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Editorial

"Hypertension in the Children- Do we miss it?"

Bangladesh Institute of Child Health

Dhaka Shishu (Children) Hospital

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DHAKA SHISHU (CHILDREN) HOSPITAL JOURNAL

CONTENTS

VOLUME 30 **NUMBER 2** **DECEMBER 2014**

DS (Child) H J 2014; 30 (2) : 80-83

EDITORIAL

Hypertension in Children- Do we miss it?

Md. Jahangir Alam

Hypertension in children has increased significantly in recent times because of its increasing prevalence in recent years and also of its significant impact on the health and well-being of children and adolescents. Existing evidence suggests that hypertension in adult originates in childhood because childhood Blood Pressure (BP) predicts BP in the adult. Consequently, early identification and treatment of hypertension in childhood are likely to have important impact on long-term outcomes of hypertensive cardiovascular disease. Several studies have suggested that elevated BP in childhood correlates with atherosclerosis in adulthood and carotid-medial thickness (marker of hypertension end organ damage) of young adults.

The true incidence of hypertension in the pediatric population is not known in our country as well as developed countries. Prevalence of children with systemic hypertension appears to be increasing and is estimated to be 2 to 5%, especially with the growing population of children with obesity. The epidemic of overweight and obesity in youth is increasing the prevalence of hypertension among children and adolescents. In both developed and developing countries childhood obesity continues to increase and in association with hypertension, dyslipidemia and diabetes mellitus forms the 'metabolic syndrome.

The prevalence of overweight children in the United States in the 1990s was 11% which is more than double the prevalence of 5% in the 1960s. In a 2002 school based hypertension and obesity screening study, the prevalence of hypertension was 3 times greater in obese (33%) compared with non obese adolescents (11%). The prevalence of obesity itself is high as 23%. There has also been a shift in primary hypertension becoming more evident in late childhood and early adolescence which may be related to relatively recent epidemic of childhood obesity. While most childhood hypertension has been previously considered secondary to renal, cardiovascular or endocrine etiology, a substantial number of children aged 6 to 20 years are now diagnosed with primary or essential hypertension. Early detection and intervention in children with hypertension are potentially beneficial in preventing long-term complications of hypertension.

Identification of hypertensive children continues to be problematic because of incomplete blood pressure screening during routine pediatric clinical visits. In children, it is not possible to use a single BP level that is used in adults to define hypertension since the BP in children increases with increasing age and body size. The definition of elevated BP throughout childhood is based on the percentiles of BP specific to age, gender and height. According to the criteria of the Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure (BP) in Children and Adolescents, normal BP in children is defined as Systolic BP (SBP) and Diastolic BP (DBP) less than 90th percentile for age, sex and height, whereas hypertension is defined as SBP and/or DBP persistently 95th percentile or more, measured on at least three separate occasions with the auscultatory method. Children with average SBP or DBP 90th percentile or more but less than 95th percentile are classified as having high-normal BP. Adolescents with BP 120/80 mmHg or more even if less than 90th percentile are also considered as having high-normal BP.

Additionally, the Fourth Report provides criteria for staging the severity of hypertension in children and adolescents which can then be used clinically to guide evaluation and managements. Stage 1 hypertensionis defined as BPs from the 95th percentile to the 99th percentile plus 5 mmHg. Stage 2 hypertension denotes any BP above the 99th percentile plus 5 mmHg. Children or adolescents

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with stage 2 hypertension should be evaluated and treated more quickly and/or intensively than those with a lower degree of BP elevation. The term white-coat hypertension defines a clinical condition in which the patient has BP levels that are >95th percentile when measured in physician's office or clinic, whereas the patient's average BP is <90th percentile outside of a clinical setting. Ambulatory BP monitoring (ABPM) is usually required to make this diagnosis.

The preferred method for blood pressure measurement is auscultation and Use of an oscillometric device is preferred for BP measurement in newborns and young infants, in whom auscultation is difficult, and in the intensive care setting, in which frequent BP measurement is needed.

The screening for hypertension is very important. BP screening has taken place in only two-thirds of routine pediatric visits, one third of ambulatory pediatric visits and that 20% of overweight and obese children are not being screened at their routine visits. Younger children, who are more likely to have secondary hypertension, are commonly not being screened as often as older children. Even when blood pressures are measured, 75% cases of hypertension and 90% cases of pre-hypertension in children andadolescents remain uninvestigated.

Pediatric Hypertension is categorized into two major types, primary (essential) and secondary hypertension. The true cause of primary hypertension in children is not known and is generally considered

Multi-factorial, including family history, increasing BMI, sleep disorder, black race and metabolic syndrome. Most childhood hypertension, particularly in preadolescents, is secondary to an underlying disorder. Renal parenchymal disease is the most common (60 to 70 percent) cause of hypertension. Other causes include endocrine disease (e.g. pheochromocytoma, hyperthyroidism) and pharmaceuticals (e.g. oral contraceptives, sympathomimetics, some over the counter preparations, dietary supplements).

Identification and thorough evaluation of children with primary and secondary hypertension is a clinical challenge and is vital for successful treatment. In the initial evaluation of the hypertensive patient, a thorough search for an underlying cause of secondary hypertension must always be undertaken along with co-morbid risk factors such as obesity, diabetes and kidney disease. A detailed history and physical examination are essential for securing key information to unveil the type of hypertension and presence of a systemic disorder. With the appropriate information, unnecessary and often expensive laboratory and imaging studies can be avoided.

Primary hypertension is a diagnosis of exclusion after secondary causes are excluded. Therefore, severe hypertension in a younger child is more likely related to secondary hypertension and should undergo comprehensive evaluation searching for underlying causes. Once the cause of secondary hypertension is identified, it should be treated accordingly. The initial approach of primary hypertension for children and adolescents with mild hypertension and no hypertensive target-organ disease is to incorporate therapeutic lifestyle changes with a focus on diet modification and exercise. Emphasis on weight loss and increasing physical activity is of vital importance, especially with the growing childhood obesity epidemic. Pharmacologic therapy is indicated along with non pharmacologic therapy if significant improvement not achieved.

Blood pressure should be monitored every 2 to 4 weeks in the office setting until good control is achieved and thereafter, every 3 to 4 months. Home blood pressure measurement may improve compliance.[32] Gradual reduction of medications should be considered after an extended period of good BP control.

Finally hypertension in the Children is an emerging paediatric health problem. It is mostly due to increase prevalence of obesity along with other secondary causes. Proper screening, prompt identification, exclusion of secondary causes, non-pharmacological (diet and exercise) intervention followed by drug therapy and continued follow up are essential to control paediatric hypertension. Every paediatrician should properly address and give emphasize to this issue so that, we can not miss this emerging childhood burden in our country.

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DS (Child) H J 2014; 30 (2) : 84-87

SPECIAL ARTICLE

Spirulina-the Nature's Superfood

Mahbubur Rahman[1] Rabi Biswas[2], Farhana Ahmed[3], Manzoor Hussain[4]

Abstract

Spirulina has become popularly known as a superfood due to the great diversity and concentration of nutrients it contains. It is the most nutritious, concentrated whole food source found in nature. It boosts the immunity and increases resistance to various infections. The antioxidant and anti-inflammatory effects are well known. Other effect of Spirulina are varied, such as- protection of the liver and kidneys, prevention of anemia, benefits for diabetes and hypertension, cancer prevention etc. These potential health benefits of Spirulina make it nature's wonder food for human health.

Arthrospira platensis (Spirulina) Description

Arthrospira platensis (here after referred to as 'Spirulina') is a unicellular microalgae which grows in fresh water, in salt water**.**

It grows best in a highly alkaline environment of pH 10-12. Such conditions currently exist in certain lakes in Sub-Saharan Africa and formerly in Mexico and Central America. Spirulina has been used as a food source for centuries, and is still commonly consumed in Chad and surrounding countries in Africa.[1] Spirulina has served as the sole source of nutrition in some African communities in times of famine, during which entire native population have existed eating only Spirulina for over a month at a time.[2]

Current use

Spirulina is marketed throughout the world as a food supplement or as an active ingredient in functional foods and beverages. It has attained considerable acceptance for the health benefits it bestows on consumers in Europe, North America, parts of Asia and Oceania. Spirulina's concentrated nutrition makes it an ideal food supplement for people of all ages and lifestyles.[2] it gained prominence more recently after it was used as a dietary supplement for astronauts on space missions. NASA has stated that the nutritional value of 1000 kg of fruits and vegetables equals one kg of spirulina.[3]

Composition

Spirulina is about sixty percent complete, highly digestable protein; it contains all essential amino acids; Spirulina contains more beta-carotene than any other whole food; it is the best whole food source of gamma linolenic acid (GLA); it is rich in B vitamins, minerals, trace elements, chlorophyll, and enzymes; and it is rich in other nutrients, such as carotenoids, sulfolipids, glycolipids, phycocyanin, superoxide dismutase, RNA, and DNA. Table 1 shows the typical nutrient content of a commercially available Spriulina product.[2]

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Spirulina: Nutrient Value

Spirulina is one of the natural sources containing the highest amount of protein - five times that of meat.[2] Spirulina provides the majority of essential and nonessential amino acids. It contains the highest amount of beta-carotene, a precursor of vitamin A.[2] It is the only vegetable source of vitamin B12 having two and half times the amount in liver.[2] The constituents of spirulina include protein (50-70%) including all essential amino-acids, essential fatty acids, polysaccharides, B vitamins particularly vitamin B12, beta-carotene and minerals particularly iron.[4] Moreover, Spirulina supplies common nutrients at high levels; comparing Spirulina with other foods shows its unusual nutrient profile (**Table 1**).

Nutrient profile of Spirulina vs other foods

180% more calcium than whole milk, 670% more protein than tofu, 3100% more beta carotene than carrots, 5100% more iron than spinach, more antioxidant and anti-inflammatory activity in 3 g of Spiurlina than in five, servings of fruits and vegetables.[5]

Typical analysis per 100 grams for Spirulina pacific[1]

General: Total Calories 333 (Kcal), Calories from Fat 50 (Kcal), Total Fat 5 (g), Saturated Fat 2.2 (mg), Cholesterol 0 (mg), Total carbohydrates 16 (g), Dietary Fiber 7 (g), Sugar 0 (g), Protein 67 (g)

Vitamins: Vit A (as Beta carotene) 375000 (IU), Vitamin E 7 (IU), Vitamin K1 2000 (µg), Vitamin K2 500 (µg), Thiamin (B1) 117 (µg), Riboflavin (B_2) 4667 (µg), Niacin (B3) 13333 (µg), Vitamin B6 1000 (µg), Folate 200 (µg), Vitamin B_{12} 300 (µg), Biotin <33 (µg), Pantothenic acid 150 (µg)

Minerals: Calcium 333 (mg), Iron 217 (mg), Phosphorous 1100 (mg), Iodine 500 (µg), Magnesium 500 (mg), Zinc 3 (mg), Selenium 30 (µg), Copper 0.7 (mg), Manganese 13 (mg), Chromium 1333 (µg), Sodium 1000, (mg), Potassium 2000 (mg).

Carotenoids & Phytonutrients: Gamma Linolenic Acid (GLA) 1067 (mg), Zeaxantenoids 300 (mg), Total carotenoids 500 (mg), Chlorophyll 1000 (mg), C-Phycocyarin 8000 (mg), Superoxide dismutase 36000 units)

Effect spirulina on malnourished children

Spirulina has a positive impact on weight and other parameters like arm circumference, height, albumin, pre albumin, protein improved after spirulina supplementation.[6] Children with the malnutrition and deficiency of micro nutritients are in greater danger of infections.[7] To promote immunity and to improve the nutritional status it becomes imperative to give better nutrition and food supplement with greater calorific values. [7] Spirulina offers remarkable health benefits to an undernourished children. It is rich in beta-carotene that can overcome eye problems caused by vitamin A deficiency. The protein and B-vitamin complex make a major nutritional improvement in an infant's diet. It is the only food source other than breast milk containing substantial amounts of essential fatty acid, essential amino acids and GLA that helps to regulate the entire hormone system.[7] The United Nations World Health Organization (WHO) has confirmed that spirulina represents an interesting food for multiple reasons, rich in iron and protein, it can be safely administered to children without any risk.[8]

Health benefits of spirulina

Research on Spirulina's health benefits has been far-ranging. In addition to antioxidant and anti-inflammatory effects other potential health applications are:

Protection of the liver and kidneys, improvement of blood quality and prevention of anaemia, benefits for diabetes, reduction in Blood Pressure, removal of heavy metals from the body, radioprotection, prevention of liver and renal toxicity, antioxidant action, immune protection, relief in allergic reactions.[2]

Role of Spirulina in Immunity

Spirulina helps in building immunity and improving resistance to viral infections. Spirulina can enhance components of the mucosal and systemic immune system as it activates the cells of innate immune system. Several pre-clinical animal studies have shown good immunostimulatory effects in a variety of species. In humans, mammals, chicken and fish Spirulina produces an immune stimulating effect by enhancing the resistance to infections, the capacity of influencing haemopoieses and stimulating the production of antibodies and cytokines. Ingestion of spirulina contributes to the functional preservation of the intestinal epithelium which acts as a first line of mucosal barrier against infections.[2]

Anti-Viral Properties

Certainly, a food, a nutritional supplement or a drug that has documented anti-viral activity as well as an ability to positively affect the immune response would be of considerable clinical interest. Based on the existing research, Spirulina shows great potential in both of these related areas of disease resistance. Unique nutrients found within Spirulina once again play an important role in Spirulina's function as an antiviral. An interesting paper related to this antiviral research from Japan against HIV proposed that consumption of algae on a regular basis may inhibit the replication of HIV in consumers.[1] They cite the literature demonstrating HIV inhibition by algae *in vivo* and *in vitro*, and also epidemiological evidence that populations with high algae consumption have correspondingly low rates of HIV infection. It concludes that the regular consumption of Spirulina could help prevent HIV infection and decrease viral loading of those infected.[9] Additionally, a group of researchers in 2002 found a hot water extract of Spirulina to be effective against Herpes simplex virus types 1 and 2, pseudorabies virus and human cytomegalovirus.[10]

Cancer Preventive Potential

Although there is not a great deal of human clinical research, there are numerous studies showing Spirulina's potential to prevent carcinogenesis and to shrink tumors in animal models.[1] One such study from 2001 concluded, 'The polysaccharide of *Spirulina platensis* has chemo-protective and radio-protective capability, and may be a potential adjunct to cancer therapy.[11] Water extracts from Spirulina contain the water soluble pigment C-phycocyanin. There are several recent studies over the last few years that show cancer related benefits to both unrefined water extracts of Spirulina as well asisocated C-phycocyanin.[1]

Spirulina as Antioxidant

One of most important characteristics of Spirulina is its antioxidant property. Antioxidants are the substances which neutralize the free radicals generated due to oxidative stress.[2] Free radicals can damage the concerned cell & lead to the death of these cells.[2] Oxidative stress directly or indirectly leads to various disorders like diabetes, atherosclerosis, rheumatoid arthritis, recurrent aphthous stomatitis, cancer, etc. Spirulina a very good source of natural antioxidant along with high protein.[12] These antioxidants can become pro-oxidants and protect the body from oxidative stress.[12]

Antidiabetic Property of Spirulina

Diabetes mellitus, a metabolic disorder, is becoming a major health problem. Long time use of various drugs can lead to various side effects. Antidiabetic effect was also seen by supplementing spirulina 2 g/day doses for two months on blood glucose levels, glycosylated hemoglobin and lipid profile. The lowering of fasting and postprandial blood glucose levels and in the HbA1c level showed the antidiabetic property of spirulina.[13]

Spirulina in Hypertension & Hyperlipidemia

Spirulina has hepatoprotective properties by decreasing liver lipid profile and lipoperoxidation products.[14] Spirulina has a hypolipemic effect,especially on the concentrations of triacylglycerols and the cholesterol associated to low density lipoprotein and indirectly on total cholesterol and cholesterol associated to high density lipoprotein values. It was also shown that spirulina reduced systolic and diastolic blood pressure when given by oral route (4.5 g/day, for 6 weeks).[14]

Spirulina in Anaemia

Spirulina possibly enhances red cell production and function. Over a 12-week study period, there was a steady increase in average values of mean corpuscular haemoglobin with spirulina intake. Levels of anaemia also decreased in children when their diet was supplemented with spirulina.[15]

Radio-protective role of Spirulina

Spirulina has a protective role in Protection against Radiation and its Effects. Feeding children subjected to low level of radiation over a long period of time with 5 grams of Spirulina a day resulted in the reduction of Cesium-137 in urine by 50%.[16] Some of the beneficial aspects of Spirulina in radiation effects may be due to its ability to bind to heavy metals and radioisotopes.

Conclusion

Spirulina has emerged as the wonder food supplements. The highly diverse nutritive nature of spirulina together with its antioxidant and protective health benefits have been utilized in vagarious health related problems. The potential health benefits of spirulina must be adequately recognized and implemented thus making full use of this nature's gift.

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DS (Child) H J 2014; 30 (2) : 88-93

ORIGINAL ARTICLE

Blood Pressure Profile among school children of Dhaka city

Rabi Biswas[1], Md. Zakirul Islam[2], Md. Jahangir Alam[3], Md. Mahbubur Rahman[4], Manzoor Hussain[5], Parveen Ahmed[6]

Abstract

Background: *Data on hypertension among Bangladeshi children are very limited. Recently alarmingly raised prevalence of hypertension has been showed in many literatures from different countries.*

Objective: *This cross-sectional study was done to find out the prevalence of hypertension and prehypertension among school children aged 5-15years.*

Methodology: *A total of 880 apparently healthy students from a school of Dhaka city were examined during January 2012 to June 2012. School was selected purposively, where students from various socioeconomic status studied together. This study was done using a predesigned questionnaire and making measurements of height, weight, BMI and Blood pressure using standardized physical instruments following standard guidelines. The data was collected and analyzed using appropriate statistical tests.*

Results: *Hypertension and prehypertension was found in 1.5% and 3.8% respectively. Hypertension was documented more in the 12+ years and 13+ years age group. There was no statistically difference in mean SBP and mean DBP among boys and girls is observed in this study. Rates of elevated Blood Pressure were significantly higher in children with raised Body Mass Index and family history of hypertension.*

Conclusion: *In conclusion, as childhood hypertension is gradually increasing in our setting, need for checking blood pressure should be emphasized during examination of children and more study is imminent to find out the aetiology of this rising trend of Blood Pressure in our kids.*

Keywords*: Blood pressure, Hypertension, Prehypertension, Body mass index, Obesity*

Introduction

Hypertension is a major health problem in developed and developing countries. By 2015, it is estimated that almost 20 million people will die from CVDs, mainly from heart disease and stroke.[1] An increasing number of healthy children and adolescents across the world are being diagnosed with hypertension.[2] High blood pressure (BP) in childhood is a major risk factor for heart disease and stroke in adulthood.[3] There is enough evidence to suggest that essential hypertension in adult starts from childhood.[4]

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Systemic hypertension is an important condition in childhood, with estimated prevalence of 1-2% in the developed countries[5] and 5-10% in the developing countries like India.[6] Although overall prevalence of hypertension is low in children, studies suggest that it tends to develop during first two decades of life.[7] Primary HTN, once considered a rare occurrence in pediatric patients, is seen more often particularly in obese patients. Other factors responsible for increased prevalence of hypertension in children include life style changes such as decrease physical activity, increased intake of high calories, high sodium and low potassium foods, use of caffeinated and alcohol beverages, smoking, mental stress and sleep deprivation.[8] The American Heart Association recommends that all children aged 3 years and older should have yearly blood pressure measurements. The long-term health risks for hypertensive children and adolescents can be substantial; therefore, it is important that measures be taken to reduce these risks and optimize health outcomes. Early detection of high blood pressure will improve health care of children. The rising prevalence of overweight worldwide has led to an increased prevalence of essential hypertension among younger population.[5] The present study was aimed to detect the prevalence of hypertension and risk factors for hypertension among school students in Dhaka city.

Materials and Methods

This cross-sectional study was carried out in a school of Dhaka city from January 2012 to June 2012. School was selected purposively, where students from various socioeconomic status studied together. The target age for the study was 5-15 years.

Date, time and place of study were decided having prior consent of school authority. Both boys and girls of 5-15 years were listed. Then total 880 children were selected, 80 from each class (started from KG to class-X, total 11 classes) for the study according to roll number serially as of the class register. Equal number of boys and girls were enrolled. If one student was absent or not eligible for the study, then the next roll number was considered. Age was determined with the help of school records. Children with any disability were excluded from the study. Children were given a questionnaire to be filled up by their parents about the family history of hypertension and their complications, education, occupation and monthly income of their parents.

In order to make the students relaxed, the purpose and procedure of the study was explained to them. Then their heights were measured by height scale (Brand ZT-20 with precision of 0.2cm) and weights by bathroom scale (Digital machine, Brand TANITA-Japan with precision of 0.1Kg). BP was recorded one by one by mercury sphygmomanometer using the same machine throughout the study. Age appropriate cuff covering 2/3rd of the length of the arm and encircling its whole circumference was used.[9,10] Measurements were taken by the same qualified medical doctor.

While measuring BP the child was asked to sit comfortably. The cuff was wrapped around the right arm keeping the arm at the level of heart. The bladder of the cuff was inflated to about 200 mm Hg level, then it was deflated slowly at a rate of 1 mm per second. Systolic BP was measured at the level of first appearance of sound (Korotkoff phase 1) and Diastolic BP was measured at the level of muffling of sound (Korotkoff phase IV).[11] The children were considered hypertensive if the systolic or diastolic blood pressure or both were equal to or more than the 95th percentile for height for age and sex. Prehypertension was defined as systolic or diastolic blood pressure or both between 90th and 95th percentile for height for age and sex, or if the systolic blood pressure (SBP) was more than 120 mm of Hg or the diastolic blood pressure (DBP) was more than 80 mm of Hg.[12] Height for age standards was determined using the CDC 2000 growth charts.[13] Readings were taken for three times at an interval of at least one minute. All these three readings were recorded and their average was considered as the BP of that child at that time.

Children whose BP were found above 95th centile for age and sex were measured for the second time after four weeks. Those children having BP above 95th centile on two occasions were identified to have hypertension.[11,14] Data were entered into computer and analyzed using SPSS program.

