.

Results:

Table I- Shows there were no significant differences in demographic data including age, weight and sex between the study groups.

Table II- Shows the base line, preintubation and postintubation hemodynamic changes. Basal MAP and HR are comparable in all three groups. There is significant difference of MAP and HR between control and other two groups during postintubation period ($p<0.05$).

Table III- Shows the overall incidence of pain on propofol injection was lower in group F (fentanyl group) (20%), group D (dexamethasone group) (24%) than in group C (control group) (72%) ($P<0.05$). There was no significant difference in the incidence of pain between fentanyl and dexamethasone group ($P>0.05$). Four (16%) and three (12%) patients in control group had moderate and severe pain respectively. Five patients (20%) in fentanyl group, six patients (24%) in dexamethasone group and eleven patients (44%) in control group had mild pain. There was no moderate or severe pain in fentanyl and dexamethasone group. There were no complications related to study drugs in the groups.

Table I: Comparison of demographic data between the groups

Parameter	Group F (Fentanyl)	Group D (dexamethasone)	Group C (Control)	p value
Age in year (mean±SD)	44.63±7.84	46.23±8.93	45.97±7.91	p>0.05
Weight in kg (mean±SD)	71.72±6.84	69.86±9.76	69.95±9.23	p>0.05
Sex (M/F)	12/13	14/11	13/12	p>0.05

Table II: Changes of mean arterial pressure and heart rate between the groups

Hemodynamic parameter	Basal Group F/D/C	Pre intubation Group F/D/C	Post intubation Group F/D/C
Mean arterial pressure (mm Hg)	92/89/91	82/80/83	95/97/117
Heart rate/ min	80/82/83	68/73/75	82/84/104

Table III: Incidence and severity of pain following propofol injection between the groups

Characteristics of pain	Group F (Fentanyl) (n=25) %	Group D (Dexamethasone) (n=25) %	Group C (Control) (n=25) %	p value
No pain	20 (80%)	19 (76%)	7 (28%)	p<0.05
Pain	5 (20%)	6 (24%)	18 (72%)	p<0.05
Mild pain	5 (20%)	6 (24%)	11 (44%)	p<0.05
Moderate pain	0	0	4 (16%)	p<0.05
Severe pain	0	0	3 (12%)	p<0.05

Discussion:

It seems that the prevention of painful irritation caused by propofol injection is necessary and important because it causes discomfort for patient and hemodynamic changes in response to pain by irritation can lead to myocardial ischemia in high-risk patients. Studies have shown that the mechanism of painful irritations by intravenous injection of propofol had several factors and propofol in the injected site releases NO[23]. Nerve endings sensitive to NO which cause painful irritations are well known in human veins.

This study shows the overall incidence of pain on propofol injection was lower in fentanyl group (20%), dexamethasone group (24%) than in control group (72%) (P<0.05). There was no significant difference in the incidence of pain between fentanyl and dexamethasone group (P>0.05). Four (16%) and three (12%) patients in control group had moderate and severe pain respectively. Five patients (20%) in fentanyl group, six patients (24%) in dexamethasone group and eleven patients (44%) in control group had mild pain. There was no moderate or severe pain in fentanyl and dexamethasone group.

Shreyasi et al[24] had a study on prevention of POPI using lignocaine and fentanyl and they observed pain on propofol injection was in the lignocaine pretreatment group 14.3%, fentanyl 42.9% and normal saline 71.4%.In our study fentanyl group had lower pain (20% vs 42.9%) but control group pain was same (72% vs 71.4%).

In the study conducted by Karbasi et al[25] concluded that dexamethasone can be used as an effective and routine drug in the operating room to reduce propofol injection pain in children before the induction dose of propofol, hence increased satisfaction of children from anesthesia.

Leili et al[26] conducted a study on prevention of propofol injection pain using granisetron and dexamethasone .The results of this study revealed that pretreatment with dexamethasone and granisetron can be effective on the incidence and intensity of pain caused by the injection of intravenous propofol and pain was experienced 88%, 50.7% and 49.4% in the placebo group in the granisetron and dexamethasone groups respectively.

Ahmad et al[27] compared the effect of dexamethasone and intravenous lidocaine on intravenous propofol pain along with saline. The results of the present study indicated the effect of dexamethasone on reducing the pain by intravenous injection of propofol; however, we used lower doses of dexamethasone.

Conclusion:

It can be concluded after this study, that fentanyl 2mcg/kg or dexamethasone 0.1 mg/kg intravenous

pretreatment appears to be effective in reducing both the incidence and severity of the pain during propofol injection when compared to saline placebo.

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Original Article

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Clinicopathological Profile and Outcome of 58 Lymph Node Tuberculosis Cases in Tertiary Care Hospital in Dhaka City

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Abstract:

In countries like Bangladesh, tuberculous lymphadenitis is a common extrapulmonary site of tuberculosis. Objectives: The objective of the present study is to describe the clinicopathological profile and outcome of tuberculous lymphadenitis (TB) cases in our setting. Methods: This is a non randomized prospective observational study was carried out in two teritiary care hospitals. Patients more than 12 years of age and Patients presenting with cervical lymph node enlargement are included in this study. After taking informed written consent, clinical points are noted and fine-needle aspiration cytology (FNAC) or biopsy of lymph nodes were done and histologically evaluated and the patients were followed up further. Results: Most patients presented with fever (62.1%), weight loss (51.7%), night sweating 62.1%), anorexia (55.2%), and cough (27.6%). Among all, 40 (69%) patients presented with multiple enlarged lymph node group and 18 (31.0%) had involvement of single group. Cervical group involvement was the most common 48 (82.8%), axillary was 8 (13.8%) and mediastinal was 2 (3.4%). Matting of lymph node was present in 39 (67.2%) cases. Among all, 48 (82.8%) cases were diagnosed by FNAC and 10 (17.2%) was diagnosed by biopsy. In microscopic evaluation, 36 (62.1%) cases had caseous necrosis, 54 (93.1%) had epithelioid cells and 15 (25.9%) had giant cells. Regarding other investigations, 16 (27.6%) patients had positive Mantoux test (MT), 9 (15.5%) had radiological opacity suggestive of pulmonary TB, and three cases were found sputum positive for acid-fast bacilli. Regarding outcome evaluation, 40 (69%) cases were declared cured, 14 (24.1%) were lost to follow-up, one case died, and four cases was declared multi drug resistant tuberculosis (MDR-TB). Conclusion: In this study, bacteriological evaluation of the response to treatment cannot be done due to difficulty in obtaining follow-up specimens from the lymph node. Response was judged on the basis of clinical features and local examination findings.

Keywords: Extrapulmonary tuberculosis, FNAC, lymph node tuberculosis

Introduction:

Tuberculosis (TB) is one of the most ancient diseases of humankind, and it is prevailing in the society perhaps for several million years[1]. Tuberculosis is caused by a group of closely related bacterial species termed Mycobacterium tuberculosis complex. Today, the principal cause of human TB is M. tuberculosis. Other member of the M. tuberculosis complex that can cause TB include Mycobacterium bovis,

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Mycobacterium microti and Mycobacterium africanum[2]. Regarding TB burden, 2 million people, equal to one third of the world's total population, are infected with the TB bacilli, among them 1.8 million people died every year due to TB. Surprisingly, 98% of TB deaths are in developing world, affecting mostly young adults in their most productive years[3]. In Bangladesh, the prevalence rate of TB is 404/100,000 and the incidence rate was 225/100,000. Regarding the development of multidrug-resistant cases, it is 29% in retreatment cases and 1.6% in new cases. TB/HIV is 0.01% and extrapulmonary TB is around 20% in Bangladesh. It is to be noted that missing cases of TB after diagnosis and initiation of therapy are 39%, which is the alarming data of Bangladesh[4]. Worldwide, between 10% and 25% of TB infections occur in extrapulmonary sites. Those sites are pleura (most common), lymph nodes (LNs), bones and joints, central nervous system (CNS; usual meningitis, but can occur in brain or spine), larynx, pericardium, abdominal sites, kidneys, genitourinary tract, and disseminated (miliary). Data of tuberculous lymphadenitis in Bangladesh are scarce. It is a good opportunity to do a study in this context.

Materials and methods:

This is a non randomized prospective observational study was carried out in the Department of Medicine, Department of ENT & Head Neck Surgery and Department of Surgery of Bashundhara Ad-din Medical College & Hospital and Dhaka Central International Medical College & Hospital, a tertiary care hospital between the period of July 2017 to December 2018.

Inclusion critera:

1. Patients clinically suspected tuberculous lymphadenitis.
2. Patients more than 12 years of age.
3. No history of TB & Anti tubercular therapy

Exclusion critera:

1. Patients where FNAC and/or biopsy of lymps node could not be carried out.
2. Patients less than 12 years of age.

Ethical clearance from the hospital authority was taken before starting the study. After written informed consent, clinical points of suspected (tuberculous lymphadenitis) were noted. Candidates fulfilling the clinical criteria of tuberculous lymphadenitis, a plan for fine-needle aspiration cytology (FNAC) or biopsy, were done. After explanation of the procedure, all cases were undergone either FNAC or biopsy of lymph node. If cytological or histological proof of tuberculous lymphadenitis was found, then that patient was finally included in the study. Diagnosis of tuberculous lymphadenitis was done as per the cytology or tissue report, and all reports were done by same pathologist. TB diagnosis was based on the findings of granulomatous inflammation in the specimen. Acid-fast bacilli (AFB) culture was not done on cytological or tissue specimen. According to the national guideline of Bangladesh, all patients were given CAT-1 anti–TB, and all patients were tagged with DOT's corner of the hospital. Patients were followed up for next 6 months. Follow-up was extended to those who were advised to extend their anti-TB course further. Treatment response and drug toxicities were noted. Follow-up reports were collected physically or by phone call. After collection of all data, it was compiled and analyzed by SPSS version 20 (IBM, Armonk, NY, USA).

Results:

Table-1: Among 58 cases of tuberculous lymphadenitis, females 37 (63.8%) were more than the male 21 (36.2%) patients and most of the patients were at the age group of 21–30 years 14 (24.1%).

Table-2: Most patients presented with fever 18 (62.1%), weight loss 15 (51.7%), night sweating 18 (62.1%), anorexia 16 (55.2%), and cough 8 (27.6%).

Table-3: Among all, 40 (69%) patients presented with multiple enlarged lymph node group and 18 (31.0%) had involvement of single group. Cervical group involvement was the most common 48 (82.8%), axillary 8 (13.8%), and mediastinal 2 (3.4%). Matting of lymph nodes were present in 39 (67.2%) cases, 39 (67.2%) had tenderness, and 5 (8.6%) had discharge.

Table-4: Among all, 48 (82.8%) cases were diagnosed by FNAC and 10 (17.2%) were diagnosed by biopsy. Among 58 cases, 36 (62.1%) had caseous necrosis, 54 (93.1%) had epithelioid cells, and 15 (25.9%) had Langhan's type giant cells.

Table-5: Regarding other test results, 16 (27.6%) cases had positive MT test, 9 (15.5%) had concomitant radiological suggestive of pulmonary TB, and three cases (5.2%) were found sputum positive for AFB.

Table-6: Regarding outcome analysis on 58 cases, 40 (69%) were declared cured, 14 (24.1%) were lost to follow-up, one case died, and four cases were declared MDR TB. Extension of treatment >6 months was given in 41 (70.7%) cases, surgical excision of involved LN was done in 6 (10.3%) cases, four cases developed drug toxicity, and one case was diagnosed lymphoma later.

Table -1: Gender, age, and occupation of the study patients

	Frequency (%)
Gender	
Male	21 (36.2.)
Female	37 (63.8)
Age group (years)	
<20	6 (20.7)
21-30	14 (24.1)
31-40	4 (13.8)
41-50	2 (6.9)
>51	3 (10.3)
Mean±SD	30.48±12.68years
Occupation	
Student	3 (10.3)
Homemaker	11 (37.9)
Service	5 (17.2)
Factory work	4 (13.8)
Others	6 (20.7)

SD=Standard deviation

Table- 2: Clinical parameters

Features	Frequency (%)
Fever	18 (62.1)
Weight loss	15 (51.7)
Night sweating	18 (62.1)
Anorexia	16 (55.2)
Cough	8 (27.6)

Table- 3: Lymph node study findings

	Frequency (%)
Number of group involved	
Single	18 (31.0)
Multiple	40 (69.0)
Name of the group	
Cervical	48 (82.8)
Axillary	8 (13.8)
Mediastinal	2 (3.4)
Matting of LN	
Present	39 (67.2)
Tenderness	
Present	39 (67.2)
Discharge	
Present	5 (8.6)

Table 4: Cellular and tissue diagnosis

	Frequency (%)
Method of diagnosis	
FNAC	48 (82.8)
Biopsy	10 (17.2)
Caseous necrosis	
Present	36 (62.1)
Epithelioid cell	
Present	54 (93.1)
Giant cell	
Present	15 (25.9)

FNAC=Fine-needle aspiration cytology

Table- 5: Screening test results

	Frequency (%)
MT test	
Positive	16 (27.6)
Negative	6 (10.3)
Not done	36 (62.1)
CXR PAV	
Xray positive	9 (15.5)
Xray Negative	33 (56.9)
Not done	16 (27.6)
Sputum for AFB	
Present	3 (5.2)
Absent	16 (27.6)
Not done	39 (67.2)

AFB=Acid-fast bacilli, TB=Tuberculosis

Table- 6: Outcome

Outcome	Frequency (%)
Cured	40 (69)
Lost to follow-up	14 (24.1)
Died	1 (3.4)
MDR TB	4 (6.9)
Treatment extended >6 months	41 (70.7)
Surgical excision	
Needed	6 (10.3)
Drug toxicity	
Developed	4 (6.9)
Diagnosis other than TB (lymphoma)	1 (1.7)

MDR TB=Multidrug-resistant TB, TB=Tuberculosis

Discussion:

Extrapulmonary TB affects LNs, gastrointestinal tract, musculoskeletal system, genitourinary system, CNS, pleura, and pericardium, although any organ can be involved. Hippocrates recognized the severity of abdominal TB by pointing out that "diarrhoea attacking a person with emaciation is a mortal symptom."[4,5] In Bangladesh, TB case notifications have increased significantly since 2012, mainly driven by increased numbers of extrapulmonary and clinically diagnosed pulmonary cases[4]. In the present study, among all cases of lymph node TB, females were affected more than the male patients. A study done by Khandkar et al[6] found that female-to-male ratio for tuberculous lymphadenitis was 2.8:1. Hence, the present study findings are consistent with previous studies that found that tuberculous lymphadenitis is more common among women. In Bangladesh, most poor females work in different garment factories, live in a crowded place, and are unaware of health hygiene. These may be reason of female preponderance of tuberculous lymphadenitis in our study. We found that most of the patients were at younger age group. Age differs between patient populations with tuberculous lymphadenitis and PTB. Golden documented a skewed unimodal distribution toward younger age (25–34 years) in tuberculous lymphadenitis populations, while displaying bimodal distribution in their PTB population with peaks at 25–34 years and 65+ years[5]. Most patients presented with fever (62.1%), weight loss (51.7%), night sweating (62.1%), anorexia (55.2%), and cough (27.6%). These are some common constitutional presentation of extrapulmonary TB. General signs (weight loss, sweats, fever, and asthenia) are found in 20%–50%[7]. Among all, 40 (69%) patients presented with multiple enlarged lymph node group and 18 (31.0%) had involvement of single group. Cervical group of lymph node involved was most commonly, 48 (82.8%), axillary 8 (13.8%), and mediastinal 2 (3.4%). Matting of lymph node was present in 39 (67.2%) cases, 39 (67.2%) had tenderness, and 5 (8.6%) had discharge. Involved tuberculous lymphadenitis usually presented as painful swelling of one or more lymph nodes. Most often, the disease is localized to the anterior or posterior cervical chains (70%–90%) or supraclavicular. It is often bilateral, and noncontiguous lymph nodes can be involved[8]. The jugulo-carotidian location is the most common and relapses occur in about 5% of cases[9]. Regarding diagnosis, 48 (82.8%) cases were diagnosed by FNAC and 10 (17.2%) were diagnosed by biopsy. They meet the different histopathological and cytopathological criteria. Among all, 16 (27.6%) had positive MT test, 9 (15.5%) had concomitant to radiologically suggestive to pulmonary TB, and three cases were found sputum positive for AFB.

When the bacillus is not found, histology may help by showing an epithelioid and giganto cellular granuloma with caseous necrosis in immunocompetent patients. Excision biopsy of the lymph nodes are the best examination for diagnostic confirmation, with a sensitivity of 100% for histological analysis and 60%–90% for the bacilli culture[10]. Outcome analysis on 58 cases revealed that 40 (69%) were declared cured, 14 (24.1%) were lost to follow-up, one case died, and four cases were declared MDR TB. These 4 cases were not responding to Anti TB drugs and referred them to National Institue of Chest Disease and Hospital, Mohakhali, Dhaka for PCR for MTB & RIF test after taking specimen by excisional biopsy from affected region. Extension of treatment >6 months was given in 41 (70.7%) cases, surgical excision of involved LN was done in 6 (10.3%) cases, four cases developed drug toxicity, and one case was diagnosed as lymphoma later. Six months' regimen showed variable response in the outcome of lymph node TB,[11,12] and in the present study, treatment regime needed to extend beyond 6 months.

Conclusion:

Tuberculous lymphadenitis represents about 10% of cases of TB in Bangladesh and is frequently the sole manifestation of extrapulmonary TB. Disease rates are highest among patients aged 21–30 years, and disease is more common among women. Tuberculous lymphadenitis may respond slowly to standard antibiotic treatment, with persistent discomfort. Frequent patient follow-up during treatment is recommended for reassurance and management of local discomfort, and further study is needed as an adjunct to standard antibiotic therapy to improve the condition. Financial support and sponsorship are nil. There are no conflicts of interest.

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Original Article

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Effect of Perioperative Oral Ascorbic Acid in Combination with β Blockers in the Prevention of Atrial Fibrillation after Off Pump Coronary Artery Bypass Grafting

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Abstract:

Background:Adrenergic beta antagonists are not sufficient to prevent atrial fibrillation (AF) after coronary artery bypass grafting. The purpose of thisstudy was to quantify the effect of perioperative oral ascorbic acid in combination with beta blockers in the prevention of AF in patients having off pump coronary artery bypass surgery (OPCAB). Methods: This prospective observational study included 100 patients who underwent OPCAB surgery from July, 2017 to June, 2018 at the dept. of cardiac surgery, NICVD.Among the 100 patients 50 patients (50%) were randomly allocated in the ascorbic acid group who received both ascorbic acid and β-blockers and other 50 patients (50%) were in control group who received only β-blockers. In ICU & HDU 12 lead ECG, hemodynamic stability (e.g. pulse, BP) in each patient up to 5th postoperative day evaluated and detected an episode of atrial fibrillation lasting >10 minutes or the requirement for urgent intervention due to atrial fibrillation (profound symptoms of atrial fibrillation or of hemodynamically unstable situations due to atrial fibrillation). Results: In both groups patients were homogenous regarding baseline and perioperative characteristics. Incidence of post-OPCAB atrial fibrillation in our control population (treated with β-blockers alone) was 24% and 6% in ascorbic acid group which was statistically significant (p-0.006). The highest incidence of atrial fibrillation onset falls on postoperative days 2 and 3. Postoperative hospital and ICU stays tended to be lower in those patients treated with ascorbic acid in combination with β-blockers than in those treated with β-blockers alone, but statistically insignificant.Conclusion: Perioperative oral administration of ascorbic acid in combination with β-blockers can prevent the incidence of atrial fibrillation better than β-blockers alone in patients who undergone OPCAB surgery.

Keywords: Ascorbic acid, atrial fibrillation, β-blockers, off pump coronary artery bypass

Introduction:

Atrial fibrillation (AF) is the most common complication following heart surgeries; it often occurs in patients after both conventional and off pump Coronary Artery Bypass Graft (CABG)[1]. This dysrhythmia can cause significant hemodynamic instability and thromboembolic events with morbid sequel longer time of hospital stay and higher costs[2]. Atrial fibrillation (AF) after OPCAB most often develops between the second and fifth postoperative day with a peak incidence in the 2nd to 3rd postoperative days[3]. Although often transient, self-limited and benign, AF usually results in the patient requiring additional medical treatment, laboratory tests, nursing time, and a prolonged hospital stay even when uncomplicated[4]. Patients who develop postoperative atrial fibrillation have significantly higher 30-day and 6-month mortality rates[5].Risk factors for developing atrial fibrillation include inflammation, oxidative stress, and atrial morphology[6].

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The presence of severe right coronary artery stenosis is an independent and powerful predictor of atrial fibrillation after coronary artery bypass surgery. In association with age, gender and postoperative beta-blocker therapy, these variables can be used to identify patients at increased risk for developing this arrhythmia[7]. Although AF in the early postoperative period is often sudden and self-limiting but can be continued for weeks and leads to increased morbidity, cardiac loss, embolic complications and the need for pacemaker[8]. Multiple randomized studies have shown the consistent prophylactic effectiveness of β-adrenergic blockers[9] and all patients without contraindications should receive β-blockers before and after cardiac surgery[10]. However, β-blockers alone are not sufficient to prevent post-CABG atrial fibrillation[11]. Therapeutic approaches that target inflammation and oxidative stress may exert favorable effects on atrial electrical remodeling[12]. Ascorbic acid may attenuate electrical remodeling and may decrease the incidence of postoperative atrial fibrillation[13].

The objective of our study was to examine the effect of oral ascorbic acid in combination with beta blockers in the prevention of AF in patients undergoing OPCAB surgery.

