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Impurities in Medicine- A Global Concern

Mohammad Ali

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Impurities in Medicine- A Global Concern

Medicines are life savings. When physicians and patients alike come to know that drugs adversely affect their health, then it is a matter of concern. Recently Federal Food And Drug Administration (FDA), USA along with Canada and 20 other countries announced voluntary recall of valsartan containing drugs used in high blood pressure and heart failure after N-nitrosodimethylamine (NDMA) was found in its active pharmaceutical ingredients (API)-a potentially cancer-causing impurity in animal model. The Directorate General of Drug Administration (DGDA), Bangladesh has also asked pharmaceutical companies concerned to recall all valsartan related medicine from the market. The pharmaceuticals implicated are only those who used raw materials from certain Chinese companies. Impurities are unwanted chemical that remain with the active pharmaceutical ingredients (APIs) or develop during formulation or upon aging of both API and formulation. The presence of impurity even in trace amount can influence safety and efficacy of drugs. Trace quantities of impurities is inevitable in drug products. International conference on harmonization (ICH)- a regulatory body formulated a guideline to set the limit and type of impurities that should be present with API. In late 1989 FDA recalled tryptophan a food supplement that had caused widespread eosinophilia-myalgia syndrome and many case fatalities due to presence of impurity. The incidence of Recombinant human erythropoietin (epoetin) induced pure red cell aplasia (PRCA) occurred in 1998. The polysorbate-80 were detected in pre filled syringes of EPREX (epoetin). So, presence of impurities in drugs are not uncommon. Their level should be controlled and monitored. Pharmacovigilance has got paramount importance for detection, assessment, understanding and prevention of adverse effects or other drug related problem. It will help in minimizing adverse effect and ensure quality safety and efficacy of drug products. Otherwise drug impurities, substandard drugs will have substantial impact on human health. Pharmaceutical industries are fastest growing potentially thriving sector in Bangladesh. They

contribute substantial amount of money in national economy. With regard to drug safety and efficacy their activities should be monitored. We hope, Directorate General of Drug Administration (DGDA) will strictly supervise and implement all prevailing drug regulations.

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Routine Inspection of Pesticide Container Improves Diagnosis, Treatment and Reporting of Acute Pesticide Poisoning: a Comparative Study

Sanjib Kumar Purohit¹, Gourab Dewan², Abdullah Al Faruque³, Md Rashed Mirjada⁴

Abstract

Background: Almost all acute pesticide poisoning are assumed and treated as organophosphate poisoning in Bangladesh. In reality a major portion of pesticide poisoning is not due to this compound. If pesticides are identified by examining the commercial container along with toxidromic assessment then erroneous diagnosis, treatment and subsequent misreporting can be avoided.

Objective: To determine whether identification of pesticide from container/packet label improves overall diagnosis, treatment and reporting pattern of acute pesticide poisoning.

Methods: A retrospective cross-sectional study was done in Rangamati and Comilla General Hospital. In Rangamati pesticides poisoning agents are confirmed by examining the commercial container at Medicine department but not in Comilla. We compared pesticide poisoning reporting pattern of the year 2015 in the two centers. In addition we compared initial diagnosis at emergency and final diagnosis after examining pesticide container in Rangamati.

Results: In Comilla all 330 pesticide poisoning were due to organophosphate compound and significantly differed from

the results in Rangamati ($p < 0.0001$). In Rangamati 81.8% were initially diagnosed and treated at emergency as organophosphate poisoning. Subsequent examination of pesticide container brought by patient party showed actual diagnosis was carbamates 25.5%, organophosphate 20%, pyrethroids 14.5%, paraquat 12.7%, rodenticide 12.7% and others (neonicotinoids, anthraline, fungicidal etc.) 14.4%. In addition, 75.5% of atropine and 69.2% of pralidoxime administered assuming organophosphate poisoning was found inappropriate. Examination of pesticide container allowed correct identification of 67.3% poisoning agents and corrected 75.5% initial over diagnosis of organophosphate.

Conclusion: Identification of pesticide from container improves diagnosis and reporting of acute pesticide poisoning. Adoption of this method may reduce misreporting of poisoning cases in Bangladesh.

Key words: Pesticide; Poisoning; Organophosphate; Diagnosis.

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Introduction

Pesticide self-poisoning is a common method of suicidal death in developing world.^{1,2} Accurate identification of pesticide class and active ingredient is essential for treatment and reliable case burden estimation. Unfortunately in Bangladesh exact burden of different pesticide poisoning is unknown.³ The reason is misreporting of almost all pesticides as organophosphate (OP).^{3,4} OP's are regarded as the main pesticide used in self-poisoning. Developing countries lack lab facilities to identify active ingredients of pesticides. However, there is simple and practical alternative. Identification is possible from inspection of container of pesticides. This may solve the inherent problems of misdiagnosis, subsequent ineffective treatment and inappropriate notification of acute pesticide poisoning cases.^{3,4} The purpose of this study was to observe whether identification of pesticides by container inspection routinely in acute pesticide poisoning influences diagnostic accuracy and notification pattern in Bangladesh.

Methods:

It was a retrospective descriptive study. We studied the case files of acute pesticide poisoning cases for the year 2015. Study centers were Comilla General Hospital (CGH) and

Rangamati General Hospital (RGH). Both are Government hospital and admission pattern is similar. All poisoning cases are admitted through emergency where initial diagnosis is made. Further management takes place in indoor. In CGH poisoning diagnosis is based solely on clinical presentation. The poisoning agent is not confirmed by scrutinizing the container. In RGH emergency medical officer also make initial judgment based on clinical presentation. However, the key difference between CGH and RGH is that in RGH in Medicine indoor patients are asked to bring container or packet of the poison to confirm the pesticide class and active ingredient from its label. Active ingredient was identified from container label and chemical class of the pesticide was identified using the list of licensed pesticides in Bangladesh. The list along with trade names is available from the website of Bangladesh Crop Protection Association.⁵ The pesticides were classified as insecticides (OP, carbamates, pyrethroids, neonicotinoids), fungicides, rodenticides, herbicides and mixed category.

Statistical analysis

In both centers frequency and types of pesticide poisonings were recorded in number and percentage. Comparison of nonparametric data of different centers or within same center was done with chi-square test or Fisher's exact test as applicable. A value of $p < 0.05$ was considered as significant at 95% CI. SPSS version 20 was used for analysis.

Results:

We compared results in two steps. First between RGH and CGH. Next only in RGH. In this center every patient's initial clinical diagnosis was verified by sample identification method. This allowed us to compare inaccuracies. In RGH 137 and in CGH 834 poisoning cases were recorded in register. Comparison of acute pesticide poisoning diagnosis pattern is summarized in table 1. Frequency of pesticide poisoning was significantly higher in RGH ($p = 0.001$). In CGH all pesticide poisoning were recorded as OP. The difference in frequency of diagnosis of OP poisoning in RGH (20.0%) and CGH (100.0%) was significant ($p < 0.0001$). While non-OP poisoning was reported in RGH but no such poisoning was reported in CGH ($p < 0.0001$) (table 1). In CGH pesticide information was limited to the chemical group (OP). In Rangamati chemical class as well as specific active ingredients was identified (table 1). This shows reporting pattern improves with sample identification method.

Table 1: Comparison of acute pesticide poisoning diagnosis pattern

Traits	Rangamati (n=137)	Comilla (n=834)	p
Total pesticide poisoning	74 (54.01%)	330 (39.6%)	0.001
Number of pesticides identified	55 (74.3%)	330 (100.0%)	< 0.0001
a) Identified pesticides			
OP compounds	11 (20.0%)	330 (100.0%)	< 0.0001
Carbamate compounds	14 (25.5%)	-	< 0.0001
Pyrethroids	8 (14.5%)	-	< 0.0001
Neonicotinoids	2 (3.6%)	-	< 0.0001
Herbicides (Paraquat)	7 (12.7%)	-	< 0.0001
Fungicidal	2 (3.6%)	-	< 0.0001
Rodenticide	7 (12.7%)	-	< 0.0001
Mixed ingredients			< 0.0001
a) OP + Pyrethroid	3 (5.4%)	-	< 0.0001
b) Neonicotinoid + Anthraline	1 (1.8%)	-	< 0.0001
b) Unidentified pesticides	19 (25.6%)	-	< 0.0001
			< 0.0001
			< 0.0001

In RGH active ingredients were identified in 90.9% (n = 50) cases. Among OP were Malathion (6), chlorpyrifos (3), phenthoate and diazinon. All 14 carbamate poisoning were with carbofuran. Pyrethroids compounds were cypermethrin (6), superthrin and lambda cyhalothrin one each. Fungicides were pyraclostobin and hexaconazole. Among mixed (OP + Pyrethroid) poisoning; profenofos + cypermethrine combination was one and chlorpyrifos + cypermethrin preparation were two. Two of seven rodenticide were 2% zinc phosphide, in remaining five name of active ingredient was absent in container.

In RGH in 55 cases clinical diagnosis of each of those patients at emergency was later verified at indoor by inspecting container of pesticide. Comparison of the clinical diagnosis on admission at emergency department with confirmed diagnosis (after container inspection) for same 55 patients presented in table 2. It shows in RGH the accurate diagnosis of pesticide poisoning after sample identification differed from initial clinical diagnosis at emergency.

Table 2: Clinical diagnosis Vs sample identification for accurate identification of pesticide

	Clinical diagnosis		Sample identification		p
	n	%	n	%	
OP	45	81.8	11	20.0	< 0.0001
Rodenticide	7	12.7	7	12.7	1.00
Unknown poisoning	3	5.4	-	-	0.24
Carbamate compounds	-	-	14	25.4	0.0001
Pyrethroids	-	-	8	14.5	0.005
Neonicotinoids	-	-	2	3.6	0.49
Herbicide (Paraquat)	-	-	7	12.7	0.01
Fungicidal	-	-	2	3.6	0.49
Mixed ingredients					
a) OP + Pyrethroid	-	-	3	5.4	0.24
b) Neonicotinoid + Anthraline	-	-	1	1.8	1.00

The clinical diagnosis OP poisoning at emergency was mostly inaccurate. At the emergency 45 were labeled OP poisoning but later on 34 of them (75.5%) proved incorrect (table 2). The actual frequency of OP poisoning (81.8% to 20.0%) in RGH reduced significantly ($P < 0.0001$) after inspection of pesticide container (table 2). By examination of container in 67.3% ($n = 37$) patients inaccurate diagnosis made at emergency department was corrected.

Table 3: Initial treatment pattern of poisoning cases in RGH

Pesticides	Numbe	Initial management as OP		Given initial management as OP			
				Atropine		Pralidoxime	
		n	%	n	%	n	%
With cholinergic features :							
Organophosphate compound	11	11	100.0	11	100	4	36.4
Carbamate compound	14	14	100.0	12	85.7	6	42.8
Without cholinergic features :							
Rodenticide	7	2	28.6	2	28.6	-	-
Fungicide	2	2	100.0	2	100.0	1	50.0
Neonicotinoid	2	2	100.0	2	100.0	1	50.0
Neonicotinoid + Anthraline	1	1	100.0	1	100.0	-	-
Herbicide	7	6	100.0	6	85.7	-	-
Pyrethroid	8	6	75.0	6	75.0	1	12.5
Mixed clinical features :							
OP + Pyrethroid	3	3	100.0	3	100.0	-	-

It is clear (from table 2) that due to inaccurate diagnosis a good number of patients were initially mismanaged as OP poisoning. We look at the pattern of initial treatment ordered at emergency of RGH (table 3). This table helps us to understand magnitude of mismanagement given initially. Though initial diagnosis was 45 OP poisoning as mentioned previously; however 47 (85.4%) patients received treatment as OP at the emergency. Two cases despite labeling as unknown poisoning were treated as OP (both later confirmed as non-OP poisoning). Similarly despite correct diagnosis two more cases of rodenticide poisoning received atropine at emergency. In seven cases of paraquat poisoning though presentation was different from cholinergic toxicity (e.g. oral ulceration); six were labeled as OP and one corrosive poisoning (table 3). In most cases no note of observed physical signs in patients was maintained in file.

OP and carbamate compounds both present with cholinergic symptoms. There were 27 pesticides that do not show cholinergic manifestation (table 3). However, 19 (70.4%) of them were initially managed as OP with atropine and one in addition with pralidoxime. Carbamates do not require pralidoxime; but six such poisoning received pralidoxime on assumption of OP (table 3). After correction of diagnosis in indoor it was found that 75.5% ($n=34$) and 69.2% ($n = 9$) of patients who received

atropine or pralidoxime respectively following order at emergency did not require them at all. Atropine toxicity occurred in 13 cases; 11 of them (84.61%) in non-OP poisoning.

Discussion:

Accurate identification of pesticide is important for two reasons- first to treat the patient appropriately; second for accurate reporting purpose. Identification of pesticide from label of container is encouraged in national poisoning management guideline of Bangladesh.⁶ This approach serves the practical needs though may not be scientific.³ However, in Bangladesh other than in a few research; sample identification is not commonly used in clinical practice.³ In RGH this method is routinely practiced since 2014. Here the pesticide container / packet was either brought from home or purchased by attendant from nearby market or photograph was sent via internet using mobile phone devices. We used the list of registered pesticides in Bangladesh to identify the poison after obtaining the trade name.

Impact of practice of sample identification is evident from this study. There is significant difference in reporting pattern of pesticide poisoning between the RGH and CGH (table 1). The list from RGH is more informative from epidemiological perspective. In Comilla, no such stratified reporting was available. In RGH 74.3% cases exact identification of pesticide class and active ingredient were possible from brand name. In Chittagong Medical College Hospital (CMCH) Verma et al. identified 68.1% pesticides using our method (2016) and in Dhaka Medical College Hospital identification rate was 53.3% (2005-6).^{4,7} Therefore this method is likely to be beneficial in Bangladeshi setting.

We need to carefully scrutinize the scenario in Comilla. Diagnosis was made on clinical ground and all poisoning cases were reported as OP (table 1). This is extremely unlikely to be the real scenario. Two points disagree with this observation. First, it is highly unlikely that all of 330 patients in Comilla took selectively OP for poisoning. We can refer to a similar unlikely observation reported from Rangpur where all 703 pesticide poisoning were reported as OP.³ Dewan in his review clearly pointed out why this sort of reporting from Bangladesh is unreliable and inaccurate.⁸ Second point is- 176 active ingredients belonging to six different categories (78 insecticides, 52 fungicides, 31 herbicides, 6 mitigites, 2 rodenticides and 7 miscellaneous) are approved as pesticide in Bangladesh.⁵ Of them only 14 active ingredients belong to chemical class of OP. Therefore, we cannot take for granted that OP is solely responsible for all pesticide poisoning.

It is evident that there is fault in process of pesticide poisoning diagnosis. Unfortunately this pattern of misreporting (all pesticide poisoning being reported as OP) is common in Bangladesh as identification of pesticide sample is not done routinely.³

Final frequency of OP poisoning in RGH differed from initial diagnosis after confirmation of pesticide by container inspection (81.8% Vs 20.0%). Moreover, in emergency department 75.5% diagnosis of OP poisoning was inaccurate (table 2). If verification of this initial diagnosis was not done by sample identification; in the final reporting OP would have been on top -similar to Comilla. This inaccurate diagnostic rate is higher than that in CMCH where 30.2% of poisoning initially treated as OP were later confirmed as non-OP.⁴ In CMCH 59.2% of non-OP poisoning was initially treated as OP.⁴ Whereas in RGH 80.5% of non-OP cases were initially treated as OP (n = 33).

The trend of labeling all pesticide poisoning as OP has deleterious effect. First is misdiagnosis ; second is wrong treatment and lastly unnecessary increase in cost of treatment and hospital stay. In CMCH overall 25% of pesticide poisoning cases were initially misdiagnosed and treated as OP (2016).⁴ The length of hospital stay and cost of pesticide poisoning treatment depended on whether the poisoning was initially correctly or incorrectly diagnosed as OP. Initial misdiagnosis as OP increased cost.⁴ In our series overall misdiagnosis rate was higher (61.8%; n = 34) than CMCH.⁴ Similar to Verma et al. we could appreciate that some costs of treatment increased with inappropriate use of atropine and pralidoxime. However, we could not quantify the increased costs or length of hospital made in our setting due to the retrospective study design but we noted that inappropriate diagnosis related iatrogenic atropine toxicity was high in this group. One in every third patient of non-OP poisoning that received atropine on assumption of OP poisoning had atropine toxicity (32.3%). So, initial misdiagnosis may increase morbidity in the form of atropine toxicity.

One has to wonder why such higher proportion of misdiagnosis of OP poisoning occurred in both centers? The answer lies in the initial management pattern in RGH. Most of the misdiagnosed poisons in RGH did not have cholinergic manifestations (pin point pupil, sweating etc.) but were initially treated as OP. In RGH physicians may have had limitation to make clinical (toxidromic) assessment appropriately (table 2). Toxidromic assessment to make initial treatment decision has sound scientific background. So we cannot argue that clinical diagnosis of poisoning lacks sensitivity and specificity therefore our physicians made inaccurate diagnosis. In fact there is no alternative to skilled clinical assessment.

Either our physicians have limited clinical skill / experience to identify cholinergic/non-cholinergic toxidromes or they are assuming all poisoning as OP due to inadequate knowledge. It may be they have limited / no concept on toxidromic approach to poisoning. Inadequate training on diagnosis of pesticide poisoning may be a reason.³

Poisoning is a neglected issue in Bangladesh. It attracts less attention both in academic proceedings and in policy making level. The level of basic training required for poisoning management is not available to all level of junior doctors.

Dewan first pointed out this issue and suggested that Bangladeshi physicians may have a tendency to treat all pesticide poisoning as OP.³ Verma et al. later confirmed that most of the native physicians assumed and treated all pesticide poisoning as OP in CMCH.⁴ The result is over diagnosis and inappropriate treatment.