Results

In our study we include 880 students of 5-15 years of age from a school of Dhaka city, among which equal number (440) was boys and 440 were girls. As shown in Table-I there was an increased trend in mean SBP and mean DBP with age. In boys, mean SBP was found to be increased from age 12+ years, whereas in girls both mean SBP and mean DBP increased

Table-I
Mean SBP and DBP in boys and girls according to age and increment in it

Age (in years)	Systolic BP				Diastolic BP			
	BOYS		GIRLS		BOYS		GIRLS	
	Mean	Increment	Mean	Increment	Mean	Increment	Mean	Increment
5+	83.60		84.47		53.44		52.89	
6+	87.88	4.28	87.52	3.05	55.62	2.18	55.52	2.63
7+	87.89	0.01	89.75	2.23	56.20	0.58	56.75	1.23
8+	91.31	3.44	90.36	0.61	59.00	2.80	60.73	3.98
9+	91.53	0.22	92.57	2.21	59.28	0.28	62.23	1.50
10+	97.44	5.91	95.78	3.21	61.56	2.28	62.18	-0.05
11+	98.50	1.06	103.00	7.22	64.32	2.76	67.05	4.87
12+	104.20	5.70	104.05	1.05	65.61	1.29	66.29	-0.76
13+	103.18	-0.42	103.77	-0.28	65.20	-0.41	65.44	-0.85
14+	103.55	0.37	107.45	3.68	65.73	0.53	66.29	0.85
15+	103.46	-0.09	109.91	2.46	65.24	-0.49	65.00	-0.29

with age from 11+ years. There was no statistically difference in mean SBP and mean DBP among boys and girls is observed in this study (p=0.764). As shown in Table-II there were 46 students having high BP, of which 13 were hypertensive and other 33 were pre-hypertensive. Among the boys 1.36% was hypertensive and 3.64% were pre-hypertensive. On the other hand, among the girls, 1.59% was hypertensive and 3.86% were pre-hypertensive. Overall, 1.48% had hypertension and an additional 3.75% had prehypertension.

Higher prevalence considering both hypertension and pre-hypertension was noted both in boys and girls at the age of 12+ and 13+ groups as compared to other age groups.

Among them five students had isolated high SBP and eight students had both high SBP and high DBP. None of them had isolated high DBP which also comparable to other study. During study there were seven students found hypertensive recorded on first visit but on follow-up visit they had normal BP, so they were not included in prevalence rate.

Table-II
Prevalence of high BP in boys and girls of different age group

Age	Boys			Girls		
	No of Student	Student having (HT)/ Pre-HT	Percentage of HT+Pre-HT	No of Student	Student having (HT)/Pre-HT	Percentage of HT+Pre-HT
5+	40	(0)/0	0%	40	(0)/1	2.5%
6+	40	(1)/0	2.5%	40	(0)/0	0%
7+	40	(1)/0	2.5%	40	(0)/0	0%
8+	40	(1)/0	2.5%	40	(0)/1	2.5%
9+	40	(0)/1	2.5%	40	(0)/2	5.0%
10+	40	(0)/2	5.0%	40	(1)/1	5.0%
11+	40	(1)/2	7.5%	40	(0)/3	7.5%
12+	40	(0)/4	10.0%	40	(1)/4	12.5%
13+	40	(1)/3	10.0%	40	(1)/3	10.0%
14+	40	(0)/2	5.0%	40	(2)/1	7.5%
15+	40	(1)/2	7.5%	40	(2)/1	7.5%
Total	440	(6)/16=22	(1.36%)/ 3.64%=5.0%	440	(7)/17=24	(1.59%)/ 3.86%=5.45%

This study checked the relationship of hypertension with obesity and/or family history of hypertension. Presence of any one of these was taken as positive predisposing factor. Table-III shows that out of 13 hypertensive cases, 10 had either obesity or family history of hypertension.

Table-IV shows the distribution of only hypertensive cases according to their hypertensive status and the presence of predisposing factors. In this study, 220 (23.3%) children had predisposing factors, either family history of hypertension or obesity. Of those 220 children, only 10(4.54%) were found to be hypertensive. In other 660(75.0%) children predisposing factors were absent, among them only 03 (0.45%) were found to be hypertensive. Chi-square test was done (Table-4) and the association between the children with hypertension and the presence of predisposing factors were found to be highly significant ($p<0.001$).

Table-III

Characteristics of hypertensive children (n=13) (Prehypertensive cases are not listed)

Case no	Age (yrs)	Sex	Wt (kg)	Ht (cm)	BMI	F/H of HTN	Syst. BP	Diast. BP	Predisposing factors*
1	6	male	23.5	114	18.08	-ve	132.7	86.9	absent
2	7	male	28.5	116	21.18	+ve	129.9	76.6	present
3	8	male	40.5	135	22.22	+ve	130.2	75.4	present
4	10	female	36.5	132	20.94	-ve	130.1	76.4	absent
5	11	male	80.5	150	35.77	-ve	136.7	88.4	present
6	12	female	58.0	153	24.77	+ve	137.2	76.8	present
7	13	female	75.0	148	34.24	+ve	146.3	85.9	present
8	13	male	75.0	150	33.33	+ve	145.3	78.9	present
9	14	female	78.0	155	32.46	+ve	142.1	91.7	present
10	14	female	80.0	156	32.87	+ve	140.1	92.8	present
11	15	male	83.0	157	33.67	-ve	146.0	94.2	present
12	15	female	82.5	155	34.33	-ve	143.9	95.2	present
13	15	female	62.0	156	25.47	-ve	141.0	101.2	absent

*Obesity or family history of hypertension or both

Table-IV

Relationship of hypertension with selected predisposing factors

		Hypertensive		Total
		Yes	No	
Predisposing	+ve	10	210	220
Factors	-ve	03	657	660
Total		13	867	880

Chi-square =16.26, p value< 0.00001, Odds ratio [95% CI] = 10.42 [2.84, 38.24]

Discussion

It is important to determine the prevalence of hypertension and prehypertension in children, not only because it varies from country to country or due to ethnicity, but also because it is essential to identify the population at risk. Early identification translates into early interventions and possibly prevention of later morbidity and mortality[12]. In the studied school children, overall 1.48% had hypertension and an additional 3.75% had prehypertension. This study showed higher prevalence of hypertension than a previous study[15] of Dhaka city during 1999 to 2000, which is indicative of an increasing tendency of hypertension in Bangladeshi school aged children. So a large study is warranted to know the real picture of the country.

Result of this study of hypertension correlates with other studies conducted in Maharashtra of India, where school going children of similar age group were enrolled.[16,17] Prevalence of hypertension among high school students of Turkey was shown 4.4%, which

was comparable to this study.[18] The rate of pre-hypertension in our study is closely related to a result of a study done in Ahmedabad,[19] although there was no child with true hypertension in that study. On the contrary, findings of present study are much lower than those reported in a survey among 11-17 years age group in Shimla of India, where in 5.9% of children had hypertension and 12.3% of children had prehypertension.[20] This variation may be due to considering a different age group between the studies.

In this study, higher prevalence of hypertension is noted both in boys and girls at the age of 12+ and 13+ groups, as found in other studies.[9] The reason why there was such high prevalence in adolescent age not known but it may be due to some life style modification or effect of sex hormones liberated at the time of pubertyand even may be due to increase in body mass.

In this study, on first evaluation, total 112 (12.7%) of the students had raised blood pressure, but on repeat measurement only 46(5.23%) were found with either hypertension or prehypertension. In the Muscatine study enrolling 6,622 students, 13% of school children had hypertension when first examined, but on repeated measurements less than 1% had their blood pressure in the hypertensive range.[21] Similar has been the observations of other researchers.[22,23] A more precise clinical estimate would include blood pressure measurements on e"3 separate occasions. However, multiple readings of blood pressure from the same day are considered appropriate for epidemiological studies.[5] There was no statistically difference in mean SBP and mean DBP among boys and girls which also observed in other studies.[9,24] The association between elevated blood pressure with positive family history and high BMI observed by us has been also noted by previous studies conducted in our country[15,25,26] and also from various workers including few from this part of the world.[9,27] Sorof, *et al.*also showed more prevalence of hypertension in obese children as compared to non-obese (33% *vs* 11%).[23] In a study in Turkey, blood pressure correlated positively with BMI significantly.[18]

Conclusion & Recommendation

Prevalence of hypertension including prehypertension in apparently healthy school going children of Dhaka city was found to be higher than previous study from the same area and this had a strong relationship with obesity and family history of hypertension. So, BP should be measured routinely for all children during physical examination. Further study involving larger number of children should be undertaken to find out the real prevalence, predisposing factors and aetiology of hypertension in children in our country.

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ORIGINAL ARTICLE

Correlation of cardiac impairment with the severity of hypoxic ischemic encephalopathy and its immediate outcome

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Abstract

Background: *Cardiac impairment is the major cause of mortality and morbidity of asphyxiated neonate. Cardiac impairment increases with the severity of hypoxic ischemic encephalopathy and there is a correlation between cardiac impairment of asphyxiated neonate with its immediate outcome such as mortality and hospital stay.*

Objective: *To find out the cardiac impairment in perinatal asphyxia by clinical features, measuring S.troponin-I and echocardiography in order to predict its association with severity of hypoxic ischemic encephalopathy and immediate outcome.*

Methods: *This cross sectional study was conducted in neonatology ward of Dhaka shishu hospital (DSH) during the periods of January 2012-December 2012. Total 60 neonates without congenital heart diseases, age 0-3 days, gestational age 35-42 weeks with perinatal asphyxia were selected as cases according to inclusion and exclusion criteria. Severity of HIE was categorized as group-I (HIE-I), group-II (HIE-II) and group-III (HIE-III) by sarnat and sarnat staging without EEG. Cardiac impairment was evaluated by clinical features, raised S.troponin-I and echocardiography. All cases were monitored during hospital stay. Mortality and hospital stay of cases were recorded. Then statistical analysis were done by χ^2 test, Odd ratio and Pearson's correlation co-efficient.*

Results: *Among the 60 cases, 32(53%) cases had evidence of cardiac impairment. Raised S.troponin-I was present in 32 (53%) asphyxiated newborns. Pulmonary hypertension, tricuspid regurgitation, ventricular dysfunction, LA/LV dilatation and RV/RA dilatation were present subsequently in 31(53%), 27(45%), 20(33%), 8(13.6%) and 16(26.6%) cases. One (7.7%) out of 13 in group-I, 20(43%) out of 35 in group-II and 11(91%) out of 12 in group-III had cardiac impairment and incidence of cardiac impairment increased with severity of HIE. The incidence of mortality was 31.6% and twenty eight (47%) cases had prolonged hospital stay (>10 days). Cardiac impairment was a risk factor for mortality (OR=34.7, p=0.0001) and prolonged hospital stay (OR=7.37, p =0 .04) of asphyxiated neonates and it was correlated with the mortality (r = 0.539) and prolonged hospital stay (r = 0 .434).*

Conclusion: *The incidence of cardiac impairment increases with severity of hypoxic ischemic encephalopathy of perinatal asphyxia. Cardiac impairment is a risk factor for the mortality and prolonged hospital stay of asphyxiated neonates and there is a correlation between cardiac impairment in perinatal asphyxia with the mortality and hospital stay.*

Key words: *Perinatal asphyxia, Hypoxic ischemic encephalopathy, Cardiac impairment, Echocardiography*

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Introduction

Perinatal asphyxia defined as failure to initiate and sustain breathing at birth.[1] Perinatal asphyxia is an insult to fetus or newborn due to a lack of oxygen (hypoxia) and /or a lack of perfusion (ischemia) to various organs which will manifest as difficulty in establishing spontaneous respiration evident by a delayed cry after birth.[2] The diagnosis of perinatal asphyxia may be based on the presence of fetal acidosis(pH<7.0), a 5 minutes apgar score of <5,hypoxic-ischemic encephalopathy and signs of hypoxic-ischemic injury to multiple organs.[3] Perinatal asphyxia occurs in 1% to 1.5% of live births in developed countries.[2] In developing countries, the incidence of perinatal asphyxia is greater; ranging 4.6-26 / 1000 live birth.[1] Case fatality in industrialized country is less than 0.1% whereas in developing country it is more than 40%.[4,5] The severity of perinatal asphyxia was divided according to their apgar score that are mild, moderate and severe. According to the sarnat & sarnat stages of Hypoxic-ischemic encephalopathy, brain dysfunction was divided as stage-I, stage-II and stage-III.[6,7] Immediate morbidity and mortality of perinatal asphyxia is due to multiorgan dysfunction especially cardiac impairment. The incidence of myocardial impairment in perinatal asphyxia is ranging from 29 to 62%.[8-13] The various clinical features related to cardiac impairment were respiratory distress, congestive cardiac failure, cardiogenic shock and systolic murmur (tricuspid regurgitation and mitral regurgitation).[2,14] Cardiac enzyme levels are changed in myocardial impairment of asphyxiated neonates. The enzymes are CK-MB (activity), CK-MB (mass), cardiac troponin I & troponin T etc. Among them cardiac troponin T & I is more sensitive and specific than CK-MB (activity), CK-MB (mass).[8,9,15-17] Echocardiographic changes found 56.7% cases. On echocardiography, the findings are pulmonary hypertension, RV-hypokinesia LV hypokinesia, mitral regurgitation, tricuspid regurgitation and RV/LV dilatation.[18]

Several studies showed that there is an association between cardiac impairment and severity of HIE of asphyxiated neonates. This study is aimed to observe the cardiac impairment in asphyxiated neonates and allows the targeting and implementation of management strategy for reducing morbidity and mortality in asphyxiated newborn.

Materials & Methods

This cross sectional study was conducted in neonatology ward of Dhaka shishu hospital during the periods of January 2012 - December 2012. All admitted newborns with history of failure to breathe spontaneously immediately after birth or history of delayed crying or not crying at all after birth and/or requirement of resuscitation to sustain life after birth, perinatal asphyxia evidenced by documented APGAR score (at 5 minutes <5) were taken as perinatal asphyxia. Neonates with congenital anomaly, congenital heart disease, septicaemia, meconium aspiration syndrome and congenital infection were excluded from study.

Total 60 neonates without congenital heart diseases, age 0-3days, gestational age 35-42 weeks with perinatal asphyxia were selected as cases according to inclusion and exclusion criteria. Severity of hypoxic ischemic encephalopathy (HIE) was categorized as group-I(HIE-I), group-II(HIE-II) and group-III(HIE-III) by sarnat and sarnat staging without EEG. Cardiac impairment was evaluated by clinical features, raised S.troponin-I and echocardiography. For measurement of troponin – I, 2 ml of venous blood was taken from antecubital vein aseptically by a disposable syringe. The blood was transferred to dry test tube with a gentle push to avoid haemolysis. The sample was sent to the biochemical laboratory and separate the serum and store serum at -20^0 c in refrigerator then samples was analyzed by Siemens biochemistry auto analyzer supervised by senior biochemist in biochemistry department in DSH. Two D-M mode-color Doppler echocardiography was done by qualified paediatric cardiologist in DSH. Within 12-72 hours of age of neonate, echocardiography was done and all biochemical investigations including S.troponin-

I was sent. S.troponin - I ≥0.183µg/l was taken as significant.[19] Criteria of cardiac impairment was taken by clinical feature - tachycardia/bradycardia and CRT>3Sec/ hypotension/systolic murmur, with or without S.troponin-I >0.183µg/l, with or without echocardiographic finding (pulmonary hypertension, RV-hypokinesia LV hypokinesia, tricuspid regurgitation, mitral regurgitation and RV/LV dilatation).[8,12,18] All cases were monitored during hospital stay. Mortality and hospital stay of cases were recorded. Then statistical analysis were done by χ^2 test, odd ratio and pearson's correlation co-efficient.

Results

Among all cases 44 (74%) babies were full term and 16(26%) were preterm. Thirty six (60%) babies were male and 24(40%) cases were female.

Mean gestational age was 37.2±1.29 weeks, mean birth weight was 2818.33gm±450.42gms and mean age at the time of hospital admission was 29.57±20.37 hours. Thirteen (21.7%) newborns were in group – I (HIE stage-1), 35(58.3%) in Group-II (HIE stage-II) and rest 12(20%) in group-III (HIE stage-III).

Among the 60 cases, 32(53%) cases had evidence of cardiac impairment. Tachycardia, bradycardia, hypotension and prolong CRT (>3 sec) were present consequently in 30(50%), 6(10%), 30(50%) and 32(53%) cases.

Mean S.troponin-I was 0.1538±0.1309µgm/L and raised S.troponin-I was present in 32 (53.3%) newborns. Raised S.troponin-I was consequently present in 2(3.3%) cases in group-I, 20(33.3%) cases in group-II, 10(16.6%) cases in group-III of HIE of perinatal asphyxia.

Pulmonary hypertension, tricuspid regurgitation, ventricular dysfunction, LA/LV dilatation and RV/RA dilatation were present subsequently in 31(53%), 27(45%), 20(33%), 8(13.6%) and 16(26.6%) cases.

The incidence of cardiac impairment was 53%.One (7.7%) out of 13 in group-I, 20(43%) out of 35 in group-II and 11(91%) out of 12 in group-III had cardiac impairment. That indicate incidence of cardiac impairment increased with severity of HIE (P value-0.0001).

The incidence of mortality of asphyxiated neonates was 31.6% (19). Out of 32 cases who had cardiac impairment, 18(56%) cases died.

Twenty eight (47%) cases had prolonged hospital stay (>10 days). Cardiac impairment was a risk factor for mortality (OR=34.7, p=0001) and prolonged hospital stay (OR=7.37, p=0.04) of asphyxiated neonates and it was correlated with the mortality (r = 0.539) and prolonged hospital stay (r = 0.434).

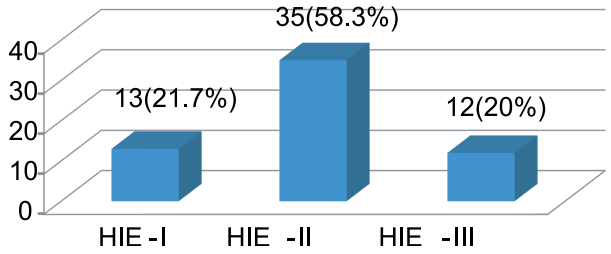

Fig 1 *Distribution of newborns according to severity of encephalopathy (n=60)*

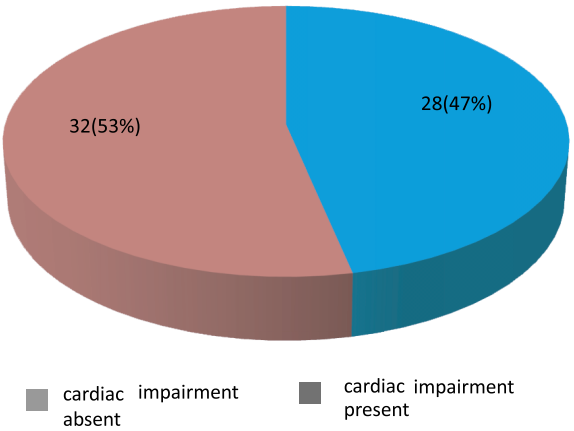

Fig 2 *Distribution of cardiac impairment among the cases (n=60)*

Table I
Clinical features of cardiac impairment in the cases

Clinical features	Number (n)	Percentage (%)
Tachypnea	33	55%
Tachycardia	30	50%
Bradycardia	6	10%
Hypotension	30	50%
Prolong CRT	32	53%
Murmur	9	15%

(Multiple response)

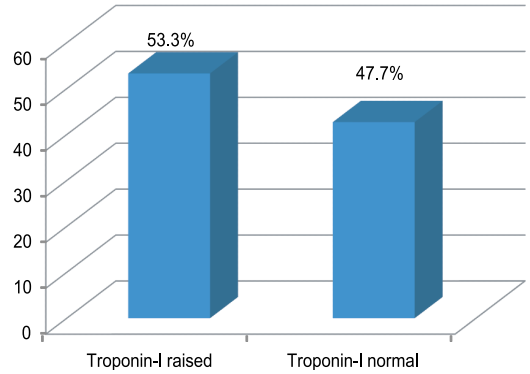

Fig 3 *Troponin-I in perinatal asphyxia*

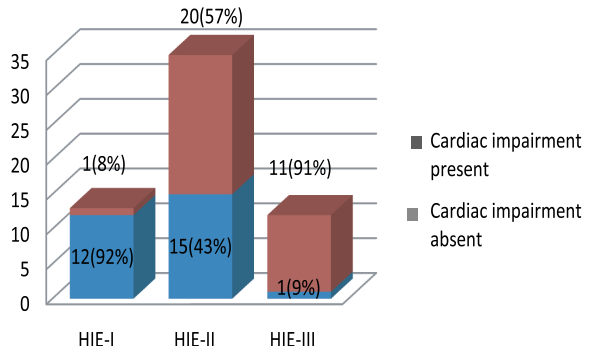

Fig 4 *Distribution of cardiac impairment according to severity of HIE of perinatal asphyxia*

Table II
Distribution of cases according to echocardiography changes

Echocardiography Changes	Number	Percentage
Pulmonary hypertension	16	26.6%
Tricuspid regurgitation(TR)	27	45%
Ventricular dysfunction	19	31.7%
RV/RA dilatation	18	30%
LA/LV dilatation	5	8.3%

Table III
Association between cardiac impairment with different group of encephalopathy of perinatal asphyxia

Organs		Group-I	Group-II	Group-III	Chi Value	P value
Cardiac impairment	Present	1	20	11	18.17	0.0001
	Absent	12	15	1		

Table IV
Risk measurement between cardiac impairment with the mortality.

Factors	Death	No Death	OR (95% CI)	P value
Cardiac impairment	18	14	34.71(4.19-287.65)	0.00001
No cardiac impairment	1	27		

Table V
Risk measurement between cardiac impairment with the prolonged hospital stay

Factors	Duration of Hospital stay(>10 days)	Duration of Hospital stay (≤10 days)	OR (95% CI)	P value
Cardiac impairment	15	17	7.35 (1.85-29.35)	.004
No cardiac impairment	3	25		

Discussion

Perinatal asphyxia is an important cause of neonatal mortality and morbidity in many countries including Bangladesh. Immediate morbidity and mortality of perinatal asphyxia is due to multiorgan dysfunction especially cardiac impairment. Among all cases 44(74%) babies were full term and 16(26%) were preterm. Thirty six (60%) babies were male and 24(40%) were female. Mean gestational age of newborns was 37.2±1.29 weeks, mean birth weight of newborns was 2818.33gm±450.42gms and mean age at the time of hospital admission was 29.57±20.37 hours. Neonates were observed for clinical signs which could be attributed to cardiac impairment on admission and during the period of hospital stay. Thirty three (55%) newborns had tachypnea. Tachycardia was present in 30(50%) and bradycardia was present in 6(10%) cases. Hypotension was present in 30 (50%), murmur in 9(15%) and prolong CRT in 32(53%) cases.