Methods:

This prospective observational study done with a total study population of 100 patients who underwent OPCAB surgery from July, 2017 to June, 2018 at the dept. of cardiac surgery, NICVD. Study protocol was approved by Ethical Committee of NICVD and informed written consent was taken from each patient before enrollment. We evaluate the effect of oral ascorbic acid in combination with beta blockers in the prevention of AF in patients undergoing OPCAB surgery. Inclusion criteria was: age >30 years and treatment with β- blockers (atenolol, propranolol, or metoprolol) for a target heart rate of about 60–90 beats/min, at least 1 week before surgery. One hundred patients entered the study: 50 patients were randomly assigned to the ascorbic acid group (those who received combination therapy with β-blockers and ascorbic acid), and the other 50 were assigned to the control group (those who received only β-blockertherapy). Exclusion criteria were patients who had a history of atrial fibrillation, medication with class I and III antiarrhythmic agents or digoxin, a permanent or temporary pacemaker, any degree of atrioventricular block or bradycardia with a heart rate of <50 beats/min, end stage renal disease, severe pulmonary disease (pneumonia or chronic obstructive pulmonary disease), or severe hepatic disease (cirrhosis or fulminant hepatitis). Preoperative ECG, serum electrolytes (e.g. potassium & magnesium), thyroid function test, liver function test and echocardiogram were done in all patients under study. Patients in the ascorbic acid group were given 2 g of ascorbic acid (trade name cevit) tablets on the night before surgery, followed by 1-g doses twice daily for 5 days after surgery. Before surgery, patients in both the control and ascorbic acid groups were treated with β-blockers (atenolol, propranolol, or metoprolol), and after surgery, the β-blockers were continued in both groups. Other medications were prescribed according to clinical indications in both groups.

After OPCAB surgery, each patient was transferred to intensive care unit and then at 3rd or 4th postoperative day was transferred to a step down or HDU. In ICU & HDU, I myself as an investigator evaluated 12 lead ECG, hemodynamic stability (e.g. pulse, BP), use of inotropic supports in each patient up to 5th postoperative day. An episode of atrial fibrillation was counted if it persisted for more than five minutes. Electrocardiography (ECG) with long lead tracing was done for all patients on the day of hospital discharge & was recorded.

The primary endpoints in our study were the detection of an episode of atrial fibrillation lasting >10 minutes or the requirement for urgent intervention due to atrial fibrillation (profound symptoms of atrial fibrillation or of hemodynamically unstable situations due to atrial fibrillation).

At the end of study, all data was analyzed by SPSS software version 22.0. The numerical data obtained

from the study was analyzed and significance of difference was estimated by using statistical methods. Continuous variables were expressed as mean values ± standard deviation and compared using student's t-test. Categorical variables were expressed as frequencies with percentages and compared using chi-square test when and where appropriate. $P < 0.05$ was considered significant.

Result:

The baseline and perioperative characteristics of patients in the ascorbic acid and control groups appear in Table: I

Table 1: Baseline and Perioperative Characteristics of Patients

Characteristic	Ascorbic Acid Group (n=50)	Control Group (n=50)	P Value
Mean age (yr)	56.38±5.2	54.9±6.1	0.39
Sex (male)	37 (74%)	33 (66%)	0.31
Hypertension	38 (76%)	34 (68%)	0.45
Diabetes mellitus	17 (34%)	18 (36%)	0.47
Hypercholesterolemia (statin therapy)	47 (94%)	48 (96%)	0.91
Cigarette smoking	31 (62%)	30 (60%)	0.32
Family history of CAD	10 (20%)	9 (18%)	0.76
History of myocardial infarction	21 (42%)	19 (38%)	0.78
LV ejection fraction <0.30	4 (8%)	3 (6%)	0.71
Body mass index (kg/m^2)	29.03±3.27	28.36±4.2	0.85
Mean diameter of left atrium (cm)	3.41±0.36	3.44±0.52	0.72
Mean LV end-systolic diameter (cm)	3.43±0.91	3.53±0.82	0.58
Mean LV end-diastolic diameter (cm)	5.12±1.23	5.29±0.65	0.37
Nitrate intake before surgery	36 (72%)	38 (76%)	0.67
Calcium channel blocker intake before surgery	14 (28%)	18 (36%)	0.28
ACE inhibitor intake before surgery	15 (30%)	19 (38%)	0.43
Mean no. of grafted vessels	2.72±0.57	2.44±0.68	0.13
Ventilation time >24 hr	1 (2%)	1 (2%)	1
Mean hospitalization time after surgery (d)	8.54±2.49	9.17±2.54	0.44
Mean intensive care unit stay (d)	2.2±1.6	2.6±1.48	0.23

Tables: II show the results of univariate analysis of some risk factors for postoperative atrial fibrillation. The overall incidence of postoperative atrial fibrillation in the ascorbic acid group was 4%, versus 26% in the control group. This study demonstrated that ascorbic acid in combination with β-blockers was the more effective for reduction of post-OPCAB atrial fibrillation.

Table II: Univariate Analysis of Some Significant Predictors of Post-OPCAB Atrial Fibrillation (Qualitative Data)

Variable	Atrial Fibrillation in variable (+) No. of pts. (%)	Atrial Fibrillation in variable (-) No. of pts. (%)	P value
Sex (male)	14/70 (20)	2/30 (6.7)	0.07
Ascorbic acid group	3/50 (6)	12/50 (24)	0.006
Hypertension	8/72 (11.1)	3/28 (10.7)	0.82
Hypercholesterolemia (statin therapy)	15/88 (17.0)	2/12 (16.7)	0.98
Cigarette smoking	10/61 (16.4)	6/39 (15.3)	0.98
History of myocardial infarction	8/40 (20)	8/60 (13.3)	0.23
LV ejection fraction <0.30	2/7 (28.6)	13/93 (13.4)	0.27
Nitrate intake before surgery	9/74 (12.1)	5/26 (19.2)	0.32
alcium channel blocker ntake before surgery	7/32 (21.8)	11/68 (16.1)	0.43
ACE inhibitor intake before surgery	8/34 (23.5)	9/66 (13.6)	0.21
Ventilation time >24 hr	1/2 (50)	14/98 (14.2)	0.28

Atrial fibrillation developed at a mean of 2.51±0.81 days after surgery. The mean ICU stay after operation was 3.21±1.34 days in atrial fibrillation patients and 2.53±1.42 days in sinus rhythm patients. The mean hospital stay after operation was 11.6±3.7 days in atrial fibrillation patients and 9.6±3.1 days in sinus rhythm patients. Adverse cerebral events (including nonfatal stroke or transient ischemic attack) occurred in 4 patients (2 in the ascorbic acid group and 2 in the control group). Two of these 4 patients had atrial fibrillation.

Discussion:

The goal of the present investigation was to examine the effect of perioperative oral ascorbic acid in combination with beta blockers in the prevention of AF in patients undergoing elective OPCAB surgery at NICVD. Carnes and colleagues1st-time prescribed prophylactic supplemental ascorbic acid to a series of bypass patients on the evening before surgery and as soon as it was possible for oral administration to resume thereafter and they found ascorbate treatment had a significant effect (*P*=0.048) on reducing post-CABG atrial fibrillation[13]. In another study,oral ascorbic acid reduced early recurrence rates after electrical cardioversion of persistent atrial fibrillation, and it attenuated associated low level inflammation[12].

Because most studies have demonstrated the consistent effectiveness of β-blockers as prophylaxis[14] we decided to supplement β-blockers with ascorbic acid. Univariate analysis of our results have confirmed that the combination of ascorbic acid and β-blockers was more effective than β-blockers alone in reducing post-CABG atrial fibrillation. Incidence of post-CABG atrial fibrillation in our control population (treated with β-blockers alone) was 26% and 4% in ascorbic acid group which was statistically significant (p-0.006). Eslami and colleagues found 26% and 4% respectively in their study[15]. In our study, the time of onset for atrial fibrillation was consistent with that reported in the medical literature.

The highest incidence of atrial fibrillation onset falls onpostoperative days 2 and 3[16,17]. In our study, postoperative hospital and ICU stays tended to be lower in those patients treated with ascorbic acid in combination with β-blockers than in those treated with β-blockers alone, but statistically insignificant.

The limitations of our study are single center study with small sample size and multiple surgical teams performed the procedure, use of purposive sampling method, lack of data regarding long term outcome.

This study concluded that perioperative oral administration of ascorbic acid in combination with β-blockers can prevent the incidence of atrial fibrillation better than β-blockers alone in patients who undergone Off Pump Coronary Artery Bypass (OPCAB).

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Original Article

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Effect of Aegle Marmelos Fruit Pulp Powder on Insulinemic Status of Type 2 Diabetic Patients

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Abstract:

Plant materials are considered to be attractive potential sources of alternate agents in the prevention and management of type 2 diabetes mellitus (T2DM). Different parts of Aegle marmelos have been claimed to explore the changes in insulinemic status. The present study was conducted at Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh from July 2010 to June 2011 to determine the anti-glycemic effect of A. marmelos unripe fruit pulp in T2DM patients. The experiment was conducted under a crossover design and the effects were analyzed during the 0-21 as well as 28-49 days with 7 days wash out period. The data were then pooled and the baseline versus endpoint values was also compared. The mean fasting blood C-peptide, HOMA%B, HOMA%S values did not significantly differ between the two groups at any time points. No significant difference between the baseline and end point values regarding fasting blood C- peptide, HOMA%B, HOMA%S. The effect on blood C-peptide, HOMA%B, HOMA%S was not significant in any of the analysis. This study did not reveal any changes in insulinemic status of A. marmelos fruit pulp in T2DM patients.

Keywords: Aegle marmelos, type 2 diabetes mellitus, insulinemic, HOMA%B, HOMA%S

Introduction:

Diabetes mellitus (DM) is one of the commonest endocrine and metabolic disorders affecting mankind all over the world. It is widely recognized as one of the leading causes of death and disability worldwide[1,2]. People of the developing countries are the worst victims of such life-long diseases because of the lack of organized health care delivery. Prevalence of diabetes in adults worldwide was estimated to be 4.0% in 1995 and to rise to 5.4% by the year 2025[3]. It has been estimated that the total diabetic patients in Bangladesh was more than three million in 2000, and this number would rise to 11.1 million by the year 2030. Type 2 diabetes develops because of defects in both insulin secretion and action (although a debated issue) and affects large numbers of people from a wide range of ethnic groups throughout the world[4]. Conventionally, Type 1 Diabetes Mellitus (T1DM) is treated with exogenous insulin and T2DM with synthetic oral hypoglycemic agents like sulphonylureas and biguanides[5]. A substantial proportion of T2DM also requires insulin. However, the existing therapeutic agents have considerable limitations in the management of this complex disorder and search for alternate agents are continuing all over the world.

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Plants are sources of multiple compounds with nutritional and medicinal value, and WHO has recognized the importance of natural products in the prevention and management of diseases. The plant kingdom has become a target for multinational drug companies and research institutes for the discovery of new biologically active compounds and potential drugs.[6] Among traditional medicinal plants, Aegle marmelos (Bael in Bengali) has enormous traditional uses against various diseases. Traditionally, various parts of the plant, Aegle marmelos, are used for the treatment of a variety of disorders. Aegle marmelos originated in India and is presently growing in most of the countries of Southeast Asia[7]. Extensive chemical investigation on various parts of the tree have been carried out and more than 100 compounds have been isolated. The bioactive compounds isolated from these fruits were marmelosin, luvangetin, aurapten, psoralen, marmelide and tannin. Aqueous leaf extract (250 & 500mg/kg, orally) produced hypoglycemic effect and increased plasma insulin level of STZ (Streptozotocin)-diabetic rats. Anti-hyperglycemic activity was seen by leaf extract (250mg/kg, orally) in glucose fed hyperglycemic rats[8]. Aqueous fruit extract (250mg/kg, twice daily for one month) produce anti-hyperglycemic effect along with decreasing glycosylated heamoglobin level in STZ induced diabetic albino wistar rats[9]. Although a number of studies in STZ and alloxan induced diabetic rat model were conducted with A. marmelos, but no study had yet been done on human with T2DM. In the above context, the present study was undertaken to explore the anti-insulinemic effects of A. marmelos unripe fruit pulp powder in patients with T2DM.

Materials and methods:

Study place and population: The study was conducted in Bangladesh Institute of Research and Rehabilitation in Diabetes, Endocrine and Metabolic Disorders (BIRDEM), Dhaka, Bangladesh from July 2010 to June 2011. It was an un-blinded clinical trial conducted under a cross-over design. Previously diagnosed thirty T2DM cases were included in the study. T2DM cases were enrolled from the out-patient department of BIRDEM. The socio-demographic data of all the participants were recorded in a pre-designed questionnaire. They were advised to take their usual diet, to do normal physical activities and to continue their prescribed drugs during the experimental period. Patients unwilling to give consent, insulin dependent DM, pregnant or lactating women, patients with cardiovascular, renal, hepatic, endocrine, metabolic disorders were excluded.

Preparation of A. marmelos fruit pulp powder: Unripe fruits of Aegle marmelos were collected from specific area of Chapainawabgonj. Fruit pulps of A. marmelos (FPAM) were dried in sunlight for 5 to 6 days, coarsely powdered by grinder machine and stored in a dry cool place.

Study procedure: The fasting blood samples of all the study participants were collected at day zero for estimation of fasting blood glucose levels (C-peptide, HOMA%B, HOMA%S, FBG). They were then divided randomly into Group A and B each consisting of 15 cases. First, one group (Group A) was given 7 gm of A. marmelos fruit pulp powder in one glass of water daily before breakfast for 21 days while another group (Group B) was on their usual diet for 21 days. The dose of 7 gm fruit pulp powder was determined based on earlier study. The fasting blood samples of both groups were collected on 21st day. After 7 days of wash out period, the fasting blood samples were again collected on the 28th day from both the groups. The groups were then crossed over and the cases who consumed A. marmelos pulp drink in the first 21 days started their usual diet and the other cases started to consume the A. marmelos pulp drink for the next 21 days. The final fasting blood sampling was collected on 49th day from both the groups. All blood samples were preserved at 20ºc until analyzed. Statistical analysis was performed using SPSS (Statistical Package for Social Science) software for Windows version-16 (SPSS Inc., Chicago, Illinois, USA). The data were expressed as proportion and mean±SD (standard deviation) as

appropriate. The statistical significance of differences between the values was assessed by paired or unpaired student's t test as appropriate. Correlation analysis between the parameters was done by using Pearson's Correlation test.

Results:

A total number of thirty T2DM cases were included in the study. The detail socio-demographic characteristics of the study participants are given in Table-1. The mean age of the study participants was 51.5 ± 12.0 years. There were 17 males and 13 females. Majority were urban residents. Table 2 shows the glycemic status of T2DM cases after 21 days of daily drink of A. marmelos fruit pulp compared to those who did not receive the intervention.

No significant difference was found between the fasting blood glucose levels of the intervention group compared to non- intervention group after 21 days of fruit pulp administration. Similarly, Table 3 shows the effects of A marmelos fruit pulp powder on glycemic status of T2DM cases during 28 to 49 days time period after cross over and 7 days of wash period. No significant difference of fasting blood glucose was observed between the intervention and non-intervention groups after 21 days of A. marmelos drink at day 49. Similarly, there was no significant change in fasting blood glucose level after 21 days of fruit pulp drink compared to the initial level in intervention group. There was no significant change of fasting blood glucose levels of all cases (Group A and B) at base point (day zero) versus end point (day 49).

Table-1: Socio-demographic characteristics of the study subjects (n=30)

Variable	Frequency	Percent
Age in years (M±SD)	51.5 ± 12.0	
WHR (M±SD)	0.91 ± 0.08	
Sex		
Male	17	57
Female	13	43
Education		
Illiterate	2	6.7
Primary	8	27.0
Secondary	10	33.0
Graduate	10	33.0
Occupation		
Service	14	47.0
Business	6	20.0
Housewife	10	33.0
Residence		
Urban	27	90.0
Rural	3	10.0

Values are expressed as M±SD or numbers and percentages as appropiate. WHR=Waist Hip Ratio

Table 2: Effect of A marmelos on high sensitive C-reactive protein and insulinemic status of T2DM subjects during 0-21 days (n=15 in each group)

Parameters	0 day	21 day	p value
C-pep (ng/ml)			
Control Group	1.02 ± 0.95	1.56 ± 1.11	0.002
FPAM Group	1.18 ± 0.87	1.35 ± 0.89	0.31
t/p value	0.49/0.63	-0.56/0.58	
HOMA%B			
Control Group	30 ± 24	34 ± 22	0.27
FPAM Group	23 ± 14	33 ± 20	0.004
t/p value	-0.94/0.36	-0.02/0.99	
HOMA%S			
Control Group	166.0 ± 157	112 ± 100	0.14
FPAM Group	164.4 ± 119	125 ± 64	0.17
t/p value	-0.02/0.98	0.43/0.67	

Comparison between 0 day 21 day values of the same individual were compared by Paired- t test (n=30).On the other hand compariscn between Control and FPAM Groups on 0 day and 21 day were done by unpaired t-test (n=15).Values were expressed as Mean± SD. P<0.05 was considered as statistically significant, n= number of subjects; FPAM group=Aegle marmelos treated group, CRP=C-Reactive protein, Cpep = Fasting serum Cpeptide; HOMA-B%= B cell function assessed by homeostasis model assessment and HOMA-S%= Insulin sensitivity assessed by homeostasis model assessment.

Table 3: Effect of A marmelos on high sensitive c-reactive protein and insulinemic status of T2DM subjects during 28-49 days (n=15 in each group)

Parameters	28 day	49 day	p value
C-pep (ng/ml)			
Control Group	1.22 ± 0.73	1.5 ± 0.88	0.08
FPAM Group	1.25 ± 0.80	1.97 ± 2.0	0.16
t/p value	*-0.06/0.95*	*-0.69/0.50*	
HOMA%B			
Control Group FPAM	29.5 ± 14.8	35.5 ± 16	0.10
Group	37.2 ± 31.0	34.0 ± 28	0.49
t/p value	*-0.87/0.39*	*0.18/0.86*	
HOMA%S			
Control Group	92 ± 37	74 ± 44	0.054
FPAM Group	106 ± 76	103 ± 78	0.84
t/p value	*-0.65/0.52*	*-1.26/0.28*	

Comparison between 28 day 49 day values of the same individual were compared by Paired- t test (n=30).On the other hand compariscn between Control and FPAM Groups on 28 day and 49 day were done by unpaired t-test (n=15). Values were expressed as Mean± SD. P<0.05 was considered as statistically significant, n= number of subjects; FPAM group=Aegle marmelos treated group, CRP=C- reactive protein, Cpep= Fasting serum Cpeptide; HOMA-B%= B cell function assessed by homeostasis model assessment and HOMA-S%= Insulin sensitivity assessed by homeostasis model assessment.

Discussion:

A number of parts of A. marmelos have been studied for the anti-diabetic properties in diabetic rat models. The present one was probably the first study in which a part of the plant was tested on human for anti-diabetic properties. The part chosen was the unripe fruit pulp of A. marmelos as this was the commonest part consumed by people as drink and prescribed by the traditional healers in Bangladesh. In fact, a few commercial preparations of the pulp are now available in Bangladesh market with wide spectrum of therapeutic claims including for diabetes. Testing the efficacy and safety of the fruit pulp has thus public health impact.

The experiment was conducted under a crossover design and the effects were analyzed for 0-21 as well as 28-49 days (with 7 days wash out period) intervention. The data were then pooled and the baseline versus endpoint values was also compared. The effect on blood glucose level was not significant in any of the analysis though, studies in animal showed insulinemic effects of different parts of A. marmelos plant.

Conclusion:

The present study did not reveal any such insulinemic effect of A. marmelos unripe fruit pulp in T2DM patients. However, the result did not indicate conclusively that A. marmelos fruit pulp had no changes in insulinemic status as we could not do a dose response curve.

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Original Article

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Recent Trends in the Presentation of Neuroanatomy Through the Quantitative Analyses of the Text in the Neuroanatomy Text Books

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Abstract:

Context: A critical challenge in Neuroanatomy is organizing, managing and accessing the explosion in Neuroanatomical knowledge. While educationists and anatomists continue with their experimentations with curricular design, variations in the implementation of the curricula prevail. Observations made through a methodical look at the way contemporary Neuroanatomy books present Neuroanatomy in terms of their approach toward the subject, weights given to different topics. One important way to know the changes in other country by analyzing the Neuroanatomy books. Objective: To estimate the weights given to different topics. Aim: To analyse the presentation of text in two Neuroanatomy textbooks.Study design: A descriptive, observational study involving quantitative analyses. Materials and methods: Ten 'topic'-headings were identified based on the types and levels of information for analysing the two textbooks. The weights given (proportions of printed area allotted) to different topics were estimated in relation to text. Results: The mean proportion (±SD) of printed areas allotted to text is maximum for 'central nervous system including autonomic nervous system' (27.13±14.28) % and minimum for 'developmental anomalies' (0.48±0.34) %. Conclusions: By incorporating the findings of the present study ideas could be formulated on improving the methods of teaching learning in Neuroanatomy.

Keywords: Contemporary neuroanatomy book, neuroanatomy, recent trends

Introduction:

In recent years, effort has been taken to improve medical care in all sectors to produce a good physician. International forces are encouraging medical institute to alter their curricula and even their basic structure[1]. Our country has not been notably successful in this regard. Most present day Neuroanatomy books usually put emphasis to the clinical aspects of Neuroanatomy[2-3]. Medical students feel difficult to understand Neuroanatomy and they also feel that it is not helpful in general practice[4]. The author believes that if the subject of Neuroanatomy is properly understood by the student it has a great clinical importance even for general practice. It seems that students are afraid of Neuroanatomy because it is a tough subject. In the postgraduate level it is believed that students coming from undergraduate background with less understanding of Neuroanatomy. So teachers start Neuroanatomy classes with the basic things of this subject. Neuroanatomy book enriched with new information and provide a more useful guide-line to the medical students at graduate and post- graduate level [5]. It is essential to make them more clinically and functionally oriented. New editions of Neuroanatomy books include several new ideas to make them more clinically and functionally oriented as well as more understandable[6].