It is likely that after admission some time may elapse before container of pesticide is available. So use of toxidromic approach for initial management of poisoning is very important. Training of physicians to use toxidromic approach specially for recognition of cholinergic toxidrome is required. Hoek et al. recommended that every health facilities should have quick access to list of active ingredients of pesticides and their trade names for consultation by medical professionals.⁹ It is also possible in Bangladesh. This sort of consultation is being used in Rangamati since 2014. The list of pesticides and trade names can be downloaded from website of Bangladesh Crop Protection Association.⁵

Conclusion:

Clinical skill of physicians for poisoning diagnosis needs to be improved. In addition, identification of pesticide from container / packet will aid to increase accuracy of poisoning diagnosis in our resource poor setting. This may have significant impact on subsequent treatment, hospital stay and proper reporting. Regular use of this method will improve quality of poisoning diagnosis, management and actual epidemiological profile will be available.

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Proteinuria and Hematocrit Value in Preeclampsia

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Abstract:

Objectives: The aim of this study is to assess the relationship between proteinuria and hematocrit value and the severity of preeclampsia.

Materials & Methods: This cross-sectional study was conducted in the department of Gynaecology and Obstetrics of Comilla General Hospital during the period of January 2017 to October 2017. A total of 50 patients were studied and they were divided into two groups- Group-A and Group-B. 25 preeclamptic patients were included in the Group-A and 25 normal pregnant women were included in the Group-B.

Results: Most of the preeclamptic women (64%) & normal pregnant women (72%) were in between the age of 20 to 30 years, with the mean ages of group-A and group-B subjects being 26.23±4.7 and 26.07±3.6 years respectively. More than half (56%) of the preeclamptic women were primigravida and 60% of the normal pregnant women were multigravida. 56% of group-A and 48% of group-B were of

low socio-economic status. Majority of the study subjects (76% of group-A & 84% of group-B) were housewives. Among the preeclamptic subjects, 11(44%) had mild or moderate hypertension (DBP<110mmHg) and 14(56%) had severe hypertension (DBP≥110mmHg). Out of the 25 preeclamptic subjects, 18(72%) had severe proteinuria (+++) and 7(28%) had moderate proteinuria (++) . The mean hematocrit value of the preeclamptic women was 35.18±2.80 and that of the normal pregnant women was 31.86±1.10. It was statistically significant (P value 0.001).

Conclusion: This study shows that proteinuria and hematocrit value of preeclamptic patients are significantly higher compared to that of the normal pregnant women (P<0.05). There is a strong association of proteinuria increased hematocrit and preeclampsia.

Key words: Proteinuria, Hematocrit, Preeclampsia.

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Introduction

Preeclampsia / eclampsia is one of the common complications of pregnancy affecting 2%-8% of all pregnancies¹. The incidence of preeclampsia is 7 times higher in low and middle income countries than in developed countries². In a baseline survey for assessment of Emergency Obstetric Care Services in Bangla-desh, 5% of total obstetric admissions in health facilities were due to preeclampsia and eclampsia³.

In Bangladesh, preeclampsia/eclampsia is a significant cause of maternal and perinatal mortality and morbidity. Eclampsia contributes 16% of the maternal mortality and the development of potentially lethal complications such as abruptio placentae, disseminated intravascular coagulation, cerebral hemorrhage, hepatic failure & acute renal failure⁴. Preeclampsia is known as “the disease of theories”, as the exact cause of the disease is not known. It is known that preeclampsia is fundamentally related to poor trophoblast invasion in the myometrium and this results in maternal spiral arteries being hampered in their normal physiological vasodilatation. It is clear that impaired intervillous blood flow results in inadequate perfusion and ischemia in the second half of pregnancy.

The increase in intravascular volume that normally occurs during pregnancy is minimal or completely absent in patients with preeclampsia. The reduced volume is predominantly of plasma and as a result, hemoconcentration develops as the disease progresses⁵. Preeclampsia thus represents a state of hemoconcentration and increased hematocrit levels. A fall in repeated hematocrit values may denote clinical improvement⁶.

Normal pregnancy is characterized by a marked expansion in plasma volume. Plasma volume and hematocrit show a significant correlation. Plasma volume reduction measured indirectly by the elevated hematocrit influences the blood viscosity. Low plasma volume or high hematocrit especially in the second trimester is associated with increased frequencies of fetal death, preterm deliveries and preeclampsia⁷. Proteinuria is the presence of urinary protein in amounts exceeding 0.3gram in a 24hour sample collection, or in concentrations more than 1gram per liter (1+ in urine dipstick). When protein excretion exceeds this level in a pregnant woman, it is considered abnormal and a sign of preeclampsia after 20 weeks of gestation. Proteinuria in pregnancy is mainly due to damage to glomerular capillary wall which allows excess albumin to be filtered & excreted with urine. Proteinuria is one of the cardinal features of preeclampsia and a potentially severe complication of pregnancy. Clinicians currently use three approaches to determine whether their pregnant patient is excreting excessive amounts of protein. One is qualitative, the classic dipstick method. The second is quantitative, the so-called "gold standard" 24-hour collection. And the third is protein-creatinine or albumin/creatinine ratio on a single voided urine⁸. Association between preeclampsia and proteinuria and hematocrit values were determined by different studies in different countries, but this study was done on Bangladeshi women to see the association between these morbid states.

Materials and Methods:

This cross-sectional study was conducted in the department of Gynaecology and Obstetrics of Comilla General Hospital during the period of January 2017 to October 2017. The study population included patients attending the antenatal clinic and admitted in the department of Gynaecology and Obstetrics of Comilla General Hospital. Study population were divided into two groups- Group-A and Group-B. Pregnant women of gestational age between 24 to 40 weeks with preeclampsia were included in the Group-A and pregnant women of same gestational age without preeclampsia were included in the Group-B.

A total of 50 subjects – 25 preeclamptic (Group-A) and 25 normal pregnant (Group-B) women were selected for the study.

Subjects were selected purposively according to the availability of the patients. Inclusion criteria for Group-A were gestational age between 24 to 40 weeks, blood pressure: diastolic ≥ 90 mmHg and systolic ≥ 140 mmHg and proteinuria (1+ or more measured by dipstick method of two random clean catch specimen of urine at least 4 hours apart) and inclusion criteria for Group-B were gestational age between 24 to 40 weeks, blood pressure: both diastolic and systolic remain within normal limits and having no medical or obstetric complications. Exclusion criteria were patients with urinary tract infection, renal disease, diabetes mellitus, essential hypertension, heart failure, chronic obstructive pulmonary disease and using diuretics.

The variables included in the study were age, socio-economic status, parity, gravidity, gestational age, systolic blood pressure, diastolic blood pressure, hematocrit value, hemoglobin concentration and proteinuria.

Structured questionnaire was prepared which includes all the variables of interest. On receipt of the informed written consent, blood samples and urine samples were collected from the study subjects. Proteinuria was measured by dipstick method. A second urine sample was collected after 4 hours to detect proteinuria again. Data was collected from the patients on variables of interest using the structured design by interview, observation, clinical examination, hematological investigations and from the history sheets of the patients. Collected data were processed and analyzed by the software SPSS (Statistical Package for Social Sciences) version 12.0. The test statistics used to analyze the data were descriptive statistics, Chi-square (χ^2) Probability Test and T-test. For all analytical tests, the level of significance was $p < 0.05$. With all aseptic precautions, 1.5mL of blood was collected from all the subjects using disposable syringe and blood was transferred to test tube containing EDTA, an anticoagulant for hematological analysis. Hematological analysis was done by an automated hematology analyzer.

The RBC were analyzed by the RBC detector.

Estimation of urine protein was done by reagent strips (Uric 2V GP, Bayer GMBH Germany).

Results:

During the study period, total 50 subjects were studied, of which 25 were preeclamptic (Group-A) and 25 were normal pregnant women (Group-B).

There was no difference in age, social class, occupation, gravidity and gestational age between the groups (Table-1). Among the preeclamptic subjects, 11(44%) had mild hypertension (DBP < 110 mmHg) and 14(56%) had severe hypertension (DBP ≥ 110 mmHg). Out of 25 preeclamptic subjects, 18(72%) had severe proteinuria (+++) and only 7(28%) had moderate proteinuria (++) . Hemoglobin

concentration of Group-A was 11.25 ± 1.20 (gm%) and that of Group-B was 10.56 ± 0.72 (gm%). Hematocrit value of Group-A subjects was 35.18 ± 2.80 (%) and that of Group-B was 31.86 ± 1.10 (%). The differences of these parameters between the groups were statistically significant ($P < 0.05$) (Table-3).

Table- 1 : Socio-demographic characteristics of the study subjects (n=50)

Characteristics	Group-A(n=25)		Group-B(n=25)		P value
	No.	%	No.	%	
Age in years					
<20	5	20	4	16	1.000
20 to 30	16	64	18	72	0.543
>30	4	16	3	12	0.999
Mean±SD	26.22±4.88		26.>>>		
Gravida					
Primi	14	56	10	40	0.257
Multi	11	44	15	60	
Gestational age					
≤32 weeks	5	20	5	20	1.000
33-36 weeks	14	56	12	48	0.571
>36 weeks	6	24	8	32	0.527
Socio-economic status					
Lower class	14	56	12	48	0.571
Middle class	6	24	8	32	0.527
High class	5	20	5	20	1.000
Occupational status					
Housewife	19	76	21	84	0.479
Service	6	24	4	16	

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

Table- 2 : Severity of preeclampsia and proteinuria of the study subjects (n=25)

Parameters	Number of patients	Percentage
Diastolic blood pressure (DBP)		
Mild (DBP < 110mmHg)	11	44
Severe ((DBP ≥ 110mmHg)	14	56
Proteinuria		
Moderate (++)	7	28
Severe (+++)	18	72

Mean distribution of hematological parameters of the study subjects (n=50)

Parameters	Group-A (n=25)		P value
	Mean±SD	Group-B (n=25) Mean±SD	
Hemoglobin (gm/dL)	11.25 ± 1.20	10.56 ± 0.72	0.267
Hematocrit (%)	35.18 ± 2.80	31.86 ± 1.10	0.001

*Unpaired t-Test was done to measure the level of significance.

Table- 3 : Mean distribution of proteinuria parameter in the study group.

Parameter	Value
24 hr urine volume (mL)	2232 ± 490 (1350-2980)
Total protein excretion per day (mg)	1446 ± 1242 (112-450)
Sport urinary protein per dL	50.9 ± 42.7 (10-191)
Urine creatinine per DL	52.8 ± 25.6 (30-190)
Urine protein: creatinine ratio (UPCR)	1.09 ± 0.86 (0.1-3.47)

Table-4: Diagnostic ability of urine protein: creatinine Ratio (UPCR) for various proteinuria range.

Proteinuria rang	Cutoff values	Sensitivity (%)	Specificity (%)	Study Group
UPCR to predict-300 mg+/day	0.45	82.1	87.5	5-(20%)
UPCR to predict-1000 to 2000 mg+/day	1.46	94.4	92.4	7-(28%)
UPCR to predict-2000 to 3000 mg+/day	1.83	91.7	86.7	13(52%)

Discussion:

Preeclampsia is a disorder of unknown etiology. It is a major cause of maternal and perinatal mortality and morbidity worldwide, particularly in developing countries. Preeclampsia occurs mostly in nulliparous women⁹.

Soffronoff et al¹⁰ found marked hypovolemia in pregnant women with severe preeclampsia and the reduction in plasma volume was particularly marked in association with severe placental failure, while the reduction in the erythrocyte volume was less pronounced. From their results, there is a high erythrocyte concentration in preeclampsia than in normal pregnancy and particularly high erythrocyte concentrations in pregnancies with a poor fetal outcome.

In this study, the Group-A (preeclamptic patients) and the Group-B (normal pregnant women) were almost identical in terms of age. Most of the subjects of both groups were of 3rd decade. Socioeconomic status of most of the study subjects of both groups was low. Most of the subjects of both groups were housewife. Regarding obstetric variables like gestational age and gravidity were homogenously distributed without any significant differences between the groups.

On analysis of the severity of preeclampsia, this study revealed that more than half (56%) of the preeclamptic women (Group-A) had severe preeclampsia (diastolic blood pressure \geq 110mmHg) and remainders (44%) had mild preeclampsia (diastolic blood pressure $<$ 110mmHg). 72% had severe proteinuria (+++ on dipstick test) and remaining 28% had moderate (++) proteinuria.

The present study demonstrated that the mean hemoglobin concentration of Group-A women was 11.25 g/dL and that of Group-B women was 10.56 g/dL. The mean hematocrit value of Group-A women was 35.18% and that of Group-B women was 31.86%. Both of these hematological parameters were significantly higher in Group-A women than in Group-B women (P value 0.001) (Table- 3). The results of this study are supported by the study done by Heilmann et al¹¹.

This study demonstrated that in preeclamptic women the hematocrit values were above those of the normal pregnant women (Table- 3). Hemoglobin concentration and hematocrit value rises both in mild and severe preeclampsia in comparison to normal pregnant women, Heilmann et al¹¹ showed that hematocrit value of both mild and severe preeclampsia were significantly different than that of normal pregnant women. They also found that the lower hematocrit of normal pregnancy is associated with a decreased oxygen carrying capacity but with an increased oxygen delivery rate. In cases with proteinuric hypertension, a hematocrit value above normal is associated with reduced systemic oxygen transport rate.

Gifford et al¹² recommended hemoglobin and hematocrit value estimation along with other laboratory evaluation for the women in whom hypertension develops after midpregnancy, as hemoconcentration supports diagnosis of preeclampsia and is an indicator of severity.

Provided that no anemia exists, estimation of hemoglobin levels during severe preeclampsia are valuable supplements to other and more sophisticated placental function tests¹³. The present study demonstrated a significant rise of hemoglobin and hematocrit values in preeclamptic women over normal pregnant women. However, it could not say about pregnancy outcome for which large scale prospective study can be performed.

The mean hematocrit value of the normal pregnant women and the preeclamptic women were 31.86% and 35.18% respectively. On the basis of the results of this study it could be concluded that hematocrit value of preeclamptic women was significantly higher compared to that of the normal pregnant women (P $<$ 0.05). So increased hematocrit value is associated with preeclampsia.

Conclusion:

Urine Protein: creatine ratio is one of the important investigation in hypertensive disorder of the pregnancy. It is simple, accurate, and convenient measurement which is not only qualitative, but also semi quantitative as it can predict the total amount of protein loss through kidneys. It can also serve as a useful gadget to monitor proteinuria on outpatient basis in hypertensive pregnant women during their regular antenatal visits.

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Study of Maternal and Perinatal Outcome of Antepartum Haemorrhage in Pregnancy

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Abstract

Background: Antepartum haemorrhage is one of the types of obstetric haemorrhage, which is defined as bleeding from or into the genital tract after 28 weeks of pregnancy until the delivery of the fetus (the first and second stage of labor are thus included). Maternal health and new born health care are closely linked. Almost three million newborn babies die every year and an additional 2.6 million babies are stillborn. APH can be due to placenta previa, abruptio placentae, unexplained or indeterminate cause or local causes of genital tract.

Objective: To evaluate the demographic profile, type of antepartum haemorrhage, maternal and perinatal complications in cases of antepartum haemorrhage and to formulate preventive guidelines so as to reduce maternal and perinatal complications in cases of antepartum haemorrhage.

Methodology: This was a retrospective study of 93 cases of antepartum haemorrhage admitted during the period of May 2012 to April 2016 at Chandpur City hospital of Bangladesh. Data was collected on a predesigned proforma and percentage analysis was done.

Result: During study period incidence of APH is 3.1%. Out of 93 sample cases, 47 cases were of placenta previa, 28

cases were of abruptio placentae and eighteen cases were of indeterminate cause. In the present study, 84.94% were emergency cases. Incidence of APH was about 70% in age group of 26 - 35 years of which about 88% cases were with parity of > 2-3. In spite of intensive care, there were 2 maternal deaths due to haemorrhagic complications. At the time of admission, 74.19% patients were anaemic and most of the patient required blood transfusion. The perinatal mortality rate is about 18.27% in both cases of placenta previa and abruptio placentae.

Conclusion: Antepartum haemorrhage is the major cause of maternal morbidity and mortality and perinatal mortality. It can be prevented by educating pregnant mothers about the importance of antenatal care, easy accessibility to emergency obstetric care (EOC), family planning program, and awareness of small family norm. These attempts will help in decreasing cases of APH in relation with age and parity. Neonatal intensive care unit also must be improved to reduce perinatal morbidity and mortality.

Key words: antepartum haemorrhage, placenta previa, abruptio placentae, perinatal mortality.

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Introduction

Antepartum haemorrhage is defined as bleeding from or into the genital tract after 28 weeks of pregnancy until the delivery of the fetus (up to the end of the second stage). It complicates about 2% to 5% of all the pregnancies¹. It is the world's leading cause of maternal mortality². It is one of the most frequent emergencies in obstetrics occurring at a prevalence of 0.5-5%³. In this case, uterine bleeding coming from above the cervix is concerning. It may follow some separation of a placenta previa implanted in the immediate vicinity of the cervical canal, it may be from a placental abruption from normal situation, indeterminate cause or local causes (such as uterine tear, cervical tear).^{4, 5}

Maternal mortality due to antepartum haemorrhage has significantly decreased in the developed countries due to better obstetrical outcome. At the country level, the countries of South Asia such as Bangladesh or India at 17%

and Nigeria at 14% accounted for 1/3rd of all global maternal deaths in 2013.⁶⁻⁷ The major complications that account for nearly 75% of all maternal deaths include severe bleeding (mostly bleeding after childbirths), infections (usually after childbirth), high blood pressure during pregnancy (pre-eclampsia and eclampsia), complications from delivery and unsafe abortion.⁸⁻¹⁰ In South Asian countries like Bangladesh and India, maternal and perinatal mortality is still very high due to associated problems like anaemia, difficulties in transport in cases of emergency and restricted medical facilities. Zeeman's study of obstetric critical care provision identifies haemorrhage as one of the most frequent reasons for admission to intensive care unit.⁹⁻¹⁴

In developing countries like Bangladesh, there is high incidence of untreated pre - eclampsia which is the main etiological factor for development of abruptio placentae. So it is important to analyze various reasons of antepartum haemorrhage in present day obstetrics in Bangladesh.¹⁵⁻¹⁷ Postpartum haemorrhage is one of the major complications of antepartum haemorrhage. Untreated anaemia and postpartum haemorrhage can result in long term suffrage of mothers. Modern obstetrics has experienced an increase in the caesarean section rates from 30% to 40%.¹⁸ If the patient has experienced caesarian section in the past, there is an increase in the incidence of placenta previa in the following pregnancy. Morbidly adherent placenta is one of the causes in these cases. Follic acid deficiency is considered as one of the etiological factors for abruptio placentae.¹⁸ Untreated anaemia is commonly found in our country. Blood transfusion facilities are still inadequate in rural Bangladesh. Late referral, lack of transport facilities and inadequate knowledge of medical and paramedical staff contributes to poor prognosis in cases of antepartum haemorrhage in developing countries like Bangladesh. This retrospective analytical study of cases from my hospital is important to understand the etiology of antepartum haemorrhage and to formulate preventive guidelines to improve the obstetric outcome.