Baki et al and Gonzalez et al also found in their study newborns affected by asphyxia presented with hypotension and arrhythmia.[9,17] Total echocardiography findings were present in 32(53%) cases. Pulmonary hypertension was present in 31(53%) cases. Then TR was found in 27 (45%) cases. Ventricular dysfunction was present in 20(33%) cases. LA/LV dilatation and RV/RA dilatation were present subsequently in 8(13.6%) and 16(26.6%) cases . PS Rajakumar et al showed cardiac impairment in neonates with perinatal asphyxia.[18] They found TR (23.3% cases), Right ventricular hypokinesia (20% cases),left ventricular hypokinesia (13% cases), RA/RV dilation (40% cases) and pulmonary hypertension (10.3% cases) on echocardiography. Cardiac troponin-I is more sensitive and specific cardiac marker than troponin-T, CK-MB. After myocardial damage, S.troponin-I level raises within 4-6 hours, reaches peak between 12-24 hours and remains elevated for 6-8 days.[16,20,21] S. troponin-I was measured. Mean troponin-I was 0.1538±0.1309µgm/L and raised S. troponin-I was present in 32 (53.3%) newborns. Raised S.troponin-I was consequently present in 2(3.3%) cases in group-I, 20(33.3%) cases in group-II, 10 (16.6%) cases in group-III of HIE of perinatal asphyxia. Anhui et al and Kanik et al also found significant raised S. troponin-I in perinatal asphyxia in their study.[17,22] Comparison between severity of encephalopathy of perinatal asphyxia and the cardiac impairment was done. It was significantly associated with severity of encephalopathy of perinatal asphyxia PS Rajakumar et al also showed similar result in their study.[14]

Regarding risk measurement between cardiac impairment with mortality of perinatal asphyxia was compared. It was found that cardiac impairment was a risk factor (OR >1, p<.05) for mortality of asphyxia. There was correlation (r = 0.539) between cardiac impairment and mortality of cases.

PS Rajakumar et al showed that cardiac impairment was a significant factor for mortality in perinatal asphyxia.[14]Regarding risk measurement between cardiac impairment with prolonged hospital stay (>10 days) of perinatal asphyxia was compared. It was found that there was association between cardiac impairment and prolonged hospital stay and it was risk factor (OR >1, p<.05) for prolonged hospital stay. There was a correlation (r =0.434) between cardiac impairment and prolonged hospital stay. Though Baki et al showed that there was no association between cardiac impairment with the prolonged hospital stay.[9] Briefly the incidence of cardiac impairment is more (53%) in this present study as that reported previously by others ranging from 29-62%.[9,-13] This was also reflected by the high mortality rate (31.6%).The higher incidence of cardiac impairment and mortality of cases may be explained by the selection of more asphyxiated babies in the study group. The more the stages of HIE of perinatal asphyxia, the more the cardiac impairment is. The cardiac impairment is a risk factor for immediate mortality and prolonged hospital stay of asphyxiated babies and there is a correlation between cardiac impairment of asphyxiated babies with mortality and prolonged hospital stay.

Conclusion

In this study it is revealed that the intensity of cardiac impairment depends on the severity of hypoxic ischemic encephalopathy which is directly related to immediate out come as duration of hospital stay and mortality, so, more attention to be paid on the management of cardiac impairment in a asphyxiated newborn.

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ORIGINAL ARTICLE

Clinical practice of management of serous pleural effusion in children in different hospital of Dhaka city

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Abstract

Background: *Bangladesh is a densely populated developing country where children constitute the major bulk of the population. Pleural effusion in children is a problem commonly encountered by the pediatricians in our country.*

Objective:*This study was carried out to evaluate the aetiology and clinical practice of management of pleural effusion in children in hospitals of Dhaka city.*

Methods: *This prospective study included 25 children between 2 months to 15 years of age admitted during April 2006 to December 2006 in different hospital of Dhaka city. Dhaka Shishu Hospital, paediatric department of Bangabhandhu Sheikh Mujib Medical University, Dhaka Medical College Hospital, Shaheed Suhrawardy Medical College children who were newely diagnosed as serous pleural effusion and did not receive treatment previously were selected as cases chest x-ray and pleural fluid aspiration was done in all cases.*

Results:*In this study among 25 cases, 20 cases (80%) were between 5 to 15 years and 5(20%) cases were less than 5 years of age. Fifteen cases (60%) were male and 10 case (40%) were female. Fever (92%), cough (84%) respiratory distress (80.0%), chest pain (64%), poor feeding (60%) were the main presenting complaints. Pulmonary tuberculsois (9/25;36%), pneumonia (8/25;32%), nephrotic syndrome (3/25;12%) and dengue fever (3/25;12%) were the commonest cause of pleural effusion. Pleural fluid analysis showed exudative fluid in 16 cases (84.21%), transudative fluid in 2 cases (15.79%). Pneumococcus was isolated in 3 (125) cases, M. tuberculosis was isolated in one (4%) case. Therapeutic aspiration of pleural fluid was done once in 19 cases and chest tube drainage was kept in situ in 2 cases. Nine cases (36%) received anti-TB chemotherapy,8 cases (32%) of parapneumonic effusion with parenteral antibiotics. Among the study case 22 case (92%) were improved 1 case was referred and 1 case was expired.*

Conclusion:*Pulmonary tuberculosis was the most common cause of pleural effusion followed by pneumonia, nephrotic syndrome and dengue fever. Most of the patients presented with fever of varying degree, cough, respiratory distress, chest pain, irrespective of the cause of pleural effusion. Majority improved after treatment.*

Key words*: Serous, Pleural effusion*

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Introduction

Pleural effusion, this term is used when at least 10-20 ml of fluid accumulate in the pleural space. The effusion may be serous,purulent (empyma) or hemorrhagic (Haemothorax). The passive tansudation of fluid into the pleural cavity occurs in cardiac failure and in conditions causing Hypoprotenemiaeg. Nephrotic syndrome, hepatic failure, malnutrition and connective tissue disorder.[1] Pleural effusion is not uncommon in children. Most of the childhood pleural effusion are seen above 5 years of age.[2] In most developing countries including Bangladesh diagnosis of pleural effusion is delayed and management is usually not optimum. Para pneumonic effusion and empyema thoracic remains a significant cause of morbidity in children though overall incidence of empyema thoracic has decreased over the past two decades.[3] Pleural effusion is the most common manifestation of pleural disorder. It may be unilateral or bilateral. Bilateral pleural effusion often occur in cardiac failure but are also seen in patients with connective tissue disorder and hypoprotenemia. Pleural effusion can be divided into, nonmalignant, malignant and paramalignant effusion.[4] In children pleural effusion is usually secondary to an underlying disorder in the lung. In developing countries pleural effusion most frequently results as a complication of bacterial pneumonia.[5] Pleural infection was first described by Hippocrates in 500BC. Open thoracic drainage was the only treatment for this disorder until 19th century when closed tube drainage was first described but not adopted.[6,7] This technique became widely practised during an influenza epidemic in 1917-19 when open pneumothroax drainage was associated with a mortality rate up to 70%. This high mortality was probably due to respiratory failure produced by large open pneumothorax left by open drainage[8].A military commission investigated this high mortality rate and produced recommendations that remain the basis for treatment today. They advocated adequate pus drainage with a closed chest tube, avoidance of bearly open drainage, obliteration of pleural space and proper nutritional support.[8]

A high index of suspicion is required to avoid delay in the diagnosis that may influence treatment and outcome of pleural effusion. The likely causes of the majority of pleural effusion can usually be identified if careful history is taken and comprehensive clinical examination is performed, chest radiograph, thoracocentesis and pleural fluid analysis are also needed to establish the diagnosis, examination of pleural fluid is useful in establishing the etiology and distinguishing whether the effusion is exudative or transudative which will detecte the management policy of the case.[9]

Inspite of extensive investigations, significant proportion (approximately 20%) of effusion defy a diagnostic label. Ultrasound and CT scan of chest have further enhanced the diagnostic yield of un diagnosed pleural effusion. The re-emergence orthoracoscopy as the latest diagnostic and therapeutic (eg.pleurodesis) tool for undiagnosed or recurrent pleural effusion, may help in narrowing the diagnostic dilemma faced clinicians.[10]

The aim of therapy of pleural effusion is not issure rapid covery with normal lung function. The optimal management of parapnumonic effusion and empyema is children remain controversial and currently there is insufficient evidence to give clear guidance on the therapy. Management strategies include a comprehensive approach with antibiotic therapy, the use of chest drains, intrapleural fibrinolytic therapy and more aggressive surgical intervention with thoracotomy and decortication,[11] and should also address the underlying disease although with large pleural effusion draining the fluid make the patient more comfortable. When diagnostic thoracocentesis is performed as much as fluid as possible up to 1 liter should be removed for therapeutic purpose. If the underlying disease is adequately treated further drainage is usually unnecessary but if sufficient fluid reaccumulate to case respiratory embarrassment repeated thoracocentesis or chest tube drainage should be performed. In older children with para pneumonic effusion tube thoracostomy is considered necessary if the pleural fluid P^H is less than 7.20 or the fluid glucose level is less then 50mg/dL.[12] They are more common in winter and spring presumably due to their infective origin. Non bacterial infectious agents such as virus &myocoplasmapnemonic cases more pleural effusion in chiuldren, then do bacterial organism throughout the world. As many as 20% of these infection can cause small and transient effusion that resolve spontenously.[8] Pleural effusion occur

in 6-12% of case pulmonorary tuberculosis in children. More recently out of 175 children with pulmonary tuberculosis from Spain 39 patient (22%) had pleural effusion.[13] Congenital effusion occur in 6-12 of case pulmonorary tuberculosis in children. Congenital effusion concluding chylothorax occur in 1 per 10,000-15,000 live births annually. In recent review of 74 patients with intrhoracic lymphomas.Chaginaud found pleural effusion in 71 (10 out of 14) of children with lymphoblastic lymphoma and in 11.7% (7 out of 60) of children with Non-Hodgkins lymphoma.[14] This study was carried out to evaluate the aetiology and current practice of management of Pleural effusion in children in hospitals of Dhaka city.

Materials and methods

It was an observational study conducted from April 2006 to December 2006 in different hospitals of Dhaka city such as Dhaka Shishu Hospital, paediatric department of Bangobhandhu Sheikh Mujib Medical University, Dhaka Medical College Hospital, National Institute of Chest disease & Hospital and Institute of Child & Mother Health. This observational study included twenty five children between 2 months to 15 years of age previously untreated cases of pleural effusion confirmed by chest radiograph and aspiration of pleural fluid. Cases having empyema thoracic, associated lung abscess, bronchiectasis, previously treated cases of pleural effusion, having developmental anomaly of the lungs and thoracic cage and any other chronic illness were excluded.Twenty five children with serous pleural effusion (2 months to 15 years) were included in the study from those admitted in the paediatric department of different hospital as Bangabhandhu Sheikh Mujib Medical University.Dhaka Medical College Hospital, Institute of Chest Disease & Hospital, Institute of Child & Mother Health and Dhaka Shishu Hospital. Cases were recorded in a pretested questionnaire by the investigator, written consent was taken from guardian of the patients. The informations included detail history of the cases, physical findings, pleural fluid aspiration, and laboratory investigation such as CBC with film with, ESR, blood culture, X-ray chest, MT and pleural fluid aspiration and analysis. Among the cases which were admitted in Dhaka Shishu Hospital, pleural fluid aspiration was done by the medical officer of the respective units of the respective hospitals. Reports were collected by the investigator. Data was recorded in a questionnaire and analyzed by using SPSS statistical soft ware.

Results

The study included 25 children between the age of 2 months to 15 years of age admitted in paediatric units of Bangabhandhu Sheikh Mujib Medical University. Dhaka Medical College Hospital.National Institute of Chest disease & Hospital, Institute of Child & Mother Health and Dhaka Shishu Hospital.

Table I
Age distribution of study case

Age (months)	Number (n=25)	Percentage (%)
2 month to 5 yrs	5	20
6 yrs to 10 yrs	9	36
10 yrs to 15 yrs	11	44
Total	25	100

Out of 25 study cases 5 (20.0%) were within the age group of 2 months to 5 years, 9 cases (36.0%) between 5 to 10 years and rest 11 cases (44.0%) between 10 to 15 years of age (Table 1). among the study children 15 cases (60.0%) were boys and 10 cases (40.0%) were girls. (Fig 1).

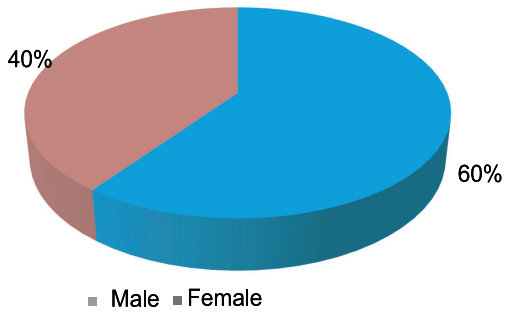

Fig 1 *Sex distribution of the study children*

As etiology of pleural effusion 9 cases (36.0%) were diagnosed as pulmonary tuberculosis, 8 cases (32,0%) as pneumonia, 3 cases (12.0%) as nephrotic syndrome, 3 cases (12.0%) as Dengue fever and 1 case (4.0%) as lymphoma and 1 case (8.0%) as neuroblastoma. (Table II).

Table II
Etiology of Pleural effusion

Disease	Number (n=25)	Percentage (%)
Pulmonary tuberculosis	09	36
Pneumonia	08	32
Nephrotic Syndrome	03	12
Dengue fever	03	12
Lymphoma	1	04
Neuroblastoma	1	04
Total	25	100

Majority of the cases presented with the history of fever (92.0%), cough (84.0%) respiratory distress (80.0%) chest pain (64.0%) and poor feeding (60.0%) (Table-III).

Table III
Clinical presentation of the study children

Presenting features	Number (n=25)	Percentage (%)
Fever	23	92
Cough	21	84
Respiratory distress	20	80
Chest pain	16	64
Poor feeding	15	60
Total	25	100

All the study children had physical signs of diminished chest movement subcostal recession, dull on percussion, diminished vesicular breath sound and 11 cases (44%) had shifting of mediastinum towards opposite side (Table-IV).

Table IV
Physical signs of study children

Physical signs	Number	Percentage
Diminished chest movement	25	100
Subcostal recussion	20	80
Dull on percussion	25	100
Diminished breath sound	25	100
Shifting of mediastinum	11	55

Among the study cases 16 (84.21%) had exudative pleural effusion and 3 (15.79%) had transudative (Figure-2).

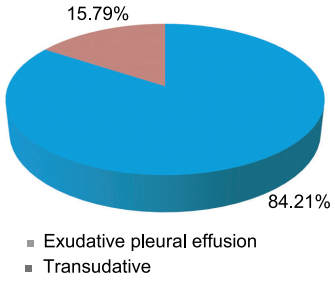

Fig 2 *Nature of pleural fluid based on protein content (n=19)*

S. Pneumonie was isolated by gram staining from pleural fluid in only 3 (12.0%) cases, only in 1 (4.0%) case AFB was found on Zeihi-Nelson staining. Malignant cells were identified in 2 (8.0%) cases of pleural effusion (Table V).

Table V
Results of cytology, gram-staining culture of pleural fluid

Staining/culture	Number (n=25)	Percentage (%)
Gram staining	3	6
ZN staining (AFB)	1	2
Staining for malignant cell	2	4
No isolation	19	38
Culture (streptococcus pneumonae)	3	6

Pleural fluid aspiration was done in 19 cases and among them 2 cases needed pleural fluid aspiration along with chest tube drainage (Table VI).

Table VI
Therapeutic intervention by aspiration of pleural fluid (n=25)

Management	Number
Pleural fluid aspiration once only	19
Chest tube drainage kept in situ	02
Not done	6

Table VII
Use of drug of the study children

Causes of effusion	Drug used	Number	Percentage (%)
Para pneumonic effusion	Ceftriaxione	03	12
	Ceftriaxione +Flucoxacillin	04	16
	Penicillin +Flucloxacillin	01	04
	Total	08	32
Tubercular effusion	Antitubercular drugs	09	36
Malignant	Chemotherapy	02	08
Nephrotic Syndrome	C. Penicillin + Prednisolone	03	12

Different drugs were given to different patients according to the causes of pleural effusion. Among the 8 (32.0%) cases of para pneumonic effusion. 3 cases (12.0%) were treated with ceftriaxone, 4 cases (16.0%) were treated with ceftriaxone and flucloxacillin, 4(16.0%) cases was treated with penicillin and flucloxacillin. All the cases were treated for 10-14 days. Cases of tubercular pleural effusion were treated by antitubercular drugs for 6 months regime and oral prednisolone for 4-6 weeks. Two malignant cases (Neuroblastoma and lymphoma) were treated with chemotherapy, nephrotic syndrome (3 cases) were treated with C-penicillin and oral prednisolone (60mg/m2/day) in divided doses for 6 weeks followed by 40 mg/m^2 on alternative day as single morning dose for the 6 weeks (Table VII).

Among the study childs 22 cases (92%) had improved, 1 case (4%) expired and 1 case (4%) was referred to the Institute of Chest Disease & Hospital from Dhaka Shishu Hospital (Figure-3).

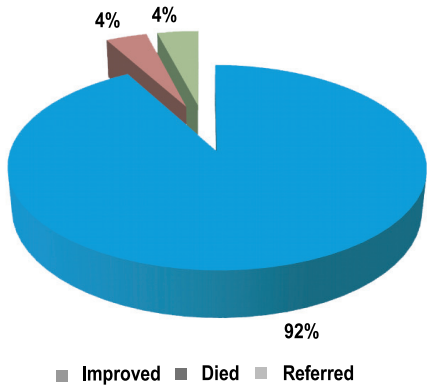

Fig 3 *Outcome of pleural effusion.*

Discussion

This is an observational study done in different paediatric units of leading hospital in Dhaka city to evaluate the aetiology and clinical practice of management of Pleural effusion in children in hospitals of Dhaka city.The present study included 25 children 25 children aged 2 months to 15 years, 15 cases (60.0%) were male and 10 cases (40%) were female. Male cases were more which is probably due to greater attention to the male children. A study found that parapneumonic effusion are more common in boys than girls and most frequency encountered in infants and young children.[16] Another study found that most of the pleural effusion in children were beyond 5 years of age.[2] In the present study majority cases were more than 5 years at presentation.

In this study fever, cough and respiratory distress were predominant presenting features. In all the cases restricted chest movement, diminished or absent breath sound were the common physical findings. Other clinical features of underlying lesions like generalized edema in case of nephrotic syndrome, weight loss in case of tuberculosis, lymphadenopathy in cervical region and hepato-splenomegaly in case of lymphoma. The present study showed pulmonary tuberculosis as the most common cause of pleural effusion (36.0%) followed by pneumonia (32.0%), nephrotic syndrome (12.0%) and dengue fever (12.0%). In many developing countries of the world the most common cause of exudative pleural effusion is pulmonary tuberculosis but this is relatively uncommon in united states.[15] The main reasons for the increasing burden of tuberculosis globally are poverty and wide gap between rich and poor in various populations.

Neglect of the disease, collapse of the health infrastructure in countries experiencing severe economic crisis or civil unrest and the impact of HIV pandemic. In developed countries heart failure, rheumatological causes and metastatic malignancy are the common causes. Less common cause of pleural effusion in developed countries include tuberculosis, systemic lupaserythromatosus, pancreatitis, subdiaphramatic absence and rheumatoid arthritis. [17] Pleural fluid protein content were analysed and showed 16 cases (76%) cases were exudative and 2 cases (8%) were transudative. Transudative is clear coloured and exudate is more amber coloured and may be turbid if the cell count is high.[22] Among 8 cases of para pneumonic pleural effusion, pleural fluid of 3 cases were clear where pleural fluid cell count was <100mm3, pleural fluid of other parapneumonic cases were hazy, where cell count was hundreds to plenty. 2 cases (8.0%) of pleural fluid due to malignancy were hemorrhagic. Uniform blood staining of pleural fluid frequency indicate pleural tumor although infarction, rheumatoid, malignant and tubercular effusion may be hemorrhagic.[18] Blood in the fluid may be due to damage to a vessel during insertion of the needle or biopsy. If this is the case the fluid withdrawn into the local anesthetic syringe is usually clear but later aspirate tend to be less blood stained than the initial ones.[19] Parapneumonic pleural effusion is inflammatory exudates dominated by polymorphonuclear leukocyte. The absolute protein values are of no values in determining the likehood of spontaneous of the effusion or chest tube drainage requirement. The pleural fluid leukocyte count shows a wide variation in values between simple effusion and frankly purulent empyemas and a predominance of lymphocyte in an exudate should raise the possibility of malignancy or tuberculosis. Some non purulent collection will show bio-chemical evidence of infection and are likely to need chest tube drainage for resolution of sepsis.[20]

In this study had parapneumonic effusion and they were treated with ceftrixaone, or in combination with flucloxacillin for 10-14 days or penicillin with flucloxacillin. Merino JM, et al[21] showed intravenous benzyl penicillin combined with quinolone has an appropriate sprectrum as an empirical therapy in community acquired parapneumonic effusion. Finegoldet al[22] showed that third generation cephalosporin and broad spructum anti pseudomonal penicillin such as piperacillin are also good alternative therapy. Neild JE et al[23] showed that continuation of antibiotics for several weeks based on experience of the clinicians managing the case providing adequate pleural drainage, long term treatment for about 3 weeks is probably appropriate.

In this study there were 9 cases (36.0%) of tubercular pleural effusion. These cases were treated with short course chemotherapy (Rifampicin, isoniazid, pyrazinamide and streptomycin) along with prednisolone for 4-6 weeks. Antituberculous chemotherapy promote rapid pleural fluid absorption and recovery and prevent fibrosis but this is usually not required for small effusion.[2] Tubercular effusion require antitubercular chemotherapy and it is usual to add corticosteroid as there is evidence that speeds the reabsorption and prevent pleural fibrosis.[24] The management of pleural effusion depends on the cause. In many cases aspiration is sufficient to cure the problem although some effusion do recur especially malignant ones. medical management of pleural effusion consists of antibiotic treatment alone or an antibiotic plus simple drainage. Many small parapneumonic effusions will respond to antibiotics without the need of further intervention. Treatment of the underlying disorder is all that is required for effusion caused by renal, cardiac or rheumatology disorder.