In the present days, the central challenge for teachers of Neuroanatomy is how to convey to their students the essential picture of Neuroanatomy according to the recent trends and concepts. In an attempt to understand the recent trends, textbooks are supposed

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to be good indices. So, analyses of contemporary textbooks may give an idea on the recent trends in the field of Neuroanatomy. Therefore, it may be assumed that good Neuroanatomy books would reflect the important aspects of the recent global trends in Neuroanatomy teaching-learning and assessment.

Methods

Materials and methods:

Two textbooks were selected for the analyses of text. These were:

1. A.K.Datta (2007): Essentials of Neuroanatomy
2. Richard S Snell (2006): Clinical Neuroanatomy

Operational definitions:

1. **Topic:** An arbitrary system was followed in the present study by dividing the presentations of Neuroanatomy (both in text and illustrations) in two commonly used Neuroanatomy textbooks into ten 'topic's. The names of the topics were based on one or more of the following:

I. The aspect of information or concept, e.g. general, basic anatomical, cytological, histological, basic functional, developmental or clinical aspect.

II. Others, e.g. Specific physiological processes, Blood supply of the Nervous system .

Thus, the 'topic's considered in the present study stood as:

1. General aspects of the Nervous system
2. Basic anatomical aspects of the Nervous system
   a. Central Nervous system
   b. Peripheral Nervous system
3. Cytological aspects of the Nervous system
4. Histological aspects of the Nervous system
5. Basic functional aspects of the Nervous system
6. Neuroanatomy of the Specific physiological processes
7. Developmental aspects of the Nervous system
8. Blood supply of the Nervous system
9. Clinical aspects of the Nervous system
   a. Clinical disorders
   b. Developmental anomalies
   c. Diagnostic images
   d. Diagnostic and treatment procedures
   e. Surface markings
   f. Clinical and problem solving question and answers
10. Others

2. Text: This term included all the printed words (information, concepts, explanations etc.) in the two textbooks. However, the legends (of illustrations), chapter numbers, chapter headings and page numbers were not included under the term.

3. Weight given: Indirect estimations of the weight given in each textbook to the texts on each 'topic' were devised. For estimating the weight of a 'topic' the proportion of the printed area allotted to the texts on the topic was measured and expressed as a percentage of the whole amount of printed area in the book.

Specific operational definitions of the different 'topic's

1. General aspects of the Nervous system:

Under this topic heading, the introductory portions like definition, nomenclature and the common portion of Neuroanatomy which can not be specified as central nervous system or peripheral nervous system were considered.

Examples: Text:

Neurons are the structural and functional units of the nervous system. Each neuron consists of a cell body and processes or neuritis which are cytoplasmic extensions[5].The nervous system is divided into two main parts, for purposes of description: the central nervous system, which consists of the brain and spinal cord, and the peripheral nervous system, which consists of the cranial and spinal nerves and their associated ganglia[2].

2. Basic anatomical aspects of the Nervous system and its support:

a. Central Nervous system (including ANS): Under this topic heading were the text of the brain and spinal cord with CSF and meninges including autonomic nervous system.

Examples: Text: The surface of the spinal cord is divided almost completely into twosymmetrical halves by an anterior median fissure and a posterior median sulcus[5].The cerebellum is connected to the midbrain by the superior cerebellar peduncles, to the pons by the middle cerebellar peduncles, and to the medulla by the inferior cerebellar peduncles[2].

b. Peripheral Nervous system (including ANS): This topic heading was chosen for all the text related to the cranial and spinal nerves and their associated including autonomic nervous system.

Examples: Text: The spinal nerves are arranged in thirty-one pairs attached to the sides of the spinal cord by two roots- ventral and dorsal[5]**.** The olfactory nerves arise from the olfactory receptor nerve cells in the olfactory mucous membrane located in the upper part of the nasal cavity above the level of the superior concha[2].

3. Cytological aspects of the Nervous System:

This topic heading was chosen for all the text related to the structural and functional aspects of neurons, receptors and supporting cells.

Examples: Text: The plasma membrane of dendrites and soma contain receptor-protein molecules which are activated by transmitters from other neurons[5]. Nissl substance consists of granules that are distributed through out the cytoplasm of the cell body except axon hillock. It is present in dendrites but absent in axon[2].

4. Histological aspects of the Nervous System:

The textual presentations related to the structural features of different tissues that are visible under microscope.

Examples: Text: The blood-brain barrier consists of non-fenestrated endothelium, basement membrane, perivascular foot and the cell body of the astrocytes, intercellular spaces, processes and cell bodies of neurons[5]. The characteristic feature of the precentral area is the most complete absence of the granular layers and the prominence of the pyramidal nerve cells[2].

5. Basic functional aspects of the Nervous system:

This topic included all the functional text of organs and parts of the nervous system.

Examples: Text: On stimulation of the parasympathetic system the heart rate is diminished, the blood pressure falls, the pupils are constricted, the peristalsis and glandular secretion of the alimentary tract arepromoted[5]. Painful and thermal sensations ascend in the lateral spinothalamic tract; light (crude) touch and pressure ascend in the anterior spinothalamic tract[2].

6. Neuroanatomy of the specific physiological processes:

This topic included all the textual information and concepts regarding different aspects of the general or systemic physiology of the human body.

Examples: Text: During quiet breathing, the expiratory neurons remain practically inactive, because the normal expiration takes place passively by elastic recoil of the lung[5]. Oxytocin stimulates the contraction of the smooth muscle of the uterus and causes contraction of the myoepithelial cells that surround the alveoli and ducts of the breast[2].

7. Developmental aspects of the Nervous System:

Under this topic heading the textual material related to the descriptions of the development of a specific organ or any structure of the nervous system.

Examples: Text: The face is developed from three processes- fronto-nasal, maxillary and mandibular, which correspond respectively with the territorial

distribution of ophthalmic,maxillary and mandibular divisions of the trigeminal nerve[5]. Neural crest cells will differentiate into the cells of the posterior root ganglia, the sensory ganglia of the cranial nerves, autonomic ganglia, the cells of the suprarenal medulla and the melanocytes[2].

8. Blood supply of the Nervous system:

Under this topic heading the textual material related to the descriptions of arterial supply and venous drainage of various organs within the nervous system.

Examples: Text: The cerebral veins consist of superficial and deep groups. The superficial veins drain the cortex and sub cortical white matter. The deep veins drain the substance of the brain including the basal ganglia and diencephalons[5]. The brain is supplied by the two internal carotid and the two vertebral arteries. The four arteries and their branches anastomose to form the circle of Willis[2].

9. Clinical aspects of the Nervous system:

a. Clinical disorder: This topic included all the text regarding the description of the disorders of the nervous system resulting from injury or pathological reason.

Examples: Text: Trigeminal neuralgia is occasionally manifested by intractable paroxysms of pain in the area of distribution of one or all divisions of trigeminal nerve[5]. Brain injuries are produced by displacement and distortion of the neuronal tissues at the moment of impact[2].

b. Developmental anomalies: Under this topic heading, all the text related to the general aspects of developmental disorders was considered.

Examples: Text: A meningomyelocele most often causes complete interruption of cauda equine, with motor paralysis, loss of reflexes and anesthesia[5]. In spina bifida, the spines and arches of one or more adjacent vertebrae fail to develop. The condition occurs most frequently in the lower thoracic, lumbar and sacral region[2].

c. Diagnostic images: The textual presentations related to the descriptions of Conventional radiograph, CT scan, MRI scan, PET scan and angiogram.

Examples: Text: Conventional radiographs are excellent for high contrast structures, e.g. bones and lungs[5]. CT is used for the detection of intracranial lesions. The procedure is quick, safe, and accurate[2].

d. Diagnostic and treatment procedure: This topic included the text regarding the investigation and treatment of various clinical disorders by surgical procedure.

Examples: Text: The operation of bilateral prefrontal lobotomy is sometimes practiced in patients with symptoms of mental illness and distressing somatic pain[5].
Lumber puncture may be performed to withdraw a sample of cerebrospinal fluid for microscopic examination or to inject drugs to combat infection[2].

e. Surface marking: Included under this topic heading were the text related to the descriptions of surface marking of different structure of nervous system.

Examples: Text: Pterion is a H-shaped sutural line, where parietal, greater wing of sphenoid, frontal and squamous part of temporal bones meets[5]. Parietal eminance is a raised area on the lateral surface of the parietal bone and can be felt about 2 inches above the auricle.

f. Clinical and problem solving question and answer: This topic included the texts regarding the description of the portion of clinical aspects which are present at the beginning and end of each chapter of the book.

Examples: Text: Carcinoma of the thyroid, breast, kidney, lung and prostate commonly gives rise to metastases in bone. The pain in the back was caused by the carcinoma invading and destroying the tenth thoracic vertebral body[2].

10. Others:

Any text that could not to be included under any of the above mentioned 'topic's and yet it is not present in the textbooks in sufficient amount to deserve a separate 'topic' heading, was included under this 'topic' heading.

Examples: Text: CSF possesses higher Na^{+}, Cl^{-} and Mg^{++} ions and lower concentration of K^{+}, Ca^{++} , and glucose than that of the plasma[5]. The smooth muscle fibers of the iris consist of circular and radiating fibers. The circular fibers form the sphincter pupillae and the radial fibers form the dilator pupillae[2].

Methods of estimating the weights given to different 'topics' ('text'):

After selecting ten 'topics' as described in the previous section, the selected textbooks were analysed for estimating the weights given to different 'topics' in terms of the amounts of text used for presenting each 'topic'. The amounts were expressed as proportions of printed material allotted to each 'topic' for text separately.

Determination of proportions of printed area allotted to text on different 'topic's:

The weight given to each topic was estimated by considering the proportion of printed area allotted to that particular topic in terms of text material.

Primary considerations:

In doing the above, the following points were kept in mind.

1. In analyzing Datta, a new chapter 'Yoga and its impact in medical sciences' and 'References' provided in each chapter were excluded from the study due to these do not represent any particular topic[5].

2. In case of the textbook by Snell, 'Appendix' was included due to they represent particular topic. On the other hand Chapter Outline, Chapter Objectives, Review Questions, Answers and Explanations to Review Questions, Additional Reading were excluded from the study as these do not represent any particular topic[2].

3. All the figure legends in Datta (2007) and Snell (2006) were excluded.

4. In case of the text inside tables, the usual way of measuring the proportion of area allotted to the text on a 'topic' was followed.

5. The blank space between two columns of text of a page was divided into two equal parts that were considered as a part of the text close by and was measured as such.

6. Any blank space between two paragraphs was considered as part of the previous paragraph and was measured as such.

7. In course of analyses of text, the headings and subheadings were not considered under the text area since most of them represent more than one topic. However, those subheadings which were followed by text on the same line were counted under the corresponding text area.

8. All measured and calculated values were approximated to their nearest values with two digits after the decimal point.

The basis of measurement:

This method of estimating weight was based on the age-old method of estimating weight (coverage) of news in a newspaper by measuring the column-length allotted to the news, as the newspaper columnwidthis constant. However, as the column width varied among the textbooks, the proportions (%) of printed area allotted to text on different 'topic's were calculated by multiplying the column lengths by the corresponding column widths in the present study[7].

The measurement procedure:

To determine the proportion of printed area allotted to text on each 'topic', the 'topic' symbols were used first to mark each text as belonging to one or more 'topic's. The column length allotted to each 'topic' was marked with a different coloured pen as shown in Figure 1. For example, the topic 'Basic functional aspect of the Nervous system' was marked with a light green coloured pen. Thus, any text belonging to the topic was marked with a light green coloured pen. Then, with a linear measuring scale as shown in Figure1 the texts were separately measured in centimeters. When two separate topics presented in a same text line the total line included under the particular topic which occupied more spaces of that line. However total line was included in the initial topic if the line presents same area for two topics. In measuring the areas of tables, the 'length' (height) of a table represented the distance between the upper most and lower most horizontal line of the table. The 'breadth' represented the length of the uppermost/lowermost line. However, as the tables varied in the number of topics presented, the following arbitrary rule was devised for measurement. If a table as a whole covered a single topic, thus the whole length (height) and the whole breadth of the table were measured.

If a table covered more than one topic in separate columns, than the combined breadth of all the columns each topic was measured separately. If a table covered more than one topic in separate rows, than all the rows covering each topics were considered together and the combined length (height) was measured for that topic. The total area allotted to text on each 'topic'in each textbook was also calculated and expressed as a percentage of the total printed area (text). Mean proportions of the two books were then calculated.

The calculation:

Using the above-mentioned measurements, further calculations were done according to the following method.

Proportion of printed area allotted to text on a 'topic' in a textbook

$$(PA_t) = \frac{L_t \times B}{L_p \times B_p} \times 100\%$$

Where,

L_p: Overall length of the printed matter of a particular textbook.

B_p: Overall breadth of the printed matter of a particular textbook.

L_t: Total column length of printed text allotted to a specific 'topic' in a textbook.

B: Column breadth in that textbook.

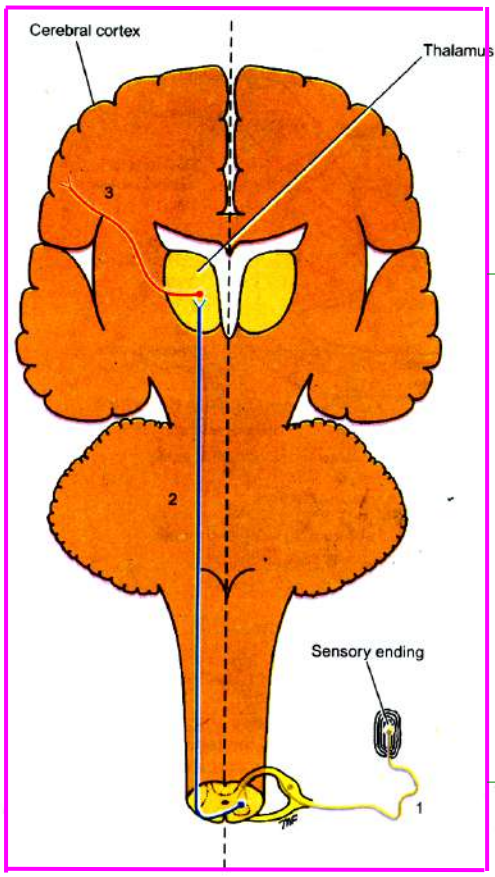


Figure 4-8 Simplest form of the ascending sensory pathway from the sensory nerve ending to the cerebral cortex. Note the three neurons involved.

ANATOMICAL ORGANIZATION

General information from the peripheral sensory endings is conducted through the nervous system by a series of neurons. In its simplest form, the ascending pathway to consciousness consists of three neurons (Fig. 4-8). The first neuron, the **first-order neuron,** has its cell body in the **posterior root ganglion** of the spinal nerve. A peripheral process connects with a sensory receptor ending, whereas a central process enters the spinal cord through the posterior root to synapse on the second-order neuron. The **second-order neuron** gives rise to an axon that decussates (crosses to the opposite side) and ascends to a higher level of the central nervous system, where it synapses with the **third-order neuron** (Fig. 4-8). The third-order neuron is usually in the thalamus and gives rise to a projection fiber that passes to a sensory region of the cerebral cortex (Fig. 4-8). This three-neuron chain is the most common arrangement, but some afferent pathways use more or fewer neurons. Many of the neurons in the ascending pathways branch and give a major input into the reticular formation, which, in turn, activates the cerebral cortex, maintaining wakefulness. Other branches pass to motor neurons and participate in reflex muscular activity.

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FUNCTIONS OF THE ASCENDING TRACTS

Painful and thermal sensations ascend in the lateral spinothalamic tract; light (crude) touch and pressure ascend in the anterior spinothalamic tract (Fig. 4-9). Discriminative touch, that is, the ability to localize accurately the area of the body touched and also to be aware that two points are touched simultaneously, even though they are close together (two-point discrimination), ascends in the posterior white columns (Fig. 4-9). Also ascending in the posterior white columns is information from muscles and joints pertaining to movement and position of different parts of the body. In addition, vibratory sensations ascend in the posterior white column. Unconscious information from muscles, joints, the skin, and subcutaneous tissue reaches the cerebellum by way of the anterior and posterior spinocerebellar tracts and by the cuneocerebellar tract (Fig. 4-9). Pain, thermal, and tactile information is passed to the superior colliculus of the midbrain through the spinotectal tract for the purpose of spinovisual reflexes (Fig. 4-9). The spinoreticular tract provides a pathway from the muscles, joints, and skin to the reticular formation, while the spinoolivary tract provides an indirect pathway for further afferent information to reach the cerebellum (Fig. 4-9).

Fun

Pain and Temperature Pathways

Lateral Spinothalamic Tract[3]

The pain and thermal receptors in the skin and other tissues are free nerve endings. The pain impulses are transmitted to the spinal cord in fast-conducting delta A-type fibers and slow-conducting C-type fibers. The fast-conducting fibers alert the individual to initial sharp pain, and the slow-conducting fibers are responsible for prolonged burning, aching pain. The sensations of heat and cold also travel by delta A and C fibers.

The axons entering the spinal cord from the posterior root ganglion proceed to the tip of the posterior gray column and divide into ascending and descending branches (Fig. 4-10). These branches travel for a distance of one or two segments of the spinal cord and form the **posterolateral tract of Lissauer** (Fig. 4-10). These fibers of the first-order neuron terminate by synapsing with cells in

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[3] Many accounts of the ascending tracts now combine the lateral and anterior spinothalamic tracts as one tract since they lie alongside one another; the combined pathway is known as the anterolateral system. The ascending tracts in the posterior white column have also been called the lemniscal system.

Fig.1 Method of determining the proportion of printed area for text allotted to different 'topic's in a page of a Neuroanatomy textbook (Snell 2006, p. 142). The coloured lines represent the way the portions of the text were marked with coloured pens for different 'topics'- Pink: General aspects of the Nervous system. Green: Basic functional aspects of the Nervous system. Blue: Central Nervous system including autonomic nervous system.

Results:

In the present study, ten 'topic's were selected for the measurement of the proportions of printed area allotted to text for each of the 'topic's in two commonly recommended Neuroanatomy textbooks. The amounts of printed areas analysed in the two textbooks were as follows:

- Datta (2007): 64,465.44 cm^2
- Snell (2006): 63,633.58 cm^2

Thus, a total of 1, 28099.02 cm^2 of printed area was analysed. The proportions of printed area allotted to the text on different 'topic's (Table1and Figure 2) show that the topic 'central nervous system including autonomic nervous system' has got the greatest mean proportion (27.13%). The 'topic's with the lowest mean proportions (between 0.20 % and 1.70%) include 'general aspects of the nervous system', 'Neuroantomy of the specific physiological processes', 'developmental aspects of the nervous system', 'developmental anomalies', 'diagnostic images', 'surface marking' and 'others'. It is observed from Table 1 that mean value of the text on 'clinical disorders' is 16.35% and 'basic functional aspects of the nervous system' is 11.91% of the total text area. It is observed from Table 1 that Snell has given more emphasis on topic 'clinical and problem solving question and answers' that cover 22.67%area of text but this topic is absent in Datta[2,5]. The mean value of the text on 'clinical disorders' is 22.39% in Snell[2]. But in Datta, the mean value of that 'topic' is 10.31%[5]. This means that the former (Snell) has put about twice the emphasis on this particular 'topic'. The Table also shows that mean value of the text on 'basic functional aspects of' the Nervous system' is 15.41% in case of Datta. But, in Snell, it is 8.40%. In this case, Datta has given about twice the emphasis on this particular 'topic'[2,5].

Table- 1 Weights given (proportions of printed area allotted) to the text on different 'topics in two commonly recommended Neuroanatomy textbooks

Sl. no.	Topic	Proportion of printed area allotted to text in an individual textbook †(%)		Mean Proportion for the two textbooks ± SD (%)
		Datta	Snell	
1.	General aspects of the Nervous system	2.31	0.94	1.63±0.97
2.	Basic anatomical aspects of the Nervous system and its support			
	• CNS(including ANS)	37.23	17.03	27.13±14.28
	• PNS(including ANS)	5.00	3.43	4.22± 1.11
3.	Cytological aspects of the Nervous system	9.39	9.04	9.21±0.25
4.	Histological aspects of the Nervous system	8.09	4.82	6.46±2.31
5.	Basic functional aspects of the Nervous system	15.41	8.40	11.91±4.96
6.	Neuroanatomy of the specific physiological processes	1.46	0.39	0.93±0.76
7.	Developmental aspects of the Nervous system	1.05	2.35	1.70±0.92
8	Blood supply of the Nervous system	4.68	2.20	3.44±1.75

Table-1 (Continued)

9.	Clinical aspects of the Nervous system			
	• Clinical disorders	10.31	22.39	16.35±8.54
	• Developmental anomalies	0.24	0.72	0.48±0.34
	• Diagnostic images	1.87	1.01	1.44±0.61
	• Diagnostic and treatment procedures	1.78	4.20	2.99±1.71
	• Surface marking	1.05	0.14	0.60±0.64
	• Clinical and problem solving questions and answers	0.00	22.67	11.34±16.03
10.	Others	0.13	0.26	0.20±0.09

† 'Proportion' means the number of printed areas, allotted to each topic

- **'CNS (including ANS)' means Central Nervous system including autonomic nervous system**
- **'PNS (including ANS)' means Peripheral Nervous system including autonomic nervous system**

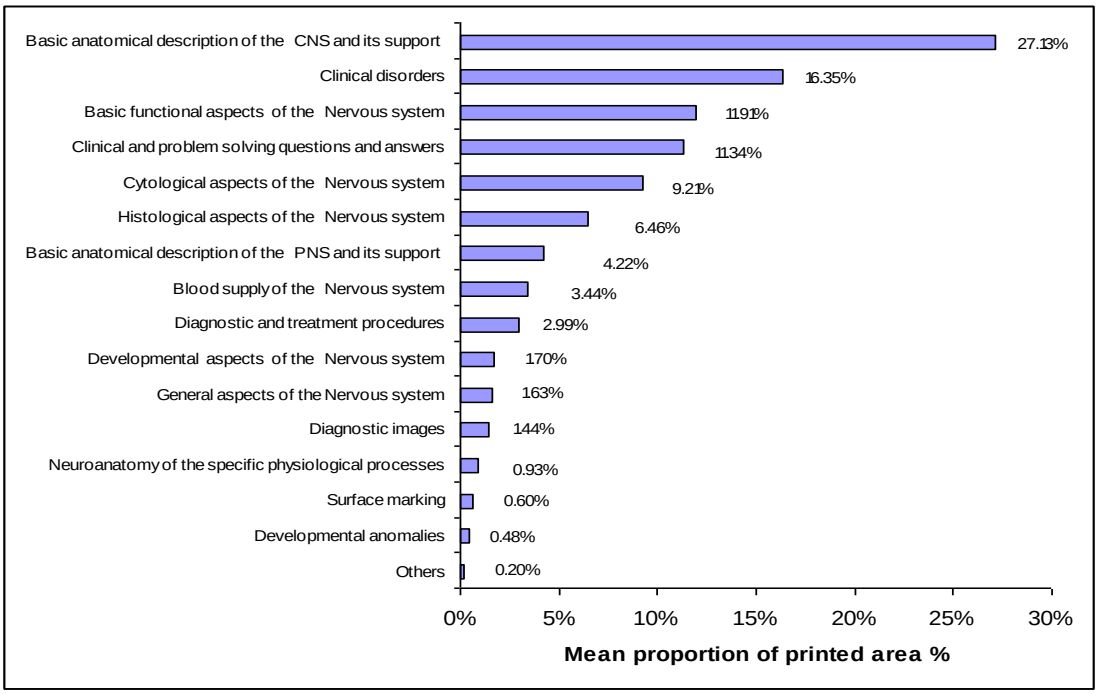


Fig. 2 Mean proportions of printed areas allotted to text on different 'topics' in the two commonly recommended Neuroanatomy textbooks (arranged in the descending order of proportion). The mean value for each topic represents the mean of the proportions in the two textbooks for the particular topic.