Methodology:

This retrospective study was conducted at Chandpur City Hospital in Bangladesh between May 2012 to April 2016. The data was collected from the case record files. Inclusion criteria: 93 cases of diagnosed antepartum haemorrhage were included in this study. Exclusion criteria: The haemorrhage in first and second trimester of pregnancy were excluded from this study. Statistical data analysis and percentage analysis have been done.

Results:

The medical records of 93 diagnosed cases of antepartum haemorrhage out of the total 3000 deliveries conducted during this period, 93 cases were of APH. The incidence of APH is 3.1%. Out of 93 cases the number of placenta previa were 47 (50.53%), abruptio placentae were 28 (30.10%) and other causes were 18 (19.35%).

Table 1: Shows the maternal demography. Majority of the patients 79 (84.95%) were unregistered (emergency) and referred to our hospital from rural areas. Rest of the 14(15.05%) patients were registered. APH is more common in the age group of 26-35 years (about 69%) and in multigravida (about 88%). Placenta previa occurs mostly between 34-36 weeks of gestation (41.93%), abruptio placentae occurs mostly at term (46.42%) and indeterminate cause of APH is 5.37% at this time of gestational age.

Table-1: Maternal demography (n=93)

	Placenta previa	Abruptio placentae	Other causes	Total Percentage
Booking status				
Unregistered	41 (44.08%)	23 (24.74%)	15 (16.12%)	79 (84.95%)
Registered	6 (6.45%)	5 (5.38%)	3 (3.22)	14 (15.05%)
Age in years				
21-25	2 (2.15%)	7 (7.52%)	6 (6.45%)	15 (16.12%)
26-30	17 (18.28%)	7 (7.52%)	5 (5.38%)	29 (31.19%)
31-35	19 (20.43%)	13 (13.98%)	3 (3.22)	35 (37.64%)
>36	9 (9.68%)	1 (1.08%)	4 (4.30%)	14 (15.05%)
Parity				
1	4 (4.30%)	3 (3.22)	4 (4.30%)	11 (11.82%)
2-4	38 (40.86%)	19 (20.43%)	9 (9.68%)	66 (70.98%)
>5	5 (5.38%)	6 (6.45%)	5 (5.38%)	16 (17.20%)
Gestational age (weeks)				
28-33	3 (3.22%)	7 (7.52%)	6 (6.45%)	16 (17.20%)
34-36	39 (41.93%)	8 (8.60%)	5 (5.38%)	52 (55.91%)
37-40	5 (5.38%)	13 (13.98%)	7 (7.52%)	25 (26.89%)

Table 2 : Shows the associated obstetric complications in my study. Most of the patients (74.19%) were anaemic (<10gm%). At the time of admission (25.80%) of the patients had pre-eclampsia. Incidence of associated previous caesarean section was (22.58%). Among the patients of antepartum haemorrhage, 13.97% patients had malpresentation and 2.15% had multiple pregnancy.

Table 2 : Associated obstetric complications (n=93)

	Placenta previa	Abruption placenta	Other causes	Percentage
Anaemia	39 (41.93%)	21 (22.58%)	9	69 (74.19%)
Pre-eclampsia	5 (5.38%)	19 (20.43%)	0	24 (25.80%)
Previous Caesarean section	17 (18.27%)	2 (2.15%)	2 (2.15%)	21 (22.58%)
Malpresentation	10 (10.75%)	3 (3.22%)	0	13 (13.97%)
Multiple Pregnancy	2 (2.15%)	0	0	2 (2.15%)

Table 3: Shows the maternal complication and management of APH. Blood transfusion was required in about 68.81% of the patients. The rate of caesarean section was 77.41% & the rate of vaginal delivery was 22.58%. The rate of PPH was 3.2%, ruptured uterus 1.07% and convelaire uterus 1.07%. There is no incidence of DIC. The incidence of maternal death was 2.15% due to haemorrhagic complications.

Table 3: Maternal complication and management of APH (n=93)

	Placenta previa	Abruption placenta	Other causes	Percentage
Blood transfusion	39 (41.93%)	22	3 (3.22%)	64 (68.81%)
Post partum haemorrhage	2 (2.15%)	1 (1.08%)	0	3 (3.2%)
Ruptured uterus	1 (1.08%)	0	0	1 (1.07%)
Convelaire uterus	0	1 (1.08%)	0	1 (1.07%)
Coagulation failure	0	0	0	0%
LSCS	47 (50.53%)	19 (20.43%)	6 (6.45%)	72 (77.41%)
Vaginal delivery	0	9 (9.67%)	12 (12.90%)	21 (22.58%)
Maternal death	1 (1.08%)	1 (1.08%)	0	2 (2.15%)

Table 4: Shows the perinatal outcome where the perinatal mortality rate is 18.27% due to low birth weight, birth asphyxia, congenital malformation or intracranial haemorrhage. In my study rate of prematurity was 33.33% and low birth weight was 63.44%.

Table 4: Perinatal outcome (n=93)

Complications	Placenta previa	Abruption placenta	Other causes	Percentage
Perinatal mortality	4 (4.30%)	13 (13.97%)	0	17 (18.28%)
Intrauterine growth retardation	9 (9.67%)	3 (3.22%)	0	12 (12.90%)
Prematurity	22 (23.65%)	7 (7.52%)	0	27 (29.03%)
Low birth weight	39 (41.93%)	17 (18.28%)	3 (3.22%)	59 (63.44%)

Discussion:

In this present study, the incidence of APH is 3.1% which is significantly less as compared to Sheikh et al (5.4%) but slightly higher than Singhal et al (3.01%).^{3, 8} In my study, 79 cases of antepartum haemorrhage were of unregistered emergency patients (84.94%) that accounted for majority

of patients. Among unregistered cases, those patients who did not have regular antenatal visits as they had been referred to our hospital from rural centers had higher incidence of abruption placenta, placenta previa and associated complications. Repeated pregnancies at short intervals may be responsible for 70% of cases of antepartum haemorrhage in the combined age group of 26 - 35 years. 88.17% of APH occurred in multigravida. Present study shows that a multigravida is more prone to APH than a primi gravida which is comparable to the study of S. Singhel who also reported that incidence of APH increases in multigravida.⁸ Abruptio placenta is more common in pregnancy around term but Placenta Previa with a bout of bleeding is more commonly found between 34 weeks and 36 weeks of gestation resulting in pre - term delivery.¹⁹ In this study, it is (31.18%). Malpresentation was seen in 13.97% of 93 studied cases. Among those malpresentations, 10 (10.75%) were in placenta previa and 3 (3.22%) were in abruption placenta. Siddhartha cites Raksha et al who found fetal malpresentation to be 23% in placenta previa and 11% in abruption placenta, which is higher than that is observed in my study.¹⁹ Anaemia was found in 74.19% of patients, which reflects the existing poverty and ignorance of our country. Incidence of pre - eclampsia was observed in 25.80% of patients and it is mostly seen in the patients of abruption placenta (20.43%). In modern obstetrics, there is an increase in the rate of LSCS which is about 30% - 40%.¹⁸ We know that there is an increased chance of placenta previa if the patient has already undergone caesarian section in the past. Previous caesarian sections may cause morbid adhesion of placenta in the uterus resulting in maternal morbidity and mortality. In my study, the rate of previous caesarian sections was 22.58%. In majority of patients, a definite association between placenta previa and previous caesarian section was present, which was 17 (18.27%). As the majority of patients were affected with haemorrhage in third trimester and pre-existing anaemia, incidence of blood transfusion rate was very high (68.70%). In spite of maximum care, there were two maternal deaths out of 93 cases due to haemorrhagic complications and high incidence of perinatal mortality (18.27%). In my study, postpartum haemorrhage (3.2%) is significantly less in comparison to Singhel et al⁸ (21.84%) and Sheikh et al³ (19%). The decreased incidence of postpartum haemorrhage may be due to prophylactic measures taken for prevention of postpartum haemorrhage such as use of prostaglandin (misoprostol), methyl ergometrin and use of other oxytocic drugs.

Caesarian section is necessary practically in all cases of placenta previa. LSCS in cases of APH reduces maternal and fetal mortality due to haemorrhage. As a result, there is a high incidence of LSCS in cases of APH in my study (77.41%). This rate is higher in comparison to Singhel⁸ and Sheikh³ studies. Perinatal mortality rate in my study is 18.27% which is lower than the S. R. Singhel and Sheikh studies due to early diagnosis and timely intervention. The incidence of low birth weight is more or less equal to Sheikh³ and Singhel⁸ studies. Perinatal loss is higher in babies with low birth weight and higher number of cases of abruptio placentae during pregnancy explains high perinatal mortality rate⁵.

Conclusion:

Antepartum haemorrhage is a grave and potentially life threatening condition for both the mother and the fetus. Multigravida was the major risk factor observed in this study (88%), which is one of the main causes of placenta previa. So educating the pregnant mother about the importance of antenatal care, importance of institutional delivery, importance of family planning, reducing the family size to 1-2 child norm will decrease the maternal and perinatal morbidity & mortality due to APH. Improved referral transport facilities, adequately trained medical and paramedical staff, improved blood transfusion facilities can aid in decreasing the incidence of APH. Neonatal intensive care unit also must be improved to reduce perinatal morbidity and mortality.

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Role of Oral Zinc Supplementation on Serum Glycated Hemoglobin Level in Patients with type 2 Diabetes Mellitus

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Abstract

Background: Diabetes mellitus may affect the homeostasis of trace elements. Zinc is an essential trace element that is directly involved in synthesis, storage, secretion and action of insulin and also plays an important role in antioxidant defense.

Objective: To find out the role of oral supplementation of zinc on serum glycosylated haemoglobin (HbA1c) level in patients with type 2 diabetes mellitus.

Methods: This prospective interventional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from January 2016 to December 2016. During the study total 51 diagnosed type 2 diabetic patients were selected randomly and divided into two groups from outpatient department of Endocrinology, Dhaka Medical College Hospital, Dhaka and personal contacts from Comilla city. Type 2 diabetic patients without

supplementation of oral zinc were considered as control group (Group A) and patients with supplementation of oral zinc (40mg/day) for 12 weeks were considered as study group (Group B).

Results: Among 51 diagnosed type 2 diabetic patients, 5 patients were excluded and 46 patients completed the study. Significant improvement was observed after intervention in study group. In this study, HbA1c level was significantly ($p < 0.001$) lower in diabetic patients after supplementation with oral zinc in comparison to that of their baseline value. Again, after 12 weeks, HbA1c ($p < 0.05$) level was significantly lower in diabetic patients supplemented with oral zinc in comparison to that of diabetic control group. **Conclusions:** It can be concluded that oral zinc can decrease the HbA1c level in patients with type 2 diabetes mellitus.

Key words: Type 2 Diabetes mellitus, serum HbA_{1c} level.

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Introduction

Diabetes mellitus is a clinical syndrome characterized by hyperglycemia caused by relative or absolute deficiency of insulin in the body¹. There are two general types of DM, one is type I or insulin dependent diabetes mellitus (IDDM) and other is type II or non insulin dependent diabetes mellitus (NIDDM). Among them, type II diabetes is more common and about 90 to 95 % of all cases of DM². According to American Diabetes Association (2016), diagnostic criteria of diabetes mellitus are fasting blood glucose level ≥ 7.0 mmol/L (126mg/dl) or 2 hours after 75gm glucose ≥ 11.1 mmol/L (200mg/dl) or HbA_{1c} ≥ 6.5 ³. According to International Diabetes Federation, it is the fourth leading cause of death in most of the high income countries⁴. World Health Organization (WHO) estimated that about 180 million diabetes mellitus patients worldwide during 2000 and expected to be increased to 399 million by the year 2030⁵. According to International Diabetic Federation (IDF), there were 382 million people had diabetes in 2013 and by the year 2035, this will rise to 592 million, whereas the national prevalence in Bangladesh is about 5.52%⁶. In Diabetes mellitus, chronic hyperglycemia produces macrovascular complications like coronary artery disease, peripheral arterial disease, stroke and microvascular complications like retinopathy, nephropathy, neuropathy⁷.

Diabetes mellitus may affect the homeostasis of trace elements. It causes significant decrease in some trace elements which leads to development of diabetic complications⁸. Zinc is an essential trace element with multiple roles in human nutrition. Zinc is inevitable for maintaining optimum health because of its diverse metabolic functions. It acts as a cofactor of more than 300 enzymes and over 200 metallo-enzymes. Zinc is required for various cellular process including DNA and protein synthesis and intracellular signaling^{9, 10}. It plays an important role in antioxidant defense and in the metabolism of carbohydrate, fat and protein¹¹. Zinc is an important trace element that is directly involved in synthesis, storage, secretion and action of insulin. It helps to increase the binding ability of insulin to its receptor and thus facilitates transport of glucose into cell and its deficiency leads to insulin resistance and impaired glucose tolerance¹².

Within beta cell, proinsulin is converted into insulin monomer in presence of zinc. It then assembles firstly into a dimeric and further to a stable form of hexameric crystal. These hexamers dissociate during secretion and enable the hormone insulin to function into the blood. Thus, zinc is essential for processing, synthesis, storage and secretion of insulin from beta cell¹³. Hyperglycemia can interfere the active transport of zinc back into tubular cells of kidney causing hyperzincemia¹⁴. Thus the lower level of zinc may decrease the production, secretion and action of insulin from pancreatic islets cells¹⁵.

Zinc improves glycemic status by reducing glycated hemoglobin level through several mechanisms. These mechanisms may include by potentiating the action of insulin, by acting at multiple steps in insulin signaling pathway, by increasing glucose uptake in insulin sensitive cells and by preventing beta cell damage through acting as an antioxidant. Thus zinc has insulin-mimetic action¹⁶.

In type 2 diabetes, lowered insulin action decreases glucose transporter (GLUT4) activity and causes hyperglycemia. Zinc causes increased activity of GLUT4 and increase in glucose uptake that potentiate insulin activity. Zinc stimulates tyrosine phosphorylation of β subunit of insulin receptor (IR- β) by stimulating of PI3-K pathway. These changes cause glucose transport by GLUT4 translocation to plasma membrane. Zinc also activates protein kinase C (PKC) which leads to translocation of GLUT4 to plasma membrane. It enhances glucose uptake into cell leading to lowering blood glucose level. Thus, zinc promotes insulin signaling pathway^{17, 18}.

Zinc helps to convert glucose to pyruvate and lactate by stimulating glycolytic enzymes through glycolysis by increasing activity of glycolytic enzymes such as hexokinase, phosphofructokinase (PFK) and pyruvate kinase. Zinc is a co factor of key enzymes like activator of fructose 1-6 diphosphatase aldolase and inhibitor of fructose 1-6 diphosphatase involved in glucose metabolism. Thus, zinc lowers blood glucose level by utilizing glucose that potentiates insulin activity^{19, 20, 21}. Glycogen synthase kinase 3 β (GSK-3 β) is a serine/threonine kinase enzyme that decreases activity of glycogen synthase enzyme which is essential for glycogenesis. In healthy adults, insulin inhibits activity of enzyme GSK-3 β . But in type 2 DM, GSK-3 β is significantly higher due to lack of insulin. Zinc inhibits this GSK-3 β by phosphorylating and activating of Akt/protein kinase. Thus it causes activation of glycogen synthase enzyme leading to glycogenesis and enhances storage of glucose results decreasing blood glucose level²². As zinc suppresses hepatic clearance of insulin by clathrin-dependent internalization of insulin receptor, it leads to increase plasma level of the insulin²³. Zinc also increases the binding ability of insulin to its receptors leading to increases sensitivity of insulin by activating PI3K, MAPK, PTPs pathways that regulate blood glucose. Like insulin, zinc also causes cell growth and protein synthesis by activating mTOR pathway. In type 2 DM, there is evidence of β cell damage. Zinc prevents cytokine and immune cell mediated β cell damage. It inhibits cyclic nucleotide phosphodiesterase (PDE) which inhibits the release of IL-1 β and TNF- α from monocyte and by suppression of activation of NF κ B (nuclear factor kappa B) and NO (nitric oxide)^{24, 25}. So, the improvement of HbA1c level was initiated by beneficial effect of antioxidant on β cell.

Methods:

This prospective interventional study was conducted in the Department of Physiology, Dhaka Medical College, Dhaka from January 2016 to December 2016. Protocol of this study was approved by Ethical Review Committee of Dhaka Medical College, Dhaka. Among 51 diagnosed type 2 diabetic patients, 5 patients were excluded and 46 patients completed the study. For this study, these 46 diagnosed type 2 diabetic patients of both sexes were selected with age ranging from 40 to 55 years. Among them, 21 type 2 diabetic patients with supplementation of oral zinc (40mg/day) for 12 weeks were considered as study group (Group B). Another 25 age matched type 2 diabetic patients without supplementation of oral zinc were considered as control group (Group A) for

comparison. They were selected from outpatient department of Endocrinology, Dhaka Medical College Hospital, Dhaka and personal contacts from Comilla city. After selection of the subjects, the nature, purpose and benefit of the study were explained to each subject in details. Informed written consent was taken from the participants. All the information's were recorded in a prefixed data collection form. Serum MDA level was estimated in Institute of Nutrition and Food Science, University of Dhaka. This parameter was studied 2 times in all subjects of control and study group, i.e., at the beginning of study (base line) and after 12 weeks of study period. Type and dose of oral hypoglycemic drugs, diet, and physical activity of the patients remained unchanged during the course of study.