Majority received antibiotic therapy as soon as pleural effusion is identified and where possible antibiotics should be chosen based on the results of pleural fluid culture and sensitivities. In this study nephrotic syndrome (3 cases) were treated with Inj. C. penicillin and oral prednisolone (60mg/m^2/day) in divided dose for 6 weeks followed by 40mg/m^2 on alternate day as single morning dose for 6 weeks. It was seen that in all the cases pleural fluid resorbed promptly along with the course of the therapy as a treatment of the primary disease process. This study also had 3 cases of dengue fever with effusion and this effusion also resolved spontaneously along with conventional therapy (Fluid management, paracetamol& other supportive measures). Most of the cases needed single theraputic aspiration of pleural fluid, only 2 cases needed chest tube drainage kept in situ. Most of the study children (92.0%) had improved, 1 case (4.0%) expired and a case (4.0%) was referred to NIDCH.

Conclusion

Pulmonary tuberculosis was the most common cause of pleural effusion followed by pneumonia, nephrotic syndrome, dengue fever and malignancy. Most of the patients presented with fever of varying dengue, cough respiratory distress, chest pain, irrespective of the cause of pleural effusion.Physical examination of cases showed tachypnoea, mediastinal shifting to the opposite side in unialteral effusion, dull percussion note, reduced or absent breath sound on affected side and diminished vocal resonance in all cases.Majority improved after treatment.

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ORIGINAL ARTICLE

Short term results of cleft lip and cleft palate repair in unilateral complete cleft lip and palate patients

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Abstract

Background: *Delaying in surgical repair of complete cleft lip and palate patient may lead to several difficulty. It may cause wide, extensive and difficult dissection. There are always chances of wound infection, wound dehiscence, complete wound disruption, fistula formation, even there is also chance of maxillary hypoplasia and failure to articulate life long.*

Objective: *In this study we observed the short term outcome of cleft lip repair and later on cleft hard palate repair in patients with unilateral complete cleft lip and palate (UCLP).*

Methods: *A prospective observational study was carried out in 25 patients with unilateral complete cleft lip and palate who under went cleft lip at first admission and then after 3 months cleft palate was repaired. During 1st and 2nd operations the gap of cleft alveolus and posterior border of the cleft hard palate were measured. Age, gender, side of the cleft, associated anomalies, family history of cleft, cleft alveolar and cleft palatal gap noted, postoperative complications were also recorded.*

Results: *A total of 25 patients included in this study. Age ranged from 4 months to 8 years. 15 patients were male and 10 were female. Right side was involved in 8 and 17 patients involved in left side. Only 3 patients had positive family history. 3 had associated congenital anomalies. Cleft alveolar and palatal gap reduced more in patients who were below the age of 18 months. Postoperative complications were mild respiratory distress, notching of vermilion border and oronasal fistula.*

Conclusion: *Repair of cleft lip leads to reduction of gap of cleft alveolus and cleft hard palate, specially in the patients who came for cleft lip surgery in early age.*

Keywords: *Unilateral Complete Cleft Lip-Palate; Cleft alveolar gap; Cleft palatal gap*

Introduction

Cleft lip and cleft palate is the third most common congenital anomalies in our country. The incidence of cleft lip or/and cleft palate in Bangladesh is 3.9 per 1000 live births.[1] Due to environmental pollution, misuse of drugs by pregnant women, radiation hazards etc, incidences of multi factorial congenital malformation like cleft lip, palate are increasing day by day.[2] Every year more than 5000 patients with cleft lip and palate are born. But most of the cleft patients come to the doctor only when their parents are aware or when the child had some problem like repeated respiratory tract infection, feeding difficulty, social problem e.g. even maternal divorce etc.

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Patients presents with abnormal teeth eruption, permanent articular problems, repeated ear infection, deafness etc. For these regions, we get patients of varying ages.[3]

In many centers the cleft lip is repaired before mother and newborn go home from hospital. Most of the surgeons prefer to wait for "Rule of 10", that is 10 Ib weight, 10 gm Hb%, 10 wks, that is around 3 months of age for repair of cleft lip. Cleft palate should be closed within 9-18 months of age before development of speech.[4]

There are many procedures for the closure of the cleft lip and palate.[5-8] Repair of cleft lip alone in unilateral complete cleft lip-palate needs extensive dissection during palatoplasty, takes more time for operation and more chances of wound distruption or oronasal fistula formation and if cleft palate repair is done earlier there may be mid facial growth disturbance.[9,10]

Even after repair, there may be chances of wound disruption, oronasal fistula formation. Some parents prefer cleft lip repair first irrespective of the age of the child only for aesthetic region and do not come again for cleft palate or oronasal fistula closure due to poverty, transport problem, lack of knowledge.[2,11]

Late repair of this defect is complicated by high fistula formation and which may persist for an extended period of time.[10] Early complete closure of the cleft allowed for earlier intelligibility of speech compound to the staged later closure.[12]

Materials and methods

This prospective observational study was carried out in the department of surgery, Dhaka Shishu (Children) Hospital; Dhaka, during the period of July 2007 to December 2008. We included only the patients with unilateral complete cleft lip and cleft palate from 3 months to 10 years in this study to see the short term results of this type of cleft patients. The patients with previous surgery for cleft lip-palate and unilateral cleft with other deformities of face were excluded. After admission history was taken and clinical examination was done thoroughly. Age, gender, side of cleft, family history of cleft, associated anomalies were recorded. Patients were included with unilateral complete cleft lip-palate the following investigations were commonly performed: hemoglobin percentage, bleeding time, clotting time, blood grouping. All patients underwent cleft lip (Millard's procedure) repair and then after 12 to 13 weeks cleft palate were repaired. Plain water was given orally after 4 to 6 hours of the operation. All the patients were discharge on 2nd or 3rd post operative day, with the advice to be on topical and oral antibiotics, analgesia, liquid diet (at least for 2 weeks for palate repair) followed by semisolid diet with spoon for four weeks and should take plenty of water after each feeding. They were also advised to come for follow up and for lip stitch removal on 5th to 7th day and on 4-6 weeks after operation. On immediate post operative and subsequent follow up we checked for any complications like bleeding, respiratory distress, flap necrosis, wound disruption, wound dehiscence, wound infection, fistula formation etc. All the information about each patient was obtained in separate data sheet, arranged in systemic manner, presented in various table and figures

Results

This study included a total of 25 patients with unilateral complete cleft lip and palate.

The age of the patients in this study group ranged from 4 months to 8 years. Mean ± SD was 25.6 ± 25.2 months and median was 11.5 months. Maximum patients were (n = 10) within 6 months to 12 months. A total of 15 patients were male (60%) and 10 were female (40%) ratio in whole study group was M: F = 1.5: 1. Among 25 patients, right side was involved in 8 (32%) patients and 17 (68%) patients involved in left side.

Only 3 (15%) patients had positive family history of cleft lip. The Mother of only one of them had isolated cleft palate only, and other two's had paternal or maternal relatives with a history of cleft lip ± palate.

Among the study group, three patients had associated anomalies, of one had atrial septal defect, one had external ear anomalies and third one had bilateral talipes equino varus.

All 25 patients were subdivided in two groups according to their age. In first group (3-18 months) there were 16 patients and in second group (> 18 months) there were 9 patients. Measurements of cleft alveolar gap and cleft palatal gap at the posterior border were taken at first before cleft lip operation and then before cleft palate operation in every patients. Then data were tabulated in Table –I and II.

Table I
Cleft alveolar gap

Age (month)	Gap before cleft lip repair (mm)		At cleft palate repair Total gap reduced (mm)	
	Up to 7.50	> 7.50	Up to 5.00	>5.00
3-18	9	7	11	5
>18	6	3	9	0
Mean ± SD	6.90 ± 2.96	4.49 ± 1.55		
Median	7.22	4.31		

Table II
Cleft palatal gap

Age (month)	Gap before cleft lip repair (mm)		At cleft palate repair Total gap reduced (mm)	
	Up to 12.00	> 12.00	Up to 3.50	> 3.50
3-18	7	9	16	0
>18	6	3	9	0
Mean ± SD	12.18 ± 3.13	2.1 ± 0.59		
Median	12.47	2.09		

Mean cleft alveolar gap and gap in the posterior border of hard palate before 1st operation (cleft lip repair) were 6.90 mm and 12.18 mm respectively. After cleft lip repair, mean cleft alveolar gap was reduced, 4.49 mm. Cleft alveolar gap reduced more than 5 mm in only 5 patients and none of them was above 18 months of age group. Mean cleft palatal gap reduced 2.1 mm. But cleft palatal gap of none of the patients of any age groups had reduced more than 3.5 mm in any age group.

No immediate post operative complication observed after cleft lip operation. On 5-7th postoperative day (during lip stitches removal) in 2 (8%) patients were found notching of vermilion border and 3(12%) developed oronasal fistula. The age of these 3 patients was above 2 years.

Table III
Post-operative complications in 1st and 2nd operation between two groups

Complications	Immediate post operative		On 5th -7th POD	
	After cleft lip repair	After palatoplasty	After cleft lip repair	After palatoplasty
Mild Bleeding	_	_	_	_
Mild respiratory difficulty	_	7(28%)	_	_
Vermilion border notching	_	_	2 (8%)	
Oronasal fistula.				3(12%)

Discussion

Cleft lip and palate is one of the common correctable congenital deformities in Bangladesh.[12] We get patients of varying ages. Most of the cleft patients come to the doctor only when their parents are aware or when the child has some problem such as repeated respiratory tract infection, social problem, etc. They presents with permanent articular problems, abnormal teeth eruption, deafness, etc. Even after surgery, there may be chances of wound disruption o recurrent oronasal fistula formation. Some parents prefer cleft lip repair first irrespective of the age of the child, only for esthetic reasons, and do not come again for cleft palate or oronasal fistula closure.[2]

Palatoplasty in UCLP needs extensive dissection, specially if the age of the patients is more and there may be more chances of oronasal fistula formation, which is very difficult to repair, and may cause mid-facial growth disturbance.[8,9] The purpose of this study was to evaluate the patients of unilateral complete cleft lip and palate and to observe the short term result of surgery. Especially, whether the cleft lip repair procedure can reduce the gaps of cleft palate and alveolus and the incidence of oronasal fistula formation.

In some studies on cleft lip and cleft palate surgery,[9,1014,15] the age of the patients was 3–7 months. But the age of the patients of this study ranged was higher, from 4 months to 8 years. The wide age range of our patients was probably due to the parents' educational, socio-economic and cultural influences regarding whether these children would be brought to the hospital or not.[13] In some case some parents bring their cleft babies just after birth, and advised how to deal with the cleft babies and to come at time for surgery. But, surgery was delayed, as patients were malnourished. The male female ratio in our study group was 1.5:1, In other studies,[2,9,13] male: female ratios were 1.5:1 to 2.1:1.

In some literatures,[2,9,13] showed more cleft involvement in the left side than the right, our study also similar to those, right side involved 32% and in the left side 68%. A study was done in 1998 on cleft lip with or without palate (n=60) in Dhaka Shishu hospital congenital heart disease was in 1.6%, and other anomalies were congenital bands in limb (3.3%), Polydactyle (3.3%), Apart's syndrome (3.3%).[13] We also found some of these types of anomalies 3 (12 %) patients in our study. Only 3 (12%) patients had positive family history of cleft lip. The Mother of only one of them had isolated cleft palate only, and other two's had paternal or maternal relatives with a history of cleft lip ± palate. In another study in 1998 on cleft lip with or without palate done in Dhaka shishu hospital positive family history was found also in 15% patients.[13] Family history has significantly increased of cleft lip and palate among the relatives of cleft lip and palate parents but isolated cleft lip and palate occur frequently in general population.[16] It is generally believed that isolated cleft palate is a genetic entity distinct from unilateral cleft lip with or without cleft palate.[17] Before cleft lip repair, the cleft alveolar gap ranged from 3.94 to 9.86 mm. But after cleft lip repaired gap was reduced and reduction ranged from 2.94 to 6.04 mm, median was 4.31 mm, and mean 4.49 mm. The cleft alveolar gap was reduced by more than 5 mm in five (20%) patients who were under 18 months of age.

Before cleft lip repair, the cleft palatal gap ranged from 9.05 to 15.31 mm. But after cleft lip repaired gap was reduced and the range of cleft palatal gap reduction after cleft lip repair in this study, was 1.51–3.5 mm, median 2.09 mm and mean 2.1 mm. The cleft palatal gap was reduced by up to 3.5 mm in 16 (64%) patients who were under 18 months of age. In other two studies,[2,9] on unilateral complete cleft lip-palate patients, cleft alveolar and cleft palatal gap were reduced significantly as they used vomer flap to repair hard palate during simultaneous repair of cleft palate. After cleft lip repair, no immediate postoperative complication was observed in any patient. But, after palatoplasty six patients needed blood transfusion after the second operation, due to extensive palatal dissection, and seven patients were observed with mild respiratory difficulty, probably due to reduction of oral cavity space and less space for tongue. On the 5th–7th postoperative day of the lip repaired, two patients was found with vermilion line notching. On the 5th–7th postoperative day following the palatoplasty. Three (13%) patients the age of whom was above 2 years, developed anterior oronasal fistula. In other studies[13,18-20], fistula rates were higher. But oronasal fistula rate may reduced by using vomar flap.[2,9]

Conclusion

Repair of cleft lip results, in reduction of gaps of alveolar cleft and that of hard palate remarkably,

specially in the patients who came for this surgery in appropriate time. So, it is better to repair cleft lip in appropriate age in order to easy repair of cleft palate and to reduce postoperative complications.

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ORIGINAL ARTICLE

Risk factors of Enteric fever among 2 years to 12 years old hospitalized children

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Abstract

Background: *Enteric fever is a leading cause of morbidity and mortality of children in developing countries due to different risk factors. The aim of the present study is to see the risk factors for enteric fever.*

Materials and Method: *A case controlled study was carried out in the Department of Pediatric Medicine, Dhaka Shishu Hospital for a period of six (06) months. All the children within the age of 2 to 12 years who presented with fever were included in this study. One hundred febrile children aged 2 to 12 years were selected. Among them, 50 were in case group and 50 were in control group. Case group was diagnosed as enteric fever by the positive Widal Test and Blood culture yielding growth of salmonella typhi . Control group was diagnosed as negative Widal test and unyielding Blood culture. The probable risk factors for enteric fever between both case and control group were compared by univariate analysis and. The p value <0.05 were considered as significant.*

Results: *-Most of our patients were in the 2 to 5 years age group. Soap use for hand washing was 34% in case and 34% in control. Taking food from street vendors was 46% in case and 33% in control. Consumption of half boiled egg was found in 33% cases of the case and 19% of the control group.*

Conclusion: *In conclusion, it was found that, use of soap for hand washing, taking food from street vendors, eating half boiled eggs are the significant risk factors for enteric fever in 2 to 12 years old hospitalized children admitted to tertiary care pediatric hospital.*

Key words*: Enteric fever, Risk factors, Salmonella typhi*

Introduction

Enteric fever (more commonly termed typhoid fever) remains endemic in many developing countries. Typhoid fever is caused by *Salmonella enterica serovar* Typhi (S. typhi) a gram-negative bacterium. A very similar but often less severe disease is caused by S. paratyphi A and rarely by S. paratyphi B (Schottmuelleri) and S.paratyphi C (Hirschfeldii).[1] In most endemic areas approximately 90% of enteric fever is with S. typhi.[2] It is transmitted through the ingestion of uncooked food or drinks contaminated by the feces or urine of infected people. Also fly has an important role in transmission especially in summer. S. typhi can live in dry and cool

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environment so that the agent can spread with contaminated ice, dust, food and sewer system. Epidemics are more common in spring and summer, sporadic in other seasons.[3]

Enteric fever continues to be a major public health problem in Bangladesh.[4] The overall incidence of typhoid fever in Dhaka was 3.9 cases per 1,000 population per year as per a study done in 2001. The incidence of typhoid fever in >5 years of age was 2.1 episode per 1,000 population per year and among children <5 years old was 18.7 cases per 1,000 children per year. Children <5 years of age had an 8.9 fold increased risk of infection when compared with all others.[5] The incubation period is usually 7-14 days but it also depends on the infecting dose (ranges from 3-30 days). The clinical presentation varies from mild illness with low grade fever, malaise, and to a severe clinical picture with abdominal discomfort and multiple complications. Enteric fever usually presents with high-grade fever with a wide variety of associated features such as generalized myalgia, anorexia, abdominal pain, hepatosplenomegaly. In children, diarrhea may be present in the earlier stages of illness and sometimes followed by constipation. The fever may rise gradually, but the classic stepladder rise of fever is relatively rare due to use of antipyretics. In about 25% cases, a macular or maculopapular rash (rose spots) may be visible around the 7^{th}-10^{th} day of the illness on the lower chest and abdomen and last for 2-3 days.[1] Complications occur mostly in untreated patients. These are gastrointestinal perforation or hemorrhage, cholecystitis, myocarditis, meningitis, encephalopathy or focal abscess. [6,7]

Continued excretion of large number of bacteria by asymptomatic carriers or individuals who are recently recovered from enteric fever is a major source of spread for an epidemic.[8] The definitive diagnosis of enteric fever requires the isolation of S.typhi or S.paratyphi from specimen of blood, bone marrow, extra intestinal site. Blood culture is the standard diagnostic method and the result can be positive in 60%-80%.[6] However the sensitivity of blood culture in diagnosing typhoid fever in many parts of the developing world is limited as wide spread antibiotic prescribing may render bacteriologic confirmation difficult[1]. Moreover, due to lack of new developments of diagnosis of enteric fever e.g. tests using monoclonal antibodies, nested PCR, in most of the developing world the mainstay of diagnosis of typhoid fever remains clinical and also the Widal test though this investigation is nonspecific. Stool and urine culture becomes positive after 1^{st} week. Typhoid fever can be prevented by avoiding foods foods and drinks at risk and getting the subjects vaccinated against typhoid fever. Typhoid vaccine 51-67% prevents the disease and loss effectiveness after several years. Antibiotics do not prevent enteric fever but they are only used to treat disease.[9] Prevention of infection with pathogenic strain should focus on personal hygiene, proper sewage treatment, hand washing prior to food handling, pasteurization of milk, proper cooking of eggs, poultry and other meats. [10] Typhoid fever has a worldwide distribution and it is endemic in Bangladesh.[4] It has life threatening complications and death. Hence it is important to control the morbidity and mortality from enteric fever. Therefore, this study was carried out to find out the risk factors of enteric fever among 2 to 12 years of age so that adequate steps can be taken to prevent the occurrence of enteric fever and its related complications.

Materials and Methods

A Case control study was performed in inpatient department of Dhaka Shishu Hospital, Dhaka, from April 2012 to October 2012. Total 100 children were selected according to the inclusion criteria and then randomly allocated to one of the two groups, each group contained 50 patients. Children aged 2 to 12 years of age of both sex with documented fever and characteristic clinical features (toxic appearance, abdominal tenderness, hepatomegaly and or splenomegaly, coated tongue, diarrhea or constipation, rose spot, caecal gurgling) , significant Widal titre (1:160 or more somatic antigen and or 1:320 or more flagellar antigen or presence of rising titre). Children below 2 years and above 12 years old and Seriously ill patients were excluded. After taking informed consent from the parents or attendants, a detail history was taken. A preformed questionnaire containing relevant information's

were recorded for this study. Complete physical examination was done for each patient. After initial evaluation relevant investigations, Widal test and blood cultute were sent. Widal test was sent after 7 days of fever and blood culture was sent before 7 days of fever. Children having a positive Widal and or S.typhi or S. paratyphi were found in blood culture were diagnosed as enteric fever. A total of 50 patients with positive widal or blood culture were assigned to experimental group and 50 with negative widal and blood culture were considered as control group. All data were recorded systematically in questionnaire and quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Risk factors between two groups were statistically compared by univariate analysis. Distribution between two groups are compared by Student's 't' test and chi-square test. Statistical analysis was performed by using SPSS for windows version 12.0. 95% confidence interval was calculated. Probability value <0.05 was considered as level of significant.

Results

In the present study we enrolled total 100 patients of both sexes from age 2 to 12 year who were admitted in the Department of Pediatric Medicine, Dhaka Shishu (Childen) Hospital during the period of April 2011 to April 2012. Among them 50 patients were in case group and another 50 were in control group. The findings from the data analysis are documented below.

Table I

Distribution of the patients by Widal test in case group

Laboratory investigation	Number of patients	Percentage (%)
Widal test		
Positive	40	80.0
Negative	10	20.0

Regarding Widal test, 40 (80%) patients had the positive response i.e. only 10 (20%) patients had the negative response.

Table-II

Distribution of case and control group by blood culture

Blood culture	Group I (Case) (n=50) No. %	Group II (Control) (n=50) No. (%)	OR	P value
Blood culture done				
Yes	48 (96.0)	50 (100.0)	0.18	0.15
No	2 (4.0)	0		
Blood culture				
Positive	15 (30.0)	0	0.00	0.001
Negative	35 (70.0)*	50 (100.0)		

*Among 35, 2 patients who were refused to do blood culture were considered as negative result.

In case and control group, 48 and 50 patients had done blood culture respectively. Among the patients who had done blood culture, 15 patients were positive for S.typhi in case group.

Table-III
Univariate analysis of risk factors for typhoid fever among 50 cases and 50 controls

Risk factors	Cases (%)	Controls (%)	OR	95% CI	P value
Residence					
Urban	36	40	0.64	0.25-1.62	0.35
Rural	14	10			
Housing					
Semi Pacca	18	23	0.66	0.29-1.47	0.31
building	32	27			
Purification of water					
Purified	35	38	0.74	0.30-1.79	0.49
Not purified	15	12			
Hand washing before meal					
Yes	34	43	0.35	0.13-0.94	0.03
No	16	7			
Hand washing after toilet					
Yes	23	33	0.44	0.19-0.98	0.04
No	27	17			
Soap use for hand washing					
Yes	34	44	0.29	0.10-0.82	0.01
No	16	6			
Eating food from street vendors					
Yes	46	33	5.92	1.82-19.23	0.003
No	4	17			
Nature of home-made food					
Well cooked	46	44	1.57	0.41-5.93	0.51
Not well cooked	4	6			
Nature of cooking milk					
Proper boiling	40	45	1.33	0.54-3.30	0.53
Not proper boiling	10	5			
Nature of cooking eggs					
Boiled	17	31	0.32	0.14-0.72	0.005
Half boiled	33	19			

The risk factors such as hand washing before meal, hand washing after toilet, soap use for hand washing, eating food from street vendors, nature of cooking eggs were statistically significant.