Discussion:

While writing Neuroanatomy textbooks, the authors usually take the contemporary and new information into consideration[7-8]. The present study was aimed at assessing how the present day Neuroanatomy books approach and deal with different aspects of Neuroanatomy in their presentation. This study was done to improve the teaching learning methods of Neuroanatomy. During the undergraduate course, the nervous system is present in the last part of the session as the brain eyeball card. Students have less time for understanding the subject. They also have no enough time for revision of the subject. Therefore they are weak in Neuroanatomy. They rote memorize the subject for passing the examination. When these students come for higher education they usually feel difficult to understand the subject. Most of the postgraduate students' loss their interest in the subject due to they don't know where Neuroanatomy will be implemented in professional / clinical life. The present study may have been able to make some important points and create an evidence based foundation upon which positive steps may be taken in future towards fulfilling the objectives set in the postgraduate curriculum.

It is observed from the results chapter that proportionately more area (text) for a topic has been allotted for 'central Nervous system including autonomic nervous system, (27.13%). It has been also observed that Snell has highlighted the topic 'clinical and problem solving question and answers'[2]. It helps the students for assessing their abilities and also it makes the students confident for facing various problems related to diagnosis the diseases during their practice.

In the two Neuroanatomy textbooks commonly recommended bythe postgraduate medical courses of Bangladesh, ten 'topic's can be identified. Among them 'central Nervous system includes autonomic Nervous system' carries the greatest weight in terms of text in 'Datta'. But in 'Snell' the greastest weight for 'clinical disorders' and for 'clinical and problem solving questions and answers' in terms of text. Second greatest value in 'Datta' for 'basic functional aspects of the Nervous system' for text and in 'Snell' for 'central Nervous system includes autonomic nervous system' in terms of text. Third most value in terms of text for 'clinical disorders' in case of 'Datta" and 'basic functional aspects of the various system' in case of 'Snell'.

Concluding remarks:

The understanding developed from the above findings and the contemporary ideas and trends in Neruoanatomy in the developed world can be integrated in order to plan for improving the methods of teaching in Neuroanatomy in Bangladesh.

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Original Article

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Comparison of Ovarian Arterial Resistive Index in Polycystic Ovarian Syndrome Patients and Those of Healthy Control Subjects

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Abstract:

Background: Polycystic ovarian syndrome is the most common endocrine abnormality in women of reproductive stage. PCOS carries with it significant health risks, including infertility, endometrial hyperplasia, diabetes and cardiovascular diseases. Duplex color Doppler ultrasonography help to assess intra stromal ovarian arterial flow velocities very quickly without any invasive procedure for qualitative and quantitative assessment of blood flow velocities. Objective: This study was performed to observe the difference between Resistive index of intra stromal ovarian artery in PCOS subjects and those of normal control subjects. Materials and methods: This case-control study was attempted on180 subjects aged 16-36 years; out of them 84 PCOS patients were considered as study group and 96 healthy subjects were considered as control subjects with compatible age and weight. The study was carried out in the department of Radiology and Imaging, Enam Medical College and Hospital, Savar for the period of January 2015 to December 2017.To eliminate the bias, Doppler study was performed first by the investigator herself and subsequently confirmed by a senior radiologist. All the selected subjects underwent TVS with Doppler study of intrastromal ovarian arteries using Voluson 730 Pro 9 MHz transducer. RI was recorded for ovarian arteries. Unpaired t-test was done to compare blood flow velocity indices of ovarian artery in PCOS patients and that of healthy control subjects and a P value <0.05 was taken as significant. Results: Majority (43.3%) of patient's were in 21-25 age group. In the current study, it was found that the mean resistive index (RI) in 84 PCOS patients was (0.63 ± 0.05) ranging 0.57-0.71. And that of 96 healthy subjects was (0.79 ± 0.11) ranging 0.73-0.96. In this study the mean differences of ovarian arterial RI in PCOS patients and healthy control group was statistically significant (p<0.05) in unpaired 't' test. Conclusion: From the result of present study it can be concluded that, there is statistically significant difference between ovarian arterial resistivity index (RI) of PCOS patients and that of healthy control subjects included in this study. Lower RI of intra stromal ovarian artery was evident in PCOS subjects.

Keywords: Polycystic ovarian syndrome, resistive index, intra stromal ovarian artery

Introduction:

Polycystic ovarian syndrome was first described by Stein and Leventhal in 1935[1]. It is the most common endocrine disorder affecting female fertility[2]. PCOS is frequently associated with hyperandrogenism, obesity, hyperinsulinemia and insuline resistance[3]. PCOS has been reported to occur in 20% of general female population[4]. In 2003, joint ESHRW/ASRM consensus meeting produced a refined definition of PCOS; namely the presence of two out of the three criteria: a) oligo and/or anovulation, b) hyperandrogenism (clinical/ biochemical) and c) polycystic ovaries[5].

The morphology of the PCO was redefined as an ovary with 12 or more follicles measuring 2 - 9 mm in diameter and/or increased ovarian volume (> 10 cm3)[6]. Ultrasound assessment of ovarian morphology is considered to be essential in the diagnosis of PCOS and the gold standard for defining polycystic ovary (PCO)[7].

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Transvaginal ultrasound with color Doppler is increasingly used as a non-invasive method to assess blood flow changes in the pelvic organs[8]. The introduction of transvaginal Doppler sonography has contributed markedly to the refinement of ultrasound diagnosis. In addition, it has provided much new morphological and pathophysiological information on blood flow dynamics within the uterus and ovaries[9].

Battaglia and co-workers, Zaidi and co-workers and Aleem and co-workers successively confirmed that, in patients with PCOS, significant changes occur within the intraovarian vessels. Furthermore, uterine artery resistance was shown to be increased in PCOS [6,9]. Zaidi and co-workers and Aleem and co-workers, confirming that Doppler analysis of ovarian stromal arteries in PCOS may be useful to improve the diagnosis, and to provide further information about the pathophysiology and evolution of the syndrome[10].

This study aims to differentiate ovarian blood flow in women with PCOS and normal control group. If difference in vascularity can be demonstrated, this information may provide us with an additional parameter for the ultrasound diagnosis of PCOS[11.]

Methodology:

This case-control study was attempted on 360 ovarian arteries of 180 subjects aged 16-35 years in the department of Radiology and Imaging, ENAM from January 2015 to December 2017. Out of them 168 ovarian arteries of 84 PCOS patients, clinically and biochemically confirmed were considered case group and 192 ovarian arteries of 96 healthy subjects were considered as healthy control subjects. The equipment used was voluson 730 pro 9 MHz transducer. Transvaginal sonography was done followed by Duplex colour Doppler study with spectral analysis of intra stromal ovarian artery. The colour Doppler study was performed first by the investigator herself and subsequently confirmed by a radiologist of the same department to eliminate bias. Data were collected from primary sample study for clinical history. Duplex color Doppler and spectral analysis were recorded in data collection sheet.

Statistical analysis of the result was done by computer software device statistical package for social science (SPSS-17). The results were presented in table. For significant difference, unpaired t-test and chi square test were performed. A P value of < 0.05 were considered significant.

Result:

A total 180 subjects are included in this study. Age of the patients ranged from 16 to 35 years. The largest group was of age (21-25 years) contributing 43.3 % of total case in the study. Mean (± SD) age of the patients was 22.5 ± 9.8 years. (Table I)

Table-I: Distribution of respondents according to age. (n= 180)

Age	No of respondents	Percentage
16-20	8	4.4
21-25	78	43.3
26-30	70	39
31-35	24	13.3
Total	180	100

In the current study, it was found that the ovarian volume, number of follicles were found increased in PCOS cases than that of normal control subjects. On the other hand, size of the follicles are more in control group.(Table II)

Table II: Ultrasonographic features of ovaries in control and PCOS patients (n= 180)

Criteria	Control	PCOS	P
Ovarian volume	3.9 ± 1.23	9.02 ± 2.11	<0.001
Number of follicles	2.50 ± 3.72	12.7 ± 4.55	<0.001
Size of the follicles	10.11 ± 6.23	6.7 ± 1.87	<0.001

The study also revealed that there was no significant difference (p>0.05) in ovarian arterial mean resistive index(RI) between right and left ovarian arteries of case group as well as in control subjects.



Picture:1. Ovarian volume in a normal control subject.

Picture: 2. Ovarian volume in a patient with PCOS.

In the present study, it was also found that stromal thickness and echogenicity is increased in PCOS cases and thickness and echogenicity is normal in control group and was statistically significant (p<0.05) in unpaired 't' test. (Table III)

Table III: Ultrasonographic findings of stromal thickness and echogenicity in control and PCOS patients (n= 180)

Criteria	control	PCOS	P
Stromal thickness	5.0 ± 0.31	8.9 ± 0.20	<0.001
Stromal echogenicity	not increased	increased	<0.001



Picture: 3. Size of follicles in patients with PCOS.

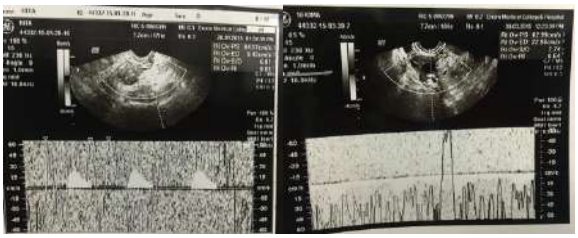
Picture: 4. Increased stromal thickness in case group.

In the current study, it was found that the mean resistive index (RI) in 168 ovarian arteries of 84 PCOS patients was (0.63 ± 0.05) ranging 0.57-0.71. And the mean resistive index (RI) value measured in 192 arteries of 96 healthy subjects was (0.79 ± 0.11) ranging 0.73-0.96. The mean difference was statistically significant (P<0.05) between two groups (Table IV).

Table IV: Comparison of ovarian arterial mean resistive index (RI) between 96 control subjects and 84 PCOS cases (n=180)

RI	Mean ± SD	Range	t value	p value
Control group (n=96)	0.79±0.11	0.73-0.96	10.53	0.039
Case group (n=84)	0.63±0.05	0.57-0.71		

*P value was achieved from unpaired t-test and was considered as significant where it was less than 0.05



Picture: 5. RI of ovarian artery in normal control group.

Picture: 6. RI of ovarian artery in case group.

Discussion:

PCOS is the most common female endocrinopathy, effects 6-8% of women in their reproductive years with unknown etiology[3]. It has been suggested that development of a state of chronic anovulation may be result in the classical picture of PCOS, displaying numerous follicle in early stage of devolopment and atresia and echogenic stromal tissue[8].

In this study 180 patients were divided into four age groups. The ages of the patients ranged from 16 to 35 years with the maximum number of cases found in the 21-25 years age group. Observation revealed no statistically significant ($p<0.05$) mean age differences in study and control group. A similar study done by dolz et al. showed no significant difference between the study and reference groups with respect of age[12].

The theory that the hemodynamics of the uterine and ovarian vessels are required for adult feature of this syndrome. Neovascularization have been demonstrated throughout the cycle[13]. Color Doppler imaging is the most promising modality regarding the direction and velocity of blood flow. Here, uterine blood flow velocity was shown to be significantly higher in women with PCOS[14].

According to Adam et al. ovarian volume is greater in women with PCOS compared to normal control group. My study showed the same findings in PCOS groups[11].

When compare with normal ovaries, polycystic ovaries are more vascular and have vessels with greater calibre[15]. I also found a direct correlation between ovarian size, presence of vascular flow pattern, number of follicles and degree of stromal echogenicity. In this study, comparison between resistivity index (RI) of right and left ovarian arteries of PCOS patients and control subjects were evaluated but no significant ($p>0.05$) difference were found.

Sophisticated new computerized ultrasound system can now be used to measure the area and volume of the ovary and may provide a valuable opportunity for truly comparative study of the normal ovary and PCOS[13].

Goswamy and Steptoe were the first to report significantly elevated RI and PI values in the uterine arteries of women who had PCOS[16]. Another study also showed, RI of intraovarian vessel is decreases in PCOS patients[13].

In this study the ovarian arterial mean resistive index (RI) measured in 84 PCOS patients was (0.63 ± 0.05) ranging 0.57-0.71 and the previous investigator dolz et al. who found the mean RI value of (0.53 ± 0.05)[12].

Mean resistive index (RI) value measured in healthy subjects was (0.79 ± 0.11) ranging 0.73-0.96. and the previous investigator pellizzari et al. discovered the mean RI value of (0.93 ± 0.005)[17].

So, the result of present study coincides with those of the previous studies and RI of intra ovarian arteries in case group were significantly decreased than that in healthy control group[13] and was statistically significant ($p<0.05$) in unpaired 't' test.

In summary, my observation with TVS and color Doppler confirmed that, in comparison to ovulating women with normal cycles, patients with PCOS have decreased impedance of ovarian artery.

Conclusion:

From the result of present study it can be concluded that, there is statistically significant difference between ovarian arterial resistivity index (RI) of PCOS patients and that of healthy control adult subjects included in this study. So, it can be concluded that color Doppler evaluation of intra stromal ovarian artery may be a new USG marker in the diagnosis of PCOS. Longitudinal studies with follow up are necessary to confirm and expand my findings.

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DCIMCJ

Original Article

DCIMCJ 2019 January;6(1):71-75

Pedigree Analyses of Type 2 Diabetes Mellitus in Bangladeshi Population

Begum F[1], Iqbal M[2], Nahar N[3], Akter S[4], Zisa RS[5], Rahman KMS[6]

Abstract:

Objective: To determine how type 2 diabetes is distributed in families of Bangladeshi males having type 2 diabetes. Methods: A descriptive cross-sectional study was carried out in the Department of Anatomy, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from July 2008 to June 2009. Fifty male patients diagnosed as and treated for type 2 diabetes mellitus at Bangladesh Institute of Research and Rehabilitation in Diabetic, Endocrine and Metabolic Disorder (BIRDEM) were selected for this study. The present researcher interviewed each subject by herself using a structured questionnaire. Paternal and maternal family histories were taken to know about the presence of diabetes in the family. The data were analyzed via Statistical Package for Social Sciences (SPSS version- 20). Results: This study shows 39 (78%) gave a positive family history. Among the siblings, the presence and absence of diabetes were almost similar in case of brothers and sisters (around 40%). Positive history about the father was a little more frequent than that about mother (22% compared to 16%). Paternal uncles and aunts, gave a positive history in 16% cases. For maternal uncles and aunts, the frequency was 26%, for paternal cousins a positive history came form 32% probands, while for maternal cousins it was 10% only. In case of category 'unknown' information varied from about 10-98% of the probands. Conclusion: There is significant familial aggregation in T2DM. The first-degree relatives of T2DM patients are high risk populations, so long term monitoring and early screening should be performed.

Keywords: Type 2 diabetes, first-degree relative, high risk population

Introduction:

Diabetes mellitus is a multifactorial disease resulting from interaction of both genetic and environmental factors[1,2]. Type 2 DM is the commonest form of diabetes (90-95% of the diabetes population) resulting from insulin resistance combined with relative insulin deficiency. Type 1 DM is an autoimmune disease, which accounts for 5-10% of diabetic cases.

In the year 2000, 171 million people were estimated to be diabetic worldwide, which is projected to rise to 366 million in 2030[3]. India was estimated to have the highest number of diabetes cases in 2000 which was 31.7 million and by 2030 it is estimated to rise to 79.4 million[3]. There is an increase in the percentage of population being exposed to diabetes in addition to the decrease in age of onset. It therefore becomes important to analyse the epidemiology of the disease. Diabetes is known to have a strong genetic component. There is a familial influence on the frequency of diabetes[4] .

In Framingham population study maternal and paternal diabetes conferred equivalent risk for occurrence of Type 2 DM in offspring[5] while

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existence of excess of maternal transmission of Type 2 DM was observed in the analysis carried out in Northern California[6]. Familial clustering of diabetes and a significant maternal influence as well as a male sex-specific paternal effect was reported in a Chinese population study[7]. In this study to evaluate pedigree analyses of type 2 diabetes Mellitus, in Bangladeshi Population.

Material and methods:

A descriptive cross-sectional study was carried out in the Department of Anatomy, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from July 2008 to June 2009. Fifty male patients age 25 years or more diagnosed as and treated for type 2 diabetes mellitus at Bangladesh Institute of Research and Rehabilitation in Diabetic, Endocrine and Metabolic Disorder (BIRDEM) were selected for this study. A systemic sampling technique was used for the study taking every alternate patient coming to the Health Education Department of BIRDEM and fulfilling the selection criteria.

The present researcher interviewed each subject by herself using a structured questionnaire. Paternal and maternal family histories were taken to know about the presence of diabetes in the family. Confirmation of the presence of the disorder in the family members was made by making telephone calls to the member as far as feasible. The data were analyzed via Statistical Package for Social Sciences (SPSS version- 20).

Results:

This study shows 39 (78%) gave a positive family history. Among the siblings, the presence and absence of diabetes were almost similar in case of brothers and sisters (around 40%). Positive history about the father was a little more frequent than that about mother (22% compared to 16%). Paternal uncles and anunts gave a positive history in 16% cases. For maternal uncles and aunts, the frequency was 26%, for paternal cousins a positive history came form 32% probands, for maternal cousins it was 10% only. In case of category 'unknown' information varied from about 10-98% of the probands.

Table 1: Frequency of diabetes mellitus among family members of the proband (n = 50)

Relationship	Present		Absent		Unknown	
	Abs. freq.	Perc. Freq. (%)	Abs. freq.	Perc. Freq. (%)	Abs. freq.	Perc. Freq. (%)
Father	11	22	22	44	17	34
Mother	8	16	26	52	16	32
Brother	20	40	24	48	6	12
Sister	21	42	22	44	7	14
H-B (Half- brother)	0	0	3	6	5	10
H-S (Half- sister)	0	0	1	2	2	4
Son	2	4	15	30	33	66
Daughter	1	2	13	26	36	72
Paternal grand father	1	2	0	0	49	98
Paternal grand mother	1	2	0	0	49	98
Paternal uncle	5	10	15	30	30	60

Table 1: (Continued)

Relationship		Present		Absent		Unknown	
		Abs. freq.	Perc. Freq. (%)	Abs. freq.	Perc. Freq. (%)	Abs. freq.	Perc. Freq. (%)
Paternal aunt		3	6	11	22	36	72
Paternal cousin	Brother	11	22	2	4	37	74
	Sister	5	10	7	14	38	76
Maternal grand father		1	2	1	2	48	96
Maternal grand mother		0	0	3	6	47	94
Maternal uncle		8	16	17	34	25	50
Maternal aunt		5	10	20	40	25	50
Maternal cousin	Brother	3	6	2	4	45	90
	Sister	2	4	3	6	45	90

Abs. freq. **:** Absolute frequency
Perc. freq. **:** Percentage frequency

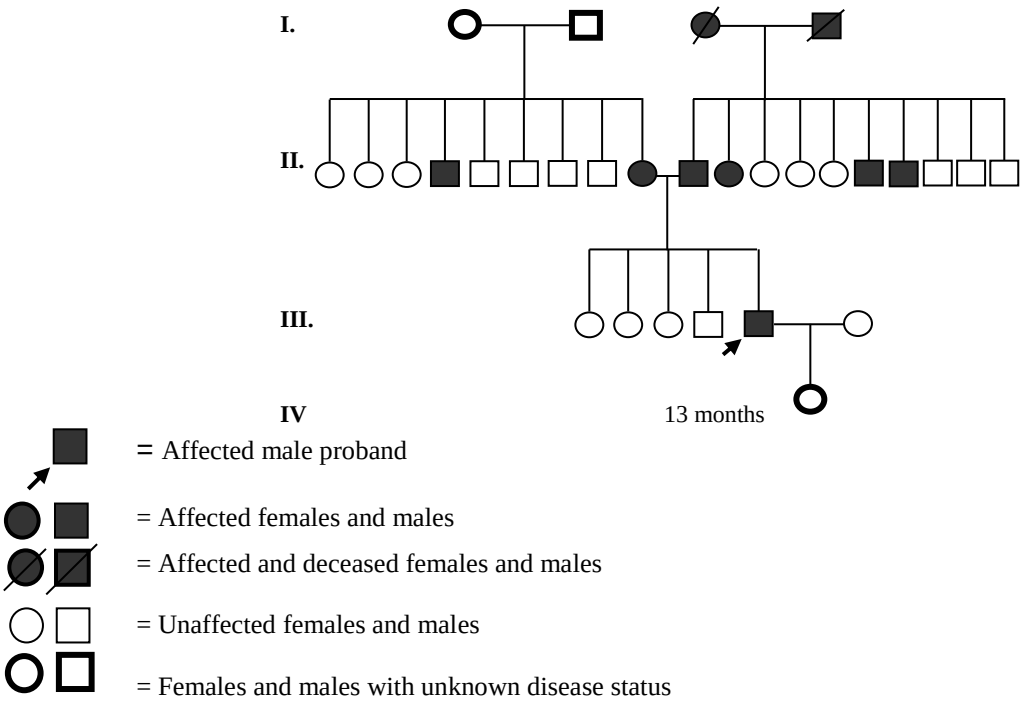


Fig. 1: A sample pedigree chart of a proband of the present study with type 2 diabetes mellitus showing the presence of diabetes at least in three generations.