Data analysis

This parameter was expressed as mean ± SD (standard deviation) and range. Paired Student's 't' test and unpaired Student's 't' test were used as the tests of significance as applicable. The p value < 0.05 was accepted as level of significance. Statistical analyses were performed by using a computer based statistical program SPSS (Statistical package for social science) version 22.0.

Results:

General characteristics are presented in table I. In this study, serum HbA1c level was significantly (p<0.001) lower in patients with type 2 diabetes mellitus with zinc supplementation (Table II, III, IV and figure I).

Table I: General characteristics of the subjects in both groups (n=46)

Parameters	Groups		p value
	Group A Type 2 DM (n =25)	Group B Type 2 DM with Zinc supplementation (n =21)	
Age (years)	47.72 ± 4.77	48.76 ± 5.25	0.485
Sex			
Male	10 (40.0)	10 (47.6)	
Female	15 (60.0)	11 (52.4)	
BMI (kg/m ²)	26.00 ± 2.08	24.79 ± 2.97	0.114
Duration of DM (years)	4.84 ± 1.70	5.23 ± 2.32	0.506
Systolic BP (mmHg)	132.40 ± 8.18	137.14 ± 8.88	0.066
Diastolic BP (mmHg)	86.20 ± 4.39	88.71 ± 5.02	0.077

Baseline characteristics are comparable between study and control groups

Table II: Comparison of serum HbA_{1c} level in type 2 diabetes mellitus before intervention with zinc between study and control group (group A₁ and group B₁)

Parameter	Control group(A ₁)	Study group (B ₁)	p value
HbA _{1c} (µmol/L± SD)	6.93 ± 0.99	7.02 ± 1.48	0.804

Serum HbA_{1c} level was comparable between study and control group before treatment with oral zinc supplementation

Table III: Comparison of serum HbA_{1c} level in type 2 diabetes mellitus before and after intervention with zinc (study group B)

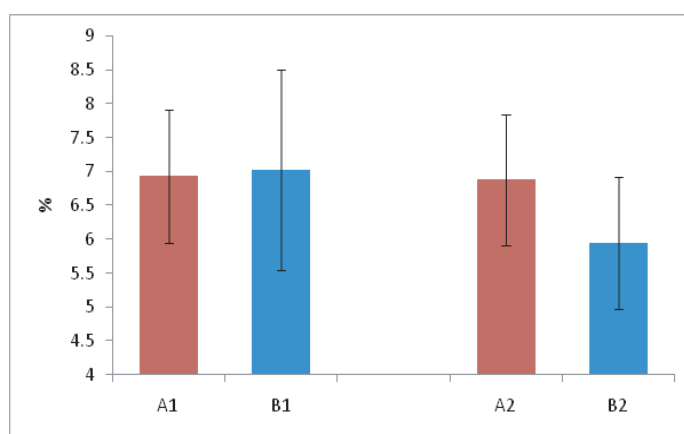
Parameter	Study group B (n=21)		p value
	Before intervention(B ₁)	After intervention(B ₂)	
HbA _{1c} (µmol/L± SD)	7.02 ± 1.48	5.95 ± 0.97	<0.001

Serum HbA_{1c} level significantly (<0.001) reduced after 12 weeks of therapy with zinc supplementation

Table IV: Comparison of serum HbA_{1c} level in type 2 diabetes mellitus after intervention with zinc between study and without intervention in control group (group A₂ and group B₂)

Parameter	Control group(A ₂)	Study group (B ₂)	p value
HbA _{1c} (µmol/L ± SD)	6.88 ± 0.97	5.95 ± 0.97	0.002

Figure-I: Mean glycated hemoglobin(HbA_{1c})level in different groups(n=46)



A₁: Control group (Patients with type2 DM at baseline)

A₂: Control group (Patients with type 2 DM after 12 weeks)

B₁: Study group (Patients with type 2 DM at baseline)

B₂: Study group (Patients with type 2 DM with oral zinc supplementation after 12 weeks)

n= Number of the subjects

Discussion:

This prospective interventional study was carried out to evaluate that, supplementation of oral zinc can improve the HbA_{1c} level by increasing transporter activity and utilization of glucose in type2 diabetes mellitus. Type 2 DM, insulin and serum zinc level presents a complex relationship which exhibits lower zinc status. Nasil-Esfahani et al. found significantly lower level of serum zinc in type2 diabetes mellitus due increase urinary zinc loss as a consequence of hyperglycemia²⁶. Thus the lower level of zinc may decrease the production, secretion and action of insulin from pancreatic islets cells leading to insulin resistance and impaired glucose tolerance^{27, 28, 29}.

In this study, we have found that the mean Serum glycated hemoglobin (HbA_{1c}) level was significantly ($p < 0.001$) lower in diabetic patients after 12 weeks of supplementation with oral zinc in comparison to that of their baseline value. In current study, the result is in agreement with previously published data that showed improvement in HbA_{1c} level after supplementation of oral zinc^{30,31,32,33,34,35}. However, this finding was not in consistent with the findings of previous study done by Parham et al. who found no significant difference in HbA_{1c} level in patients after supplementation of oral zinc in comparison to that of their base line value and diabetic control group who were not supplemented with oral zinc³⁶.

Type 2 diabetes mellitus is one of the major metabolic abnormalities. It affects structural and functional integrity of cell by spontaneous non-enzymatic glycosylation of proteins which causes microangiopathy. This is responsible for most of the complications of DM like retinopathy, neuropathy, nephropathy etc. Thus; zinc is an essential trace element that can decrease the complications related to diabetes by improving glycemic status through decreasing HbA_{1c} level.

Conclusions:

From the results of the study, it can be concluded that oral zinc can decrease the glycated hemoglobin level in patients with type 2 diabetes mellitus. Therefore, estimation of serum zinc level and supplementation of oral zinc in routine management may be helpful to minimize the complications in type 2 diabetes mellitus.

Limitation:

- The study was conducted in a selected hospital. So, the study population might not represent the whole community.

Recommendation:

- Similar type of study can be done with large sample size.

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Mother's Awareness on Tuberculosis of Under Five Children

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Abstract

Background: Tuberculosis (TB) is one of the leading causes of morbidity and mortality of children in tuberculosis endemic areas and account for approximately 11% of the total TB burden. Maternal awareness can play important role for prevention and control of childhood TB in the community.

Objective: to assess the level of awareness of mother on prevention and control of tuberculosis among under 5 children

Materials and methods: This cross-Sectional study was done from January 2015 to July 2015 in some selected slam Area of Khilgaon, Dhaka city. A 106 mother having at least one under five children were included in this study by purposive sampling. Knowledge about sign/ symptom, prevention, diagnosis, treatment of childhood TB, knowledge regarding the place of DOT Centre, the source of knowledge was recorded. If respondent provide >3 correct answer considered as good knowledge. If provide 2-3 correct answer considered as average knowledge. If provided <2 or no correct answer, then considered as poor knowledge. Data were analyzed by SPSS version 12.

Result: The mean age of the study cases was 22.72 years. Most of them(34%) completed their primary education, 30.25% were illiterate, 60.4% were housewife, majority of the cases (47.2%) belong to lower socioeconomic status. Most of the families (65.1%) were nuclear and 67.9% had at least 1 under five children. Majority of them(48.15) had average knowledge and had poor knowledge (36.8%) regarding sign symptoms of TB. 13.4% had good knowledge about TB diagnosis. Regarding TB treatment most of the mother had poor knowledge (54%). Maternal educational level, husband's education, occupation, socioeconomic status had significant impact on knowledge regarding childhood TB.

Conclusion: The present study provides some baseline information regarding knowledge of mother about child tuberculosis. This information will help policy makers to improve vaccination program, women's educational program & economic status of poor people which will ultimately reduce childhood TB and child mortality.

Key words: Childhood TB, awareness, maternal knowledge

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Introduction

Childhood tuberculosis (TB) is a preventable and curable infectious disease that remains a major public health problem. Childhood TB contributes significantly to the burden of disease and represents the failure to control transmission in the community.

Tuberculosis (TB) is one of the leading causes of morbidity and mortality of children in tuberculosis endemic areas¹. World Health Organization (WHO) in 2014, estimated that 1 million children (<15 years) suffer from TB worldwide and 140,000 die each year, representing 10% and 9% of global caseload and mortality, respectively. Childhood TB (CTB) remains a neglected aspect of the TB epidemic, despite its contribution to 20% or more of the TB caseload in many countries with high TB incidence². Among the 4,452,860 new cases reported in 2010 by the 22 highest TB burden countries, only 157,135, i.e. 3.5% (range, 0.1 to 15.0), were reported as CTB. However, the best estimates suggest that children (under 15 years of age) account for approximately 11% of the total TB burden, reflecting that just over 332,000 (7.5%) of CTB went undiagnosed or unreported in these countries³.

Bangladesh stands 7th amongst the 22 high TB burden countries in the world. As in many high-TB burden countries, childhood tuberculosis is also grossly under-detected in Bangladesh⁵. In 2007, Bangladesh National Tuberculosis Programme (BNTP) reported incidence of childhood TB as 9 per 100 000⁶. In 2011, of the total 155,673 newly reported TB cases, only 4,672 (3%) cases occurred in children under 15 years⁷. The National incidence of CTB among 0-14 years old children were 9 per 100,000 reported by the NTP in 2007 and 8.6 per 100,000 reported by the Damien Foundation in 2009⁸. However, extrapolating data of best estimate (CTB: 11% of total case load), the estimated incidence and prevalence of CTB is likely to be 25/100,000 and 45/ 100,000 respectively in Bangladesh⁹.

Childhood tuberculosis which is a marker for ongoing infection of TB in the community and indicator of level of adult TB control within the population^{10,11} poses significant threat for a resource poor country like Bangladesh for several reasons. Existing high burden of adult TB, prevalence of childhood malnutrition, poverty and high density of population in Bangladesh are among the critical ones. There are still some major gaps in our epidemiological data on transmission dynamic of TB where the fact that TB is endemic and highly prevalent in Bangladesh. So, the need for knowledge about tuberculosis is raised to prevent & control childhood TB. In this issue mother can play important role. Maternal awareness about where they can get health service, their role in the promotion of health within their family and community, will be informed about their share of responsibility in the prevention of diseases so that their children and they will not be victims of many of the health problems. This study will help to find recommendations for arranging advocacy as well as awareness programme for mother to prevent child TB. So, the aim of the study to assess the level of awareness of mother on prevention and control of tuberculosis among under 5 children.

Methodology:

This cross-Sectional study was done from January 2015 to July 2015 in some selected slum Area of Khilgaon, Dhaka city. One of the Slum were near the High way, there were about twenty families, most of them were Rikshawpuller. Another slum was situated at Chourasta, Khilgaon. In this slum different type of occupation were found eg Garments Worker, NGO Worker, Driver, Shopkeeper etc. Reason for selecting the study area as this area represents the urban area in Bangladesh, were well communicated, and connected with multiple broad roads with available transportation. Study population was easily approachable and convenient to get adequate and reliable information from the respondents. 106 mother having at least one under five children, age was within reproductive period and lived in slam area Khilgaon were included in this

study by purposive sampling. Informed consent was taken and data were collected by predesigned structured questionnaire. Details socio demographic information (maternal age, religion, educational status, occupation, family members, type of family, Housing condition) was taken. TB related information (I. Infectious diseases, II. male, female, child all are affected, III. it is curable disease, IV. it can be prevented, V. it is caused by mycobacteria), Knowledge about sign/ symptom of childhood TB (I. Chronic Cough, ii. Weight loss, iii. Cough with blood, iv. Fever, v. Weakness), Awareness about prevention of child TB (Vaccination, Modern Medicine), Information about BCG vaccination. Knowledge regarding diagnosis of childhood TB (sputum examination, X-ray, blood test), Information regarding treatment of childhood TB (How will you treat childhood TB? How long you treat? Where it is available? How much money you have to spend? Side effect), Knowledge regarding the place of DOT Centre, the source of knowledge regarding TB (Radio, TV, Newspaper, Husband, Relative, Field Worker)

If respondent provide >3 correct answer about sign/ symptom, prevention; diagnosis and treatment of TB considered as good knowledge. If provide 2-3 correct answer considered as average knowledge. If provided <2 or no correct answer, then considered as poor knowledge. Data were analyzed by SPSS version 12. Results on continuous measurements are presented on Mean ±SD (Min-Max) and categorical measurements are presented in number (%). Chi-square test has been used to find the significance on categorical scale between two variables.

Result:

The mean age of the study cases was 22.72 years and majority of the cases were >25 years (59.4%). Most of them completed their primary education (34%), 30.25% were illiterate and 3.8% were completed their graduation. Among the study cases 60.4% were housewife, 17.9% were service holder and 18.9% had business Majority of the cases (47.2%) belong to lower socioeconomic status (Table1).

Table I: Demographic profile among the study cases

Variable	Frequency n=106
Maternal age	
<20 years	13(12.3%)
20-25years	30(28.3%)
>25 years	63(59.4%)
Maternal educational level	
Illiterate	32(30.2%)
Primary	36(34.9%)
Secondary	13(12.3%)
Higher secondary	5(4.7%)
Graduation	4(3.8%)
Non institutional	13(12.3%)
Occupation	
House wife	64(60.4%)
Service Business others	19(17.9%)
Socioeconomic status	
Poor	50(47.2%)
Middle Good	41(38.7%)
	15(14.2%)

Most of the family (65.1%) was nuclear, joint family (32.1%) and only 2.8% were extended family. Among the study cases most of the family had 4-5 child (46%) and 67.9% had at least 1 under five children (Table II).

Table II: Family status among the study cases (n=106)

Variable	Frequency (%)
Number of family member <34-5>5	26%46%28%
Number of under five children OneTwo≥ Three	67.9%20.8%11.3%
Types of family Nuclear familyJoint familyExtended family	65.1%32.1%2.8%

Very few mother had good knowledge about overall TB 16(15.4%) and majority of them had average 51(48.15) and poor knowledge 39(36.8%). Regarding sign symptoms of TB most of the mother had poor knowledge 48(45.8%) followed by average knowledge 41 (38.7%) and good knowledge 17(16%). About TB diagnosis 13(13.4%) had good knowledge, 29(27%) had average and most of them had poor knowledge 64(60.37%). Regarding TB treatment most of the mother had poor knowledge 58(54%), had average knowledge 35(33.01%) and 13(12.26%) had good knowledge (Table III).

Table III: Maternal knowledge regarding TB among the study cases (n=106)

Maternal knowledge	Poor knowledge	Average knowledge	good knowledge
Overall knowledge about TB	39(36.8%)	51(48.11%)	16(15.1%)
About sign/symptom of TB	48(45.8%)	41(38.7%)	17(16%)
About diagnosis of TB	64(55.3%)	29(32.3%)	13(13.4%)
About management of TB	58(55.3%)	35(32.3%)	13(13.4%)

Among the cases who were illiterate had poor knowledge about childhood TB. Very few had good knowledge. On the other hand, literate mother had good knowledge then illiterate mother, which was found statistically significant. Among the study cases whose husbands were illiterate had poor knowledge then literate husband. Most of the mother who were housewife had poor knowledge. On the other hand, working mother had more good knowledge about childhood TB. Rickshaw puller, day labor, unemployed husband had poor knowledge about childhood TB then employed husband. Among the study cases that were belonging to poor socioeconomic status had poor knowledge then middle/average socioeconomic group. Maternal educational level, husband’s education, occupation, socioeconomic status had significant impact on knowledge regarding childhood TB (Table IV). Most of the

mother (37.7%) does not know about DOT center. Very few mother got some information from TV Channel & Radio, most were unknown about child tuberculosis.

Table IV: association between sociodemographic status and maternal knowledge about childhood TB (n=106)

	Poor and average knowledge	Good Knowledge	P value
Maternal age			
<25 years(43)>25 years(63)	36(33.96%)54(50.94%)	7(6.60%)9(8.49%)	0.167
Maternal educational level			
Illiterate (45)Primary (33)Secondary (10)Graduate(4)	44(41.50%)33(31.13%)10(9.43%)0(0%)	1(0.94%)3(2.83%)8(7.54%)4(3.77%)	0.04
Husband’s educational level			
Illiterate (69)Literate(37)	67(63.205)23(21.69%)	2(1.88%)14(13.20%)	0.05
Maternal occupation			
Housewife(64)Working mother(42)	58(54.71%)32(30.18%)	6(5.66%)10(9.43%)	0.091
Husband’s occupation			
Unemployed (10) Rickshaw puller (32)Service (25)Day labor (24)Businessman (15)	9(8.49%)31(29.24%)17(16.03%)22(20.75%)11(10.37%)	1(0.94%)1(0.94%)8(7.54%)2(1.88%)4(3.77%)	0.034
Socioeconomic status			
Good (15)Poor/middle (87)	3(2.83%)87(82.07%)	12(11.325)4(3.77%)	0.001

Discussion:

The development of knowledge in specific issues always depends on education, occupation, family history and especially the level of standard of the community or country. So, the knowledge about TB and childhood TB also depend on these issues.

One study found that the literacy rate in Bangladesh aged above 15 years is 59.82%^{12,13}. In present study, most of the study cases were housewife and had lower socioeconomic and academic status. But the trend was upward than 2007¹⁴ and all most similar with Haqueet al.¹⁵This slum area is highly crowded and transmission of Mycobacterium Tuberculosis is strongly associated with degree of crowding^{16,17,18}

However, a paper has recently been published on the knowledge and associated factors regarding adult TB based on a nationwide survey in Bangladesh¹⁹. This study found that approximately 67% of respondents knew the mode of TB transmission in adults. Being a female had 2 times higher odds of having poor knowledge about adult TB. Another study done among TB patients at urban DOTS centres in Bangladesh documented even poorer knowledge about adult TB where only 56% knew accurate mode of TB transmission. This proves lack of awareness in the community even for adult TB.