Table -IV

Nutritional status	Group I (Case) (n=50) No. %		Group II (Control) (n=50)No. (%)		OR		P value	
	W/H	H/A	W/H	H/A	W/H	H/A	W/H	H/A
Normal	34 (68%)	41 (82%)	46 (92%)	44 (88%)	0.01	2.13	0.009	0.68
Mod. Wasted	11 (22%)	7 (14%)	2 (4%)	5 (10%)				
Severely wasted	5 (10%)	2 (4%)	2 (4%)	1 (2%)				

Distribution of the patients by nutritional status of W/H and H/A

W/H of 68%, 22%, 10% were normal, moderately wasted and severely wasted in case group while 92 %, 4% and 4% in control group respectively.

Table-V

Distribution of the case and control group by history

History	Group I (Case) (n=50) No. %	Group II (Control) (n=50) No. (%)	OR	P value
H/O enteric fever previously	7 (14.0)	7 (14.0)	-	1.0
H/O enteric fever in the family	5 (10.0)	12 (24.0)	0.06	0.06
Typhoid vaccine	3 (6.0)	2 (4.0)	1.78	0.64
Contact with enteric fever patients	6 (12.0)	0	0.01	0.01

H/O similar illness previously(who was admitted in hospital for enteric fever or diagnosed as enteric fever by registered physician) 14% patients in case group and 14% patients in control group. H/O similar illness in the family(whos family member was admitted in hospital for enteric fever or diagnosed as enteric fever by registered physician) 10% patients in case group and 24% in control group.

Table-VI

Univariate analysis of symptoms among 50 cases and 50 controls.

Risk factors	Cases (%)	Controls (%)	OR	95% CI	P value
Fever	50 (100)	50 (100)	1.0	0.40-2.52	1.0
Duration of fever					
< 7 days	4 (8.0)	22 (44.0)	0.11		0.01
> 7 days	46 (92.0)	28 (56.0)		0.035-0.35	
Anorexia	44 (88.0)	42 (84.0)	1.39	0.45-4.37	0.56
Vomiting	26 (52.0)	24 (48.0)	1.17	0.55 - 2.57	0.68
Abdominal pain	18 (36.0)	8 (16.0)	2.95	1.14-7.65	0.02
Diarrhea	8 (16.0)	0.0	20.0	1.13- 360.29	0.04
Constipation	2 (4.0)	1 (2.0)	2.04	0.18- 23.27	0.56
Chills & rigor	3 (6.0)	1 (2.0)	3.12	0.31-31.14	0.33
Headache	9 (18.0)	1 (2.0)	10.75	1.31 - 88.47	0.02

Table VII
Univariate analysis of signs between case and control group

Signs	Cases (%)	Controls (%)	OR	95% CI	P value
Toxic	39 (78.0)	34 (68.0)	1.66	0.68 - 4.08	0.26
High temperature	43 (86.0)	38	1.93	0.69- 5.43	0.20
Coated tongue	41 (82.0)	4 (8.0)	52.38	14.99- 182.99	0.01
Rose spot	4 (8.0)	0	9.77	0.51-186.53	0.12
Pallor	12 (24.0)	17 (34.0)	0.69	14.99-182.99	0.39
Jaundice	1 (2.0)	5 (10.0)	0.18	0.02-1.63	0.13
Abdominal distension	2 (4.0)	2 (4.0)	1.0	0.13-7.39	1.0
Abdominal tenderness	2 (4.0)	4 (8.0)	0.47	0.08- 2.74	0.40
Hepatomegaly	23 (46.0)	5 (10.0)	7.66	2.61-22.54	0.01
Splenomegaly	8 (16.0)	1 (2.0)	9.33	1.12-77.71	0.03

Discussion

This case control study was carried out with an aim to evaluate the risk factors of enteric fever among 2 to 12 years old hospitalized children. In the present study we enrolled 100 patients of both sexes from age 2 to 12 years who were admitted to Dhaka Shishu Hospital during the period of April 2012 to October 2012.

Stoll BJ, Glass RI, Banu H et al (1983) of International Centre for Diarrheal Disease Research, Dhaka, Bangladesh, found older children and young adults had the highest age-specific rates of this disease. [11] Khan MI et al (2012) conducted a study in Seoul, South Korea and showed that the risk of typhoid was lower with increasing age . The risk found was higher with an increase in population density and lower in the households using a safe drinking-water source.[12] In our study the age risk was observed higher in lower age group.

H.H.Tran et al (2005) showed recent contact with a typhoid patient , no education and drinking untreated water were associated with typhoid fever.[13] Srikantiah P et al(2007) showed that consumption of unboiled surface water outside the home, use of antimicrobials in the 2 weeks preceding onset of symptoms , and being a student were independently associated with typhoid fever.[14]

Mohammad Hatta et al (2009) identified independent risk factors related to typhoid fever like consumption of uncooked vegetables, consumption of water with a poor quality, use of water that is contaminated with coliform bacteria, not washing hands before eating and not using soap for washing hands .[15] This findings correlated with the findings of our present study.

Ayesha Ayaz et al (2006) showed that risk factors of enteric fever include age, educational status of parents, consumption of street vendors food, water intake, history of contact with patient of enteric fever in family. Enteric fever spreads through consumption of unhygienic food and beverages which are being handled by typhoid career.[16] It also correlated with the findings of the present study.

In present study showed that proper boiling of milk was not significant risk factor but proper boiling of egg was a significant risk factor.

Vollaard AM et al (2004) found that paratyphoid fever among cases was independently associated with consumption of food from street vendors and flooding, recent typhoid fever in the household, no use of soap for handwashing, and no toilet in the household.[18]

In this study showed that contact with enteric fever patients was a significant risk factor.

Regarding Widal test, 40 (80%) patients had the positive response i.e. only 10 (20%) patients had the negative response. On the other hand, regarding Blood culture 15 (30%) patients had positive results and consequently 35(70%) patients had negative results. Widal test is a screening test for the disease which is positive at the end of first week. It is one of the most widely used method for diagnosis of typhoid fever in developing countries.[19]

Conclusion

The present study concludes that hand washing before meal,use of soap for hand washing , eating food from street vendors, nature of cooking eggs are the significant risk factors for Enteric fever of 2 to 12 years old hospitalized children admitted to a tertiary care Pediatric Hospital. A multi centre should be recommended for other probable risk.

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ORIGINAL ARTICLE

Serum magnesium level in hospitalized nephrotic syndrome patients and its relation to albumin

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Abstract

Background: *Nephrotic syndrome(NS) is the second most common renal disorder in developing countries in children leading to high morbidity.*

Objective: *To evaluate the magnesium level in patients with nephrotic syndrome and its relation to albumin.*

Methods: *An observational cross sectional study was conducted in the Department of Pediatrics, Dhaka Shishu Hospital, Dhaka from January 2015 to June 2015. Fifty four diagnosed cases of nephrotic syndrome admitted during the study period were included in this study. Patients of nephrotic syndrome with associated illnesses such as diarrhoea, severe vomiting, metabolic disturbances and seizure were excluded in this study. Serum magnesium and albumin levels were assessed in every enrolled patients.*

Results:*The mean level of serum magnesium during initial attack was 2.28±0.36, and it was 2.04±0.29 during first relapse, 2.06±0.29 during infrequent relapse and 1.76±0.32 during frequent relapse. The difference found among the mean level of serum magnesium level in different pattern of nephrotic syndrome by ANOVA test (one way) is statistically significant (P <0.01).Among the patients with severely low (< 2.5 gm/dl) albumin level, about 29.6% of them had less than 1.8 mg/dl magnesium level, 44.4% of them had Mg level at 1.8-2.4 and about 25.9% had Mg level at greater than 2.4. Among the patients with moderately low albumin level, 14.8% had Mg level at < 1.8 mg/dl, 59.3% had Mg level at 1.8-2.4 mg/dl and 25.9% of the patients had Mg level greater than 2.4 mg/dl. None of the patients had greater than 2.9 albumin level. The p value at 0.01 signifies statistically significant correlation between the albumin and Mg level. Hypomagnesemia was mostly found in frequent relapse nephrotic syndrome cases. The positive correlation between serum magnesium level with serum albumin, the correlations were statistically significant (r = 0.34, p = 0.01).*

Conclusion: *Serum magnesium level is low in most (64.3%) cases of frequent relapse nephrotic syndrome. Positive correlation was found between serum magnesium with serum albumin in children with nephrotic syndrome (albumin level was decreased their magnesium level also be decreased) and that was statistically significant.*

Key words: *Nephrotic syndrome, magnesium, albumin*

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Introduction

Magnesium is needed for more than 300 biochemical reactions in the body. It helps maintain normal muscle and nerve function, keeps heart rhythm steady, supports a healthy immune system, and keeps bone strong. Magnesium also helps regulate blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism and protein synthesis. There is an increased interest in the role of magnesium in preventing and managing disorders such as hypertension, cardiovascular disease, and diabetes. Dietary magnesium is absorbed in the small intestines. Magnesium is excreted through the kidneys.[1] Nephrotic syndrome (NS) is a clinical entity characterized by massive loss of urinary protein (primarily albuminuria) leading to hypoproteinemia resulting in edema. Hyperlipidemia, hypercholesterolemia, and increased lipiduria are usually associated with Nephrotic Syndrome. Although not commonly thought of as part of the syndrome, hypertension, hematuria, and azotemia may be present.[2]

The most common primary cause in children is minimal change glomerulopathy; in adults, it is idiopathic membranous glomerulopathy. The overall prevalence of NS in childhood is approximately 2–5 cases per 100,000 children. Minimal change nephrotic syndrome (MCNS) is the most common form in children, and its prevalence is inversely proportional to the age (i.e., the younger the child, the more likely the histology will show minimal abnormalities on light microscopic evaluation of glomerular histology). In children below eight years at onset, the ratio of males to females varies from 2:1–3:2 in various studies.[3] In older children, adolescents, and adults, the sex ratio is appro- ximately equal.

Biochemical alteration is a common phenomenon in all kidney diseases including nephrotic syndrome and as most intracellular magnesium is bound to proteins, membrane leakiness in nephrotic syndrome causes hypoalbuminemia as well as hypomagnesemia. Mg deficiency causes hypertrophy of juxtraglomerular apparatus located in the kidney. This releases renin which ultimately increases aldosteron, lowering serum Mg and K. It is fairly well established that aldosterone plays an important part in regulation of magnesium metabolism and increases renal excretion of this ion.[4]

So, Magnesium level should be checked as a part of evaluation of the severity of the kidney problems. And as serum magnesium level is related to calcium, potassium, cholesterol level and albumin, so proper supplementation of magnesium can properly manage the disease as they are altered in nephrotic syndrome. Serum magnesium level in nephrotic syndrome has never been assessed in our country. A particular long list of prescription medications have been shown to reduce the body's supply of magnesium. Several types of diuretics, loop diuretics like frusemide have been shown to compromise magnesium status. Antibiotics can also lower magnesium availability. Other medications that reduce the body's supply of magnesium include corticosteroids and immunosuppressant drug cyclosporine.[5] For these reasons the serum magnesium level in patients with idiopathic nephrotic syndrome is an important issue.

Methodology

An observational cross sectional study was conducted in the Department of Pediatrics, Dhaka Shishu (Children) Hospital, Dhaka from January 2015 to June 2015. Fifty four diagnosed cases of nephrotic syndrome admitted to this hospital were included in this study. Patients of NS with associated illnesses such as diarrhoea, severe vomiting, metabolic disturbances and seizure were excluded from this study. All children of nephrotic syndrome were given biochemical and other routine investigations like CBC, urine R/E, urine C/S, serum albumin, cholesterol, spot urine protein creatinine ratio, HBs Ag . On admission, 2 ml of blood were collected from a patient at a time. Samples were centrifuged and stored in a refrigerator. Serum magnesium were assessed.

The ALB method used on the Dimension clinical chemistry system is an in vitro diagnostic test intended for the quantitative determination of albumin in human serum and plasma. Data were collected by interviews of the patients, clinical examination and laboratory investigations using the research instrument.

The MG (megnesium method) method was used on the Dimension clinical chemistry system. It is an in vitro diagnostic test intended for the quantitative determination of magnesium in human serum, plasma and urine.

The magnesium method is a modification of the methylthymolblue (MTB) complexometric procedure described by Connerty, Lau and Briggs. The barium salt of ethylenebis (oxyethylenenitrilo) tera acetic acid (Ba-ETA) is used to reduce interference due to calcium which also reacts with MTB.

Data were processed and analyzed using software SPSS (Statistical Package for Social Sciences) version 22.The test statistics used to analyze the data were descriptive statistics and correlation coefficient and student t test. Level of significance was set at 0.05 and $p < 0.05$ was considered significant.

Results

In present study mean age was 5.51 (±2.56) years, minimum age was 1 year and maximum age was 10 years, maximum age group was > 5 years of old which was 53.7%. Majority of them were male baby (72.2%)and male female ratio 2.6 :1. (Table I)

Table I
Demographic characteristics of the study population

	Number	Percentage
Age in years		
1yr	02	3.7
2-5 yrs	23	42.6
>5 yrs	29	53.7
Mean SD	5.51 (±2.56)	Range 1-10 years
Sex		
Male	39	72.2
Female	15	27.8
Total	54	100.0

Presenting complaints show that majority of the patients had swelling of face (96.3%), swelling of leg (83.3%),ascitis(85.2%) and cough 172.2%). Swelling of genitalia, fever, abdominal pain, vomiting, respiratory distress, burning sensation during micturation were found in 31.5%, 48.1%, 40.7%, 35.2%, 22.2% and 18.5% of cases respectively. (Table II)

Table II
Distribution of patients by presenting complaints (n=54)

	Number	Percentage
Swelling of face	52	96.3
Swelling of leg	45	83.3
Swelling of abdomen	46	85.2
Swelling of genitalia	17	31.5
Fever	26	48.1
Pain abdomen	22	40.7
Vomiting	19	35.2
Cough	39	72.2
Respiratory distress	12	22.2
Burning sensation during micturition	10	18.5

Among nephrotic syndrome cases 16(29.6%) patients were in first attack, 12(22.2%) were in 1st relapse, 13(24.1%) were in infrequent relapse and 13(24.1%) were in frequent relapse nephrotic syndrome. |(Table III).

Table III
Distribution of patients by type of attack

Type of attack	Number	Percentage
First Attack	15	27.8
First Relapse	12	22.2
Infrequent Relapse	13	24.1
Frequent Relapse	14	25.9
Total	54	18.5

24.1% percent of the patients had hypomagnesmia (< 1.8 mg/dl) and 13.0% had hypermagnesemia (> 2.4 mg/dl). The rest of the cases had magnesium level within normal range (1.8 – 2.4 mg/dl) (Table IV).

The mean level of serum magnesium during initial attack was 2.28±0.36, and it was 2.04±0.29 *during first relapse, 2.06±0.29 during infrequent relapse and 1.76±0.32 during frequent relapse.* The difference found among the mean level of serum magnesium level in different pattern of

Among the patients with severely low (< 2.5 gm/dl) Albumin level, about 29.6% of them had less nephrotic syndrome by ANOVA test (one way) is statistically significant (P <0.01).(Table V)than 1.8 mg/dl magnesium level, 44.4% of them had mg level at 1.8-2.4 and about 25.9% had mg level at greater than 2.4. Among the patients with Moderately Low Albumin level, 14.8% had mg level at < 1.8 mg/dl, 59.3% had mg level at 1.8-2.4 mg/dl and 25.9% of the patients had mg level greater than 2.4 mg/dl. None of the patients had greater than 2.9 Albumin level. The p value at 0.01 signifies statistically significant correlation between the albumin and mg level.(Table 6) Hypomagnesemia was mostly found in frequent relapse nephrotic syndrome cases.The positive correlation between serum magnesium level with serum albumin, the correlations were statistically significant (r = 0.34, p = 0.01).(Fig.1)

Table IV
Magnesium level of the study population

Magnesium level	Number	Percentage
< 1.8	13	24.1
1.8-2.4	34	63
> 2.4	7	13
Total	54	100

Table V
Magnesium status in different states of nephrotic syndrome (n=54)

Type of Attack	N	Magnesium Level (mg/dl) [Mean±SD]
Initial attack	15	2.28±0.36
1st relapse	12	2.04±0.29
Infrequent relapse	13	2.06±0.29
Frequent relapse	14	1.76±0.32
*P value		<0.01

*ANOVA Test

Table VI
Association between albumin level with magnesium level

Magnesium level (mg/dl)	Albumin level Severely low (< 2.5 gm/dl) n(%)	Moderately low (2.5-2.9 gm/dl) n(%)	Mild (>2.9 gm/dl) n(%)	Total	p value
< 1.8	08 (29.6%)	04(14.8%)	00	12	0.01
1.8-2.4	12(44.4%)	16(59.3%)	00	28	
> 2.4	07(25.9%)	07(25.9%)	00	14	
Total	27(100%)	27(100%)	00	54	

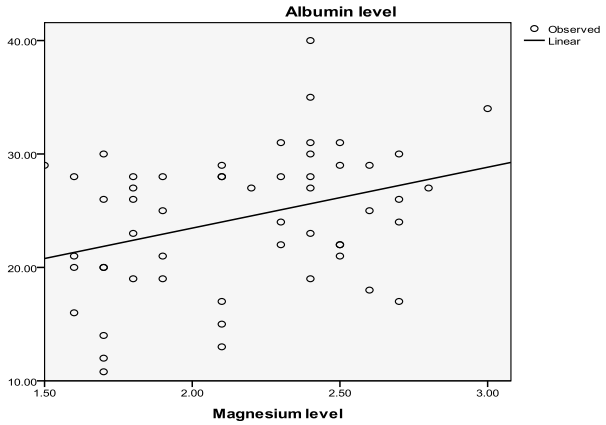

Fig 1 *Correlations of serum magnesium with albumin level in children with nephrotic syndrome*

Discussion

Observational cross sectional study was carried out in department of Nephrology Dhaka Shishu (Children) Hospital. There were total 54 children enrolled in the study out of these 39 males and 15 female children in this study group. The mean age was 5.51 (±2.56) years, minimum age was 1 year and maximum age was 10 years, maximum age group was > 5 years of old which was 53.7%, majority of them were male baby 72.2%, male female ratio 2.6:1.

There was no history in this study which suggested antecedent renal parenchymal disease. Oedema, proteinuria, hypoproteinemia and hypercholesterolemia were uniformly present at the onset of the disease. Haematuria was absent, no history of hypertension, blood urea nitrogen was normal. Kidney biopsies not done as there was no indication.Thus the diagnosis of nephrotic syndrome based on clinical parametres.

Kobayashi A[6] study revealed that serum magnesium level was significantly reduced in the untreated condition of the disease and serum magnesium level showed direct correlations with serum protein and albumin.Serum magnesium level was gradually elevated to the normal range as the disease improved.

Sah et al.[7] *study showed low serum total protein and albumin level are associated with NS in*

children,in their study serum albumin level -2.0 to 3.4 g/dl was found in most of the patient and low number of patients had 1.5 to 1.9 g/dl which was co-related with other studies[8-11] Proshad, Flink and Mc-Collister[12] described that in the nephrotic syndrome the total magnesium was somewhat lower than normal, probably because of hypoprotinaemia and that the percentage of ultrafiltrable magnesium was increased in some patients associated with hypoalbuminaemia.

In one of the first cases of primary hyper aldosteronism reported, that of Mader and Iseri,[13] a very low serum magnesium was noted, and in the first case studied by Milne, Muehrcke and Aird.[14] a low serum magnesium was also present and was restored to normal by removal of the aldosterone secreting adenoma, the change being accompanied by a strong positive balance for magnesium.

Present study reveals that, hypomagnesemia is mostly found in frequent relapse nephrotic syndrome cases. This may be partly due to secondary hyper aldosteronism which is thought to develop in nephrotics with generalized oedema and partly due to loss of protein. Present study also showed the correlations of serum magnesium with serum albumin in children with nephritic syndrome. Serum magnesium bears linear correlation with serum albumin, when serum magnesium level decreased, serum albumin also decreased, the correlations were statistically significant (r = 0.34, p =.01).

Conclusion

In conclusion, serum magnesium is low in most cases of frequent relapse nephrotic syndrome and direct correlation with serum magnesium with serum albumin in children with nephrotic syndrome, where albumin level was decreased their magnesium level also be decreased and that was statistically significant. A large multicentre should be under taken to look for any tubular problem in thoracic patients.