The sequential arrangements of the siblings do not represent their birth sequence in any generation.

Discussion:

Diabetes is a disease that has a strong clustering in families and has a genetic component[7-9]. However, environmental factors such as diet and oxidative stress equally contribute to the disease occurrence. When the patterns of inheritance of diabetes were analysed in different populations, specific trends were observed in these sets of population with respect to different parameters e.g. excess of maternal transmission[6] lack of excess of maternal transmission[10], male sex specific paternal effect[6], maternal and paternal diabetes conferring equivalent risk[5], and so on. Thus there is a familial influence on the transmission of diabetes and different genetic and environmental factors contribute to the transmission of disease in different populations and influence penetrance, variability and epidemiology.

In this study shows 39 (78%) gave a positive family history. Out of them, 20% gave a positive family history in the father, 16% in the mother and among 40% in siblings. Ostavan[11] reported that, 61% of type 2 diabetic patients had a positive family history, of which 11.9% in father, 21.4% was in mother and around 30% cases in siblings. One interesting results of the present study was the paternal inclination of family history. Present study shows that in case of category unknown information varied form about 10-98% cases. Similar study Deo et al,[12] found in case of type 2 DM, 58% of the cases showed family history, 28% cases had no family history of type 2 DM.

Ostovan[11] reported that, his findings provide evidence suggesting more significance of family history among type 2 DM than type 1 diabetic patients and also importance of maternal inheritance than paternal one.

In western India showed the age of onset of diabetes decreased with generations in families with history of diabetes, both the parents conferred equal risk in transmission of diabetes as previously reported in Framingham offspring study;[5] and sons were more susceptible to the disease when both parents were diabetic. Deo et al[12] also observed absence of excess of maternal transmission as previously reported in the Korean population and the south Indian population.

Conclusion:

The pedigree analysis of genetic transmission thus gives valuable insight into genetic epidemiology and leads to better understanding of the pattern of occurrence of diabetes. The involvement of multiple genes and mutations in occurrence of diabetes reported earlier could influence the inheritance patterns observed. These variations in the transmission pattern could be related to the clustering of different mutation in the gene pool.

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Original Article

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Serum Magnesium Level in Chronic Kidney Disease Patients and Patients with Maintenance Hemodialysis

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Abstract:

Background: The burden of Chronic Kidney Disease (CKD) is increasing rapidly worldwide and has become a major health problem. Serum magnesium has protective role in the cardiovascular system in CKD and MHD patients. Objectives:To observe the serum magnesium level in Chronic Kidney Disease Patients and Patients with maintenance hemodialysis. Methods:A cross sectional study was carried out for a period of one year in the Department of Biochemistry, Dhaka Medical College in collaboration with department of medicine.Total number of 150 subjects of both sexes, age ranging from 18 to 60 years. Among them, 50 CKD patients (stage IV& V) were included in group I, 50 CKD patients with maintenance hemodialysis (MHD) in group II and 50 health subjects ingroup III. Results: Serummagnesium was significantly higher in CKD [3.00± 0.33] than in CKD with MHD [2.02±0.61] patients. Conclusion: Serum magnesium level is increased in patientswithCKD (CKD Stage IV & V) than in patients with maintenance hemodialysis. Regular checkup of serum magnesium level in CKD patient with MHD patients in view with magnesium supplementation might prevent cardiovascular & cerebrovascular disease due to hypomagnesaemia.

Keywords: CKD, MHD, serum magnesium

Introduction:

Chronic kidney disease (CKD) is recognized as a major public health problem worldwide. It is characterized by progressive deterioration in renal function ultimately leading to irreversible loss of nephron number and function. This decline can occur over several months or can take years to progress[1]. Kidney Disease Outcomes Quality Initiative (K/DOQI) of the National Kidney Foundation (NKF) has developed a definition of CKD. According to the organization, CKD is either kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of kidney, with or without decreased glomerular filtration rate (GFR) or GFR < 60 ml/min/1.73 m^2 for ≥ 3 months, with or without kidney damage [2].The incidence and prevalence of chronic kidney disease (CKD) are increasing worldwide. According to the 1999 – 2004 National Health and Nutritional Survey (NHANES), the prevalence of CKD in the US population is 15.3% [3].

Incidence of CKD in Bangladesh is 19%[4]. To observe the prevalence of CKD a review was done on 26 studies of different countries of the world. The researchers found the average worldwide prevalence of CKD was 7.2% in persons aged > 30 years[5]. It has been found that, in Bangladesh there are about 20 million people suffering from CKD. Among them, 20,000 people die of end stage renal disease (ESRD) in each year[6]. The most common complications are cardiovascular, cerebrovascular and peripheral vascular disease[7]. The incidence of cardio vascular

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disease (CVD) is also high in patients on hemodialysis. CVD is the leading cause of death among the patients with chronic kidney disease[8]. End-stage renal disease (ESRD) is a devastating medical, social and economic problem in the community and needs dedicated supervision andhealth care. It is fatal unless treated properly. Cardiovascular and cerebrovascular diseases are the two most important causes of morbidity and mortality in ESRD patients especially in diabetics and those with lupus erythematous[9]. Cardiovascular diseases are the leading cause of death in ESRD patients; cardiac arrest accounts for 47.1% of total deaths[10].

Magnesium is predominantly an intracellular cation that plays a critical role in cellular physiology. Serum levels are often slightly elevated in patients on chronic hemodialysis and older reports suggests that total body stores may also be increased, based on bone biopsies in patients treated with higher dialysate magnesium levels than are currently in use today. Several studies have shown that magnesium, particularly in the form of magnesium carbonate, is an effective phosphate binder and can decrease patients' exposure to calcium[11]. Magnesium (Mg) plays an important role in the regulation of vascular tone and heart rhythm. Magnesium also reduces total peripheral resistance by stimulation of nitric oxide synthesis and is a potent inhibitor of vascular calcification[12]. Disorders of magnesium are hardly mentioned in most educational books of medicine[13]. Magnesium status depends on three organs: uptake by the intestine, storage in the bone and excretion through the kidneys. Hypermagnesaemia is therefore often due to problems in these organs, mostly intestine or kidney.The kidney has a vital role in magnesium homeostasis and, although the renal handling of magnesium is highly adaptable, this ability deteriorates when renal function declines significantly. In moderate chronic kidney disease (CKD), increases in the fractional excretion of magnesium largely compensate for the loss of glomerular filtration rate to maintain normal serum magnesium levels. However, in more advanced CKD (as creatinine clearance falls <30 mL/min), this compensatory mechanism becomes inadequate such that overt hypermagnesaemia develops frequently in patients with creatinine clearances <10 mL/min. In patients undergoing dialysis, the effect of various magnesium and calcium dialysate concentrations has been investigated in hemodialysis (HD) and peritoneal dialysis (PD). Results generally show that dialysate magnesium, at 0.75 mmol/L, is likely to cause mild hypermagnesaemia, results for a magnesium dialysate concentration of 0.5 mmol/L were less consistent, whereas serum magnesium levels were mostly normal to hypomagnesaemic when 0.2 and 0.25 mmol/L were used. While dialysate magnesium concentration is a major determinant of HD or PD patients' magnesium balance, other factors such as nutrition and medications (e.g. laxatives or antacids) also play an important role[14].

Our body needs magnesium to regulate a variety of biochemical reactions. The kidney plays a major role in magnesium homeostasis and the maintenance of plasma magnesium concentration. The plasma magnesium concentration is a major determinant of urinary magnesium excretion[15]. Vascular calcification is an important factor for increased morbidity and mortality in CKD and dialysis patients[16]. Hypomagnesaemia has been linked with increased co-morbidity and cardiovascular risk factors; including C-reactive protein (CRP), atherosclerosis, hypertension, and dyslipidemia[17].

Keeping in view, the mortality associated with CVD and the association of serum magnesium levels with CVD in CKD and MHD patients and its relation with comorbidity we have planned to study the serum magnesium profile of CKD patients, CKD patients with MHD and healthy subjects in our centre. Magnesium is a metallic chemical element; it has the symbol Mg and atomic number 12. It is the second element in group 2 of the periodic table[18].

CKD stages [19]

The stages of CKD (Chronic kidney disease) are mainly based on measured or estimated GFR (Glomerular filtration rate). There are five stages but kidney function is normal in Stage 1, and minimally reduced in Stage 2. The K/DOQI Stages of kidney disease are:

Stage	GFR*	Description	Treatment stage
1	**90+**	Normal kidney function but urine findings or structural abnormalities or genetic trait point to kidney disease	Observation, control of blood pressure.
2	**60-89**	Mildly reduced kidney function, and other findings (as for stage 1) point to kidney disease	Observation, control of blood pressure and risk factors.
3A	**45-59**	Moderately reduced kidney function	Observation, control of blood pressure and risk factors.
3B	**30-44**		
4	**15-29**	Severely reduced kidney function	Planning for end stage renal failure.
5	**<15 or on dialysis**	Very severe, or end stage kidney failure (sometimes call established renal failure)	Treatment choices.

Methods:

It was a cross sectional study, which was conducted in the Department of Biochemistry, Dhaka Medical College, Dhaka during the period from July 2014 to June 2015. A total number of 150 subjects of both sexes were selected purposively according to selection criteria with age ranging from 18 to 60 years. Among them 50 patients were CKD patients (Stage IV& V) (Group I), 50 patients were CKD with maintenance hemodialysis (Group II) and 50 healthy subject had taken for comparison group (Group III). The fasting magnesium level of all group were assessed. All data were tabulated and analysis was performed by using a computer based statistical program SPSS Version 20 . Result was presented as mean and standard deviation (mean ± SD). Comparison was done by unpaired Student't' test, Chi-square test, ANOVA test and Pearson's Correlation coefficient Test was done to see correlation . P value of <0.05 was considered as significant.

Reference value:

Serum Magnesium
Male/ Female : 1.9 – 2.5 ml/dl

Results:

In this study total 150 subjects were selected according to selection criteria. Among them, 50 CKD patients (stage IV & V) were included in group I, 50 CKD patients with maintenance hemodialysis (MHD) were included in group II and 50 health subjects were included in group III. Serum magnesium, fasting blood glucose, lipid profile of all the groups was assessed and statistically compared.

Table I: General characteristics of the subjects of study groups.

Baseline characteristics	Groups			p value
	Group-I (CKD) (n=50)	Group-II (CKD ē MHD) (n=50)	Group-III (Healthy) (n=50)	
Age (mean ±SD)	43.86 ± 9.21	47.14 ± 9.02	43.32 ± 8.73	0.075*
Gender				0.395#
▪ Male n (%)	32 (64.0)	37 (74.0)	31 (62.0)	
▪ Female n (%)	18 (36.0)	13 (26.0)	19 (38.0)	
BMI (mean ±SD)	22.8 ± 1.7	23.3 ± 2.6	23.8 ± 3.4	0.139*
Systolic BP (mmHg)	176 ± 29	154 ± 40	118 ± 8	<0.001*
Diastolic BP (mmHg)	100 ± 10	90 ± 14	76 ± 9	<0.001*

#Chi-square test was done to measure the level of significance

*t test was done to measure the level of significance

Table I shows general characteristics of the study subjects. Mean ±SD age was 43.86 ±9.21, 47.14 ±9.02 and 43.32 ±8.73 in CKD, CKD ē MHD and healthy subjects respectively. BMI was almost similar in all groups. Blood pressure was higher in CKD patients followed by CKD ē MHD and healthy subjects. Study subjects are age and sex matched.

Table II: Serum magnesium (mg/dl) level in study subjects.

	Groups			p-value
	Group-I (CKD) (n=50)	Group-II (CKD ē MHD) (n=50)	Group-III (Healthy) (n=50)	
S. Mg (mg/dl)	3.00± 0.33	2.02 ± 0.61	2.05 ± 0.27	<0.001#

Group-I (CKD) (n=50)		Group-II (CKD ē MHD) (n=50)	
S. Mg (mg/dl)	3.00± 0.33	2.02 ± 0.61	<0.001*
Group-I (CKD) (n=50)		**Group-III (Healthy)** (n=50)	
S. Mg (mg/dl)	3.00± 0.33	2.05 ± 0.27	<0.001*
Group-II (CKD ē MHD) (n=50)		**Group-III (Healthy)** (n=50)	
S. Mg (mg/dl)	2.02 ± 0.61	2.05 ± 0.27	0.801*

[#] ANOVA test was done to measure the level of significance

* t test done to measure the level of significance.

Table III shows serum magnesium in study subjects.

Mean ± SD serum magnesium was 3.00 ± 0.33 mg/dl, 2.02± 0.61 mg/dl and 2.05 ± 0.27 mg/dlin CKD, CKD ē MHD and healthy subjects respectively.

Serum magnesium was significantly higher in CKD [3.00±0.33] than CKDē MHD [2.02±0.61] patients.

Serum magnesium was significantly higher in CKD [3.00±0.33] than healthy [2.05±0.27] study subjects.

Serum magnesium was almost similar in CKD ē MHD [2.02±0.61] patients and healthy [2.05±0.27] study subjects.

Discussion:

Chronic Kidney Disease (CKD) is increasing rapidly worldwide and has become a major health problem. Studies have shown that more than 50% of deaths in CKD patients are attributable to cardiovascular events. Serum magnesium has protective role in the cardiovascular system in CKD and Dialysis patients.

To establish the purpose of study a cross sectional comparative study was carried out to evaluate and assess the serum magnesium level of all group. The serum Magnesium of both groups were assessed and statistically compared in among groups to observe magnesium in CKD patients and patients with MHD. In our study, serum creatinine level was estimated in the study groups for determination of estimated GFR (eGFR). Staging of CKD was done based on eGFR.

Nakamura also found similar result that is age and BMI was matched in between groups[20].

In this study S. Magnesium was significantly higher in CKD [3.00±] than CKD with MHD [2.02±0.61] patients. Similar type of observation was found by Cunningham et al[15] where S. magnesium was significantly higher in CKD [3.00±0.33] patient than healthy [2.05±0.27] study subjects.

In this study S. Magnesium in different stages of CKD patients. S. Magnesium was significantly higher in stage-V (3.09±0.35) than that of stage-2.79±0.17. Cunningham et al. also found in healthy people, intestinal magnesium absorption and renal excretion are regulated so as to maintain magnesium balance in more advanced CKD (as creatinine clearance falls <30mL/min), this compensatory mechanism becomes inadequate such that overt hypermagnesaemia develops frequently in patients with creatinine clearances <10mL/min[15].

So from above discussion it may be concluded that Serum magnesium level is increased in patients with End Stage Renal Disease (CKD Stage IV & V) than patients with maintenance hemodialysis. Regular checkup of serum magnesium level in CKD with MHD patients in view with magnesium supplementation might prevent cardiovascular & cerebrovascular disease due to hypomagnesaemia.

Conclusion:

Serum magnesium level is increased in patients with End Stage Renal Disease (CKD Stage IV & V) than patients with maintenance hemodialysis. Regular checkup of serum magnesium level in CKD with MHD patients in view with magnesium supplementation might prevent cardiovascular &cerebrovascular disease due to hypomagnesaemia.

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Original Article

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Childbirth Practice and Attitude among the Rural Women in a Selected Community of Bangladesh

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Abstract:

Childbirth is a normal physiological process which can become pathological due to the adoption of certain practices consequently affect the health and survival of the new born and mother. Good ante- natal and post- natal care and trained assistance at the time of child birth are thus very important to ensure survival of both mother and child. A cross- sectional descriptive type of study was carried out to find out the childbirth practice among the rural women. A total of 151 cases were selected purposively from the village of Islampur of Dhamraiupazilla under Dhaka district. The study revealed that the most of the respondents (49.01%) were young aged women (21-25 years), more than 79% of the cases were Muslims, higher proportion of the respondents (25.83%) was educated up to primary level, mostly the respondents (51.05%) were from a large family that is 5-7 family members and about 93% of the respondents were housewives. The socio- economic status of the respondents showed that 41.72% of the women had family income between 5,001-10,000 taka. The reproductive health status revealed that most of the women (64.9%) got married in their younger age (15-20 years), 29% conceived for one time before the study was done, about 60% of the women had < 2 children. Utilization of antenatal care related information found that about 55% of women received antenatal care during their last pregnancy and among them 69% of women received from the local Upazilla Health Complex, about 60% of women received antenatal visit only for 2 times and 73.51% of the respondents were immunized against tetanus during their last pregnancy. About 76% of the respondents denied having any health problems during their last pregnancy. Among them who had problems most of the women (46.36%) in the study had faced leg edema during their last pregnancy. Place and person conducting delivery revealed that the most of the respondents (73.51%) delivered at home during their last delivery and about 69.54% had their delivery by the local dais, 84% of the women in the study normally delivered, about 84% of the respondents in the study denied having any problems during their last delivery and who had problems among them the most of the women (46.36%) had prolonged labour. Childbirth practice in the rural community is more or less similar in the developing countries. Bangladesh is not out of this trend. The present study revealed the same fact which warrants actions targeting specific factors and further study is recommended.

Keywords: Childbirth, ante- natal care, rural women

Introduction:

Bangladesh is a developing country. Population nearly 160 million, per capita GDP is 470 US dollars, infant mortality, maternal mortality, under-5 children mortality are 37/ 1000 live birth, 1.94/ 1000 live birth, and 52 / 1000 live birth respectively. Bangladesh is fighting against three curses: poverty, illiteracy and over population[1]. Eighty percent are rural population. Rural women are underprivileged in education, health care and in other social activities. They are ignorant in seeking health care. Maternal mortality rate (MMR) 1.96/ 1000 live birth, at least one antenatal check up by medically trained provider (doctors, nurses, midwives) 53.7%, facility based delivery 23.4%, delivery assisted by doctors, nurses or midwives (medically trained person) 26.5%. 85% of births take place at home, attended by unskilled birth attendants[2]. In the developing countries women's attitudeto deliver at home more than to deliver at hospital.

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Most women attended for antenatalcheck up but very few childbirths takes place at heath facilities. Most home deliveries are attended by untrained dais, mother in laws and other senior relatives, neighbours. Skilled birth attendants and health professionals conduct negligible number of deliveries. In case of complicated pregnancies and deliveries, husband or the family head is supposed to give decision[3]. Monetary constraints, absence of knowledge about the need of health care services and restrictions on the movement of the women also cited as reason for not accessing antenatal care. Behaviour of health workers discourage women to use the services provided by health facilities for antenatal care and child delivery. In developing countries, rural women never care for birth preparedness which includes selecting a skilled birth attendant, arranging delivery kit needed for safe delivery, identifying where to go in case of emergency and arranging money and transport for delivery[4]. In the context of rural Bangladesh different people are found to conduct home delivery in a traditional manner. Sometimes it may be the mother, relatives or the neighbours of a pregnant woman are found in this task. Quite often the Dai or the traditional birth attendant, in short TBA is the first priority for the pregnant women in rural Bangladesh.[5] Dais (trained or untrained birth attendant) are called only at the onset of labour. It is not customary for them neither to perform ante-natal care (ANC) nor to examine the position of the baby in the weeks preceding the birth. If no complications are present, TBAs do not refer the mothers for ANC as they feel it is not mandatory. To speed up delivery, abdominal massage is routine during labour. Introduction of various substances, such as juices of Chalta fruit, mustard oil, coconut oil, soap water, juices of tree buckle into vagina, make it slippery and facilitate delivery is common. Molasses juices are given to mothers to eat and hair rag other items even kerosene oil in extreme cases is put into the mouth of the mothers to induce vomiting and speed up delivery[6].

In Srilanka the high maternal mortality rate of 16.1/ 1000 live birth 1940 due tocomplications during Delivery hassignificantly declined reaching a level of 0.5/ 1000 live births by 1981. The impact of the common practice of delivering at a medical institution is lowering of maternal mortality rate in Srilanka to a lower level of 0.5 maternal deaths per thousand live births. Attendance at ante-natal clinics, visiting family doctors or even obstetric consultants was mostly done alone by the women when she felt sick or developed symptoms of confinement. She usually does not wait for her husband but accompanied one of her relatives or neighbors when went to the hospital immediately[7].

In Uganda, attendance for antenatal care represents a unique opportunity to improve the health of women and their infants. At delivery, the importance of skilled attendance has long been recognized. However, distance to health facilities, inadequate transportation and the need for immediate and specialized services havehampered women's ability to access these services[8]. The national Maternal Mortality Ratio is estimated to be 505 per 100,000 live births. Levels of antenatal care attendance are high (94%) but this is not reflected in care at delivery. Around a quarter of women are assisted during labour by a relative or friend and one in seven mothers receives no assistance at all.[9]

Presence of a professional attendant at each birth can lead to a marked reduction in maternal mortality and morbidity[10, 11]. Professional health care during childbirth is one of the process indicators to assess progress towards the Millennium Development Goal of improving maternal health[12].