Islam et al found in their study that community awareness in their study group increased significantly²¹. During their study period they made community awareness by providing IEC materials, training of service providers and distributing posters, leaflets, handbooks, folksongs and flipcharts on childhood TB management. So this is reasonable to argue the improvement of knowledge among the target groups regarding child TB can be attributed to their awareness building intervention. The awareness campaign indicates that program uptake of these IEC materials could be very useful for Bangladesh NTP in raising community awareness on childhood TB.

Present study showed that Maternal age >25 years (50.94%) had poor knowledge compared to <25 years. Fahim et al found similar findings²², which indicates after adopting the DOTS strategy the rate of knowledge dissemination on TB management has increased in Bangladesh but it is still so poor. Frustratingly, only 16% mothers were concerned about it. Developing countries adequacy of treatment and TB contact history are the most important exposure variables²² but still the knowledge of TB burden and its trends is imprecise in Bangladesh^{23,24}. Cough <3 weeks and low Body Mass Index (BMI) should be considered for suspecting TB cases and these issues should be addressed in the current NTP guidelines and awareness campaign which usually addresses only those with cough for at least three weeks even malnutrition is also associated with TB^{25,26,27}. Where the NTP guidelines and awareness campaign were not well addressed, it is tough to find adequate amount of mothers having good knowledge on TB or childhood TB. So, proper strengthening of control activities and knowledge dissemination may contribute in prevention, early diagnosis and treatment of TB though till now total cost of diagnosis and treatment bare by Government. But, need much more specific community oriented campaign for dissemination of info ware. Literacy always increases knowledge, so the information disseminated by television, radio, newspapers were easy to understand by the literate person and this study showed significant relation between education and knowledge about TB and childhood. Most of the Bangladeshi housewives are generally not well educated. They not even well informed about the present status of the world and also not involved with regular activities accept home management which may be a great reason behind the knowledge gap on TB and childhood TB. A foreign funded TB CARE-II project is working throughout Bangladesh to raise awareness of TB among vulnerable groups, including children, urban and rural populations, and low-income populations. Targeted community oriented programs may help to develop awareness more effectively with higher rate of success. But this obviously need proper pre assessment of maternal knowledge of Bangladesh by matching with the present government policy framework.

Conclusion

The present study provides some baseline information regarding knowledge of mother about childhood tuberculosis. This information will help policy makers to improve vaccination program; women's educational program & to improve economic status of poor people which will ultimately reduce childhood TB and child mortality.

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Risk Factors for Relapse in Childhood Nephrotic Syndrome

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Abstract:

Background: Nephrotic Syndrome (NS) is a common childhood illness characterized by massive proteinuria, hyperlipidemia, hypoalbuminemia & edema. NS is a disease of relapse and it is a major problem to manage the cases with frequent relapse.

Objective: To find out the risk factors for relapse of nephrotic syndrome.

Methods: This cross sectional comparative study was conducted in the Department of Pediatric Nephrology, Cumilla Medical College Hospital, Cumilla, from January 2017 to December 2017. Total 100 children with relapsed NS out of them 40 had Frequent Relapse NS (FRNS) and 60 had Infrequent Relapse NS (IFRNS) were included in the study.

Results: NS was more common among less than 5 years of age (67%) with male to female ratio 1.5:1. Most (67%) of patient with frequent relapse had age <5 years, came from rural area (65%) and belongs to poor social class (64%)

compared to that of infrequent relapse. The mean age at first onset was significantly (<0.001) less in frequent relapse group) than that of infrequent relapse group (20 vs 36 months). Majority (52%) of atopic child belongs to frequent relapse cases. Low serum albumin level, Urinary Tract Infection (UTI), Respiratory Tract Infection (RTI) at initial attack were observed to be statistically significant risk factors in relapse and more in case of frequent relapse group.

Conclusion: It was concluded that poor socioeconomic condition, rural residency, early age of onset, history of atopy, low serum albumin at the time of initial attack, UTI and RTI are significantly associated with the risk factors for relapse of childhood NS.

Key word: Risk factors, Relapse, infection, atopy.

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Introduction

Nephrotic syndrome is a pathological entity characterized by massive proteinuria and hypoalbuminemia. Nephrotic range proteinuria is defined as proteinuria exceeding 1000 mg/m² /day or spot urinary protein to creatinine ratio exceeding 2. The proteinuria in childhood nephrotic syndrome is relatively selective, constitute primarily by albumin¹. Estimate on the annual incidence of nephrotic syndrome range from 2-7 per 100000 children and prevalence² from 12-16 per 100000. There is epidemiological evidence of a higher incidence of nephrotic syndrome in children from Asia³. The condition is primary in 95 percent cases. An underlying disorder that might be identified in less than 5 percent cases, includes Systemic Lupus Erythematosus, Henoch Schonlein Purpura, Amyloidosis and Infection with HIV, parvovirus B19 and hepatitis B and C virus.^{4,5} More than 80 percent patients with nephrotic syndrome show minimal change disease (MCD) characterized by normal histology on light microscopy. The remaining is contributed by focal segmental glomerulosclerosis (FSGS) and mesangioproliferative glomerulonephritis (MesPGN). MCD and FSGS are often considered to represent the same

pathophysiological process. Membranous nephropathy and membranoproliferative conditions are uncommon in children.^{6, 7, 8}

About 90% children with MCNS responds promptly to corticosteroid therapy with complete clinical and biochemical remission and have excellent long term prognosis. Among who responds to prednisolone, 20-40% have infrequent relapse and 40% have frequent relapse and remaining are steroid dependent⁹. Relapse can be defined as the reappearance of massive proteinuria for 3 consecutive days after having gone into remission on previous occasion⁹. Relapse can be of two types i.e. infrequent and frequent. Infrequent relapse can be defined as 3 or <3 relapses in any consecutive 12 months⁶, and frequent relapse can be defined as 4 or >4 relapses in any 12 months¹³.

Regarding socioeconomic condition following common three-stratum model is used. Concepts of social class often assume three general categories: a very wealthy and powerful upper class that owns and controls the means of production; a middle class of professional workers, small business owners and low level managers; and a lower class, who rely on low-paying wage jobs for their livelihood and often experience poverty.^(Encyclopedia)

Materials and Methods

The aim of this cross sectional comparative study was to find out the risk factors of relapsed nephrotic syndrome and to compare those between frequent relapse and infrequent relapse and carried out in the Department of Paediatric Nephrology of Cumilla Medical College, Cumilla, from January 2017 to December 2017. A total 100 children between 2-12 years of age with relapsed NS out of them 40 having FRNS and 60 having IFRNS were taken using simple random sampling technique. Patient had features of systemic illness causing NS were excluded from the study. Several demographic, clinical and laboratory variables were studied by a structured questionnaire from discharge paper to find out the risk factors for relapse. Patients having less than 4 relapse within 12 months were diagnosed as infrequent relapse nephrotic syndrome(IFRNS) and that those 4 or more relapse within 12 months were diagnosed as frequent relapse nephrotic syndrome(FRNS). Data were coded, edited and entered into computer and were analyzed by using SPSS program. Chi-squared test and Student's t-test were used to analyze. and p value < 0.05 was taken as significant.

Results

Nephrotic syndrome was more common among less than 5 years of age (67%) with male to female ratio 1.5:1. Most

(67%) of patient (Table:II) with frequent relapse had age <5 years, came from rural area (65%) and belongs to poor social class (64%) compared to that of infrequent relapse. The mean age(Table: III) at first onset was significantly(<0.001) less in frequent relapse group than that of infrequent relapse group (20 vs 36 months with a p value <0.001). Majority (52%) of atopic (Table:III) child belongs to frequent relapse cases. Low serum albumin level at initial attack (Table.III), Urinary Tract Infection (UTI) and Respiratory Tract Infection (RTI) were observed (Table. IV) to be statistically significant risk factors in relapse and more in case of frequent relapse group.

Table I: Baseline characteristics of patients: (n=100).

Parameter	Frequency	Percentage
Sex	Male	60
	Female	40
Age(Years)	< 5 years	67
	>5 years	33
Socio economic condition	Poor	64
	Middle	31
	Upper	5
Residence	Rural	65
	Urban	35

Table II: Association of demographic features with type of relapse (n = 100).

Demographic Features		Groups		p value
		Frequent relapse(40)	Infrequent relapse (60)	
Age	< 5 years	27(67.0)	20(33.0)	<0.05
	>5 years	13(33.0)	40(67.0)	
Sex	Male	25(62.0)	37 (61.0)	>.005
	Female	15(38.0)	23(39.0)	
Socioeconomic Condition	Poor	30(75.0)	26(43.0)	<0.05
	Middle class	8(20.0)	33(55.0)	
	Upper class	2(5.0)	1(2.0)	
Residence	Rural	28(70.0)	32(53.0)	<0.05
	Urban	12(30.0)	28(47.0)	

Table III: Association between disease related variables and type of relapse. (n = 100)

Variable	Group		P value
	FRNS(40)	IFRNS(60)	
Age at first onset (months)	20.2 ± 6.4	36.4 ± 9.1	< 0.001
Serum albumin (gm/dl)	1.4 ± 0.2	1.8 ± 0.3	< 0.001
Number of relapse within 1st yr	4 ± 1	2 ± 1	< 0.001
Total number of relapse	5.3 ± 1.3	2.1 ± 1.1	< 0.001
History of atopy	21(52.0)	15(25.0)	<0.05

Table IV: Association between infection and type of relapse (n =100).

Name of infection	Group		p value
	FRNS(40)	IFRNS(60)	
UTI	18(45%)	14(23%)	<0.05
RTI	14(35.%)	11(18%)	<0.05

Discussion

A total 100 cases of relapsing Nephrotic Syndrome of which 40 with FRNS and 60 with IFRNS were studied. Out of 100 children, majority (67%) were less than 5 years of age, this findings is consistent with the finding of Desman Situmorang et al¹⁴. Among the studied cases male to female ratio 1.5:1 which is comparable with the finding of Gulati et al¹⁵. In this study, majority of patients (59%) came from poor class family and they were significantly prone to develop FRNS than the children belongs to middle and upper class. This is comparable with the finding of Biswas et al¹⁶. Significantly higher incidence of FRNS was found in rural children than that in urban children ($p < 0.05$) which may be caused delay in the initiation of specific treatment in rural area. Children with FRNS had early age of onset (20.2 ± 6.4 months) than that with IFRNS (36.4 ± 9.1 months), this comparison is statistically significant ($P < 0.001$). This is comparable with the finding of Mendoza et al¹⁷. Statistically significant number of children with FRNS had history of atopy. Meadow et al¹⁸ described that children with steroid sensitive NS had a higher incidence of atopic disorder. Mean serum albumin level in FRNS group was significantly lower than that of IFRNS group ($P < 0.001$). This finding is consistent with study conducted by Takeda et al¹⁹. UTI and RTI were found significant risk factors for relapse of nephrotic syndrome ($P < 0.05$). This is confrontation with many other studies^{15,16}.

Conclusion: It was concluded that poor socioeconomic condition, rural residency, early age of onset, history of atopy, low serum albumin at the time of initial attack, UTI and RTI are significantly associated with the risk factors for relapse of childhood NS.

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Duodenal Nodular Lesions in Patients With Upper Abdominal Pain- A Study of 86 Cases.

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Abstract

Background: Upper abdominal pain is extremely common among patients attending at Gastroenterology and Hepatology outdoors. It is also a very common reason for hospital admission under gastroenterology/Hepatology departments. Though, somehow, the pain can be managed for the time being, many a time, underlying cause could not be found out. These patients suffer a lot because of diagnostic difficulties.

Objective: The aim of this study was to identify gastrointestinal lesions endoscopically in patients with upper abdominal pain when the other investigations are normal. To determine the usefulness of endoscopic procedure in the diagnosis of underlying causes of upper abdominal pain.

Methods: This hospital based cross sectional study was conducted to evaluate upper abdominal pain in adult patients during the period of July 2017 to December 2017

in the department of Gastroenterology and Hepatology, Comilla Medical College Hospital. 86 eligible patients with upper abdominal pain were taken purposively. All study subjects were underwent endoscopic procedure having adequate preparation. Data were collected through face-to-face interview, observation, endoscopic findings and admission file review. Data were recorded and analyzed.

Result: On endoscopy, 19.77% patients had normal upper GIT; 80.23% had lesions. Among the lesions- ulcer was 18.60 %; erosions 32.56%, mucosal nodularities 21%, and others (GIST/Pancreatic rest) was 04%.

Conclusion: In this study a significant number of patients had gastric and/or duodenal mucosal nodularities, more in the younger age group which may be attributable to their abdominal pain.

Keywords: nodular lesions, duodenum, abdominal pain

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Introduction

Upper abdominal pain is a very common complaint among adults as well as in younger age groups. It is probably the most common abdominal complaint causing patients to attend to physicians and hospital admission¹. The common causes of upper abdominal pain are peptic ulcer disease, pancreatitis, cholecystitis, cholelithiasis, reflux oesophagitis, hepatitis, gastric and oesophageal malignant disease and others².

Most of the above mentioned diagnosis can be reached by some routine or some specific investigations such as ultrasonography, plain x ray, laboratory test e. g. serum amylase, lipase, Liver function tests or endoscopy of upper GI tract.

In our day to day practice, we find a number of patients with upper abdominal pain in whom diagnoses can not be reached by these investigations. This group comprises functional disease of abdomen and a group with other diagnoses³.

Endoscopic evaluation of upper abdominal pain is done when clinical evaluation points towards upper GIT lesions, or, when other investigations such as ultrasonography, plain x ray or laboratory investigations reveals normal study. We usually find ulcer, erosions, gastritis, and a large group of patients having no lesion in upper GI tract⁴. While in a

group we find diffuse small sized nodules in the mucosa of the stomach but more at the duodenum. This is called nodular lymphoid hyperplasia⁵.

Duodenal nodular lesions of the gastrointestinal tract represents a rare disease that is grossly characterized by the presence of numerous visible mucosal nodules measuring up to, and rarely exceeding, 0.5 cm in diameter⁶. Histologically, hyperplastic lymphoid follicles with large germinal centres are seen in the lamina propria and superficial submucosa called nodular lymphoid hyperplasia(NLH)⁷. There is enlargement of the mucosal B cell follicles caused by hyperplasia of the follicle centres; surrounded by a normal appearing mantle zone. Disease may involve the stomach, the entire small intestine, and the large intestine⁸. NLH involving the colon can mimic a variety of polyposis syndromes and this may cause difficulties in diagnosis⁹. Disease has been reported to cause pulmonary disease as well. The etiology is unknown.

In children, NLH is often associated with viral infection or food allergy; tends to have a benign course and usually regresses spontaneously^{10,11}. The disease in adults is rare and poorly described. It has been suggested that NLH is a risk factor for both intestinal and extra intestinal lymphoma¹². Approximately 20% of adults with common variable immunodeficiency are found to have NLH. Some patients have low or absent IgA and IgM levels, decreased IgG levels, susceptibility to infection, small intestine bacterial overgrowth, diarrhea with or without steatorrhea¹³⁻¹⁵. *Giardia lamblia* is often present in such patients¹⁶. There is also an association with familial adenomatous polyposis and Gardner's syndrome¹⁷. It has also been reported in patients with human immunodeficiency virus infection. The disease may be associated with other pathologies, especially gastrointestinal malignancies¹⁸.

Dominant clinical features of these patients with NLH are epigastric pain, bloating, occasional vomiting, diarrhea, weight loss etc.

In this study we want to see how frequent this duodenal nodular lesions are present in patients with upper abdominal pain attributing to this pain when other relevant investigations for upper abdominal pain are normal.

Method

This cross sectional study was conducted to evaluate upper abdominal pain in patients having normal study in other routine investigations like ultrasonography, x ray, S. amylase etc. Total period of study was from January 2017 to December 2017. The study was undertaken at the department of Gastroenterology and Hepatology, Comilla

medical college hospital.

Adult patients with upper abdominal pain were included: patients attended at endoscopy unit of Gastroenterology and Hepatology department. Patients who fulfilled criteria in our private chambers were also included and were enrolled after informed consent.

Inclusion criteria were: adult patients with long standing upper abdominal pain, having normal USG of upper abdomen, plain X ray abdomen and normal pancreatic enzymes level.

Patients with unstable cardiopulmonary status, severe anaemia patients and younger patients below 18 years were excluded.

All study subjects were underwent upper GI endoscopic procedures after adequate preparation along with history and physical examination and investigations review. Sample size was 86. Purposive sampling technique was used. Data were collected by face to face interview and from procedures results. Data were analyzed manually.

Result

Upper abdominal pain is a common complaint among patients attending outdoors, private chambers and also a frequent reason for hospital admission. It is often associated with upper gastrointestinal (GI) lesions. This hospital based cross-sectional study was carried out to identify GI lesions diagnosed endoscopically in patients with upper abdominal pain at the department of Gastroenterology and Hepatology of Comilla medical college hospital. Total 86 adult male and female patients were selected purposively. Majority of patients were in younger age group (18-32 yrs) (39.54%) with maximum and minimum age 78 and 18 years respectively. More than half of the patients were male (55.81%) and rests were female (44.19%). On endoscopy, 18.60% patients had ulcers (gastric/duodenal), 32.56 % (gastric/duodenal), 24.42% had mucosal nodularities (gastric/duodenal), 4.65% had GIST or pancreatic islets, and 19.77% had normal upper GIT.

Table I: Age group of the study subjects (N=86)

Age group (in Years)	Frequency (n)	Percent (%)
18 -32	34	39.54
33 - 47	26	30.23
48 -62	15	17.44
63 -77	09	10.47
> 77	02	2.33
Total	86	100.00

Figure I: Male-Female ratio of the patients (N=86).