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ORIGINAL ARTICLE

Pattern of infection in neutropenic patients of acute leukaemia

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Abstract

Background: *Neutropenic children with Acute leukemia suffers from variety of infection which may leads to death. Detection of infection in neutropenic patients with acute leukemia by doing blood and urine cultures is not so much helpful as these are found positive only in few percentage. CRP and chest x-ray may be done for detection of infection in these patient as both are found positive in more than 50% cases. However fever, which present in almost all cases, still remains most important indicator of infection in these patients.*

Objective: *To determine the pattern of infection in neutropenic patients by identifying the organisms or localizing causes of infection. To recommend appropriate measures for these patients to reduce mortality.*

Methods: *This was a cross sectional study done in Dhaka Shishu (Children) Hospital, over 6 months from 15th November 2006 to 15th May 2007. Forty (40) acute leukaemic patients of both sex, aged 2 to 9 years in whom absolute neutrophil count was less than 500/cumm either during diagnosis or during treatment were selected as cases. Detailed history, clinical examination including local signs of infection, relevant investigations like CBC with film, bone marrow study, CRP, chest x-ray, ZN staining of stool for cryptosporidium, blood & urine for culture and sensitivity were done in all cases. Then all data were collected and statistical analysis was done by student t-test and chi-square (χ^2) tests with SPSS version -17.*

Results: *Positive blood culture were found in 8(20%) cases among them E. coli were present in 5 (12.5%) cases and acinetobacter in 3(7.5%) cases. Positive urine culture were present in 9(22.5%) cases, among them E.coli were found in 5 (12.5%) cases and K. pneumoni were found in 4(10%) cases. CRP titre was 20-40 mg/l in 30(75%) cases and 10-20mg/l in 5(12.5%) case. Abnormal CxR consistent with pneumonia was present in 50% cases. Fever was present in 100% cases.*

Conclusion: *Among all cases of acute leukamia with neutropenia, positive blood and urine culture were present subsequently only in 20% and 22.5% of cases. In 62.5% cases, CRP was positive. Abnormal CxR consistent with pneumonia was present in 50% cases. Among all the parameters, fever was the consistent feature in neutropenic patient with acute leukemia.*

Keywords *Acute leukemia, Infection, Neutropenia, Prospective study*

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Introduction

Infection is the commonest cause of death in children with cancer.[1] Compromised host defenses, either from the malignancy itself or as a consequence of chemotherapy, radiotherapy, splenectomy or indwelling catheter, all contribute to the high risk of infection in cancer patients.[2] The diagnosis of infection is sometimes made difficult by the absence of an inflammatory response or lymphadenopathy in the granulocytopenic patients. Fever should be considered to be of infectious etiology unless proven otherwise. Fever is defined as a temperature of 38°c 3- times in 24 hours or 38.4c once.[1] Neutrophils play a critical role in protecting the body from infection by the micro-organism that colonize the oropharynx ,gastrointestinal tract and the skin and in the acute response to most infectious and inflammatory disease; whenever there are breaks in the surface barrier, it is the capacity to recruit neutrophils to the site rapidly that determining of an overt infection will occur. At the inflammatory focus, neutrophils ingest and kill bacteria limiting their production of endotoxin and allowing tissue repair to begin. Neutropenia is defined as an absolute neutrophil count (ANC) less than 500/µl or less than 1000/µl and falling.[1] Bacteria account for most of the acute infections in such patients. Previously Gram negative organisms were predominant but now a days Gram +ve organisms are emerging as major causes of bacterial infection[1]. Anerobic bacteria are rare. Fungal and protozoal infections are also observed, when there is prolonged granulocytopenia or immunosuppression and when corticosteroid therapy is used. The frequency & severity of infections in patient with severe neutropenia depends on several factors.

These include the severity of neutropenia and duration of neutropenia, the integrity of the skin & mucous membranes, level and function of monocytes, lymphocytes, immunoglobulins & complement components, & function of the spleen & reticuloendothelial system. A patients general well being including nutritional status, physical strength, capacity to cough & clears secretions, level of consciousness, previous antibiotic exposure and many other factors are also important in determining the occurrence & severity of infectious. In general, a weak & debilitated person with a poor nutritional status, whose body surfaces are perpetuated by catheters & colonized by resistant microorganism after days of antibiotic treatment, is very prone to infection with even a transient period of neutropenia. On the other hand, a relatively healthy individual often can tolerate severe neutropenia for several days.[3,4]

A study was conducted a randomized-controlled, open-label, multicenter clinical trial among high-risk patients from 34 university-affiliated tertiary care medical centers in the United States, Canada, and Australia who were undergoing treatment for leukemia or hematopoietic stem cell transplantation and were hospitalized for empirical treatment of febrile neutropenic episodes, about 60% have been suffering from various magnitude of infection.[5] All of them due to severe neutropenia. Death from ALL mainly due to uncontrollable infection.[5] Inspite of continuing struggle, the problem with mortality among the leukaemic patient with neutropenia still high. Keeping this in view & working under such circumstances we designing a study to detect the organisms or localize cause of infection & appropriate measure for these patient.

Materials and Methods

This was a prospective study done in Dhaka Shishu(Children) Hospital, Sher-e-Bangla Nagar, Dhaka-1207, over 6 months from from 15th November 2006 to 15th May 2007. We included 40 acute leukaemic patients of both sexes with age 2 to 9 years in whom absolute neutrophil count was less than500/cumm either during diagnosis or during treatment were selected for this study. Neutropenia other than acute leukaemia eg. Lymphoma, NHL, Aplastic anemia and age <2 years and > 10 years were excluded. After admission, a detailed history was taken & through clinical examination was conducted in all cases and were recorded in the preformed questionnaire. After clinical diagnosis, a complete blood count with film was done for every patient & subsequently the diagnosis was confirmed by bone marrow study. During neutropenia patients were throughly examined for signs of infection in the sites such as mucosal surface of alimentary tract and skin, where vascular catheter may give as portal for systemic infection. Other sites are gums, pharynx, lungs perineum, bone marrow aspiration sites, venepuncture sites, and the nail bed. Then the patients are screened for infection by doing CRP titre, blood C/S, urine C/S, CXR and stool ZN staining for cryptosporidium. Investigation results were collected in prescribed form. Blood culture and urine culture

were done after 2 days omission of antibiotics. For blood culture 2cc of venous blood after proper aseptic precaution were drawn and send to microbiology department where initial culture were done in Triptone soya broth then subculture were done in three medias such as-Mac conkys agar, blood agar and Chocolate agar. For urine culture 5 cc mid stream urine or from catheter were send to micro biology department, where 2 medias were used such as blood agar and Mac conkys agar and reports were recorded . For CRP 2 cc of venous blood were send to biochemistry department and CRP titre were measured by Dimension clinical chemistry systrem by using Flex reagent cartridge and more than 10 mg/l taken as positive.The data was analyzed according to standard procedure. SPSS version 12.0 for Windows (SPSS Inc, Chicago, IL, USA) software was used for data entry and analysis. Results of the findings was verified by conducting standard tests for significance (p-value < 0.05), including unpaired student T-test and Chi-square (c^2) tests, as appropriate. After explaining the procedures of the study to the parents/caregivers, informed written consent was taken and permission from ethical board of Dhaka Shishu Hospital was taken.

Results

Total 40 patients of acute leukaemia of both sexes in whom absolute neutrophil count is less than 500 who were admitted in Dhaka Shishu Hospital during the study period,were selected as case.

Table I
Age distribution of study population

Age	Number	Percentage
2-3 years	17	42.5%
3-6 years	10	25%
6-9 years	13	32.5%
Total	40	100%

Among all 40 cases 17(42.5%) were within 2 to 3 years age group,10(25%) were 3-6 years age and 13(32.5%) were 6-9 years age.

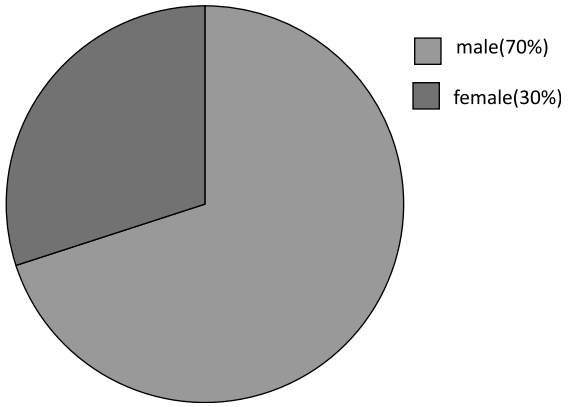

Fig 1 *Pie chart showing male and female distribution of study population.*

Among all 40 patients, majority are male. The ratio is M:F-2.3.1

In this study 100% patients sufferin from fever, majority patients having bone pain, bleeding, lymphadenopathy and organomegaly.

Table II
Characteristics of study population

Patient characteristics		No. of patient	Percentage
Fever during admission	Present	40	100%
	Absent	0	0%
Bone pain	Present	25	62.5%
	Absent	15	37.5%
Bleeding	Present	30	75%
	Absent	10	25%
Lymphadenopahy	Present	30	75%
	Absent	10	25%
Splenomegaly	Present	35	87.5%
	Absent	5	12.5%
Hepatomegaly	Present	36	90%
	Absent	4	10%
Fever during neutropenia	Present	40	100%
	Absent	0	0%
Pulmonary infection(by CXR)	Present	20	50%
	Absent	20	50%

In this study 20(50%) patients Hb was 6 gm/dl (<40%) at the time of diagnosis, majority patients TC of WBC was 10000-20000/cumm in 14(35%) cases at diagnosis, marked leucopenia (<2500/cumm) was found only in 2(5%) cases, absolute neutrophil count in most of the cases were more than 2000/cumm, absolute neutrophil count in most of the study population(23) 57.5% were 201-<500.

Table III
Hemoglobin conc, total leukocyte count and absolute neutrophil count among study population.

Hemoglobin concentration	Hb%	Number	Percentage
	< 6 gm/dl	20	50%
	6-10 gm/dl	15	37.5%
	>10 gm/dl	05	12.5%
Total Leucocyte count during admission	Total leukocyte count	Number	Percentage
	<2500/cumm	2	5%
	2501-5000/cumm	7	17.5%
	5001-10000/cumm	7	17.5%
	10001-20000/cumm	14	35%
	20001-50000/cumm	6	15%
	>50000/cumm	4	10%
Total Leucocyte count . during neutropenia	Total leukocyte count	Number	Percentage
	<1000/cumm	20	50%
	1000-2000/cumm	10	25%
	2001-3000/cumm	10	25%
Absolute neutrophil count in study population during Neutropenia	Absolute neutrophil count	Number	Percentage
	<100	5	12.5%
	100-200	12	30%
	201-<500	23	57.5%

Among all 40 patients, documented infection found in 42.5% patients.

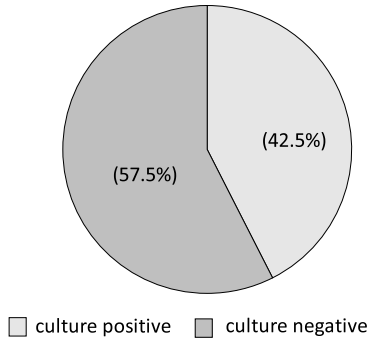

Fig 2 *Pattern of infection in study population*

Among all 40 patients, 62.5% cases CRP titre was positive.

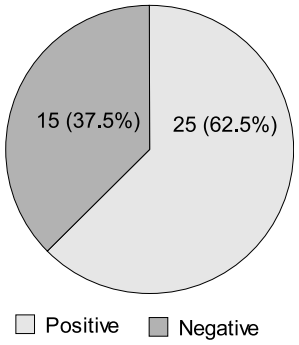

Fig 3 *CRP during Neutropenia in study population*

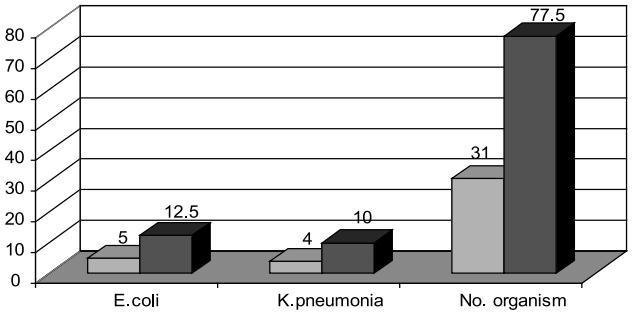

Fig 4 *Urinary organisms isolated in study population during Neutropenia.*

Table VII
Sensitivity pattern of isolated organisms both from blood C/S and urine C/S during neutropenia.

Organism	Sensitive to
E. coli	Imiphenem, Chloramphenical and Amikacin
K. pneumoniae	Imiphenem, Amikacin, Cotrimoxazole and Gentamycin
Acenetobacter	Imipenam

All organisms are resistant to conventional antibiotics.

Discussion

A total of 40 patients studied among all 40 cases, 17 (42.5%) were within 2 to 3 years age group, 10 (25%) were 3-6 years age & 13(32.5%) were 6-9 years. The duration of fever ranged from 7 days to 150 days. Among them 2(5%) were less than 10 days, 21(52.5%) were 10-50 days & 17(42.5%) were more than 50 days. Fever occurred initially at presentation & continued throughout the induction period. Infections, especially septicemia was the commonest cause of fever and must always be considered as likely cause particularly in patient with granulocyte count below 1000/cumm. Bone pain was present in 25 (62.5%) case and absent in 15 (37.5%) , which coincide with previous study where it was 65.6%.[6] But in western study it was 25%.[7] Site of bone pain mostly were in multiple site 13 (32.5%) predominantly in lower limbs 9(22.5%) which coincide with previous study. Bleeding manifestation were present in 30(75%) case only. Bleeding sites involved mostly in the gum & skin in about 17(42.5%) it is always secondary to severe thrombocytopenia, caused by marrow failure. Highest risk of bleeding in patient with platelet count <20,000/cumm. Duration of bleeding in most case was less than 5 days (40%). Pallor was present in 100% of case but severity varied. Anaemia was due to marrow failure which was almost due to direct reduction in steam cells and may associated with ineffective erythropoiesis.[8]There was no patient found where there was H/O cancer in the family. Lymphadenopathy was present in 23(57.5%) & absent in 17(42.5%) patients. In majority of the patients cervical lymph nodes were involved in 13 (32.5%) others were generalized (27.5%) which coincide with Western study where Lymphadenopathy was in 50% of cases.[9] Splenomegaly was found in 35(87.5%) cases & absent in 5(12.5%). It didn't coincide with the previous study where it was 68.8%.[7] Most of the spleen measured within 3-4 cm of the 24(60%) cases and below 2cm in 8(24%).In this study, 20 (50%) patients Hb was 6 gm/ dl (40%) at the time of diagnosis,Hb was 40-60% in15(37.5%) cases.

Among this patients some might have received blood transfusion which has been commonly practiced in our ward. During neutropenia blast cells were <10% in 80(20%) patients in most of the case it was 10-30%. Blood culture positive found in 20% cases which coincide with previous findings which was 20-25%.[10] Among all organism 50% are Gram negative organism such as E. coli, K. pneumoniae and P.aeruginosa[10] but in our study we found E. coli and Acinetobacter.

In our study 8 patients found blood C/S positive E.coli found in 12.5% cases (5 patients), Acinetobacter found in 7.5% cases (3 patients). Urine culture positive found in 22.5% patients, E. coli found in 12.5% patients (5 patients), K. pneumoni found in10% patients (4 patients), which coincides with previous finding,[11] where most common organisms were E.coli and other Gram negative enterics. CRP titre were positive in 62.5% patients & negative in 37.5% patients, but previous finding was 87% in patient of leukemia developed neutropenia due to chemotherapeutic agents , where CRP titre was equal or more than ninety.[12]

Conclusion

Acute leukaemia in children having neutropenia is an omnious sign which may lead to death due to infection. Detection of infection with neutropenia in a leukaemic patient is very difficult as blood culture and urine culture positivity is very less (20% & 22.5% respectively). Fever, CRP and CXR is helpful tools for detecting infection.

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ORIGINAL ARTICLE

Electro Clinical Profile of Children Attending For Electroencephalogram (EEG) at Neurophysiology Laboratory of A Tertiary Care Hospital

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Abstract

Background : *Electroencephalography (EEG) remains the most important investigative modality in the diagnostic evaluation of individuals with epilepsy and other organic brain disease.. Children living with epilepsy in the developing world are faced with challenges of lack of access to ideal centre for EEG Recording and remains a high risk of misdiagnosis and inappropriate therapy.*

Objective : *The aim of the study is to evaluate the EEG findings of the children and corelate them with provisional diagnosis.*

Material and methods : *EEG records of the entire 1417 consecutive cases referred from OPD and IPD during a 1 year period were analyzed. Information on biodemographic data, clinical description of symptoms and provisional diagnosis made by referring physicians and the EEG diagnosis were obtained from the records. The EEG findingss were then compared with the clinical information of the patient and provisional diagnosis made by the physician.*

Results: *The most common age group of children were 0-3 year (59.8%), followed by age group >3-5years (16.4%) respectively. Mostly male (60.06%). EEG was normal in 49.12% and abnormal in 50.88% (epileptic discharge were 33.74% and background abnormalities were 17.14%). About 60.56% of the childrens had h/o of seizure and among them, EEG was found abnormal in 60.48%patients. High abnormal EEG was found in those patients who had provisional diagnosis of CNS infection with seizure (76.09%), then Seizure with comorbidity (69.88%). Generalized seizure (17.15%) and special pattern of discharge (12.77%) were found more than focal seizure(3.81%).*

Conclusion: *Most of the patients referred for the EEG had their reports inconsistent with clinical suspicion. EEG was found to be a useful tool in diagnosis and management of patients with epilepsy and other organic brain disorder.*

Key words*: EEG, Epilepsy, epileptiform discharges*

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Introduction

EEG refers to the recording of the brain's spontaneous electrical activity over a period of time.[1] Electroencephalography was introduced by the psychiatrist Hans Berger of Jena, Germany, in 1929, primarily to study brain dysfunction in mental illnesses.[2] Since it is a convenient, safe and relatively inexpensive way to demonstrate the physiological manifestations of abnormal cortical excitability that underlies epilepsy, EEG continues to play a central role in diagnosis and management of patients with epilepsy in conjunction with the remarkable variety of other diagnostic techniques.[3] A single interictal EEG often helps to classify epilepsy and can provide support for a diagnosis of epilepsy when the clinical features are highly suggestive.[4-6] However, EEG is rarely, if ever, the sole determinant of this diagnosis.[7] EEG can help to predict the risk of recurrence after a first seizure and the risk of relapse after drug withdrawal.[8-9] It may also be recommended to exclude other conditions such as headaches, head injuries, fainting spells, organic brain disorders[10]and psychiatric disorders.[10 14] Several studies have shown that the commonest reason for EEG referral is to diagnose epilepsy.[10,15-16] A study in Kano, Northern Nigeria found that 92% of patients referred for EEG came with a clinical suspicion of seizure disorder.[15] A seizure is any clinical event caused by abnormal electrical discharge in the brain, whilst epilepsy is tendency to have unprovoked recurrent seizure.[17] Epilepsy is the most common cause of morbidity in children worldwide, 80% of whom live in developing countries.[18] In Bangladesh epidemiological surveys confirm that seizure disorders are common, one study showing a prevalence rate of 68 out of every 1000 for 'any seizure history' and 9 out of every 1000 for 'any unprovoked seizure', in children aged 2 to 9 years [19].Even with the tremendous advances in neurodiagnostic procedures, the role of EEG for the diagnosis of epilepsy, organic brain diseases like sub acute sclerosing pan encephalitis (SSPE), Jakob-Creutzfeldt disease(JCD), Herpes simplex virus encephalis (HSV) and to exclude mental health disease is not abolished. Thus, we have attempted to study the relationship between provisional diagnosis and electrophysiological findings of the paediatric patients referred for EEG.

Material and Methods

This retrospective study was carried out in Neurophysiology Laboratory of Dhaka Shishu Hospital (DSH) from 1st January 2015 to 31st December 2015 from different outpatient department (OPD) and inpatient department (IPD) of DSH during this period. Appropriate preparations as hair wash with shampoo and little sleep in the last night were advised, so that patient can sleep on EEG table in the following morning. An EEG database had been maintained for all the cases at EEG laboratory, which included sociodemographic profiles, relevant clinical history and source of referral. Provisional diagnosis was made by referring physicians. EEG diagnosis was obtained from the records. Each recording of EEG were obtained through digital equipments with minimal duration of 30 minutes and electrode positioned on scalp according to international 10 ~ 20 systems. Recording was done in both awake and sleep state, except in very few cases, who didn't sleep following all measures, only awakened state recording was taken. Activation procedures like hyperventilation, sleep, and eyes closure and opening, photic stimulation and tactile stimulation were given for every patient. The EEG was interpretated by consultant neurologists, trained and experienced in neuro-physiology. Different Montages like longitudinal, transverse, average, multiphotic etc were used during review. Electroencephalographic findings of each case were divided into normal and abnormal. The abnormal EEG were categorised as epileptiform discharge and background abnormalities. Epileptiform discharges includes generalized epileptiform discharges, focal epileptiform discharges and special epileptiform patterns like hypsarrythmia, periodic discharge etc. Background abnormalities like polymorphic morphology, generalized or localized slow wave activities.[20] The data was analyzed using the Statistical Package for Social Sciences (SPSS) version 21. Tables and figures are shown for relevant data. Chi-square test is used to see the significance of associations for categorical variables.

Results

Among 1417 patients were referred for EEG, 778 patients came from OPD and 639 patients from IPD (Table I). The most common age group of children were 0-3 year (59.8%), followed by age group >3-5years (16.4%). Mostly male (60.6%) and male female ratio was 1.5:1 (Table 1).

Table I
Sociodemographic factor of the childrens

Variables	Number of Patients (n=1417)	Percentage %
Age groups		
0-3yr	846	59.8
>3-5 yr	233	16.4
>5-7 yr	133	9.4
>7-15yr	182	12.8
>15 yr	23	1.6
Sex		
Male	859	60.6
Female	558	39.4
Residence		
Urban	1082	60.6
Rural	558	39.4
Source of referral		
0PD	778	55
IPD	639	45

Among 1417 patients, 858 (60.56%) patients had history of seizure and 559 (39.44%) patients had no history of seizure. EEG was normal in 696(49.12%) patients and abnormal in 721(50.88%) patients (Fig 1). Among the abnormal EEG epileptiform activity was found in 33.74% and background abnormalities was found in 17.14% (Polymorphic background 5.4%, generalized slow wave 4.7%, localized slow wave 3.7%, nonspecific dysfunction 2.3% and diffuse slow waves 1.1%) (fig 2).