Materials and methods:

This was a cross- sectional type of descriptive study.To find out the childbirth practice among the rural women in a selected community in Bangladesh. Total study required six months from November 2015 to April 2016. The study actually started with protocol preparation and finished with final report submission. The study was conducted at Islampur village in DhamraiUpazilla. By using conventional method of cross- sectional study sample size was determined. Although maximum effort was given by the researcher, due to time limitation only 151 cases could be included in the study. A non- probability purposive sampling was done due to scarcity of cases.

A structured questionnaire was developed in the light of objectives and variables of the study for collection ofdata.The questionnaire was pre- tested among the mothers residing in a selected rural community for clarity, accuracy, unambiguity.Data were collected ensuring the privacy and confidentiality by face to face interview of the mothers.

Results:

This cross sectional type of descriptive study was carried out among 151 married women who have at least one child. Data were analyzed using appropriate statistical procedure and presented in this current chapter through tables and graphs.

Table 1: Distribution of the respondents by background characteristics

Background	Number	%
Age in years		
15-20	15	9.93
21-25	74	49.01
26-30	10	6.62
31-35	15	9.93
36-40	19	12.58
> 41	18	11.92
Religion		
Muslim	120	79.47
Non- Muslim	31	20.53
Educational qualifications		
Illiterate	27	17.88
Can write	25	16.55
Primary	39	25.83
Secondary	35	23.17
S.S.C/ Equivalent &	25	16.57
Occupation		
Housewife	140	92.71
Others	11	7.29
Number of family members		
2-4	75	49.67
5-7	62	51.05
8 and above	14	9.27

Table-1 shows that the most of the respondents were young (49.01 %), Muslims (79%) and housewives (92.7%). Among the non-muslims (Hindu, Buddhist, and Christian) were Hindus mostly (20.53%). Table shows higher proportion of the respondents (25.83%) among the cases was educated up to primary level and 51.05% were from a large family that is 5-7 family members.

Table- 4.3 shows that among the respondents about 96% women's age of menarche was within the age of 12-15 years.

Table 2: Distribution of the respondents by their antenatal care during the last Pregnancy

Antenatal care during last pregnancy	Number	%
Yes	83	54.97
No	68	45.03

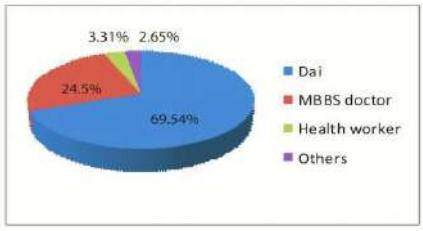
Table 2 shows that among the respondents about 55% of women received antenatal care during their last pregnancy.

Table 3: Distribution of the respondents according to their place of last delivery

Place of last delivery	Number	%
Home	111	73.51
Institutional	40	26.49

Table 3 shows that most of the respondents (73.51%) delivered at home during their last delivery.

Figure 1: Distribution of the respondents according to the person conducting the last delivery.



Discussion:

This cross sectional study was designed to determine the childbirth practice among the rural women in a selected community. A total of 151 married women of having at least one child were selected from the village of Islampur in DhamraiUpazilla under Dhaka district.

In this study, most of the respondents (49.01%) were young aged women (21-25 years) who were included in the study. Similar result was found in a study of Uganda that 13-25 years aged women 94/135 (70%) were mostly found who were younger of all age group included in that study[13]. Also a study among the ultra poor women of Bangladeshi household revealed that the majority (15 out of 20 respondents) of the women were in their twenties.[5]This recent study revealed that more than 79% of the cases were Muslims. Among the non-muslims (Hindu, Buddhist, and Christian) were Hindus mostly (20.53%). In a study of Bangladesh also found that most of the interviewees were Muslims.[4]Amongthe study women most (94%) of them were Muslim, and the remaining 6% were primarily Hindu revealed a study in Dhaka slum[14].

Here higher proportion of the respondents (25.83%) among the cases was educated upto primary level. And then upto secondary level education (23.17%) was also mentionable here. Similarly upto primary level education among the women of a community of Uganda was seen [87/146 (60%)].[13] similarly in a study of rural Kenya found that women who did not visit an ANC were more likely to have < 8 years of education (adjusted OR [AOR] 3.0, 95% CI 1.5-6.0)[15]. In this study most of the respondents (51.05%) were from a large family that is 5-7 family members. In rural Nepal, similarly since children are seen as divine blessings, family sizes tend to be large[16].

In the recent study the respondents were asked about their average monthly family income. Among the respondents 41.72% of the women had family income 5,00110,000 taka. And then about 35% of the respondent's income was the lowest as <5000 taka monthly.

Also in astudy of rural Kenya found that women who did not visit an ANC were more likely to have a low socio-economic status (SES) (AOR 2.8, 95% CI 1.5-5.3)[15].

In the current study most of the women in the study (64.9%) got married in their younger age (15-20 years) of their life. About 60.26% of the women had < 2 children among the total respondents. It is here to be mentioned that fertility declined dramatically in Bangladesh; women reporting 5 or more children declined from 35.9% in 1991-93 to 17.9% in 2000-04[12].

Among the respondents about 55% of women received antenatal care during their last pregnancy. It is also revealed in a study of Bangladesh that upwards trends for antenatal care between 1991 and 2004[12]. In the recent study among the respondents 76.8% received ante-natal services and of them 57.9% received more than three ante natal care[17]. Rahman et al. have also found that previous visits to the Upazilla Health & Family Welfare Centres (UHFWCs) was associated with greater seeking for antenatal care services[18].

Among the respondents about 60% of women received antenatal visit only for 2 times. But opposite scenario was seen in a community survey of Uganda found that on an average the pregnant women had 4-6 antenatal visits.[13] Also in a community based survey among the rural Kenyan women 90% visited the antenatal clinic (ANC) at least once during their last pregnancy (median number of visits 4)[15].

In this recent study about 73.51% of the respondents were immunized against tetanus during their last pregnancy. Similarly another study of Bangladesh revealed that 83% received tetanus toxoid (TT) vaccination during their ANC visits[19].

It is similar to a community survey of Uganda that tetanus vaccination (91%) was the one of the services most frequently reported. Also tetanus vaccination was high (>90%) in a study of Kenya[13].

This recent study revealed that about 76% of the respondents denied having any health problems during their last pregnancy. Among them who had problems most of the women (46.36%) in the study had faced leg oedema during their last pregnancy. Similarly a study of Bangladesh found that women did not associate complications of pregnancy with danger signs[20]. But oppositely according to a recent survey more than 60% pregnant women suffered from some complication during their pregnancy. Here most of the respondents (73.51%) delivered at home during their last delivery. According to NIPORT 2003, for all over Bangladesh, 91% delivery taka place at home[6]. Similar findings (82% deliveries were at home) was seen in a study of Dhaka slums[14]. Also in rural Kenya eighty percent of women delivered outside a health facility; among these, traditional birth attendants assisted 42%[15]. But an opposite scenario was seen in a community survey of Uganda that although 63% delivered their newborn at a local hospital, 11% still delivered at home with no skilled assistance[13]. And about 69.54% of the respondents had their last delivery by the local dais. According to a recent study, three- fourths of all births in Bangladesh are carried out by Dais, the traditional birth attendant.[6] TBAs attended also 75.6% of the home deliveries was found in another review study of Bangladesh.[20] Similar findings (98% deliveries were attended by dais) was seen in a study of Dhaka slums[14]. Also the majority of the births (68.8%) were conducted by untrained personnel in a study of Indian slum areas[20]. Here about 84% of the women in the study normally delivered in their last delivery. In the study about 84% of the respondents in the study denied having any problems during their last delivery. In this current study, who had problems among them the most of the women (46.36%) had prolonged labour during their last delivery. As per BDHS 2004, 52% of women identified prolonged or obstructed labour as potentially life threatening[1]. It is here to be mentioned about a community survey amongthe rural Kenyan women where 64% of those who delivered outside a health facility were aware of the potential risks, and could identify one or more complications that could occur[13].

A study of childbirth practice among the slum areas of India women also revealed that almost two-fifths (59.8 per cent) of the women had delivered at home while the remaining (40.2 %) had had their babies delivered at Government or private hospitals. A study among the indigenous populations of Australia also revealed that the majority of women had a vaginal birth (67%)[21]. Maternal mortality, deaths during pregnancy, birth or the postpartum period, is a key indicator of women's health and status.

Conclusion:

This cross- sectional type of descriptive study found out the childbirth practice among the rural women in a selected community in Bangladesh.

The study revealed that the most of the respondents (49.01%) were young aged women (21-25 years), more than 79% of the cases were Muslims, higher proportion of the respondents (25.83%) among the cases was educated upto primary level, mostly the respondents (51.05%) were from a large family that is 5-7 family members and about 93% of the respondents were housewives. The socio-economic status of the respondents showed that 41.72% of the women had family income between 5,00110,000 taka.The reproductive health status of the respondents showed that about 96% women's age of menarche was within the age of 12-15 years, most of the women (64.9%) got married in their younger age (15-20 years) of their life, 29% conceived for one time before the study was done, about 60% of the women had < 2 children.

Utilization of antenatal care related information of the respondents found that about 55% of women received antenatal care during their last pregnancy and among them 69% of women received from the local Upazilla Health Complex, about 60% of women received antenatal visit only for 2 times and 73.51% of the respondents were immunized against tetanus during their last pregnancy.

Place and person conducting delivery related information revealed that the most of the respondents (73.51%) delivered at home during their last delivery

and about 69.54% had their delivery by the local dais, 84% of the women in the study normally delivered, about 84% of the respondents in the study denied having any problems during their last delivery and who had problems among them most of the women (46.36%) had prolonged labour.Childbirth practice in the rural community is more or less similar in the developing countries. Bangladesh is not out of this trend. The present study revealed the same fact which warrants actions targeting specific factors and further study is recommended.

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Original Article

DCIMCJ

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Estimation of Serum Zinc, Copper and Magnesium Levels in Second Trimester of Bangladeshi Gestational Diabetes Attending in a Tertiary Care Hospital

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Abstract:

Background: The term Gestational Diabetes Mellitus (GDM) is becoming a major health problem in developing countries undergoing rapid changes in lifestyle, dietary habits and body mass index. GDM is associated with an increase incidence of congenital abnormalities which is also aggravated by mother's some trace elements deficiency such as zinc, copper, magnesium. Zinc, Copper, Magnesium are essential trace element for normal embryogenesis and fetal growth and its deficiency increase mortality and morbidity rate of mothers, embryos and neonates. Objective: To evaluate the association of serum copper, zinc and magnesium with GDM in second trimester. Methods: It was a case control study to evaluate the association of Copper and Zinc levels of pregnant women with GDM. A total number of 172 subjects were participated in this study; among them eighty six women diagnosed with GDM were selected as case (Group-I) and eighty six healthy pregnant women were control (Group-II). Student's unpaired t test was used to analyse the data between groups. For analytical purpose 95% confidence limit ($p<0.05$) was taken as level of significance. Results: There was significant difference in serum Copper levels in cases compared to control group. Serum Copper level was significantly increased in cases compared to control group in second trimester ($p<0.01$). We found very significant difference ($p<0.01$) in serum Zinc level when GDM compared to normoglycemic pregnant women in second trimester. Conclusion: Estimation of serum copper and zinc levels should be incorporated in every GDM cases for prevention of complications.

Keywords: Diabetes mellitus, GDM, OGTT, Trace elements

Introduction:

Gestational diabetes mellitus is defined as glucose intolerance resulting in hyperglycemia, with first onset or detection duringpregnancy[1,2]. Usually initiation of GDM is in middle and late gestational period and continues to term. Glucose intolerance usually returns to normal range within 6weeks after delivery[3]. Approximately 1-14 % of all pregnancies are complicated by GDM[4]. The incidence of GDM in Bangladesh is 6.7% among all Bangladeshi pregnant mothers[5]. Frequency of congenital malformation in infants of diabetic mothers is estimated to be 6-10%[6] Pregnancy is associated with physiological changes that result in increased plasma volume and red blood cells and decreased concentrations of plasma proteins and micronutrients[7]. It is a time of increased nutritional needs, both to support the rapidly growing fetus and to allow for the changes occurring in the pregnant[8]. Gestational diabetes is associated with excessive nutrient losses due to glycosuria[9]. Different researchers demonstrated that micro and macro nutrients are essential for thedevelopment offetus. With the progress of pregnancy, the level of plasma

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copper increased and it was high in all trimesters[10]. Serum copper is significantly increased in GDM patients as compared with healthy pregnant women[11].

Among the micronutrients, Zn is important, especially early in the life for the development and maintenance of fetal organs and tissues. Wang et al also showed serum zinc contents decreased in gestational diabetes compared with healthy pregnant women[8]. Magnesium (Mg) has been found to be linked to fetal and maternal wellbeing. Mg deficiency during pregnancy is associated with intrauterine growth retardation and metabolic syndrome in later life of the offspring[12,13]. There is report of low and variable serum Mg level during second and third trimester of normal pregnancy[14]. It has been found that serum Mg is depleted at a greater extent in women with GDM[15].

Aim of the study:

We aimed to see whether the changes in serum zinc, copper and magnesium could help in better understanding of the biochemical and metabolic abnormalities in GDM.

Materials and methods:

This case control study was carried out from July 2013 to June 2014 in the biochemistry department of Mymensingh Medical College. Total 172 subjects were selected by purposive sampling technique from the outpatient department of Obstetrics and Gynaecology and department of Endocrinology in Mymensingh Medical College Hospital. Clinically diagnosed GDM (n=86) was in the case group as Gr-I and it was done on the basis of OGTT by WHO criteria 2013[16]. The normoglycemic pregnant women at second were taken as control group (n=86) as Gr-II. All those pregnant women with the previous history of diabetes, hypertension, and other endocrine disorders were excluded from this study. This study protocol was approved by the institutional review committee. Data were collected through a preformed data collection sheet (questionnaire). The variables were age, education, occupation,socioeconomic status, residential address, dietary habit, height, weight, family history of diabetes, previouspregnancy history and previous history of gestational diabetes mellitus. Written informed consent was obtained from all the participants of the study groups prior to their enrolment into this study. Blood samples, from pregnant women, which was withdrawn for OGTT during screening for GDM was used for this study. In this study serum glucose was determined by Enzymatic method with GOD-PAP serum, serum zinc was determined by colorimetric method with 2-(5-Brom-2-pyridylazo)-5-[-N-propyl-N-(3 sulfopropyl) amino]-phenol,Serum copper was determined by colorimetric method with the 3,5-DiBr-PAESA stain and and Mg by Xylidyl Blue-I Method as per manufacturer's instruction.

The results were analyzed statistically and values were expressed as mean ± SD. The level of significance was determined by employing Student's unpaired t test. Only when the p value was less than 0.05; the difference between two groups and subgroups were considered as statistically significant.

Result:

A total of 172 pregnant women in their second and third trimester were enrolled in the study of which 86 had GDM and 86 were euglycemic by OGTT test. Pregnant women without GDM (euglycemic) were considered as control group. The mean age of GDM and control groups were 28.6±3.2 years and 27.3±3.1 years while the mean BMI was 26.4±1.5 m/kg^2 and 26.3±1.3 m/kg^2 respectively (Table-1). Also the mean Systolic & Diastolic Blood pressure in GDM and Control group were 125.33±10.24, 85±7.08 and 120.50±9.82& 80.50±6.84 respectively. Mean Serum Zn levels in GDM cases as Gr-I group were significantly ($p< 0.001$) low in both second trimester (43.93±75.479 µg/dl) compared to those without GDM (67.30± 7.812µg/dl) Gr-II group. In this study, 58 out of 86 GDM patients had family history of diabetes mellitus. The present study showed that serumCopper level was very significantly ($p<0.01$) increased in the GDM women in second trimester as Gr-I group compared to healthy controls in the second trimester Gr-II group. Serum Mg level was significantly low ($p<0.001$) in 2nd trimesters in GDM cases 1.4±0.3 mg/dl compared to control group 1.7±0.3 mg/dl.

Table-1: Age, BMI SBP DBP and Zinc in GDM and euglycemic pregnant women

GROUP	AGE (yrs)	BMI	SBP (mm of Hg)	DBP (mm of Hg)
GDM	28.6±3.2	26.4±1.5	125.33±10.24	85±7.08
Control	27.3±3.1	26.3±1.3	120.50±9.82	80.50±6.84
P value	0.778	0.774	0.65ns	0.695ns

GDM- Gestational diabetes mellitus, Control-Pregnant women without GDM (Euglycemic)

Table-2: Serum concentration Cu Zn and Mg in GDM and euglycemicPregnant women

Variables	Mean ± SD (cases Gr-I)	Mean ± SD (controls Gr-II)	P value
Copper(µg/dl)	240.09± 7.618	234.33± 3.809	0.002
Zinc(µg/dl)	43.93±75.479	67.30± 7.812	0.001
Magnesium (mg/dl)	1.4±0.3	1.7±0.3	0.001

(Student' s t test was used to analyses the data between groups)

Discussion:

Copper are important trace element in metabolism, growth, development and reproduction. Copper is of particular importance, especially early in life for the development and maintenance of myelin sheath[17]. Deficiencies of copper have been implicated in various reproductive events like infertility, pregnancy wastage, congenital abnormalities, pregnancy induced hypertension, placental abruption, premature rupture of membranes, still birth and low birth weight[18]. Different researchers demonstrated that micro and macro nutrients are essential for the development of fetus. With the progress of pregnancy, the level of plasma copper increased and it was high in all trimesters[10]. Serum copper is significantly increased in GDM patients as compared with healthy pregnant women[11]. In this study, the values of copper in GDM subjects were significantly higher ($p<0.05$) when compared to the control. Our finding is supported by the studies of Wang[8]. Copper in the blood also depends on the time of gestation. The possible causes of the changes are due to the hormonal, metabolic and enzymatic changes in pregnancy.

The increase in serum copper may be due to the increase in the inflammatory response especially in copper containing enzyme (ceruloplasmin)[19]. In diabetes mellitus, oxidative stress seems primarily due to both increased plasma free radical concentrations and a sharp reduction in antioxidant defense. Loven et al. found that there is no statistically significant difference in serum copper concentrations between healthy pregnant women and women with GDM[20].

Serum Zinc concentration declines 15%-35% by late pregnancy[10,21]. Zn may be involved in maintaining normal glucose use, and reducing the severity of insulin resistance and diabetes. Evidence for increased requirement of zinc during pregnancy has been reported by Al-Saleh et al[10]. The current study showed highly significant differences in zinc levels between pregnant women with gestational diabetes and control. This finding is similar to previous reports of Bo et al.[19] and Khadhem[11]. Diabetes causes oxidative stress, which damages the insulin-producing cells of the pancreas, and this can worsen

diabetes[22]. Zinc exerts a number of indirect antioxidant functions, and its deficiency can decrease the response to insulin, possibly by increased oxidative stress damage, apoptosis and inflammation [23,24]. Zinc improves insulin signaling, which promotes glucose uptake. Therefore, zinc supplementation appears to have beneficial effects on glucose homeostasis. The findings of the current study is in contrast to previous reports of H.Z.hamdan et al.[25] which showed no significant differences in zinc levels between pregnant women with gestational diabetes and controls.

Serum Mg concentration in women with GDM was significantly low compared to that of control. The decrease in serum Mg might be caused by osmotic diuresis and by indirect hormonal effects. The low serum Mg levels seen in the diabetic population could be a consequence of insulin resistance and low dietary Mg intake and decreased intestinal absorption[26]. Goker et al.[12] found that there is no statistically significant difference in serum magnesium concentrations between healthy pregnant women and women with GDM.

Conclusion:

Analyzing the finding of the present study, significant alteration in Serum Copper, Zinc and magnesium levels were observed in GDM Patients. This study was done within the context of the facilities available to us, it has got some limitation. As the study was case-control the population size was small. Further studies with large number of subjects and with the application of modern sophisticated technology was required to give a conclusive decision. Therefore it might be recommended that estimation of this biochemical parameter in GDM patients should be carried out for earlier detection and management the complications of GDM.

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Review Article

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Acinetobacter Baumannii: an Emerging Nosocomial Pathogen

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Abstract:

Acinetobacter baumannii is an opportunistic nosocomial pathogen and one of the six most important multidrug-resistant microorganisms in hospitals worldwide. This human pathogen is responsible for a vast array of infections, of which ventilator-associated pneumonia and bloodstream infections are the most common, and mortality rates can reach 35%. Furthermore, the frequency of community-acquired infections has been increasing gradually. Infection outbreaks are often associated with multidrug resistance, extensive drug resistance and even pan drug resistance. To overcome this problem, knowledge of pathogenesis and antibiotic resistance mechanisms of A. baumannii is important. This review summarizes the virulence factors of A. baumannii, antibiotic resistance mechanism of this organism. Lastly, novel prospective treatment options available for treating A. baumannii infections.

Keywords: Acinetobacter, nosocomial pathogen, multidrug-resistant, virulence factor.

1. Historical background of the genus Acinetobacter:

Acinetobacter was most probably first described in 1911, when Beijerinck, a Dutch microbiologist, described an organism named Micrococcus calcoaceticus that was isolated from soil by enrichment in a calcium acetate-containing minimal medium[1]. The current designation of the genus Acinetobacter from the Latin word akinetos (meaning non-motile) which was proposed in 1954 by Brisou and Prevot and it was accepted in 1968[2].

2. Morphological characteristics:

Acinetobacter species are glucose non-fermentative, non-motile, non-fastidious, catalase positive, oxidase negative, indole negative, citrate positive, strictly aerobic, Gram-negative coccobacilli (Figure-1) with DNA G + C content of 39 – 47%[3]. Acinetobacter includes 55 species and the numbers of species are increasing[4]. Among Acinetobacter species, Acinetobacter baumannii is the most important member associated with hospital-acquired infections worldwide[5].