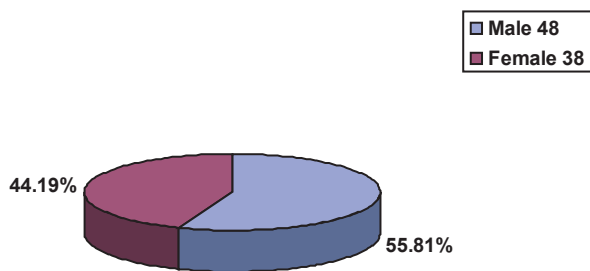


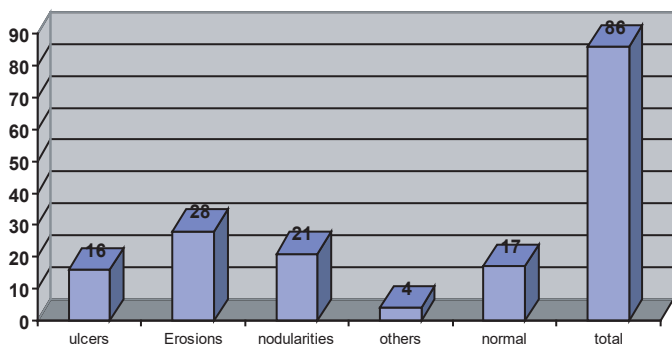
Table II: Frequency of Findings on upper GI Endoscopy among the study subjects (n=86).

Lesions	frequency (n)	Percentage (%)
Ulcers (gastric and/ or duodenal)	16	18.60
Erosions(gastric and/ or duodenal)	28	32.56
Muocosal nodularities	21	24.42
Others(GIST/ Pancreatic rests)	04	04.65
Normal findings	17	19.77
Total	86	100.0%

Table III: Endoscopy findings of the patients (N=86)

Upper GI Endoscopy	Frequency (n)	Percent (%)
Normal	17	19.77
Lesions	69	80.23
Total	86	100.00

Figure - II: Endoscopy findings among the study subjects (N=68)



Discussion:

Common causes of upper abdominal pain are peptic ulcer disease, pancreatitis, cholecystitis, cholelithiasis, reflux oesophagitis, hepatitis, gastric and oesophageal malignant disease etc. There are many uncommon causes of upper abdominal pain as well. Nodular lymphoid hyperplasia of

upper GIT especially of stomach and duodenum is an occasional finding in upper endoscopy¹⁹. Patients with this finding usually present with upper abdominal pain, bloating nausea, vomiting, diarrhea, weight loss etc. In our day to day practice we find this NLH on upper GIT endoscopic procedures in patients with upper abdominal pain. Our effort was to correlate this duodenal nodular lesions with upper abdominal pain.^{20, 21}

There are many studies on duodenal nodular lesions regarding its pathogenesis, association with Helicobacter Pylori, association with immunodeficiency etc²². But no study showed what is the most common form of presentation of this group of patients with NLH. In this study, we found patients with NLH presented with upper abdominal pain as dominant symptom.

In our study the respondents aged between 18-78 years. Maximum patients were in the younger age group (18-32). Maximum and minimum age was 78 and 18 years respectively where range was 60 years. There was a male preponderance. Male patients were 48 (55.81%) and Female were 38 (44.19%).

In this study endoscopic finding were ulcers (18.60%), erosions (32.56 %), nodular lymphoid hyperplasia (24.42%) and others including GIST and pancreatic rests (4.65%), and, 19.77% had normal upper GIT.

Study showed that a significant number of patients (24.42%) had NLH on endoscopy who presented with upper abdominal pain having all other relevant investigations normal indicating that NLH is one of the cause of upper abdominal pain; it is also noted that NLH is more common in younger age group than others. On history, we did not find significant history of diarrhea, weight loss or other features in this group which were mentioned in other studies²³.

Study also showed a significant portion of patients (19.77%) had normal upper GIT on endoscopy. This may be attributable to one of functional bowel disorder like Irritable bowel syndrome (IBS).

Conclusion:

Upper abdominal pain is a very common complaint among general population. Upper GIT causes of upper abdominal pain are ulcers, erosions, inflammation, malignancy etc. Nodular lesions of stomach and/or duodenum is another uncommon endoscopic finding we frequently encountered in daily practice in patients presenting with upper abdominal pain. In this study we found this lesions in a significant number of patients with upper abdominal pain. We also observed that it is more common in younger age group.

Limitations of the study

- The study was conducted in a selected population. So the study population might not represent the whole community.

- Probability sampling technique could not be employed to recruit the study unit; they were selected purposively. As a result, there might be some selection bias.
- Due to resource limitation biopsy was not taken in all cases which might give a better result.
- Further in depth research should be conducted to clarify the association of duodenal nodular lesions with upper abdominal pain.

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Incidence of Carcinoma in Patients Presenting with Breast Lump

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Abstract

Background: Carcinoma breast is one of the leading causes of death in women. More than a million of women are diagnosed breast cancer a year. Carcinoma breast may present from an extent of non-palpable to a fixed mass with distal metastasis.

Objectives: To find out the incidence of carcinoma breast in patients presenting with breast lump.

Study Design: Prospective study.

Setting: Department of Surgery, Cumilla Medical College Hospital, from April 2009 to September 2010.

Methods: This prospective study of 100 cases of breast lump was done from May, 2009 to September, 2010. All patients were female, except one. They were admitted and treated in Cumilla Medical College Hospital.

Palpable breast lump in the present study was defined by clinical examination as a palpable desecrate swelling with in an otherwise normal breast. It was further confirmed by USG of the breast and / or mammography and FNAC. Patient with true lump were included in this study.

Results: Out of 100 cases of breast lump 65 were benign and 35 were malignant. In this study common age group of carcinoma breast patient was 45-54 years, which comprised 28%. Regarding presentation, 56% cases presented with pain, 30% cases with nipple retraction and 15% with ulceration in the breast. In the present series 18 (51%) patients had carcinoma of the left breast and 15 (43%) patients had on the right breast and 2 (6%) patients bilateral and simultaneously affected. 37% cases involved upper outer quadrant, 9% cases lower outer, 22% upper inner, 9% lower inner, 14% cases central and 9% cases diffuse involvement of the breast. In this study 80% of cases, metastasis were present in axillary lymph nodes.

Conclusions: An attempt has been made to find out the incidence of carcinoma among the patients presenting with breast lump. Certainly such small study cannot represent the total incidence of cancer breast in this country.

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Introduction

Breast cancer has become a major health problem over the last 50 years, affecting as many as one in eight women during their lifetime.¹ Breast cancer is a significant health problem in the industrialized western world, where it is the most common form of cancer among women in North America and almost all of Europe. It is estimated that each year the disease is diagnosed in over one million women worldwide and is the cause of death in over 400,000 women.² The incidence of the disease is increasing, in both industrialized and developing countries. In the United States for instance, the incidence rate for breast cancer has increased steadily by about 1-2% per year since 1960.²

A woman's reaction to any actual or suspected disease of breast may include fear of disfigurement, loss of sexual attractiveness and death. Hence it is important for the surgeon to rule out malignancy with minimal invasive investigations and thereby prevent the patient from undergoing mutilating surgery, on the other hand not missing the diagnosis of malignancy as well as to rule out the fear of cancer. In majority of cases a provisional diagnosis can be made on the basis of thorough history taking, careful assessment of physical characteristics and use of an orderly sequence of investigation is required in nearly all the cases of breast lump to attain a definite diagnosis.³

Aims of the study: To find out the incidence of carcinoma breast in patients presenting with breast lump.

Materials and Methods

This prospective study was conducted in the department of Surgery, Comilla Medical College Hospital, Comilla from April 2009 to September 2010. 100 patients presented with breast lump were included in the study. All patients were female, except one. Breast disease without palpable lump, pregnant and lactating women, patient with bacterial mastitis (breast abscess) were excluded from the study.

History was taken in patients with palpable breast lump attending the surgical out patient with particular emphasis on the duration of the breast lump, history of recent rapid growth, pain over the swelling, menarche, menopause, pregnancy, lactation, family and drug history. Physical examination included general examination as well as examination of the breast. Attention was given to the site, size, skin change, consistency, mobility and both axillary lymph node. Investigations included ultrasonography of the breast, mammography, fine needle aspiration cytology of breast lump (FNAC).

Ethical clearance was taken from the institution ethical committee and informed written consent was taken from all the enrolled patients. All the data will be collected, recorded systematically in questionnaire, analyzed by computer and presented in tabulated forms.

Results

In this series, out of 100 cases 99 (99%) cases female and 1 (1%) was male and 65 patients had benign disease and 35 patient malignant breast diseases.

Youngest patient of the carcinoma breast was a 23 years old and the eldest was 74 years. Highest incidence 10 (28%) in this series was in the age group of 45-54 years.

Table- 1: Clinical presentation of disease (n=100)

Presenting features	No. of cases	Percentage
Lump in the breast	100	100
Pain the breast	56	56
Ulceration over the lump	15	15
Nipple discharge	10	10
Peau d orange	12	12
Skin fixation over lump	16	16
Fixation of lump to pectoral's muscle / chest wall	4	4
Nipple retraction	30	30

Table-2: Clinically suspected carcinoma breast Tumour Size (n=35)

Size of tumour	No. of cases	Percentage
T1	2	6
T2	8	23
T3	18	51
T4	7	20
Total	35	100

Table-3: Lymph node involvement (n=35)

Regional lymph node involvement	Clinically involved lymph node	Histologically positive lymph node	Total	Percentage
Positive involvement	26	26	28	80
Negative involvement	9	2	7	20

Table-4: Clinical evidence of distant metastasis (n=7)

Site of metastasis	No. of patients	Percentage
Skeletal	3	42
Lungs	2	29
Liver	2	29
Total	7	100

Table-5: Relationship between tumour size and lymph node involvement (n=35)

Size of tumour	Total number of patients	Number of patients involved	Percentage
T ₁	2	1	50
T ₂	8	5	62
T ₃	18	15	83
T ₄	7	7	100

Out of 35 cases, 28 cases has regional lymph node involvement. In this series original lymph nodes involvement sharply increased as the tumour size increased, in T1 cases 50% of patients regional lymph nodes were involved. In T2 cases 62% patients had regional lymph nodes involvement. Similarly, in T3 and T4 cases 83% and 100% of patients had regional lymph nodes were involved, respectively.

Table-6: Clinical staging of breast carcinoma according to TNM classification (n=35)

Stage	No. of patients	Percentage
I	1	3
II	9	26
III	20	57
IV	5	14
Total	35	100

In this series 20 patients (i.e. 57%) were in stage III, 9 patients (i.e. 26%) were in stage II. Next common stage of this series is stage IV, which comprise of 5 patients (i.e. 14%) and stage I which comprise of 1 patients (i.e. 3%).

Table-7: Histopathological type of malignant tumour (n=35)

Disease	No. of patients	Percentage
Noninvasive duct carcinoma	3	9
infiltrating duct cell carcinoma	30	85
Invasive lobular carcinoma	2	6
Total	35	100

Table-8: Histopathological types of benign tumour (n=65)

Types	No. of patients	Percentage
Fibroadenoma	52	80
Fibroadenosis	7	11
Others	2	3
• Tuberculosis	1	1.5
• Lipoma	2	3
• Galactocele	1	1.5
• Duct ectasia	1	1.5
Total	65	100

Discussion

In this study, commonest age of presentation was 45-56 years (28%) Next common age group was 35-44 years (23%). So maximum incidence is below 50 years. According to the cancer registry of New York in 1996 largest number of incidence found in 45-49 year of age 4. In retrospective analysis in India in 1984 shown 41% of patients registered as carcinoma breast were in the 35-49 years age group⁴. So, it is evident that women in the age group of 35-50 remain at highest risk of developing breast carcinoma all over the world.

In our series, 100% of carcinoma breast cases were presented with breast lump, 56% cases with pain, 30% cases with nipple retraction and 15% with ulceration in the

breast. and fixation of overlying skin 16%, nipple discharge 10% chest wall fixation 4% But clinical evidence of distal metastasis 20%. In a western series published by Harnett et al. shows 77.4% women presented with breast lump, where axillary lymph node involvement found only in 17.6% and chest wall fixation found in 19.3% patient⁵. An Indian series has shown breast lump in 88%, axillary lymph node swelling in 54%, chest wall fixation in 27%, skin fixation 16% and metastasis features in 5% patients⁶.

In the present series, 18 (51%) patients had carcinoma of the left breast and 15(43%) patients had on the right breast and 2 (6%) patients bilateral and simultaneously affected. At the Ellis Fischel Hospital, cancers were located in the left breast in 52% of cases and in the right breast in 47% with 1% bilateral and simultaneous⁷.

In this study 37% cases involved upper outer quadrant, 9% cases lower outer, 22% cases upper inner, 9% lower inner, 14% cases central and 9% cases diffuse involvement of the breast. In Ellis Fischel Hospital (EPSCHE) showed 37% cases involved upper outer quadrant, 8% cases lower outer, 12% cases upper inner, 5% cases lower inner, 15% cases central and 20% diffuse involvement of the breast⁷. In this study 80% of cases, metastasis were present in axillary lymph nodes. Alam (1987) reported 58% axillary lymph node involvement clinically⁸. In this study percentage of lymph node involvement was higher than previous study. In the present study skeletal metastases were 42% liver metastases 29% and lung metastases 29%. Alam (1987) found 50% skeletal 25% lung metastases and 25% liver metastases⁸.

Out of 100 cases, 65 cases were benign and 35 cases were malignant. Out of 35 malignant cases, 7 cases were clinically doubtful and needed preoperative aspiration biopsy cytology Such high correlation between clinical suspicion and histopathological confirmation may be due to advanced cases of carcinoma breast in our study.

Conclusion

Carcinoma breast is the leading cause of death among middle aged women in western countries. Although it is common in western and affluent population but it is not uncommon in our country. Early detection and early treatment undoubtedly give a better prognosis. If the patients are aware of the lethal nature of the disease and if the modern technology regarding diagnosis and therapeutic of breast cancer are available, the mortality rate of breast cancer will be reduced in our country in the future.

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Importance of Cardiac Murmur in Neonatal Period regarding Diagnosis of Congenital Heart Disease

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Abstract

Introduction: Babies presenting with congenital heart diseases (CHD) in neonatal period is an important diagnostic hazards in clinical evaluation of diseases. The incidence of CHD occurs in 8/1000 live birth. Approximately one third of these neonates require intervention in the first month of life. Clinical features of CHD vary according to their type of lesion. The presence or absence of a murmur does not assure either the presence or absence of CHD. This study was conducted to determine the echocardiographic evaluation of neonate with heart murmur and contribution of neonatal examination especially in presence or absence of cardiac murmur in newborn.

Objectives: To determine the importance of cardiac murmur with echocardiographic findings to diagnose the CHD.

Materials & Methods: This cross-sectional observational study was conducted in neonatology department of Dhaka Medical College Hospital during the period from January 2011 to December 2011. Patients were categorized as CHD according to their echocardiographic finding with morphological cardiac defect. Neonates having heart

murmur or when there were some clues to doubt CHD like cyanosis, respiratory distress, heart failure, persistent low partial pressure of oxygen (PaO₂) in arterial blood gas analysis were underwent for echocardiography. CHD were classified according to the structural defect with the echocardiographic findings.

Results: Neonates of 820 were sampled out for my study. Heart murmurs were found in 35 cases. Out of 35 cases 16 (46.00%) had CHD confirmed by echocardiography. Another 8 neonates were found to have CHD without murmur after echocardiography. In total 24 (3%) neonates had CHD. Pattern of CHD were Ventricular Septal Defect (VSD), Atrial Septal Defect (ASD), Transposition of Great Arteries (TGA), Tetralogy of Fallot (TOF) and double outlet ventricle.

Conclusion: Neonates with CHD may present with variety of sign and symptom especially with or without murmur. To determine the importance of CHD with or without cardiac murmur should undergone echocardiography, so that counseling and appropriate measure can be initiated.

Key words: CHD, murmur, neonates, oxygen.

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Introduction

Babies with Congenital heart diseases (CHD) are important clinical hazards in neonatal period. CHD occurs in 7-8 per 1000 live births, with approximately one third of these neonates requiring intervention in the first month of life^{1,2}. So diagnosis of CHD at the earliest possible time is very important as early referral and appropriate intervention in some of these cases are life saving.

Clinical manifestation of CHD varies according to the type of lesion. Neonates with respiratory distress, cyanosis, feeding difficulties, low cardiac output, dysmorphic syndromes commonly have CHD³. These clinical manifestations of CHD are also the features of other non-cardiac causes in the early neonatal period like perinatal asphyxia, RDS, transient tachypnoea, congenital pneumonia, sepsis, pulmonary hypoplasia, etc. Significant cardiac murmur is one of the differentiating point between them, though the presence or absence of a murmur does not assure either the presence or absence of significant congenital heart disease. Rein et al⁴, from Israel found that 86% of asymptomatic neonates presenting with a murmur in the first days of life have structural heart disease.

In another study Anisworth et al⁵ showed that neonatal examination detects cardiac malformation presenting in infancy. Clinical evaluation could determine the presence or absence of heart disease in most neonates but echocardiography is necessary to exclude or confirm the clinical finding. The study was done to evaluate CHD by echocardiography findings

Materials and Methods

This observational prospective study was conducted in neonatology department of Dhaka Medical College Hospital during the period from January 2011 to December 2011. Dhaka Medical College Hospital is a multi-departmental 1500 bedded general hospital in Dhaka city having a big obstetrics and maternity unit and also a 120 bedded paediatric unit. Patients are admitted here as inborn and out born. After admission of the neonates, they were undergone routine physical and clinical examination (0-28 days). Neonates with heart murmur or when there were some clues to doubt CHD like cyanosis, respiratory distress, heart failure, persistently low PaO₂ in arterial blood gas (ABG), echocardiography was done to evaluate structural defect of heart. Echocardiographs were performed by a paediatrician working in paediatric cardiology unit and having training in echocardiography, using 2D echocardiograph machine of Siemens-Sonoline Prima, MC 12E6J3-MI, 1999, Japan. All babies were classified according to their cause of referral and physical findings. Patients are classified as CHD according to what type of lesion of structural defect was present.

Results

820 neonates were taken during the study period. Heart murmurs were found in 35 cases. Out of 35 cases 16(46.00%) had CHD confirmed by echocardiography. Another 8 neonates were found to have CHD without murmur after echocardiography. In total 24 (3%) neonates had CHD out of total 820 babies (Table-I). Out of 24 cases 16 were term and 8 were preterm babies. Table-II shows various presentations of CHD cases. Eight babies were cyanosed on admission and out of these 8 cases 4 were finally diagnosed as cyanotic heart disease. All the TOF cases were not blue but diagnosis was made after echocardiography. Table-III shows types of structural defects of CHD. VSD were found in 36.6% of cases followed by ASD (31.8%), TGA and TOF were diagnosed in 13.6% cases each. Table-IV shows causes of initial admission of CHD cases and their final diagnosis after echocardiography examination.