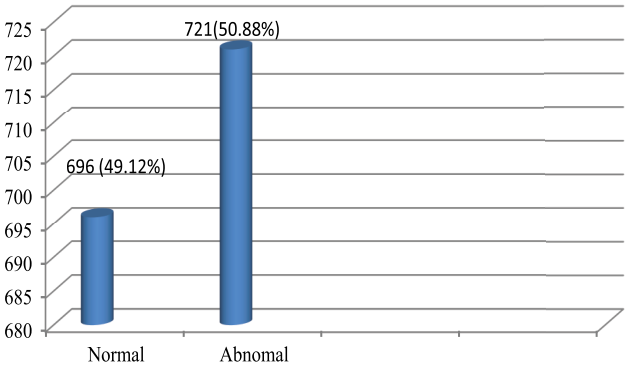

Fig 1 *EEG findings of the patient*

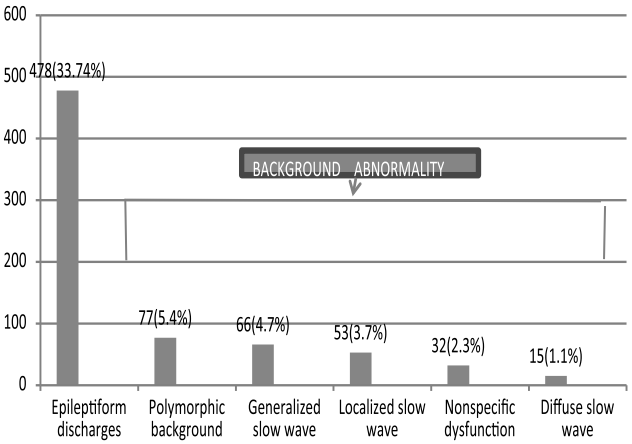

Fig 2 *Abnormal EEG*

Again among 858 patients who had history of seizure, EEG was found abnormal in 519 patients (60.48%), and those who had no h/o seizure, EEG was found abnormal in 36.14% patients (Table-II). From clinical information, number of children who had delayed cry after birth, delayed motor, cognition, vision, hearing and speech were 40%, 49%, 48%, 31%, 29% and 31% respectively and their abnormal EEG findings were 66.54%, 68.20%, 64.30%, 71.42%, 72.55%, 51.50% respectively (Table II).

The provisional diagnosis made by referring physicians were, epilepsy, seizure with co morbidity, febrile seizure, CNS infection with seizure, Breath holding attack, psychomotor delay, Mental health disease and miscellaneous were 8.89%, 35.14%, 13.27%, 3.25%, 1.48%, 15.17%, 15.31%, 7.48% and among each diagnosis abnormal EEG were found in 46.03%, 69.88%, 38.83%,76.09%, 33.33%, 47.43%, 26.26% and 38.68% respectively (Table III). EEG detected significantly high epileptiform discharges in children with h/o CNS infection with seizure (76.09%) and then seizure with co morbidity (69.88%) (Table III). Types of seizure diagnosed by the physician were generalized seizure 43.96%, myoclonic seizure 6.28%, focal seizure 10.24%, and absence seizure 0.071% (Table IV).Pattern of epileptic discharge found in EEG were, generalized epileptiform discharge 17.15%, special epileptiform pattern 12.77%, focal discharge 3.81% (Table IV). There is strong association between provisional diagnosis of seizure and EEG findings (Table IV).

Table-II
Clinical Information of the patients Vs EEG findings

Variables	Number of patients (n=1417)	EEG findings		P value
		Normal N=696	Abnormal N=721	
Birth history				
Immediate cry	855(60%)	508(59.41%)	347(40.58%)	.000
Delayed cry	562 (40%)	188(33.46%)	374(66.54%)	
Developmental History				
Motor				
normal	722(51%)	475(65.78%)	247(34.22%)	
impaired	695(49%)	221(31.80%)	474(68.20%)	
Cognition				
normal	739(52%)	454(61.44%)	285(38.56%)	
impaired	678(48%)	242(35.70%)	436(64.30%)	.000
Vision				
Normal	976(69%)	570(58.40%)	406(41.60%)	
Impaired	441(31%)	126(28.58%)	315(71.42%)	
Hearing	1009(71%)	584(57.88%)	425(42.12%)	
Normal	408(29%)	112(27.45%)	296(72.55%)	
Impaired				
Speech				
Normal	982(69%)	485(49.38%)	497(50.62%)	.329
Impaired	435(31%)	211(48.50%)	224(51.50%)	
History of seizure				
Yes	858(60.56%)	339(39.52%)	519(60.48%)	.000
No	559(39.44%)	357(63.86%)	202(36.14%)	

Table III
Correlation between provisional diagnosis and EEG findings

Provisional diagnosis	Total number of patients	EEG findings			P value
		Normal	Abnormal		
			Epileptic discharge	Background abnormalities	
Epilepsy	126(8.89%	68(53.97%)	45(35.71%)	13(10.32%)	.000
Seizure with comorbidity	498(35.14%)	150(30.12%)	243(48.80%)	105(21.08%)	
Febrile seizure	188(13.27%)	115(61.17%	60(31.91%)	13(6.92%)	
CNS infection with seizure	46(3.25%)	11(23.91%)	22(47.83%)	13(28.26%)	
Breath holding attack	21(1.48%)	14(66.67%)	6(28.57%)	1(4.76%)	
Cerebral palsy	215(15.17%)	113(52.57%)	43(20%)	59(27.43%)	
Mental health disease	217(15.31%)	160(73.74%)	35(16.13%)	22(10.13%)	
Miscellaneous	106(7.48%)	65(61.32%)	24(22.64%)	17(16.04%)	

Table IV
Correlation between pattern of seizure and epileptic discharge

Seizure type	Pattern of epileptic discharge				Total number of patient	P value
	None	Generalized discharge	Focal discharge	Special epileptiform patte\rn		
Generalized seizure	355 (25.05%)	149 (10.52%)	32 (2.26%)	87 (6.14%)	623 (43.96%)	
Focal seizure	64 (4.52%)	6 (0.42%)	1 (.07%)	18 (1.27%)	89 (6.28%)	
Myoclonic seizure	66 (4.66%)	36 (2.54%)	12 (0.84%)	31 (2.19%)	145 (10.24%)	**.001**
Absence seizure	0	0	0	1 (.07%)	1 (.07%)	
None	454 (32.04%)	52 (3.67%)	9 (.64%)	44 (3.10%)	559 (39.45%)	
Total	939 (66.27%)	243 (17.15%)	54 (3.81%)	181 (12.77%)	1417 (100%)	

Discussion

In socio demographic strategies of our study we found male is more than female with a male female ratio was 1.5: 1 and the most common age group was 0-3 yr (60%). In a study done in Nepal during the three-year study period, the number of male children undergoing EEG was almost three times more than that of female and most common age group was between one to five years.[21] The study found that 60.56% patients had history of seizure and among them EEG was found abnormal in 60.48%, This findings is almost similar to a study done in Nigeria where 92% of patients referred for EEG was for seizure but only about 58% had abnormal EEG findings.[22] Another study in Nigeria showed that 79.5% of attendees were referred with a provisional diagnosis of seizure disorder.[23] Seizure with co-morbidity (35.14%) was the most common referral cases for EEG, followed by mental health disease15.31% and cerebral palsy 15.17%. Others were febrile seizure 13.27 %, miscellaneous 7.48%, CNS infection with seizure 3.25% and Breath holding attack 1.48%. This study did not match with a previous study in Nepal where epilepsy (59.39%) was the most common referral cases for EEG, followed by febrile seizure (15.08%), CNS infection with seizure (6.26%), seizure with co-morbidity (2.56%) and cerebral palsy (1.60%).[21] In CNS infection with seizure EEG recording was abnormal in 76.09%, which is very high in this study compare to other studies in Nepal and India where abnormal EEG was found in meningitis/encephalitis in 48.71 % and 50 % respectively.[21,24] In seizure with co morbidity, EEG recording was abnormal in 69.88% which is very similar to a previous study in Nepal where 68.75% children had EEG abnormalities.[2] [1]In cerebral palsy without history of seizure EEG were abnormal in 47.43% cases in this study. Other studies showed that there is relatively high incidence (44%) of epileptiform discharges even in children without clinical evidence of seizures peaking between the ages of four and six years.[25] In febrile seizure and breath holding attack EEG were abnormal in 38.83% and 33.33% respectively and normal in 61.17% and 66.67% cases respectively. Overall, EEG detected significantly less epileptiform activities in febrile seizure and breath holding attack. Studies have shown that the yield of routine EEG is low in neurologically normal children with febrile seizures even if the seizure is complex.[26] Other showed that 15% of all EEGs recorded for febrile seizures and only 4.85 % were abnormal with background rather than epileptiform abnormalities.[27] Therefore, there are suggestions that the routine practice of obtaining EEG in neuro developmentally normal children with febrile seizures is not justified.[28] Our findings are supported by these reports though abnormal EEG was more in our study than in those studies. In Mental Health disease EEG was abnormal in 26.26% cases and normal in 73.74%cases**.** This is almost

similar to a retrospective observational study of clinical EEG of patients with acute psychiatric problem, where abnormal EEG was identified in 17 % of the patients.[29] So EEGs were conducted when there were sudden changes of behaviour, signs of excessive irritability, hyperactivity, sleep complaints, and any other paroxysmal events. On the basis of clinical history and examination, 858 patients had h/o seizure, among them generalized epilepsy was found in a majority of children (43.96%), followed by myoclonic (10.24%), and focal (6.28%) seizure. This study did not differ much with a study in a paediatric unit of a Nigerian hospital, where generalized tonic–clonic seizures accounted for 62.2% of cases and partial seizures for 17.4% on the basis of clinical evidence.[30] When EEGs were considered, this study found generalized epileptiform discharge (17.15%) more than focal epileptiform discharge (3.81%). This is almost similar to a study where retrospective analysis of 493 EEG tracing from 180 generalized epilepsy patients showed that 33% had generalized spike or polyspikes, while 22% had focal discharges [31.] But this study differ from a study done in Nigeria and Bangladesh where they found focal epileptiform discharge more than generalized epileptiform discharge.[30,32] High abnormal EEG was found in this study who had history of delayed cry after birth and impaired or delayed in one or more domain of development. These predictive risk factors findings were important for future prognosis and outcome of seizure remission. Previous study done in Bangladesh had shown that neurodevelopment morbidities (high rates of seizures, multiple seizure types, associated motor disability, and poor cognition) were found to be significant predictors of poor seizure remission.[32]

Interestingly this study found almost half of the patients had normal EEG (49.12%). Published figures for diagnostic sensitivity of EEG range between 25 to 55 %, 29 to 38%.[33,34] On a first standard EEG recording, around 40 % of children with seizures will have a normal record or up to about half of patients with epileptic disorders may have one normal inter-ictal EEG. [33-35] Hence, a normal or negative EEG cannot be used to rule out the clinical diagnosis of Epilepsy.

There is some limitation of the study. First of all it is a single centre study. Another limitation of this study is its retrospective study design. Some of the EEG records had incomplete information about clinical signs, symptoms and provisional diagnosis.

Conclusion

The study showed significant relationship between provisional diagnosis and EEG findings. Most of the EEG findings were inconsistent with clinical suspicion. EEG was found to be a useful tool in diagnosis and management of patients with epilepsy and other organic brain disorder if it is done with appropriate preparations and procedures.

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REVIEW ARTICLE

IgA Nephropathy (Igan) : Recent Advances and Opportunities

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Introduction

Immunoglobulin A (IgA) nephropathy, or Berger disease, is the most common form of glomerulonephritis worldwide which was first described by Berger and Hinglais in 1968, based on the finding of predominant IgA deposition in the mesangium with a mesangial proliferation . It was initially considered a benign condition, but extended follow-up showed that IgA nephropathy can lead to significant kidney damage, and progression of disease usually develops at 15-20 years after disease onset.

Due to increased collaborative efforts of well powered clinical and genetic studies recent years have brought remarkable progress in the field of IgAN. Landmark developments include the discovery of new genetic susceptibility loci, formulation of the multi hit pathogenesis model , introduction of the Oxford pathology scoring system, and formalization of IgAN Kidney Disease Improving Global Outcomes (KDIGO) consensus treatment guidelines. This review, mainly high light the update on these developments and outline the remaining areas of uncertainty.

Epidemiology

Depending on the geographic region, the prevelance of Ig A Nephropathy tends to be highly variable, ranging from 5% in the Middle East,[1] 10–35% across Europe[2,3,4] and up to 50% in Japan and China.[5,6] However this metric can be affected by disparities in local biopsy practices and local incidence of other glomerular diseases. Despite these limitations, some important prevalence patterns have clearly evident.[7] Most notably, there is a clear West-to-East prevalence gradient, with the disease being most common in East Asia (32–54% of primary GN in China [8] and Japan [9] compared with European countries (10–35% of primary GN).[10,11,12]

Diagnosis

IgA Naphropathy typically occurs at all age more commonly in second and third decades. The disease has a wide spectrum of clinical presentation, ranging from asymptomatic microscopic hematuria to a more severe course characterized by sustained proteinuria and rapid deterioration of renal function. Definitive diagnosis of IgAN requires a kidney biopsy; the disease is defined immune histologically by dominan or codominant glomerular deposits of IgA.[13] According to recent consensus, the IgA should be at least 1+ in intensity[14] and in most cases is 2+ or more and involves the glomeruli diffusely. Typically, there is an obvious dominant staining for IgA with weaker and more variable staining for IgG and/or IgM.[15] C3 deposits were observed in a similar distribution pattern in 64% cases. The early components of the classical complement pathway, C4 and C1q are absent. Fibrin or fibrinogen products related antigens were observed in diffuse mesangial distribution in 25-75% cases and represents injurious marker for the kidney. The deposits consist predominantly of polymeric IgA of the IgA1 subclass.[16] The stronger staining for ë light chain reflects the predominance of IgA1-ë in the circulation.[17,18] IgAN has diverse histologic features. These include no or minimal abnormalities by light microscopy, mesangial hypercellularity, endocapillary proliferative, necrotizing and crescentic lesions and rarely, membranoproliferative patterns of injury.[19]

Classification

In the past, Heuristic classification, Lee et al and Hass et al score systems were applied to IgAN,[20] which mostly based on the pattern and severity of the proliferative and sclerosing lesions. Finally, the

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Oxford IgAN classification, devised by a working group of over 40 nephrologists and pathologists representing the International IgA Nephropathy Network and the Renal Pathology is unique as the first evidence-based schema which can predict progression in a large disease cohort with known outcomes, and thus represents a scoring system. The major limitation of the Oxford system is that the study has not describes the impact of crescents and specific immunofluorescence features, such as the presence of peripheral capillary wall deposits of IgA and co deposits of IgG.[21]

A number of studies have attempted to validate the predictive value of the MEST lesions in independent cohorts from North America, Europe, and Asia, including pediatric cases. The largest meta-analysis based on 16 retrospective cohort studies and involving a total of 3893 IgAN cases validated the predictive utility of the M, S, and T lesions but did not confirm the prognostic value of the E score.[22] Although the E score exhibited some of the weakest and most heterogeneous associations with disease progression, the T score was consistently the most significant predictor of poor renal outcomes across all cohorts. In addition, 5 of 16 studies examined the association of crescents with clinical outcomes; meta-analysis of these studies showed that the C score (defined as the presence of any crescents) was strongly associated with progression to kidney failure.[23] Lastly, the recently published VALIGA (European Validation of the Oxford Classification of IgAN) study of 1147 patients from 13 European countries provided an independent validation of the predictive value of the M, S and T lesions across a broader spectrum of the disease. They have showed that the combination of MEST score with readily available blood pressure, proteinuria, and eGFR at the time of biopsy predicted the composite renal outcome similar to using clinical data over 2 years of follow-up which provide illustrations of the clinical utility and potential therapeutic implications of the earlier risk stratification provided by the Oxford Classification.[24] In summary, the Oxford scoring system represents an important step toward improved prognostication and standardization of diagnosis, but further refinements of the score may be needed to enhance its prognostic utility.

Pathogenesis and Genetics of IgA Nephropathy

Although the pathogenesis of Ig A nephropathy remains unclear, there is substantial evidence that it is a immune complex mediated disease. Galactose-

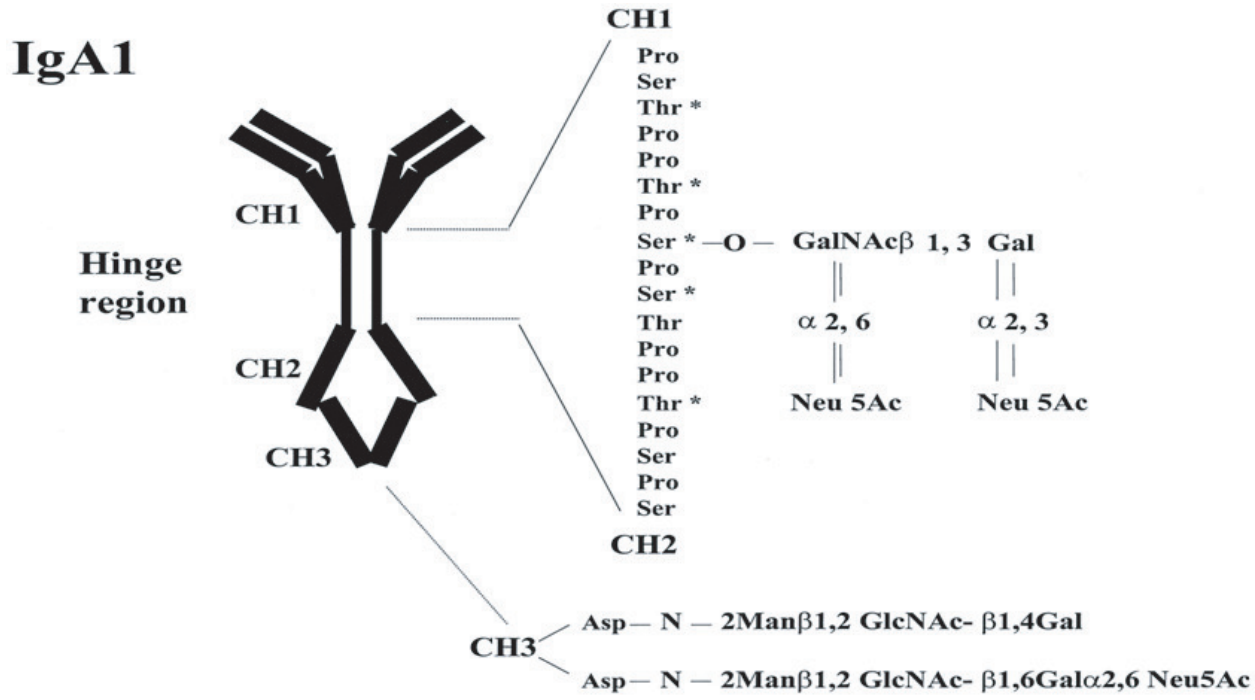

Fig 1 *Structure of Ig A IgA1 heavy chains contain a hinge region segment which is the the site of O-glycosylation, with nine potential sites for attachment of O-glycans. Normal human circulatory IgA1 has O-glycans consisting of N-acetylgalactosamine (GalNAc) with â1,3-linked galactose; each saccharide can also be sialylated.*

deficient variants of IgA1 (Gd-IgA1) are more common in the sera of IgA nephropathy patients compared with that of healthy and disease controls.[25] Recent studies suggest that some individuals with high levels of Gd-IgA1 are prone to auto-sensitization and production of anti–Gd-IgA1 antibodies with formation of immune complexes[26] which strongly implicate an auto immune etiology of IgAN autoimmune disorders.[27] Additionally, GWAS highlighted the involvement of the mucosal defense system and the alternative complement pathway.

IgA1 structure and O glycosylation pathway

Patients with IgAN have a greater fraction of circulatory IgA1 molecules with hinge-region O-glycans without galactose, i.e., consisting of terminal GalNAc or sialylated GalNAc. This galactosylation defect appears to be specific for IgA1, and this defect represent a risk for nephritis and more rapid progression of kidney disease.[27-30] Recent evidence indicates that some galactose-deficient O-glycans may be present at residues threonine 233 (Thr233) and Thr236 in normal serum Ig A.[29] The initiation of O-glycosylation is catalyzed by GalNAc transferases (GalNAc-Ts).

Additional insights from genetic studies

Numerous evidence support a strong genetic contribution to IgAN. First, significant geographic and ethnic differences exist in the prevalence of Ig A N.[30] Second, familial aggregation of the disease has been well recognized.[31]In most reported families, Ig A N follows autosomal dominant transmission with incomplete penetrance. The GWAS approach has emerged as a powerful alternative to family-based studies for complex traits and has been successfully applied to IgAN. By design, the major limitation of GWAS is that they detect only common susceptibility variants, and these typically have relatively small effects.[32] In the case of IgAN, by GWAS in the field of autoimmune and inflammatory diseases, over 500 genome-wide significant susceptibility loci discovered to date. By through careful analysis several causal candidate genes have been prioritized, providing novel insights into the pathways driving the pathogenesis of IgAN.The implicated pathways include the antigen processing and presentation pathway (three loci on chromosome 6p21 in the MHC region), the mucosal immunity pathway (chromosomes 22q12 HORMAD2 locus, 8p23 á-defensin [DEFA] locus, and 17p13 TNFSF13 locus) and the alternative complement pathway (chromosome 1q32 complement factor H [CFH] locus).[33-35]

Antigen processing and presentation pathway

All three GWAS of IgAN identified strong signals with genome-wide significance within the MHC region. Further dissection of these signals using conditional analyses defined three distinct susceptibility loci on chromosome 6p21: HLA-DRB1/DQB1, HLA-DPB1/DPB2, and TAP1/PSMB9.The strongest association was observed in the region that included the HLA-DRB1 -DQA1 and -DQB1 genes The second distinct MHC locus was centered over the region of the HLA-DPA1, -DPB1, and -DPB2 genes, but the causal variant at this locus and its involvement in IgA N are unknown at present. The third MHC locus contained the TAP1, TAP2, PSMB8, and PSMB9 genes. These genes also play an important role in modulation of cytokine production and cytotoxic T cell response.[36] In summary, GWAS support a complex pattern of association in the MHC region and strongly implicate the antigen processing and presentation pathway in the pathogenesis of IgAN.

Mucosal immunity and regulation of IgA production

Secretory IgA is plays a important role to intestinal homeostasis between the host and commensal bacteria. Patients with selective IgA deficiency often develop IBD and recurrent intestinal infections.[37] The inability of secretory IgA to activate the classical complement pathway may also play a role in creating a more tolerant non-inflammatory host-microbial relationship.Clinical associations of macroscopic hematuria coinciding with mucosal infections led to the hypothesis that defects in the regulation of local IgA response and/or abnormal mucosal antigen handling may trigger IgAN.[38] Among different pathogen classes, the strongest association was found for local helminth diversity (defined as the number of endemic helminthic species infecting humans in a given geographic.[39] In aggregate, these findings gave rise to a novel hypothesis that higher genetic risk of IgAN in Asia represents an untoward consequence of protective adaptation to worm infections. Further studies will be needed to test this intriguing new hypothesis.