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3. Natural habitats of A. baumannii:

A. baumannii is frequently isolated from reusable medical equipments such as ventilator tubing, arterial pressure monitoring devices, humidifiers, wash bins, plastic urinals, and respirometers[6]. They have also been isolated from the skin of healthcare personnel, mattresses, pillows, all types of ventilator equipment and moist solutions[7,8].

4. A. baumannii virulence factors:

Despite extensive research into the virulence potential of this emerging pathogen, little is still known about its true pathogenic potential or virulence repertoire. While it is believed that several factors may contribute to the virulence potential of A. baumannii[9]. Identified virulence factors of

A. baumannii are:

i. Outer membrane protein A (OmpA): It is essential for adherence to epithelial cells. It induces cell apoptosis by entering the cell and stimulating the release of cytochrome C and apoptosis-inducing factor. OmpA is also involved in resistance to complement and the formation of biofilms[10].

ii. Lipopolysaccharides (Endotoxins): They are potent stimulators of circulating WBCs to release pro-inflammatory substances. They are toxic to neutrophils, and inhibit their migration as well as their phagocytosis[11-13.]

iii. K1 capsule: Approximately one-third of strains produce a polysaccharide capsule that works with the cell wall lipopolysaccharide to prevent complement activation. The capsule may also delay phagocytosis[14].

iv. Siderophore-mediated iron-acquisition system: Acinetobacter can survive iron-deficient conditions for long periods of time. This is due to 'acinetobactin' a catechol siderophore that can sequester iron from the host[10].

v. Fimbriae: They help attach the organism to environmental surface[15].

5. Infections with A. baumannii:

A. baumannii is now recognized as causing a broad range of severe nosocomial infections, including skin and soft tissue infections, wound infections, urinary tract infections and secondary meningitis[16,17]. However, the most important infections, with the highest mortality rates, are ventilator-associated pneumonia (VAP) and blood stream infections[18]. Less commonly, A. baumannii can also cause community-acquired infections, including pneumonia and bacteraemia. Other possible community-acquired infections include skin, soft tissue and ocular infections, secondary meningitis and endocarditis[19, 20].

6. Transmission:

Acinetobacter species are often transmitted to patients via persistence on environmental surfaces and transient colonization of the hands of health care workers[21,22]. However, nosocomial spread by aerosolized bacteria from infected or colonized patients has been reported[23].

7. Risk factors:

A. baumannii causes opportunistic infections, mainly in immunocompromised patients. The risk factors of A. baumannii infection include prolonged hospitalization, poor overall condition, circulatory system insufficiency, respiratory system insufficiency, mechanical ventilation, prior antibiotic therapy and presence of foreign materials (such as venous, arterial and urinary catheters)[24].

8. Multidrug resistant A. baumannii:

For the past 30 years, strains of A. baumannii have acquired resistance to newly developed antimicrobial drugs; these strains are known as MDR A. baumannii. It became prevalent in many hospitals all over the world and has been recently recognized as a leading nosocomial pathogen[8,25]. The World Health Organization (WHO) declared that A. baumannii is one of the most serious "ESKAPE" organisms (Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa and Enterobacter species) that effectively escape the effects of antibacterial drugs[26]. Different terminology like multidrug resistant (MDR), extensive drug resistant (XDR), and pan-drug resistant (PDR) have been used with various definitions to describe the degree of antimicrobial resistance for Acinetobacter spp. MDR Acinetobacter spp. can refer to being resistant to a minimum of three classes of antimicrobial drugs e.g. all penicillins and cephalosporins, fluoroquinolones and aminoglycosides[27]. Another specific definition of multidrug resistance is whenever there is resistance to more than two of the following five drug classes: antipseudomonal cephalosporins (ceftazidime or cefepime), antipseudomonal carbapenems (imipenem or meropenem), ampicillin-sulbactam, fluoroquinolones (ciprofloxacin or levofloxacin), and aminoglycosides (gentamicin, tobramycin, or amikacin)[8, 28, 29]. MDR Acinetobacter

strains which show additional resistance to carbapenems will be defined as XDR. Finally, PDR Acinetobacter species is a term given to the XDR Acinetobacter species that is also resistant to polymyxins and tigecycline. These categorizations help to define the extent of resistance and rational antimicrobial therapy in a clear way[30].

9. Mechanisms of antibiotic resistance:

The mechanisms of antimicrobial resistance in A. baumannii are generally classified into five broad categories[31].

i. Antimicrobial-inactivating enzymes: Inactivation of β-lactams by β-lactamases is a major antibiotic resistance mechanism in A. baumannii. B-lactamases are divided into 4 molecular groups: Ambler class A (ESBLs), Ambler class B (metallo β-lactamases), Ambler class C (AmpC cephalosporinases), and Ambler class D (oxacillinases). These enzymes, at least partially, hydrolyze carbapenems along with other β-lactams[32].

ii. Changes in outer membrane porins (OMPs): Reduced expression or mutation in porins may be associated with carbapenem resistance. Carbapenem resistance in Acinetobacter species has been associated to the loss of proteins through porin channels from the outer membrane. It is possible that β-lactamases and outer membrane changes work together to grant resistance to β-lactam agents[30].

iii. Efflux pumps: Presence of efflux pumps (AdeABC, TetA, TetB, AbeM, AbeS) confers resistance to multiple classes of antibiotics[33]. AdeABC efflux pump has been well characterized in A. baumannii that mediates resistance to many classes of antibiotics (cefotaxime, chloramphenicol, erythromycin, aminoglycosides and fluoroquinolones). Over expression of AdeABC also confers resistance to carbapenems[34] and tigecycline[35].

iv. Changes in penicillin-binding proteins (PBPs): The resistance of A. baumannii to carbapenems is related to decreased drug uptake because of porin deficiency, and diminished affinity for the drug due to modification of the PBPs by mutations[36].

v. Resistance to antibiotics:

- Resistance to aminoglycosides: Aminoglycoside-modifying enzymes are the major mechanism by which A. baumannii confers resistance to aminoglycosides. Aminoglycoside-modifying enzymes can be classified into acetyltransferases, adenyltransferases and phosphotransferases. These enzymes are typically present on transposable elements and are transferred among pathogenic bacteria[37].

- Resistance to quinolones: Alteration in the structure of DNA gyrase or topoisomerase IV through mutations in the quinolones resistant-determining regions of the gyrA and parC genes is the main cause for resistance of A. baumannii to quinolones[38]. Plasmid-encoded quinolone resistance determinants qnrA, qnrB, and qnrS have also been identified in A. baumannii that protect DNA by inhibiting binding of quinolones to DNA gyrase and topoisomerase[39,40].

- Resistance to polymyxin: Polymyxin B and Polymyxin E (colistin) are peptide antibiotics that were first isolated in 1947 and have been progressively used as a "last resort" for the treatment of infections caused by MDR A. baumannii. Unfortunately, resistance to colistin in A. baumannii has been reported and conceived with great alarm[38]. Two major mechanisms have been reported for colistin resistance. The first mechanism consists of mutations in lipid A encoding genes (IpxA, IpxC and IpxD) resulting in loss of LPS, which is an initial target of colistin[41]. The second mechanism is the point mutation in pmrA and pmrB gene, resulting in remodeling of outer membrane[42].

10. Current treatment options:

A baumannii is considered by the Infectious Diseases Society of America (IDSA) as one of the ''red alert"

pathogens that significantly threaten the effectiveness of our current antibacterial armamentarium[4]. Unfortunately, as resistance has increased, a few antimicrobials can be reliably used for effective treatment of MDR Acinetobacter infections. Since few antimicrobials remain consistently effective in the treatment of nosocomial Acinetobacter infections, the search for new drugs and the reevaluation of older agents have become a priority[43].

- Carbapenems: Carbapenems (imipenem and meropenem) resistant Acinetobacter is increasingly reported, making MDR Acinetobacter infections difficult to treat. However, carbapenems continue to be the treatment of choice in cases where isolates are still susceptible to this antimicrobial class[30].

- Sulbactam: Sulbactam, an inhibitor of β-lactamase, demonstrates in vitro bactericidal activity against Acinetobacter species and it is suitable for mild infections[44, 45].

- Tigecycline: Tigecycline (derivative of minocycline) has bacteriostatic activity against MDR A. baumannii[45]. High-level resistance to tigecycline has been reported for some multidrug-resistant A. baumannii isolates, with a concern that this organism can quickly escape this antimicrobial mediated efflux pumps[35].

- Aminoglycosides: Tobramycin and amikacin are used as therapeutic options in cases of infection with multidrug-resistant A. baumannii isolates that retain susceptibility. These options are typically used in combination with another active antimicrobial agent. Many multidrug-resistant A. baumannii isolates maintain an intermediate susceptibility to amikacin or tobramycin to which resistance is highly correlated with aminoglycoside modifying enzymes or efflux pump mechanisms[46].

- Colistin: Colistin (polymyxin E) is a potent broad-spectrum antimicrobial agent which is used for highly drug resistant A. baumannii infections. These infections included pneumonia, bacteraemia, sepsis, intra-abdominal and CNS infection[47]. Unfortunately, the emergence of colistin-resistant A. baumannii strains has increased worldwide[48].

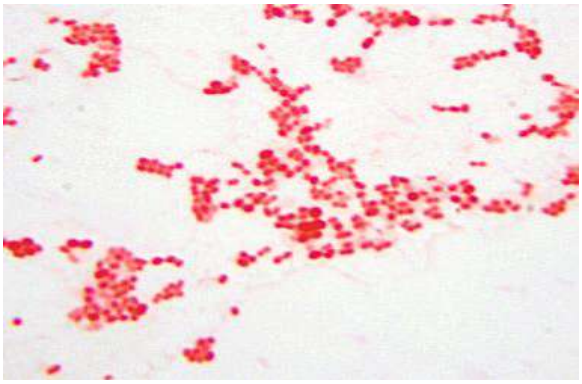


Figure-1:Morphology of Acinetobacter baumannii on Gram stain.

11. Conclusion:

Acinetobacter has been known as a major cause of nosocomial infections worldwide and have shown a broad spectrum of resistance toward commonly used antimicrobial agents. In view of this, control measures need to be implemented to control the spread of this organism in the hospital environment. It is advisable that healthcare facilities should implement proper safety programs to limit the spread of these bacteria as well as other hazardous bacteria. Novel, rationally designed strategies and screening-based approaches are required to discover new classes of antibiotics. If we continue to take all efforts at maintaining the effectiveness of antibiotics and developing novel antibiotics, effective control of A. baumannii infections can be successful.

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Review Article

DCIMCJ

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Typhoid Fever: Drug Management

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Abstract:

Despite advances in technology and public health strategies, typhoid fever remains a major cause of morbidity in the developing world. Although, the paediatric population is mostly affected by this disease, is an important cause of morbidity and mortality in adult populations also. In Bangladesh, most of the cases of typhoid fever are diagnosed clinically, or at the most by the Widal test which is not fool proof. Typhoid fever is an orally transmitted communicable infectious disease caused by the bacteria Salmonella typhi. This review addresses recent trends in global epidemiology, approaches to prevention and control, antimicrobial resistance pattern in Bangladesh and rest of the world, and treatment, conventional and newer developing diagnostic methods along with role of Widal test in diagnosing typhoid.

Keywords: Typhoid fever, prevention and control, antimicrobial resistance

Introduction:

Typhoid fever is caused by a highly specific human adapted pathogen, Salmonella enterica serotype typhi. This organism is an important cause of febrile illness and death in population living in crowded and poorly sanitized environment.The risk of disease has increased in population exposed to unsafe water and food and also the travellers visiting to endemic country[1]. Salmonella typhi Vi-positive strains are more infectious and virulent than Vi-negative strains. Following the incubation period of 7 to 14 days, there is onset of fever and malaise. The fever is then accompanied by chills, headache, malaise, anorexia, nausea, vague abdominal discomfort, dry cough and myalgia. These are followed by coated tongue, tender abdomen, hepatomegaly, and splenomegaly. Azithromycin (10mg/kg) given once daily for seven days has proven effective in the treatment of typhoid fever in some adults and children. A dose of 1g per day for five days was also found to be more effective in most adults. Of the third generation Cephalosporins, oral Cefixime (15-20mg per kg per day, for adults, 100-200mg twice daily) has been widely used. Intravenous third generation cephalosporins (Ceftriaxone, Cefotaxime) are effective. Aztreonam and Imipenem are potential third line drugs.

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Bacteriology:

The bacterium is serological positive for lipopolysaccharide antigens O9 and O12, protein flagellar antigen Hd, and polysaccharide capsular antigen Vi. The Vi capsular antigen is largely restricted to S.enterica serotype typhi, although it is shared by some strains of S. Enterica sero types hirschfeldii (paratyphi C) and dublin, and Citrobacterfreundii[2] . Polysaccharide capsule Vi has a protective effect against the bactericidal action of the serum of infected person[3].

Epidemiology:

In recent years there have been some changes in the epidemiological patterns of typhoid and related diseases in the third world countries, involving basically most of the countries in Africa, Asia and Latin America[4,5]. More than 20 million cases a year occur in the hygienically compromised areas of

developing countries and out of them Pakistan, India, and Bangladesh together bear the brunt of the attack accounting for 85% of the cases occurring globally [6]. Obviously, the highest age-specific rates of typhoid and allied diseases are borne by children and young adults. Studies in Pakistan and Bangladesh show the mean age of patients affected with typhoid fever is 7 years[7]. Typhoid is found to be a seasonal disease; in the monsoon itself there is occurrence of 45% of the total annual reported cases. In South Asia the disease occurrence is highest during July to October because of heavy rainfall during that period[8]. Proper standardization of the methods of epidemiological studies on typhoid is therefore deemed necessary[9].

Aetiology:

The disease typhoid fever is an orally transmitted infectious disease caused by the bacteria Salmonella Typhi. It is usually caused by consuming impurified water and contaminated food. As S. typhi bacteria can survive in water for days, contamination of surface water such as sewage, fresh water and ground water acts as major aetiological agent of typhoid.

Defaecation in open places is another notable cause of typhoid transmission. Amidst food, cut fruits kept uncovered for some time are an important cause of contamination in most developing countries. Papaya has a neutral pH and its cut surface can support the growth of various microorganisms.

It was observed by Hosoglu et al in a Turkish study that eating cut papaya, lettuce salad and some traditional raw foods in Turkey (e.g. cig kofte) was an important causative factor[10]. Inhabiting in a congested locality or household is significantly related with typhoid fever. Again, the habit of washing vegetables and compulsory use of sanitary latrine for defecation have been found to prevent typhoid. In a case-control study in Indonesia, paratyphoid fever was found to be associated with consumption of food from street vendors[11].

Excessive antibiotic use causes an increased risk of infection with both drug-resistant and drug-sensitive serotypes of *S.* typhi [12,13].

Prolonged antimicrobial use can cause changes in gastro-intestinal flora and a decreased barrier to bacterial colonisation facilitating Salmonella infection. Bhan et al. have found a significant association between the presence of serum anti-Helicobacter pylori IgG antibodies and typhoid fever[14]. In a study in Vietnam, lower risk of typhoid was found to be associated with nucleotide polymorphisms in specific HLA alleles and the TNF-alpha promoter[15]. HLA-DRB1*12 was associated with protection against complicated typhoid fever.

Pathogenesis:

The infectious dose of S. Enteric serotype typhi in patients varies between 1000 and 1 million organisms. Vi-negative strains of S. Enteric serotype typhi are less infectious and less virulent than Vi-positive strains. S. enteric serotype typhi must survive the gastric acid barrier to reach the small intestine, and a low gastric pH is an important defence mechanism. Achlorhydria as a result of aging, previous gastrectomy, or treatment with proton-pump inhibitors or large amounts of antacids lowers the infective doses[1,16].

In the small intestine, the bacteria adhere to mucosal cells and then invade the mucosa. They rapidly penetrate the mucosal epithelium via either microfold cells or enterocytes and arrive in the lamina propria, where they rapidly elicit an influx of macrophage that ingest the bacilli but do not generally kill them. Some bacilli remain within the macrophage of the small intestinal lymphoid tissue and some microorganisms translocate to the intestinal lymphoid follicles and the draining mesenteric lymph nodes and by which they enter the thoracic duct and the general circulation[17]. As a result of the silent primary bacteraemia the pathogens reaches an intracellular haven within 24 hours after ingestion. Salmonella organisms are able to survive and multiply within the mononuclear phagocytic cells of the lymphoid follicles, liver, and spleen and bone marrow. The incubation period is usually 7 to 14 days. The incubation period in a particular individual depends on the number of bacteria, their virulence, and the host response.

Clinical illness is accompanied by a fairly sustained but low level of secondary bacteraemia, usually one bacterium per millilitre of blood and about 10 bacteria per millilitre of bone marrow [1].

Typhoid induces systemic and local humoral and cellular immune responses, but these confer incomplete protection against relapse and reinfection. The interaction of host immunologic mediators and bacterial factors in infected tissue may contribute to the necrosis of Peyer's patches in severe disease[18].

Symptomatology:

Typhoid fever is one of the most common febrile illnesses in developing countries. Following the incubation period of 7 to 14 days, there is onset of fever and malaise. The fever is then accompanied by chills, headache, malaise, anorexia, nausea, vague abdominal discomfort, dry cough and myalgia. These are followed by coated tongue, tender abdomen, hepatomegaly, and splenomegaly [2].

However, recent advances of antibiotic treatment have changed this classic mode of presentation, such as a slow and stepladder type of fever and features of toxicity scarcely seen these days. In areas where malaria is endemic and where Schistosomiasis is common, the presentation of typhoid may be atypical. Even polyarthritis and monoarthritis are reported presentation. Adults often have constipation, but diarrhoea, toxicity and complications such as disseminated intravascular coagulation are more noticeable in infants. Vertical intrauterine transmission from an infected mother may lead to neonatal typhoid, a rare but severe and life threatening condition[2]. Both relapses and re-infection are common in typhoid and occur in less than 10 per cent of cases. Reinfection can only be distinguished from relapse by molecular typing [2,19].

Diagnosis:

The diagnosis of typhoid is usually made in the developing world from clinical criteria. In areas of endemic disease, fever without evident cause that lasts for more than one week should be considered typhoid until proven otherwise. However, malaria, deep abscess, tuberculosis, amoebic liver abscess, encephalitis should also be considered for differential diagnosis. Over and above, the following complications of typhoid should be kept in mind as they are often confusing factors during diagnosis and treatment:

Abdominal:

Gastrointestinal perforation, gastrointestinal haemorrhage, Hepatitis, Cholecystitis (usually subclinical).

Cardiovascular:

Asymptomatic electrocardiographic changes, Myocarditis, Shock.

Neuropsychiatric:

Encephalopathy, delirium, psychotic states, cranial or peripheral neuritis, Guillain- barre syndrome, meningitis, impairment of coordination.

Respiratory:

Bronchitis Pneumonia (Salmonella enterica serotype typhi, Streptococcus pneumoniae).

Hematologic:

Anaemia, Disseminated intravascular coagulation (usually subclinical), thrombocytopenia, haemolytic uremic syndrome.

Others:

Focal abscess, pharyngitis, miscarriage, relapse, chronic carrier, influenza, dengue, leptospirosis, infectious mononucleosis, brucellosis, rickettsial diseases etc. should be considered.

Routine blood tests:

Fifteen to 25% patients show leucopoenia and neutropenia. Leucocytosis found in intestinal perforation and secondary infection. In younger children, leucocytosis is common association and may reach 20,000-25,000/mm3.

Liver function tests:

Significant hepatic dysfunction is rare, some studies and case reports showed there was hepatic

derangement simulating acute viral hepatitis and also present as hepatic abscess.

Blood culture:

This is the standard diagnostic method; it is positive in 60 to 80 per cent of patients with typhoid. Culture of the bone marrow is more sensitive, around 80 to 95 per cent patients, even in patients taking antibiotic for several days, regardless of the duration of illness. Blood culture is less sensitive than bone marrow because there is lower number of organism in blood than bone marrow. The sensitivity of blood culture is higher in the first week of illness, increases with the volume of blood cultured (10-15ml should be taken from school-children and adults, 2-4ml are required from toddlers and preschool children). Toddlers have higher level of bacteraemia than adult.

Felix-Widal test:

The classic Widal test is more than 100 years old. It detects agglutinating antibodies to the O and H antigens of S. enterica serotype typhi. The levels are measured by using doubling dilutions of sera in large test tube. Although easy to perform, this test has moderate sensitivity and specificity. Its reported sensitivity is 70 to 80 per cent with specificity 80 to 95 per cent. It can be negative in up to 30% of culture proven typhoid fever, because of blunted antibody response by prior use of antibiotic. Moreover, patients with typhoid may show no detectable antibody response or have no demonstrable rise in antibody titre. Unfortunately, S. enterica serotype typhi shares these antigens with other salmonella serotypes and shares these cross-reacting epitopes with other Enterobacteriaceae. This can lead to false positive results. If paired serums are available a fourfold rise in the antibody titre between convalescent and acute sera is diagnostic[2].

Considering the low cost of Widal test, it is likely to be the test of choice in many developing countries. This is acceptable, as long as the results of the test are interpreted with care, on the background of prior history of typhoid, and in accordance to appropriate local cut-off values for the determination of positivity.

New diagnostic tools:

Tubex test detect IgM antibodies, Typhidot detect IgM and IgG antibodies against 50 kD antigen of S. typhi[1]. Tubex has not been evaluated extensively but in preliminary studies, this test performed better than Widal test in both sensitivity and specificity. Although culture remains gold standard, Typhidot-M is superior to culture method in sensitivity (93%) and has high negative predictive value. In some studies, it has shown that for total Ig estimation ELISA has superior sensitivity when compared to other tests.