Table-I: Percentage of CHD in relation to murmur

	Murmur No.	CHD No. (%)
Present	35	16 (46.00)
Absent	785	8 (1.00)
Total	820	24 (2.8)

Table-II: Presentation of CHD cases on admission

Presentation	Number
Cyanosis	8
No cyanosis	14
Resp. distress with or without cyanosis	16
Reluctance to feed	12
Heart failure	1

Table-III: Types of structural defects of CHD cases (n=24)

Structural defects	No. (%)
VSD	8 (36.6)
ASD	7 (31.8)
TOF	3 (13.6)
TGA	3 (13.6)
Corn plex cyanotic heart disease	1 (4.5)

Table-IV: Comparison of initial and final diagnosis of CHD cases (n=24)

Initial diagnosis	Number	Final diagnosis
Perinatal asphyxia Perinatal asphyxia	4	Perinatal asphyxia & ASD
Preterm, LBW, Sepsis	2	Perinatal asphyxia & TOF
N. Convulsion	3	Preterm, LBW, Sepsis & VSD
S. Pneumonia	3	Hypoglycaemia & ASD
N. Sepsis, Jaundice	2	S. Pneumonia & VSD
N. Sepsis, Inguinal hernia	2	N. Sepsis, Jaundice & ASD
CHD (acyanotic)	3+1	N.Sepsis, Inguinal hernia & TOF VSD & TOF
CHD (cyanotic)	3+1	TGA & Complex heart disease

Discussion

Patients with CHD are difficult to classify on clinical examination. Although congenital heart disease is present at birth, there are often no signs and babies may be asymptomatic. Detection of a murmur on routine examination may be due to heart disease and offers the possibilities of early presymptomatic diagnosis. According to the finding, we have found heart murmur in 35 cases out of 820 neonatal admissions. Forty five percent of the babies with heart murmur were found to have structural cardiovascular malformation after echocardiogram. Detecting heart disease at neonatal examination is very difficult as after

birth there are rapid change within the cardiovascular system (CVS) as part of adaptation to extrauterine life, which may produce some murmur that can be mistaken for CHD⁶. Anisworth et al⁵, found heart murmur in 46 (0.6%) neonates out of 7204 during routine neonatal examination of whom 25 (54%) had cardiac malformations. But Kociszewska et al³. showed high incidence of murmur during routine neonatal examination. They had found 107 (8.3%) out of 1291 newborn had murmur and 93 (86.9%) of these 107 infants had congenital heart diseases by echocardiography¹. Another study Rein et al⁴ showed 170 (0.84%) neonates out of 20323 had murmur during examination, of these 147 (86%) were found to have structural heart disease⁴. ZD Du

also concluded in his study that 84% of heart murmur in neonates was due to heart disease and 16% were due to innocent murmur⁷. Examiners skillness and experiences can help to detect a cardiac murmur. There may be a variation of reports regarding prevalence of murmur in neonates. All studies including our one supports that all the babies with murmur should undergo early paediatric cardiological assessment.

The present study showed 8(31.8%) out of 24 CHD cases did not have any murmur. These 8 babies were finally diagnosed to have CHD after echocardiography due to presence of signs and symptoms other than murmur. Anisworth et al⁵, found 48% of CHD in infancy without heart murmur and Shima et al⁸, found 40% CHD without murmur and cyanosis. In our study 8 babies were presented with cyanosis and 15 babies with respiratory distress with or without cyanosis.

The commonest lesion was found as VSD (37%) by Rein et al., followed by PDA (23%)⁴. This findings were similar to this study, we have found VSD in 36.6% cases. But we did not find any cases of Patent ductus arteriosus (PDA), probably it could be due to difficulty to identify PDA by 2D echocardiogram machine and at same time majority cases were term baby where chance of PDA is less. One study done in Japan by Takami et al⁷, he showed that ASD were 9.6% in term neonates presented with heart murmur. But ASD was found in 31.8% cases in this study. Kociszewska et al³, concluded in their study that Patent foramen ovate (PFO) was the most frequently observed abnormality in echocardiograph in infant with heart murmurs. Several echocardiography evolution is needed for differentiation between PFO and ASD.

Conclusion

Neonate with CHD presenting with murmur is not negligible. They can present with or without murmur. To determine the importance of CHD with or without cardiac

murmur should undergone echocardiography, so that counseling and appropriate measure can be initiated.

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Prediction of Development of Significant Hyperbilirubinemia in Preterm Newborn Admitted in A Tertiary Care Hospital

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Abstract

Introduction: Jaundice is one of the major concern for the parents as well as the pediatricians due to chance of neurotoxicity. Determination of early bilirubin level can predict the prevalence of development of significant hyperbilirubinemia in newborn.

Objective: To determine the prevalence of development of significant hyperbilirubinemia on the 5th and 7th days of life from the serum bilirubin values of the first and second day in preterm newborns.

Methodology: This observational prospective study was carried out in Dhaka Medical college Hospital during the period of January to June, 2011. One hundred & twenty preterm newborns of 30-37 weeks gestational age were enrolled in first day of

their life and their serum total and indirect bilirubin were estimated on the 1st, 2nd, 5th & 7th day. Their 1st and 2nd day serum total bilirubin values were analyzed statistically at different cut off points from which significant hyperbilirubinemia could develop on 5th & 7th day of life. Henceforth the definitive intervention would lessen the risk in newborn.

Results: The study included 120 premature neonates of 30-36 weeks gestation who were enrolled on first day of their life. Their mean gestational age was 34.7(±2) weeks and mean birth weight was 1725(±345) gm. Of them, 38 (34%) neonates developed significant hyperbilirubinemia within first seven days of life. Among the study population, 40 (36%) neonates had serum total bilirubin value of <2 mg/dL on first day of life. None of them developed significant hyperbilirubinemia (100% negative predictive value). Again 66 (59.5%) neonates had serum total bilirubin value of <4 mg/dL on second day of life. Among them only 8% developed significant hyperbilirubinemia (93% negative predictive value).

Conclusion: Initial first 2 days serum total bilirubin values can predict subsequent hyperbilirubinemia within seven days of life. First day serum total bilirubin value of 2 mg/dL can be taken as a safe limit from which chance of significant hyperbilirubinemia is less.

Key words: Preterm, Hyperbilirubinemia, Sepsis, Gestation

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Introduction

Neonatal Hyperbilirubinemia is a major concern for the Parents and commonest abnormal physical sign in the newborn¹. It is observed during the first week of life in approximately 60% of the term & 80% of preterm infants². Hyperbilirubinemia is defined as a total serum bilirubin level of >5mg/dL². Neonatal Hyperbilirubinemia is termed as significant when it needs close supervision, further evaluation and sometimes intervention^{3,4}. In case of term baby, serum total bilirubin >17mg/dL beyond the age of 72 hours is termed as significant hyperbilirubinemia^{3,5}. In case of preterm newborn significant hyper-bilirubinemia varies according to gestational age and birth weight^{5,6}. Neonatal jaundice may not be a major cause of mortality but is an important cause of morbidity in the neonatal period and beyond⁶. The primary concern of hyperbilirubinemia is the neurotoxicity and cell injury that results from high levels of serum bilirubin. Prematurity is one of the risk factors for neonatal hyperbilirubinemia.²

Sometimes Neonatal jaundice is the most common reason for readmission after early hospital discharge^{3,7}. The American Academy of Pediatrics recommends that

newborns discharged within 48 hours should have a follow up visit after 2-3 days for any significant jaundice and other problems⁸. This is not always possible in our country due to our limited facilities and economic constrains. The study was undertaken to know the pattern of serum total and indirect bilirubin levels in first two days of life from which significant hyperbilirubinemia may occur in the later part of first week of life. This will enable us to take right decision about the discharge of preterm babies from hospital.

Methodology

This prospective observational study was conducted in Dhaka Medical College Hospital from January to June, 2011. One hundred and twenty preterm newborn with gestational age of 30-37 weeks (210-258 days) were enrolled during their first day of life. Their gestational age was determined according to the first day of mother's last menstrual period and was additionally confirmed by the New Ballard Scoring system and antenatal Ultrasonographic examination or obstetric records. Newborns with gestational age of <30 weeks (d<209 days), 37 completed weeks (d=259 days) and with major congenital malformations, with severe perinatal asphyxia were excluded from the study Babies were enrolled as delivered by normal vaginal delivery and and also by caesarian section.

On admission into hospital, their Hb estimation, complete blood count & peripheral blood film, blood grouping with rhesus typing, serum bilirubin (total & indirect) were performed. Serum total and indirect bilirubin were repeated on the 2nd, 5th & lastly on the 7th day of life. The neonates were followed up upto 7 days of life. Phototherapy was given to them who developed hyperbilirubinemia following the guidelines for perinatal care by the American Academy of Pediatrics. Neonates who developed direct hyperbilirubinemia, Rh incompatibility, clinically or culture positive sepsis and who had evidence of hemolysis were excluded. Serum bilirubin was measured by using Colorimetric method in the Pathology Department of Dhaka medical college Hospital. Serum total and indirect bilirubin values of day 1, 2 were statistically analyzed at different cut of points from which significant hyperbilirubinemia can develop on the later part of first week. Statistical data were analyzed with the descriptive analyses. Results were presented in tabulated form. P value of <0.05 was considered significant. For the independent sample t and chi square tests by using SPSS (statistical package for social sciences) version 12 for Windows.

Results

The sample for study was all preterm newborn (30-37 weeks of gestation). They were divided into four groups according to their gestational age (Table-I). The maximum number was found in the 34-35 weeks (42.3%) gestational age. Among them 62 (56%) were male and 58 (44%) were female. Their birth weight ranges from 1050gm to 2500gm. The mean \pm SD birth weight was 1754 \pm 341 gm.

Table-I: Distribution of study population according to Gestational age (n=120)

Gestational age (wks)	No.	%
30-31	18	16.2
32-33	25	22.5
34-35	47	42.3
36-37	21	18.9
Mean \pm SD	33.7	\pm 2.0

Out of total 120 preterm, in table-II 38(34%) developed significant hyperbilirubinemia. Total 40 (36%) preterm had serum total bilirubin of <2 mg/dL on day 1. None of them developed significant hyperbilirubinemia during the first seven days of life (table II). Serum total bilirubin of <2 mg/dL on day 1 had 100% negative predictive value; sensitivity & specificity were 100% & 54.8% (Table III).

Table- II: Total serum bilirubin vs. subsequent hyperbilirubinemia

Total S bilirubin mg/dL	Total		Subsequent Hyperbilirubinemia	
	n	%	n	%
Day 1				
<2	40	36.0	nil	
2-3	27	24.3	7	25.9
3-5	25	22.5	13	48.0
>5	19	17.1	18	94.7
Day 2				
<5	65	58.5	5	7.6
5-7	23	20.7	14	60.9
7-9	19	16	11	78.5
>9	13	11.1	8	88.8

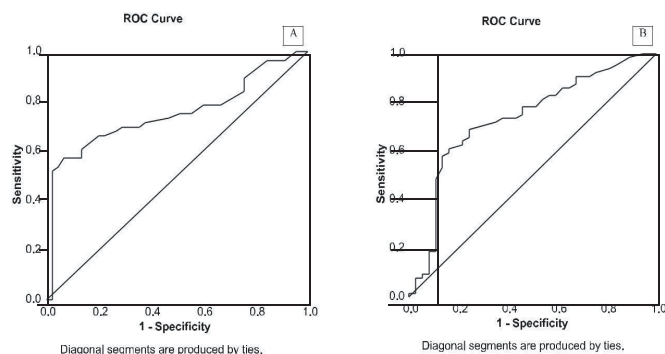
Also total 65 (58.5%) preterm had serum total bilirubin of <5 mg/dL on day 2. Only 5 (7.6%) of them developed significant hyperbilirubinemia during the first seven days of life (table-III). So, on day 2, serum total bilirubin of <5 mg/dL had 92.3% negative predictive value (table III) ie. Only 7.6% chance to develop significant hyperbilirubinemia at this level of serum total bilirubin.

The development or hyperbilirubinemia associated with day 1 serum total bilirubin values are at 5 mg/dL (OR= 64.8, 95% CI: 8.19-82.34) and at 3 mg/dL (OR= 14.14, 95% CI: 3.68-63.59).

And the Prevalence of hyperbilirubinemia associated with day 2 serum total bilirubin values are at 9 mg/dL (OR=19.20, 95%CI: 2.26-27.34) and at 5 mg/dL (OR=30.46, 95% CI: 9.01-110.64). The area under ROC curve (C statistics) was 0.750 for day 1 and 0.733 for day 2.

Table -III: Prevalence value of day 1 and day 2 serum total bilirubin at different cut off points.

S.Total bilirubin as risk demarcator	No of preterms (Total= 120)	Subsequent significant hyperbilirubinemia		Predictive Characteristics			
		Present	Absent	Sensitivity (%)	Specificity(%)	PPV (%)	NPV(%)
Day 1							
>5	19	18	1	47.4	98.6	94.7	78.3
<5	92	20	72				
>3	44	31	13	81.6	82.8	70.5	89.6
<3	67	7	60				
<2	71	38	33	100.0	54.8	53.5	100
>2	40	0	40				
Day 2							
>9	9	8	1	21.1	98.6	88.9	70.6
<9	102	30	72				
>7	23	19	4	50.0	94.5	82.6	78.4
<7	88	19	69				
>5	46	33	13				
<5	65	5	60	86.8	82.2	71.7	92.3



Receiver operating characteristic (ROC) curves with the discriminative performance of day 1 (A) and day 2 (B) serum total bilirubin for predicting subsequent hyperbilirubinemia.

Table IV: Area under the above curve

	C-statistics	Standard error	95% confidence interval
Day 1 TSB	0.750	0.050	0.653 0.848
Day 2 TSB	0.733	0.053	0.629 0.838

TSB-Total serum bilirubin

Discussion

Early detection of neonatal hyperbilirubinemia is an important tool for development of significant hyperbilirubinemia in newborn. The early postnatal discharge of neonates is a regular trial of good practice in every part of the world . Such practice increases the risk of not detecting significant as discharge happens when serum bilirubin is still increasing^{7,8}. Screening and early detection is therefore important to prevent bilirubin

induced neurological dysfunction^{9,10}. The present study was conducted to measure the risk of development of significant hyperbilirubinemia on the 5th and 7th days of life from the serum bilirubin values of the first and second day in preterm newborns. These babies are carefully noted in the hospital. One prospective study by Maisels et al.¹¹ showed that near term (35-37 weeks gestation) newborns had higher serum total bilirubin levels on days 5 and 7 in comparison with term newborns (38-42 weeks gestation).

The premature neonates also showed a rise of serum total bilirubin on 5th and 7th days. This later peak of serum bilirubin demonstrates the necessity of a relatively longer follow-up of these infants with respect to the development and duration of significant hyperbilirubinemia in present study.

Out of total 120 preterms, 38(34%) developed significant hyperbilirubinemia within first seven days of life. Total 40(36%) preterms had serum total bilirubin of <2 mg/dL on day 1 (table-II). None of them developed significant hyperbilirubinemia during the first 7 days of life. So, serum total bilirubin of <2 mg/dL on day 1 had 100% negative predictive value. Also total 65(58.5%) preterms had serum total bilirubin of <5 mg/dL on day 2. Only 5(7.6%) of them developed significant hyperbilirubinemia during the first 7 days of life. So, on day 2, serum total bilirubin of <5 mg/dL had 92.3% negative predictive value ie. Only 7.7% chance to develop significant hyperbilirubinemia by determining the serul total bilirubin at this level.

According the total population, 19(17.1%) had serum total bilirubin >5 mg/dL on day 1 (Table-II). Among them 18 (94.7%) developed significant hyperbillirubinemia within first week. The positive predictive value was 94.7 and it was 98.6% specific (table III). The day 2 serum total bilirubin value was >9 mg/dL in case of 9 preterms. Out of them 8(88.8%) developed hyperbilirubinemia within first week. The positive predictive value was 94.7 and it was 98.6% specific (table III).

A similar kind of prospective study was done by Bhat et al. 5 over 461 healthy term neonates showed that, 29.3% babies had transcutaneous bilirubin index <5 at 24 hours and 43.3% had <8 at 48 hours. None of them had later significant hyperbilirubinemia (100% negative predictive value).

The development of significant hyperbilirubinemia has increased from 25.9% to 94.7% when day 1 serum total bilirubin value raised from <2 to >5 mg/dL and also from 60.9% to 88.8% when day 2 serum total bilirubin value rose from <5 to >9 mg/dL (table-II).

The hazards for hyperbilirubinemia associated with day 1 serum total bilirubin values are at 5 mg/dL (OR= 64.8, 95% CI: 8.19-82.34) and at 3 mg/dL (OR= 14.14, 95% CI: 3.68-63.59). Similarly the risk for hyperbilirubinemia associated with day 2 serum total bilirubin values are at 9 mg/dL (OR= 19.20, 95% CI: 2.26-27.34) and at 5 mg/dL (OR= 30.46, 95% CI: 9.01-110.64). The area under curve (C statistics) was 0.750 for day 1 and 0.733 for day 2 (table IV). The C statistics for Bhat et al's studies was 0.838 and 0.836 for 24 hour and 48 hour transcutaneous bilirubin index respectively indicating good predictive value.

A study by Zakia et al.¹² done in our country over 84 healthy term and preterm newborns for predicting hyperbilirubinemia showed that 6% of their term infant and 35% of preterm infant developed significant hyperbilirubinemia. In our study 34% preterm newborn developed significant hyperbilirubinemia. In Zakia et al.'s¹² study limit for umbilical cord blood serum total bilirubin was 2.5 mg/dL In our study the safe limit for serum total bilirubin on day one is 2 mg/ dL so less chance of significant hyperbilirubinemia

Conclusion

Preterm newborn should be observed carefully for neonatal hyperbilirubinemia and should have pre discharge criteria for serum total bilirubin. Initial 1st 2 day serum total bilirubin values can predict the prevalence of significant hyperbilirubinemia within 7days of life. serum bilirubin level 2mg/ dL or less on day one can be taken as safe limit from which chance of significant hyperbilirubinemia is less and hence less chance of intervention.

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Effect of Maternal BMI on Neonatal Weight- A Study at Combined Military Hospital, Cumilla

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Abstract

Background: The intrauterine environment is assessed crudely by birth weight of the infant. BMI has a clear impact on pregnancy outcome. That is, low body mass index (BMI) is associated with LBW, IUGR, preterm birth, high BMI with increased fetal weight, possibly greater risks of neural tube defects, gestational diabetes, hypertensive diseases, risk of dystosia and shoulder dystosia with a consequent higher risk of cesarean deliveries and a higher incidence of anesthetic and postoperative complications.

Objective: This study aims at determining the influence of maternal body mass index at term pregnancy on fetal weight and improving obstetric management of condition earlier mentioned.

Methods: This retrospective cross-sectional study was conducted in antenatal ward of combined military hospital, Cumilla. During the period of 1st January 2017 to 31st December 2018. A total of hundred patients of different age group who participated voluntarily in this study was the study population. All the information was collected on predesigned questionnaire and different parameters were evaluated. Data analysis was done in SPSS version 16.

Result: Maximum number of Patient was in the BMI group of 25-29.9. Maximum number of Normal body weight patient belonged to lower middle income group (68%).

60% patients of low BMI belonged to the age group <20 years. Mean age of all groups of patients showed a positive relationship with BMI. Mean height of normal weight and overweight patient showed positive relationship with BMI. Mean weight showed a positive relationship with BMI in all the groups. Anemia (40%) was the common maternal disease in low body weight, PIH and GDM was common for overweight and obese mother 10%, 15% respectively. Incidence of GDM was (35%) was highest in obese mother. C/S was the most common mode of delivery in overweight and obese patient i.e. 60%, 80% respectively. Major indication for C/S was CPD in low body weight patient (66%) and normal weight patient (46%), h/o previous C/S in overweight (40%) and obese (50%) patient. Neonatal weight showed a positive relationship with BMI of mothers in all groups. Low birth weight (<2.5 kg) was 80% in low body weight mother. Apgar score did not show any relationship with BMI of mother.

Conclusion: In conclusion BMI of mothers showed positive relationship with neonatal weight in all groups and the relationship was positive and statistically significant ($p < 0.0001$).

Keywords: BMI, macrosomia, over weight, obese, Apgar score.

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Introduction

BMI is defined as measuring a person's weight in kilogram and then dividing by that person's height in meter squared (kg/meter^2). It denotes nutritional status of a person. According to the range of BMI it is classified as low body weight, normal weight, overweight and obese.

Maternal height and pre-pregnancy weight along with the rate and amount of weight gain during pregnancy are important in fetal development. In a study carried out by T.J. Cole, showed that birth weight is directly related to height and weight gain in late pregnancy and also to weight gain in third trimester¹

Birth weight is regarded as one simple measure of outcome of pregnancy. It is a relative indicator of fetal wellbeing and maturity and the most important determinant of the chances of newborn to survive and undergo healthy growth and

development. Thus birth weight has been a subject of clinical importance.

The average weight of a normal newborn infant, born at birth is 2.5kg. Abnormal fetal growth is defined according to percentiles: infants classified as intrauterine growth retardation (IUGR) are in the 10th percentile or below and those are large for gestational age (LGA) are in the 90th percentile or above.² Both IUGR and LGA have an increased risk of perinatal mortality and morbidity and they also alter obstetrical management.³

Detailed methodology

This is a retrospective study done on 100 patients who come for antenatal check up and later admitted for delivery in antenatal ward of combined military hospital, Cumilla. Data was collected during the period of 1st January 2017 to 31st December 2018. All the information was collected on pre-designed questionnaire and different parameters were evaluated. Data analysis was done in SPSS version 16. Women had satisfied inclusion criteria women with regular menstrual cycle, sure about LMP, singleton pregnancy, with normal liquor volume.

Multiple pregnancy, polyhydramnions, suspected intrauterine growth retardation, preterm labour, antepartum hemorrhage, eclampsia, fetuses with obvious congenital abnormalities, presence of uterine anomaly or fibroid along with pregnancy were excluded.

All the selected patient's pregnancy was dated from menstrual date, which was in good agreement with ultrasonic estimation of gestational age before 24 weeks. After taking history, both general and obstetrical examinations were done in the standard way.

Age was recorded in nearest full year as stated by the patient, weight was measured in kilograms by a weight machine. Height was measured in meter in erect posture, bare foot parallel to each other, heels, buttocks, shoulders and back of the head touching the vertical scale.

Maternal: BMI was calculated by the following formula

$$\text{BMI} = \text{weight in kg} / (\text{height in meter})^2$$

For our study purpose, we divided the patients into the following groups according to their BMI. Group A - Low body weight (BMI <18.5), Group B - Normal weight (BMI 18.5- 24.9), Group C - Over weight (BMI 25-29.9), Group D - Obese (BMI >30)(51)

Socio economic status - Our patients were classified into different social classes depending on the income of the family as follows:

Poor (<Tk.8000/month), Lower middle (Tk.8000-15000/month), Upper middle (Tk.16000-30000/month), Higher class (>Tk.30000/month)

Blood pressure was recorded in sitting position and was written as systolic/diastolic mm of Hg. Symphysiofundal height was measured in centimeter by a non-stretchable tape from upper border of symphysis pubis to the top of the centralized fundus. Birth weight (in kg) was obtained immediately after birth and classified as:

Low birth weight (<2.5 kg), normal weight (2.5-3.9 kg), macrosomia (>4 kg).

Statistical Analysis:

The data obtained was corrected and edited manually. Then the data were entered and analyzed using SPSS version 16. Data was presented in tabular form. The variables were stratified. Quantitative variables like age, weight, height, BMI and Apgar score has been presented as mean. Qualitative variables like maternal disease, mode of delivery, indication for C/S were presented as frequency and percentage.

Results:

Table-I: The number of patient in different BMI Group

BMI Group of mother	Number of patient
Group A (BMI <18.5)	5
Group B (BMI 18.5 -24.9)	25
Group C (BMI 25 -29.9)	50
Group D (BMI >30)	20
Total	100

Table I shows maximum number of Patient was in the BMI group of 25-29.9.

Table -II: Socio-economic status in different BMI Group

Socio - economic status	Group A n=5	Group B n=25	Group C n=50	Group D N=20
Poor	3 (60%)	2 (8%)	2 (4%)	0 (0%)
Lower middle	2 (40%)	17(68%)	17(34%)	2(10%)
Upper middle	0 (0%)	5(20%)	25(50%)	16(80%)
High	0 (0%)	1 (4%)	6(12%)	2(10%)

Table-II shows maximum number of group A belonged to poor income group (60%), maximum number of group B belonged to lower middle income group (68%), of group C and D majority belonged to upper middle income group 50% and 80% respectively

Table-III: Age distribution of the patients

Age group	Group A n =5	Group B n=25	Group C n=50	Group D n=20
< 20	3 (60%)	5 (20%)	0 (0%)	0 (0%)
21-30	1 (20%)	20 (80%)	35 (70%)	12 (60%)
>30	1 (20%)	0 (0%)	15 (30%)	8 (40%)

Table-III shows age distribution of patients. In group A, maximum number of patients (60%) belonged to age group <20 years and in group B, C and D the majority belonged to age group 21-30 years(80%,70% and 60%) respectively.

Table-IV: Relationship between maternal age and maternal BMI

Age	Group A n=5	Group B n=25	Group C n=50	GROUP D n=20
Mean +SD	20.87+3.76	23.50+3.70	26.12 +3.71	27.96+5.12
Range	18-31	19-30	21-35	21-40

Mean (+SD) age of the study patients were 20.87+3.76(Range 18-31), 23.50+3.70 (Range 19-30), 26.12+3.7 (Range 21-35), 27.96+5.12(Range 21-40) yrs respectively of group A,B,C and D. Age showed a positive relationship with BMI.

Table V: Relationship between maternal height and maternal BMI

Height	Group A	Group B	Group C	Group D
Mean +SD	145.25+4.50	152.50+5.20	153.90+6.50	150.55+6.20
Range	140-152	143-165	141-170	140-160

Mean(+SD) height of the study patients were 145.29+4.50 (Range 140-154cm),152.50+5.20(Range 143-165), 153.90+6.50(Range 141-170), 150.55+6.20 (Range 140-160) respectively of group A,B,C and D. Group B and C patients showed positive relationship with height.

Table VI: Relationship between maternal weight and maternal BMI

Weight	Group A	Group B	Group C	Group D
Mean±SD	39.50±3.50	55.24±4.93	65.83±4.99	71.80±7.50
Range	36-45	46-65	55-75	65-90

Mean(±SD) weight of the study patients were 39.50±3.50 (Range 36-45), 55.24±4.93 (Range 46-65), 65.83±4.99 (Range 55-75), 71.80±7.50 (Range 65-90) respectively of group A,B,C and D. Weight showed a positive relationship with BMI in all the groups.

Table VII: Maternal disease

Maternal disease	Group A	Group B	GROUP C	Group D
Anemia	2(40%)	2(8%)	0(0%)	0(0%)
PIH	0(0%)	3(12%)	5(10%)	3(15%)
GDM	0(0%)	2(8%)	5(10%)	7(35%)
Hypothyroidism	0(0%)	0(0%)	1(2%)	0(0%)
Hyperthyroidism	0(0%)	0(0%)	0(0%)	0(0%)
Asthma	0(0%)	0(0%)	0(0%)	0(0%)
Hepatitis B+ve	0(0%)	0(0%)	2(4%)	0(0%)
Chronic hypertension	0(0%)	0(0%)	0(0%)	0(0%)
None	3(60%)	18(72%)	37(74%)	10(50%)

Table-VII shows maternal diseases of the study patients. Most common diseases were anemia (40%) in group A, anemia(8%) and PIH in group B(12%), PIH(10%),GDM(10%) and hepatitis B positive (4%) in group C and GDM (35%), PIH (15%) in group D.

Table VIII: Mode of delivery

Mode of delivery	Group A n=5	Group B n=25	Group C n=50	Group D n=20
Vaginal	3(60%)	13 (52%)	20(40%)	4(20%)
C/S	2(40%)	12(48%)	30(60%)	16(80%)

C/S was the most common mode of delivery in group C and D, ie60%,80%respectively.

Table IX: Neonatal weight

Neonatal weight(kg)	Group A	Group B	Group C	Group D
<2.5	4(80%)	2(8%)	0(0%)	1(5%)
2.5-3.9	1(20%)	23(92%)	50(100%)	18(90%)
>4	0(0%)	0(0%)	0(0%)	1(5%)

$\chi^2 = 20, df=4, P < 0.001$

Table-IX shows distribution of neonatal weight in different BMI groups of patients. In group A patients, neonatal weight was <2.5 kg in 80% cases, while the birth weight was from 2.5-3.9 kg in majority of the babies of group B, in all the babies of group of C and 90% of the babies of group D.

Table X: Relationship between neonatal weight and maternal BMI

Neonatal weight(kg)	Group A	Group B	Group C	Group D
Mean±SD	2.4±0.29	2.8±0.32	3.00±0.33	3.1±0.46
Range	2-2.8	2.2-3.5	2.5-3.9	2.45-4.3

P values (One- way ANOVA)

Group A vs	<0.5	<0.5	<0.01
Group B vs		<0.5	<0.5
Group C vs			<0.05

Mean(±SD) neonatal weight of different groups of patients were 2.4±0.29 (Range 2-2.8), 2.8±0.32(Range 2.2-3.5), 3.00±0.33(Range 2.5-3.9) and 3.1±0.46(Range 2.45-4.3)kg, respectively, of group A,B,C and D. Neonatal weight showed a positive relationship with BMI of mothers in all groups.

Table XI: Effect of maternal BMI on neonatal weight

Parameters	N	r value	P value ^a
BMI <20 kg/m ² (group A) vs neonatal weight	5	+0.817	<0.05
BMI 20-24.9 kg/m ² (group B) vs neonatal weight	25	+0.002	<0.5
BMI 25.0-29.9 kg/m ² (group C) vs neonatal weight	50	+0.002	<0.5
BMI > 30 kg/m ² (group D) vs neonatal weight	20	-0.028	>0.5
Overall BMI (kg/m ²) vs neonatal weight	100	+0.117	<0.001

Table-XI shows that BMI of mothers has positive relationship with neonatal weight in all the groups, i.e. group A ($r=+0.81, P<0.05$), group B ($r=+0.002, P<0.5$), group C ($r=+0.002, P<0.5$) and group D ($r=-0.028$). Statistically the relationship was significant in group A ($n=5$), B ($n=25$) and C ($n=50$) ($P<0.5$), whereas non-significant in group D ($n=20$) ($P>0.5$) only. Overall ($n=100$), the relationship was positive ($r=+0.117$) and statistically significant ($P<0.001$). Here r value is determined by z test.

Discussion:

In modern obstetric practice, fetal wellbeing has been determined mainly by direct monitoring and testing, but it is important not to overlook the status of the mother when determining fetal wellbeing. Maternal health is obviously crucial to fetal development and must be continuously assessed during pregnancy⁴ Maternal BMI has a clear impact on pregnancy outcome. That is, low body mass index (BMI) is associated with LBW, IUGR, preterm birth, high BMI with increased fetal weight, possibly greater risks of neural tube defects, gestational diabetes, hypertensive diseases, risk of dystosia and shoulder dystosia with a consequent higher risk of cesarean deliveries and a higher incidence of anaesthetic and postoperative complications.⁵

In many studies pre-pregnancy BMI or BMI at early pregnancy was studied to see the effect on pregnancy outcome.^{6,7} This study aims at determining the influence of maternal body mass index at term pregnancy on fetal weight and improving obstetric management of conditions earlier mentioned.

In Nasiri Amiri Fatemeh's study, the incidence of macrocosmic baby was 6.8% in overweight and 4.5% in the underweight women, while the incidence of low birth weight (LBW) baby was 7.6% in overweight and 6.5% in the underweight women.⁸ In the present study, the incidence of macrocosmic baby was 5% in overweight and 0% in underweight women, while the incidence of LBW baby was 5% in overweight and 80% in underweight women (Table-IX). Like the findings of the above study, our obese mother did not give birth to macrocosmic baby. The cause behind this may be, obese women sometimes give birth to average size or LBW babies as nutrition goes towards mother.^{9,10}

Hughes K et al found that LBW babies increase with a lowering socioeconomic group,⁸ The incidence of LBW baby was 5.5% in higher class, 6.5% in upper middle class, 7.6% in lower middle class and 8.9% in poor socioeconomic class.^{11,12} In our study, the incidence of LBW baby was 5% in group D (majority belonged to upper middle and higher class), 0% in group C and 8% in group B (majority belonged to lower middle and upper middle class) and 80% in group A (majority belonged to poor and lower middle class) (Table- II, IX). During the observation of our study, it was found that LBW babies were more common in lower socioeconomic group.

Florence Galtier-Dereure's study showed that, maternal overweight was related to higher risk of caesarean deliveries.^{13,14} In the present study, caesarean deliveries were also more in group C and D, 60% and 80% respectively (Table-VIII).

A. Kirksey in Egypt found relation of BMI of mother in early pregnancy to birth weight. For that study, mothers were subdivided by BMI into quartiles <1 (BMI<22.6), 1-3 (BMI 22.6-27.4) and >3 (BMI>27.4). Mothers in the lowest quartile delivered infants of significantly lower birth weights (3154+386 gm) than mothers in the highest quartile with infants birth weight (3568+ 362 gm).^{15,16} In the present study, mothers in group-A delivered infants with birth weight (2.4±29 gm) (Table-X) which was very much lower than A, Kirksey's study. This may be due to the prevalence of underweight in women, which varies from 0.2% to 35% in different countries.⁸ The global estimates of mean birth weight and the prevalence of low birth weight (LBW), produced by World Health Organization in 1982, of the 127 million infants born in 1982, 20 million (16%) were estimated to weight less than 2.5 kg and over 90% of these infants were in developing countries.⁹ Bangladesh is one of the least developing countries of the world where disease, poverty, illiteracy and disasters are very common. Poor socioeconomic status has a lot of influence on pregnancy and pregnancy outcome due to poor nutritional status of mother. There were many low bodyweight women at term pregnancy and most of them gave birth to low birth weight baby.

In another study carried out by J. R. Backstrand in Mexico where maternal anthropometry were studied as a risk predictor for pregnancy outcome. Of the anthropometric measures, weight and BMI at third trimester showed the highest correlation coefficients 0.35 ($P < 0.005$) and 0.36 ($P < 0.001$) respectively with birth weight.^{17,18} In the present study, maternal weight showed significant relationship with birth weight in all group ($P < 0.001$) (Table-XI).

The main objective of the study was to determine the influence of maternal BMI on fetal weight, which had also positive relationship, i.e. group A ($r = +0.817$, $P > 0.05$), group B ($r = +0.002$, $P < 0.5$), group C ($r = +0.002$, $P < 0.5$) and group D ($r = -0.028$, $P > 0.5$). Statistically the relationship was significant in group A, B and C, whereas not significant in group D. Overall ($n=100$), the relationship was positive ($r = + 0.117$) and statistically significant ($P < 0.001$).

So, in this study we found that BMI of mother had positive relationship with fetal weight in all the groups, which was more significant in normal BMI group. We also found that age and weight of mother had also positive relationship with BMI.

Conclusion

BMI of mother at term pregnancy had positive relationship with neonatal weight that is with increasing BMI of mother neonatal weight was also increased. Overall the relationship was statistically significant. Age and weight of mother had positive relationship with BMI in all the groups, which was statically significant. Maximum number of low body weight and normal weight BMI group patient belonged to lower middle income group while of overweight and obese patients belonged to upper middle income group, which was statistically significant.

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