Recently DNA probes and polymerase-chain-reaction (PCR) have been developed to detect S. enterica serotype typhi directly in the blood[2],[20]. Urine antigen detection has 65-95% sensitivity. PCR has still not been used in clinical practice.

Treatment:

Prompt institution of appropriate antibiotics following early diagnosis is essential for optimal management. Knowledge of the antibiotic susceptibility is crucial in determining which drug to use. More than 90% of patients can be managed at home with oral antibiotic and regular follow-up. However, patients with severe illness, persistent vomiting, severe diarrhoea, and abdominal distension, require hospitalisation and parenteral antibiotic treatment. Chloramphenicol was the drug of choice for several decades after its introduction in 1948. However, the emergence of plasmid mediated resistance and development of serious side effect like bone marrow aplasia had pushed this drug aside. Trimethoprim-Sulfamethoxazole and Ampicillin were employed to counter Chloramphenicol resistance in 1970, but it was also discarded because of development of plasmid mediated resistance.

In 1992, emergence of multidrug resistance enteric fever (resistant to Chloramphenicol, Ampicillin and Trimethoprim-Sulfamethoxazole) was strongly addressed in Bangladesh; around 36.58% cases were reported in a large study.

In the 1980s, ceftriaxone and ciprofloxacin became the drug of choice. Although Fluoroquinolones attain

excellent tissue penetration, rapid therapeutic response and very low rate of post treatment carriage, strains of bacteria have emerged in Asia that show resistance to them in the past decade. Resistance to the Fluoroquinolone may be total or partial. The Nalidixic-acid-resistant strain has reduced susceptibility to Fluoroquinolone drug compared to Nalidixic-acid-sensitive strain. Although isolates are Nalidixic acid resistant but these can be susceptible to Fluoroquinolones in disc sensitivity testing. Disc sensitivity testing defined as a Ciprofloxacin MIC of 0.12-1 mg/L, and is not always detected by testing of nalidixic acid resistance. The available Fluoroquinolones (Ofloxacin, Ciprofloxacin, Perfloxacin) are highly active and equivalent in efficacy. For Nalidixic-acid-resistant infections, a minimum of seven days of treatment at the maximum permitted dosage is necessary and 10-14 days are usually required. Culture sensitivity data of Department of Microbiology of BSMMU showed 8.6% sensitive to Nalidixic acid, whereas Ciprofloxacin is still 67% sensitive. Even a few days earlier it was thought that gatifloxacin is better than older Fluoroquinolones. The bacteria needed dual point mutations (in the DNA-gyrase and Topoisomerase-4 genes) to become resistant to Gatifloxacin. Most studies in endemic countries have identified gyrA mutation in S. enterica as a mechanism of resistance. Because there is no reported pattern of sensitivity to Gatifloxacin in India or Bangladesh or most of the western countries for that matter and of its recent reports of some toxicities it has been withdrawn and no longer used for any systemic illness.

Azithromycin in a dose of 500mg (10mg/kg) given once daily for seven days has proven effective in the treatment of typhoid fever in some adults and children. A dose of 1g per day for five days was also found to be more effective in most adults. Of the third generation Cephalosporins, oral Cefixime (15-20mg per kg per day, for adults, 100-200mg twice daily) has been widely used in children in a variety of geographical settings and found to be satisfactory. However, in some trials Cefixime showed higher rates of failure and relapse than Fluoroquinolones.

But antibiotic sensitivity pattern in BSMMU showed higher sensitivity around 78.8%.

Intravenous third generation Cephalosporins (Ceftriaxone, Cefotaxime) are effective with low relapse (3 to 6%) and fecal carriage (<3%) rates. Ceftriaxone is effective at a dose of 2-4gm daily in single or two divided doses [4,21]. Aztreonam and Imipenem are potential third line drugs. Prevention of Typhoid: In urban areas, these measures are rapidly growing In Bangladesh, India and some other developing countries compared to other parts of the world. In several studies, data indicate higher infection rate in the urban population. Lack of safe water and inadequate sanitation is responsible for this increased incidence. In developing countries, reducing the number of cases in general population requires the provision of safe drinking water and effective sewage disposal. Food safety can be ensured by washing hand with soap before preparing food, water for drinking should be boiled, avoiding raw food shellfish, ice cream.

In one study from Dhaka city, people living close to the rivers Buriganga, Turag, and Balu had an elevated risk of typhoid [22].There are several factors responsible. Low income inhabitants of this area frequently use surface water for drinking. As S. typhi bacteria can survive in water for days, contaminated surface water act as etiological agents of typhoid.

Conclusion:

Even today, enteric fever is a global public health problem, particularly in developing countries. Studies show the number of urban cases of typhoid is around 800-900/year. Widal test, though cheap and available should be interpreted with caution. We should be aware about the higher incidence of typhoid fever in Bangladesh and other developing countries. Massive campaigns should be initiated to make people understand the preventive measures, importance of visiting doctors and the like. Doctors should be conscious about the gradually developing antibiotic resistance and the emerging safe and effective newer antibacterial agents. The latter includes newer Fluoroquinolones and Macrolides in large doses, and

lastly third generation. Cephalosporines both in oral and injectable forms and lastly Aztreonam and Imipenem are potential third line drugs. A typhoid-vaccination program for schoolchildren or, with the advent of the new conjugate Vi vaccine, as part of the Expanded Program of Immunization, should be considered. Over and above, the profession should look forward to newer curative and preventive measures.

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Case Report

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An Ectopic Breast Tissue Presenting with Fibroadenoma at Lower Abdominal Wall.

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Abstract:

Among the well-documented anomalies of the breast, polymastia or accessory breast or Supernumerary breast is the most common and usually presents along the embryonic milk line extending between the axilla and groin. The incidence of accessory breast is around 0.4-6% in females. In the EBT any disease can develop that affects the normal breast. Among benign lesions are included fibrocystic disease-like changes, intraductal papilloma, fibroadenoma, and phyllodes tumor, while malignant lesions mentioned comprise ductal, lobular, and mucinous adenocarciomas. We present herein the case of a patient with a progressive-growth at lower abdominal wall with a final report of fibroadenoma. In this case, we support the origin in ectopic mammary tissue.

Keywords: Ectopic breast tissue, fibroadenoma, lower uterine caesarean scar

Introduction:

Ectopic breast tissue (EBT), polymastia or supernumerary and accessory breast are proper synonymous words used for breast tissue at more than two places with or without nipple.Ectopic mammary tissue can occur anywhere along the primitive milk line that extends in the embryo from the axilla to the groin[1]. About 67% of ectopic breast tissue occurs in the thoracic or abdominal portions of the milk line just below the inframammary crease, 20% occurs in axilla and remaining 13% locations take place anywhere along the milk line[2,3]. Though the incidence remains low, EBT can harbor all kinds of pathological diseases as in normal breast tissue. Among the pathological changes carcinoma is the most common followed by inflammation and fibroadenoma [1,4]. We report a case of fibroadenoma in the lower abdominal wall polymastia for its rarity to emphasize the importance of considering the ectopic breast and its associated pathology in the differential diagnosis of lower abdominal wall mass and also to stress the importance of evaluating the patients to rule out renal anomalies or urological malignancies as it is an important association [5].

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Case report:

A 20 years woman presented with a painless, well defined mass in lower abdominal wall since one year, gradually increasing in size. The mass was at one end of LUCS scar. She has the H/O LUCS three years back. Physical examination revealed a 3 × 2-cm tumor located near the LUCS scar. The tumor was soft and movable and not adhered to skin or other structures. The gynecological, inguinal, and abdominal examination was reported as normal. Chest x-ray as well as abdomino-pelvic Computed tomography (CT) scan reported no masses or retroperitoneal lymph node enlargements. A provisional diagnosis of endometriosis externa was made. Patient has gone through wide tumor excision.

Pathology:

Grossly a well delimited, encapsulated, multilobular mass was received. The measures of the mass was 3x2x2 cm. Cut surface shows a lobulated white firm mass without necrosis or hemorrhage. Microscopy showed proliferating fibrous stroma in a peri and intracanalicular pattern. Some ducts were cystically dilated and others compressed into slit like spaces. The ducts were lined by bilayered epithelium, inner columnar to cuboidal and luminal the myoepithelial cells (Fig).Histopathologically a diagnosis of fibroadenoma was made. The patient was followed for one year and it was uneventful.

Discussion:

During the 6th week of embryogenesis, the mammary milk lines representing 2 ectodermal thickenings, develop on the ventral surface of the embryo, extending from the anterior axillary fold to the inside of the inguinal fold. Physiologically, most of the embryologic mammary ridges resolve, except for the pectoral 2 segments, which later become breasts. Ectopic breast tissue results from failure of involution of any portion of the mammary ridge. Therefore, ectopic breast usually occurs along the 'milk line' or mammary line [6].

There are two forms of ectopic breast tissue: supernumerary and aberrant[7]. A supernumerary breast consists of a ductal system communicating with the overlying skin, usually located along the ''milk line'', that extends from the axilla to the groin. It usually responds to hormonal stimulation and undergoes physiologic changes as a normal functioning breast [8]. Polymastia and polythelia are the two varieties of supernumerary breast. Polymastia is an accessory gland resulting from failure to regress mammary ridge during embryonic development. Polythelia presents itself in the form of an areola and/or a nipple lacking glandular tissue [9].

The second form of ectopic breast tissue, aberrant breast, consists of an isolated fragment of glandular tissue located beyond the periphery of orthotopic breasts. It is most commonly found in the axilla. However, parasternal, subclavicular, submammary, vulvar and anal cases also have been reported[10-12]. Aberrant breast is characterized by an unorganized secretory system without any connection between the inside and the outside. Despite morphologic differences, ectopic mammary tissue, whether supernumerary or aberrant, may present characteristics analogous to orthotopic tissue in terms of function and, more importantly, pathologic degeneration.

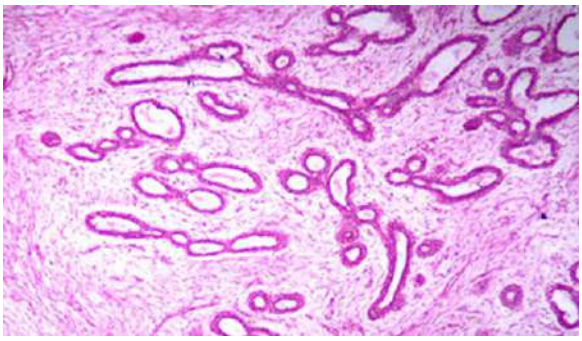


Figure: Photomicrograph showing fibroadenoma in ectopic breast tissue at lower abdominal wall. (H&E stain x 40)

Usually ectopic breast tissue occurs sporadically, but a hereditary predisposition has also been reported[12]. It occurs in 1-6% of the population and upper umbilical scar is more frequent site[13, 14]. Customarily, these are most frequently reported during pregnancy and lactation[14].

Accessory breasts are usually asymptomatic and cause nothing more than a visible distension which may resemble a tumour. Sometimes it may cause psychological disturbances in adolescence and also results in pain and discomfort especially during menstruation, pregnancy, and lactation[7]. The clinical significance of ectopic breast lies in the fact that apart from the psychological and cosmetic impact, it causes the same pathological changes as the normally located breast tissue such as inflammation, fibrosis, fibroadenoma, cystosarcoma phyllodes, and carcinoma[1, 7]. Fibroadenoma is a common benign fibro epithelial lesion of normal breast tissue.

Its occurrence in accessory breast tissue is very rare and a few cases have been reported[15,16]. Fibroadenoma of the breast is a benign tumor composed of two elements: Epithelium and stroma. It is nodular and encapsulated. The epithelial proliferation appears in a single terminal ductal unit and describes duct like spaces surrounded by a fibroblastic stroma. Depending on the proportion and the relationship between these two components, there are two main histological features: Intracanalicular and pericanalicular.Often both types are found in the same tumor. (a) Intracanalicular fibroadenoma: Stromal proliferation predominates and compresses the ducts, which are irregular, reduced to slits. (b) Pericanalicular fibroadenoma: Fibrous stroma proliferates around the ductal spaces and hence that they remain round or oval, on cross section. The basement membrane is intact. Our case is pericanalicular type.

Ectopic breast tissue patients, have been associated with urinary abnormalities such as supernumerary kidneys, failure of renal formation, renal adenocarcinoma, hydronephrosis, polycystic kidney disease, duplicate renal arteries, ureteric stenosis and other congenital anomalies such as pyloric stenosis, epilepsy and cardiac abnormalities due to corresponding development of mammary tissue and the genitourinary system[5,6].

The ectopic mammary tissue express hormone receptors which can be detected by immunohistochemistry and are potential to present with benign or malignant lesion similar to normal breast tissue [5,17].

The behavior of fibroadenoma in ectopic mammary tissue is similar to that in normal breast. Radiological non-invasive procedures are of great help in diagnosis. Though we did not perform in our case, fine needle aspiration or core biopsy could be done for appropriate surgical decision. Excision usually has good prognosis and rarely recurs[18]. Surgical excision is also important for cosmetic, psychological and therapeutic reasons.

Conclusion:

Based on the above case it can be concluded that when tumors or nodules are found along the mammary line, the presence of breast tissue should be considered during investigation[1]. Clinically it is wise to evaluate and screen carefully cases of supernumerary breast for any pathology and for any associated urogenital anomalies. Though, fibroadenoma in normal breast is quiet frequent but infrequent in EBT and should be kept in the differential diagnosis of abdominal wall swelling. Excision is the only treatment of choice for symptomatic EBT.

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DCIMCJ

Case Report

DCIMCJ 2019 January;6(1):113-115

A Young Girl with Progressive Myoclonic Epilepsy and Intellectual Decline

Mamun KAA[1], Nomany BMS[2], Ali ML[3]

Abstract:

Lafora disease a fatal autosomal recessive disease. It presents with progressive myoclonic epilepsy and intellectual decline .We report a case of 15 years old girl with severe progressive myoclonic epilepsy. Neurological examination showed cerebellar syndrome and intellectual deterioration. All investigations were normal. Skin biopsy was done to guide the diagnosis and histological examination confirmed the diagnosis .

Keywords: Lafora, epilepsy, skin biopsy

Introduction:

Lafora disease is a neurodegenerative disease characterized by progressive myoclonic epilepsy[1]. It begins to develop during the early adolescent years. The diagnosis is suggested by myoclonic seizure, progressive cognitive deterioration, drop attacks, ataxia, temporary blindness, visual hallucination and a rapidly developing dementia[2]. The EEG is characteristic and confirmation is made by histological examination[3]. The evolution is often fatal. We report the case of a 15 year old girl, who presented with seizures and myoclonus from the age of 12.

Case report:

A 15 years old girl, born from a first degree consanguineous marriage, presented with refractory epilepsy and poor school performance. She has one brother who is in healthy state. The onset of the disease was at the age of 12 by the appearance of generalized tonic-clonic and myoclonic seizures with progressive cognitive deterioration,drop attacks and ataxia Neurological examination found a cerebellar syndrome. The electroencephalogram (EEG) showed medium to high voltage epileptiform discharge in both frontal regions on a slow background which is suggestive of myoclonic seizure.

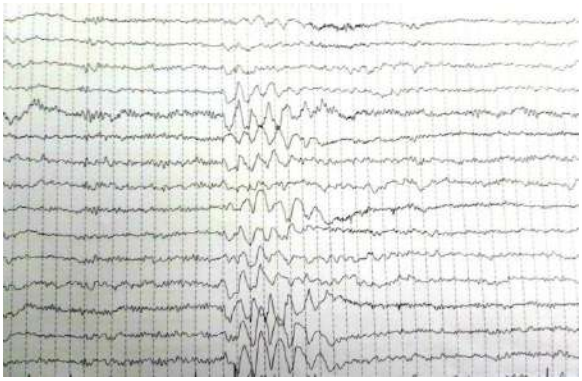


Figure-1: EEG shows generalized epileptiform discharge

All the laboratory tests were normal. The magnetic resonance imaging showed cerebral and cerebellar atrophy. Resistance to antiepileptic and progressive cognitive deterioration raised the possibility of Lafora disease.

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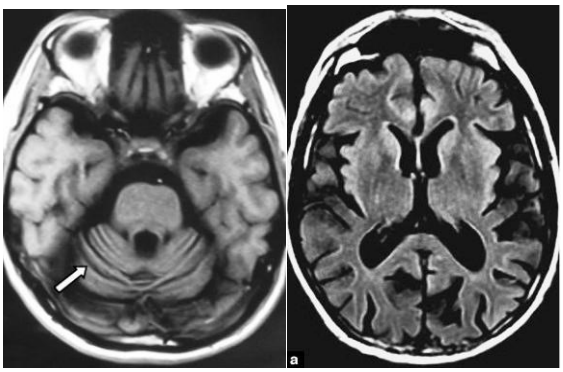


Figure-2:MRI brain shows cerebral and cerebellar atrophy

Histological study of skin biopsy(performed at the axillary region)showed the presence of Lafora bodies in cytoplasm of epithelial cells of apocrine sweat glands. These Lafora bodies were PAS positive. Thus the diagnosis of Lafora disease was finally made.

Discussion:

Lafora disease is an autosomal recessive disease[1]. It is a glycogen metabolic disorder. It was described first by White in 1988[1]. It is more common in the Mediterranean region[2]. Its first manifestations occur during adolescence with generalized tonic-clonic seizure and myoclonus[3]. With the onset of seizures, people with Lafora disease often shows signs of cognitive decline, there may be behavioral changes, depression, confusion, ataxia , dysarthria and eventually dementia[4]. By the mid-twenties, most affected people lose the ability to perform the activities of daily living; have continuous myoclonus; and require tube feeding and comprehensive care[5]. Most cases of Lafora disease are caused by mutations in either the EPM2A gene or the NHLRC1gene[4]. The electroencephalogram changes may precede the onset of symptoms[6]. In half of the cases there is generalized epileptiform activity with a gradual slowing of the background rhythm [7].

The role of skin biopsy in the axilla is to confirm the diagnosis of Lafora disease[8]. It reveals Lafora bodies in the cytoplasm of epithelial cells lining the excretory ducts of apocrine sweat glands[3]. The pathological hallmark of Lafora disease is the presence of cytoplasmic polyglucosan inclusions, the Lafora bodies.The presence of Lafora bodies in the axillary biopsy in young subjects is pathognomonic of Lafora disease[8].

Differential diagnoses are juvenile myoclonic epilepsy or subacute sclerosing panencephalitis[9]. Unfortunately, there is currently no cure of Lafora disease. Management is only supportive and palliative, limited to symptomatic management of the epileptic seizures, myoclonus, and intercurrent complications[10]. Death occurs 2-10 years after the onset with an epilepsy[7].

Conclusion:

Lafora disease has significant clinical and histopathological characteristics. Resistance to antiepileptic and progressive cognitive deterioration should guide the clinician to do axillary skin biopsy to find Lafora bodies.

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Medical Quiz

DCIMCJ 2019 January;6(1):116-117

Medical Quiz: Images

Mamun KAA[1], Parvin A[2]

A 14 year old girl presented with partial epilepsy and left sided weakness since childhood. She was suggested EEG and MRI brain.

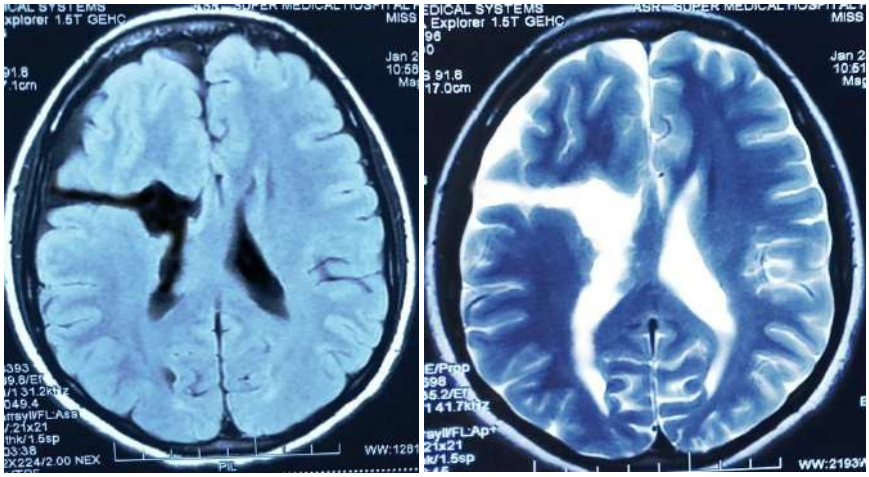


Figure 1: MRI brain



Figure 2:EEG

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- **Q1. Mention the abnormalities found in MRI Brain**
- **Q2. Mention the abnormalities found in EEG**
- **Q3. What is the diagnosis?**

Answer to Medical Quiz: Images:

1. MRI shows open lip schizencephaly in the right parietal region in axial T1 and T2 weighted images.

2. EEG shows focal epileptiform discharge.

3. Open lip Schizencephaly.

Schizencephaly is a rare developmental malformation of the central nervous system . Its incidence is up to 1.5:100,000 live births[1].

It is believed that intrauterine ischemia or expression of genetic factor damaging germinal matrix and impairing cellular migration in 6–7 weeks of intrauterine life may play a role in the development of schizencephaly[2].

Depending on the level of morphological disturbances we distinguish open and closed schizencephaly which can be uni- or bilateral. Clefts most often involve frontal or parietal lobes especially in the region of Sylvian fissure and are lined with a layer of gray matter[3].

Schizencephaly often coexists with other brain abnormalities such as ventricular enlargement, polymicrogyria, dysgenesis/agenesis of the corpus callosum[4].

Schizencephaly can be visualized in ultrasonography (USG) and computer tomography (CT) but the method of choice is magnetic resonance (MR)[5].

The most common clinical manifestations of schizencephaly are epilepsy, psychomotor retardation, hemiplegia, hydrocephalus and microcephaly[6].

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