Intestinal network of IgA production

This hypothesis is also supported by GWAS. A GWAS locus on chromosome 17p13 contains TNFSF13, which encodes a proliferation-inducing ligand (APRIL). This molecule is involved in T cell–independent generation of IgA-secreting plasma cells, as well as IgA1 to IgA2 class switching.[40,41] Serum levels of APRIL are elevated in some patients with IgAN.[42] and the 17p23 risk variant was reported to increase total serum IgA. Inactivation of Tnfsf13 in mice produces partial IgA deficiency and reduced IgA antibody responses to mucosal immunization. Conversely, over expression of B cell activation factor (BAFF), results in autoimmune disease with commensal flora-dependent mesangial IgA deposits in mice.[43] These data strongly implicate APRIL and BAFF signaling in the pathogenesis of IgAN.

Alternative complement pathway

GWAS also support alternative pathway activation in IgAN. Inheritance of a common deletion in factor H-related genes 1 and 3 (CFHR3,1-del) provides additive protection from IgAN.[44] CFHR1 and CFHR3 encode regulatory proteins that promote activation of the alternative pathway, likely through a competitive inhibition of factor H (FH).[45] Recent data suggest that CFHR3,1-del is associated with higher levels of circulating FH and lower levels of complement activation split products in IgAN.[46]

The multihit pathogenesis model

Abnormalities in the production of IgA1, leading to elevated levels of galactose deficient IgA1 (Gd-IgA1), represent the first hit in the model. More recent study suggests that elevated Gd-IgA1 elicits an autoimmune response, resulting in the generation of anti-glycan antibodies that recognize N-acetylgalactosamine epitopes on Gd-IgA.This anti-glycan response may represent a second hit in the model. The elevation of both Gd-IgA1 and anti-glycan

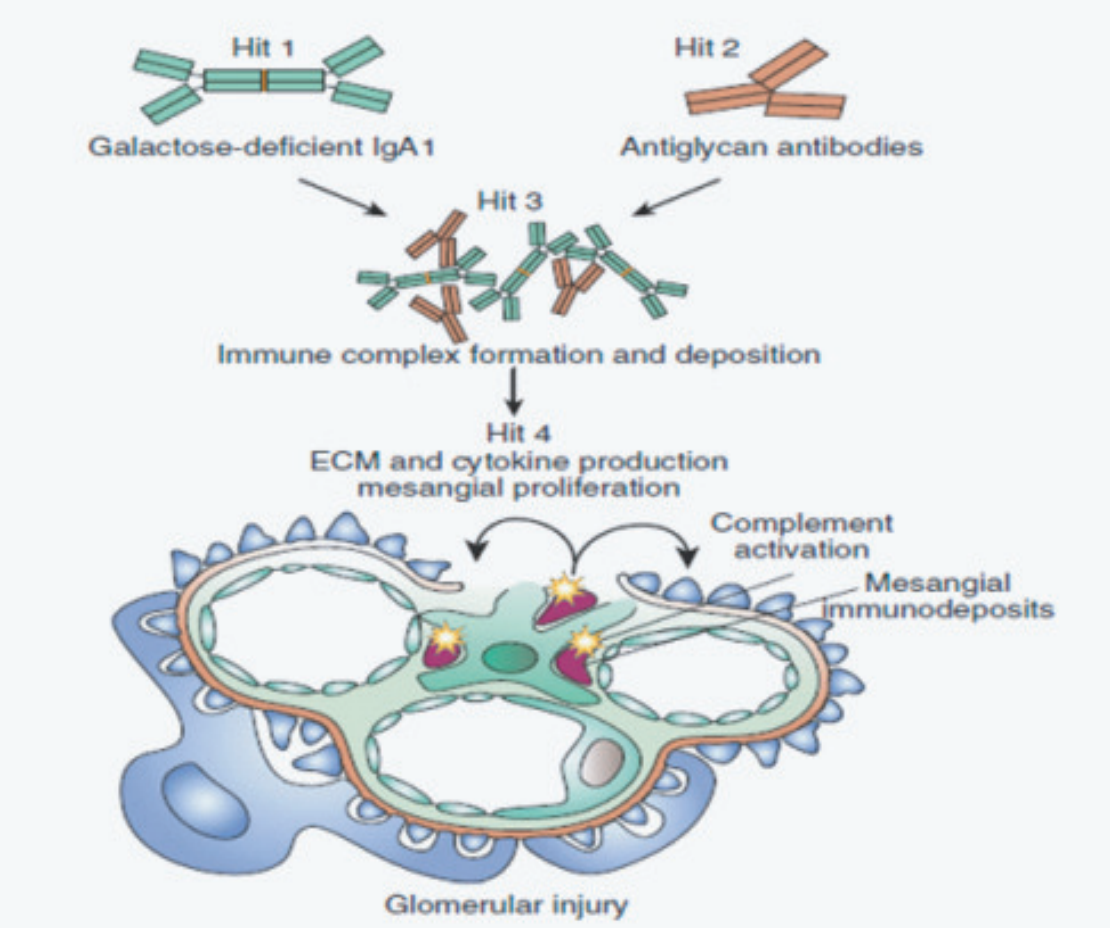

Fig 2 *Hit 1 formation of galactose deficient Ig A, Hit 2 :formation of antiglycane antibody Hit 3:immune complex formation and deposition Hit 4 : glomerular injury*

antibodies leads to the formation of immune complexes (Hit 3), which then deposit in the glomerular mesangium.[47] This deposition activates the complement pathway, stimulates mesangial cells, and induces secretion of cytokines, chemokines, and extracellular matrix proteins resulting in inflammation and fibrosis (Hit 4).

The treatment and prognosis of IgA nephropathy Treatment of Ig A Nephropathy becomes a therapeutic challenges for physician, as appropriate treatment is still a matter of controversy. At present there is no curative treatment for Ig A Nephropathy.The new Kidney Disease Improving Global Outcomes (KDIGO) clinical practice guidelines for glomerulonephritis provide an evidence-based review and appraisal of the literature on treating IgAN which was published on 2012. Based on this treatment a number of randomized controlled trials (RCTs) showed reduction of proteinuria and delay of GFR deterioration.[48] However, it remains unclear at what level of proteinuria this therapy should be initiated. Several small studies suggest a benefit in proteinuria reduction with combined angiotensin converting enzyme inhibition and angiotensin receptor blocker use [49] but there are no data showing decreased rate of renal failure or mortality The KDIGO guidelines suggest the use of a 6-month trial of corticosteroids in patients with persistent proteinuria of >1 g per day, despite 3–6 months of optimal supportive care. This recommendation is based on three RCTs performed in patients with generally preserved renal function[50] and a meta-analysis, which showed that steroids reduce kidney disease progression in this setting.[51] It is unclear at what level of reduced renal function this therapy becomes futile and whether patients with lower levels of proteinuria should also be treated.[52] The outcome of immunosuppressive therapy in addition to supporative care are uncertain. Recently a randomized control study conducted by STOP – IgAN was done which suggests that patient with early stage of IgA nephropathy ,mild disease are probably more likely to have remission of protienuria than adult patients with immunosuppressive therapy.[53] For patients with crescents involving over 50% of glomeruli required aggressively treated with pulse solumedrol followed by oral corticosteroids and intravenous cyclophosphamide.[54] Rituximab therapy has not yet been used in a significant enough number of patients to be recommended; however, data from studies on other crescentic diseases suggest a potential benefit. Similarly, the use of mycophenolate mofetil and azathioprine are generally not recommended in KDIGO guideline. Azathioprine offered no additional benefit in a recent well-designed RCT.[55] One recent study done by kang et al showed steroid-resistant IgAN children with nephrotic syndrome, whose renal pathological changes were serious, found that the therapeutic effect of MMF was dramatic which is different from the results of Maes et al and Frisch et al who reported that MMF does not affect urinary protein excretion or improve renal function in adult patients. Study also showed that most patients who had the T1 or T2 variable of the Oxford MEST classification were resistant to MMF treatment, most of those with T0 were sensitive to MMF treatment.[56] Fish oils may be potentially useful in patients with persistent proteinuria > 1 g per day, despite 3–6 months of optimized supportive car. The effect of fish oil is dose dependant and different RCTs give equivocal results on the benefit of fish oils.[57] However, this treatment should not replace corticosteroids, for which the evidence is stronger . Tonsillectomy not recommended, unless specifically indicated by recurrent episodes of tonsillitis with synpharyngitic symptoms of Ig A , as there was no supportive data.The evaluation of KDIGO guidelines made it clear that the effectiveness of the existing therapies is limited and targeted treatments, more specific to the pathogenic process in IgAN.

Future directions

There are some new important studies underway to overcome some of the most critical clinical problems outlined above.Budesonide, a glucocorticoid locally released in the ileocecal region near the Peyer's patches, is being studied in a larger controlled trial after proving successful in a small pilot trial. Other promising agents include bortezomib (proteosome inhibitor), fostamatinib (Syk inhibitor), blisibimod (BAFF inhibitor), and atacicept (humanized recombinant TACI-IgGFc fusion protein with anti-APRIL and anti-BAFF activity).[58] In addition, the discovery of the protective effect of CFHR1,3-del suggests that pharmacologic suppression of the alternative complement pathway may be of potential benefit in IgAN. GWAS loci discovered to date explain o8% of the disease risk, suggesting contributions of additional, yet unidentified, genetic and environmental factors.

Lastly, the ongoing studies aimed at refining the multihit model are likely to define new biomarkers and potential therapeutic targets. Integration of this model with additional genetic discoveries may finally lead to improved disease classification and novel personalized treatment strategies.

Conclusion

The prognosis of IgAN is quite variable and the outcome remains difficult to predict in individual patients. Early diagnosis, treatment and improvement of predictive factors for a long duration may lead to better renal prognosis in patients with IgA nephropathy.

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REVIEW ARTICLE

AFP surveillance and polio certification in Bangladesh

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Abstract

Expanded Programme on Immunization is one of the most successful program of Government of Bangladesh and surveillance activity in EPI for Vaccine Preventable Diseases (VPDs) has entered an historic new period in maintaining polio free status from 22 November 2006 after experiencing importation from the neighboring country. Poliomyelitis has appeared in epidemic form, become endemic on a global scale, and been reduced to near elimination, all within the span of documented medical history. Epidemics of the disease appeared in the late 19th century in many European countries and North America, following which polio became a global disease with annual epidemics. During the period of its epidemicity, 1900-1950, the age distribution of poliomyelitis cases increased gradually. Beginning in 1955, the creation of poliovirus vaccines led to a stepwise reduction of poliomyelitis, culminating in the unprecedented elimination of wild polioviruses in the United States by 1972. Global expansion of polio immunization resulted in a reduction of paralytic disease from an estimated annual prevaccine level of at least 600,000 cases to fewer than 1000 cases in 2000. Indigenous wild type 2 poliovirus was eradicated in 1999, but unbroken localized circulation of poliovirus type 1 and type 3 continues in 3 countries in Asia and Africa. Bangladesh along with 10 other countries of WHO South-East-Asia Region was certified polio free on March 27, 2014 by an independent commission under the WHO certification process. Bangladesh is maintaining a very high OPV3 coverage of more than 90%, national fully valid vaccination coverage of 82%, and a very strong AFP surveillance system, which are comparable to first world countries.

Key Words: *Poliomyelitis, Acute Flaccid Paralysis, Eradication*

Introduction

Poliomyelitis is a highly infectious disease caused by poliovirus and it is still an important disease which causes a substantial disability due to paralysis. Poliovirus is a member of the enterovirus subgroup, family Picornaviridae and transient inhabitants of the gastrointestinal tract. There are three poliovirus serotypes (P1, P2 and P3) and the most frequent cause of polio epidemic is P1 but the most frequent vaccine associated paralytic polio (VAPP) is caused by poliovirus type 3. Poliovirus varies substantially in their paralytogenecity; type 1 accounted for approximately 80% of paralytic cases.[1, 2] There are minimal heterotypic immunity between the three serotypes. Poliovirus is found only in human beings; there is no animal/extra human reservoir and it mainly affects children under five years of age. Since most infections are subclinical, paralytic cases represent only the tip of the epidemiologic iceberg. Flaccid paralysis occurs in less than 1% cases and approximately 1 in 200 infections leads to irreversible paralysis usually in the lower limbs. Among those

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paralyzed, 5-10% dies when their respiratory muscles become paralyzed. [3, 4] Disease surveillance may be defined as ongoing collection and analysis of information about cases of a disease as a basis for planning, implementing and evaluating disease prevention and control activities. Surveillance activities in EPI for VPDs (Vaccine Preventable Diseases) was started in 1995 with AFP surveillance for polio eradication and Bangladesh was committed to eradicate poliomyelitis as a co signatory of 1988 World Health Assembly (WHA) resolution for global polio eradication.[5,6]

Epidemiology

Though rare in the Western world, polio is still endemic in South Asia and Africa, particularly Pakistan and Nigeria respectively. Following the widespread use of poliovirus vaccine in the mid 1950s, the incidence of poliomyelitis declined dramatically in many industrialized countries which reduced the number of annual diagnosed cases by 99%; from an estimated 350000 cases in1988 to a low of 483 cases in 2001, after which it has remained at a level of about 1000 cases per year (1606 cases in 2009). [6,7] In 2012, cases decreased to 223 and transmission of indigenous wild poliovirus has continued uninterrupted in three countries (Nigeria, Pakistan and Afghanistan) and remained endemic again in 2013 in those three countries although it continued to cause epidemics in other nearby countries due to hidden re-established transmission.[8] For example, despite eradication ten years prior, an outbreak was confirmed in China in September 2011 involving a strain prevalent in neighboring Pakistan.[9] In 2013, the Center for Disease Control published reports of 183 cases of polio in Somalia, 14 in Kenya, 8 cases in the Somali Region of Ethiopia and 15 cases were confirmed among children in Syria between October and November 2013 and it was the first outbreak in Syria since 1999.[10,11,12]

History

The effects of polio have been known since prehistory. Egyptian paintings and carvings depict otherwise healthy people with withered limbs and children walking with canes at a younger age. The first clinical description was provided by the English physician Michael Underwood in 1789, where he referred to polio as debility of the lower extremities.[1,13] In the United States, the 1952 polio epidemic became the worst outbreak in the nation's history. Nearly 58000 cases reported, 3145 died and 21269 were left with mild to disabling paralysis and intensive care medicine has its origin in the fight against polio.[13] The World Health Organization estimated that there are 10-20 million polio survivors worldwide with varying degrees of paralysis. Global Polio Eradication program was initiated in 1988 when 125 countries were endemic and globally about 350000 cases were reported to WHO. The countdown for polio eradication began in 1995, when Bangladesh showed leadership in the region by conducting its first National Immunization Days (NIDs) on March 16 and April 16, 1995. From 1995 to 2014, total twenty one NIDs and one Sub- National Immunization Day (SNID) were conducted in Bangladesh. In 1999, a total of 29 polio cases were reported from 18 districts in all six divisions. Before importation in 2006, last polio case detected in a slum area of Dhaka City Corporation on August 22, 2000, was the last confirmed indigenous poliomyelitis case in Bangladesh before importation.Till then no polio case was detected until early 2006 and Bangladesh was polio free for more than five years. [5]

Polio eradication was certified in the American Region in 1994, in the Western Pacific Region in 2000, in the European Region in 2002 and in the South-East Asia Region on March 27, 2014.[14-17] The eleven countries in the region – Bangladesh, Bhutan, Democratic People's Republic of Korea, India, Indonesia, Maldives, Myanmar, Nepal, Sri Lanka and Timor-Leste- are home to 1.8 billion people and represent the fourth of six WHO regions of the globe to be officially certified polio-free. India, once deemed the most difficult place to end polio, recorded its last case in January 2011, enabling completion of regional certification. Other countries such as Sri Lanka, Maldives and Bhutan have been polio free and waited for this day for more than 15 years.[17]

South-East Asia's remarkable achievement in ending polio was made possible by unprecedented commitment from governments to hold high quality vaccination campaigns that reached a cumulative total of 7.5 billion children over 17 years, in every home the busiest city street to the remotest rural corner, with the dedication of millions of community health workers and volunteers. Between 1995 and 2012, the polio programme conducted 189 nationwide campaigns across the region and administered more than 13 billion doses of oral polio vaccine.[5, 18]

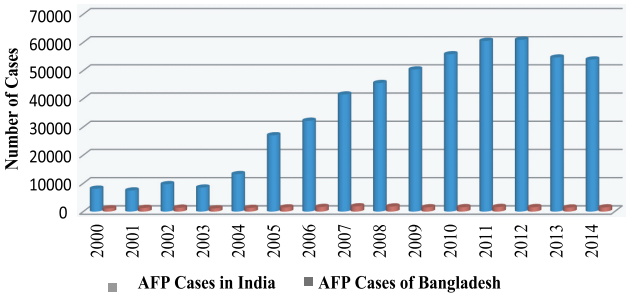

Fig 1 *Reported number of Acute Flaccid Paralysis cases of Bangladesh and India 2000-2014.*[24]

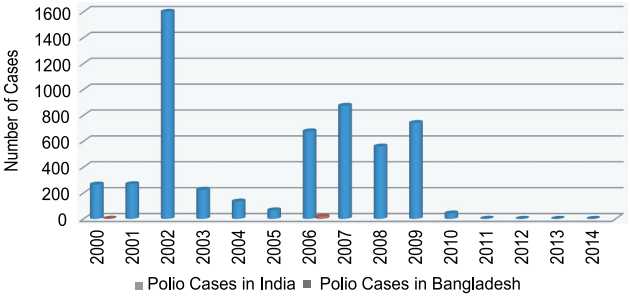

Fig 2 *Wild polio virus case report of Bangladesh and India 2000-2014.*[24]

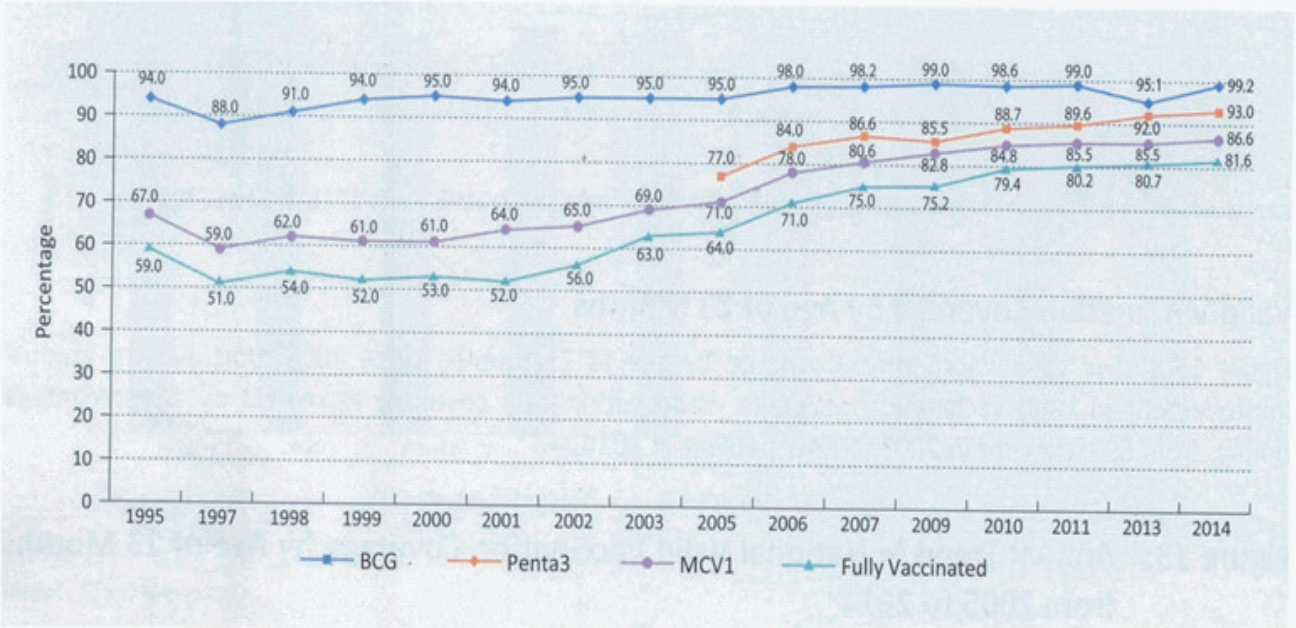

Fig 3 *Annual trend in national valid vaccination coverage by age 12 months among 12-23 months old children from 1991 to 2014*

Now 80% of the world's population lives in regions certified polio free- the WHO Regions of the Western Pacific, South-East Asia, Europe and the Americas - the goal of eradication is closer than ever. However, this progress is at risk unless the polio is ended in the three countries where it has never been stopped i. e. Afghanistan, Pakistan and Nigeria. Recent outbreaks in the Middle East and the Horn of Africa are stark reminders that polio anywhere is a threat everywhere. Until polio is stopped in the remaining three endemic areas, all countries need to maintain sensitive surveillance and high immunization rates to rapidly detect any importation of poliovirus and minimize its impact.

Strategies adopted in Bangladesh

Bangladesh has integrated disease surveillance that is called AFP and VPDs disease surveillance. The diseases under surveillance are Polio (any age), AFP (<15 years), Neonatal Tetanus (d"28 days), Tetanus (any age after neonatal period), Measles (any age), Diptheria (any age), Pertussis (any age) and Tuberculosis (<5years). Bangladesh has also incorporated AEFI (Adverse Event Following Immunization) surveillance in EPI as an effective means of monitoring immunization safety and contributes to the credibility and quality of national immunization programme.

Strategies of Polio Eradication are:

1. Strong Routine Immunization programme
2. National or Sub-National Immunization Days (NIDs/SNIDs)
3. Acute Flaccid Paralysis (AFP) Surveillance
4. Mopping-up immunization

Table I

Country	BCG					DPT3/PENTA3					OPV3					MCV				
Yr 2008-12	08	09	10	11	12	08	09	10	11	12	08	09	10	11	12	08	09	10	11	12
Bangladesh	90	94	94	95	95	95	96	95	96	96	95	96	95	96	96	96	98	94	96	96
India	87	87	87	87	87	72	72	72	72	72	70	70	70	70	70	74	74	74	74	74
Sri Lanka	99	99	99	99	99	98	97	99	99	99	98	97	99	99	99	98	97	99	99	99
Nepal	87	94	94	97	96	82	89	82	92	90	82	93	83	92	90	79	90	86	88	86
Maldives	99	99	97	98	99	98	98	96	96	99	98	98	97	96	99	97	98	97	96	98
DPR Korea	97	98	98	98	98	92	93	93	94	96	98	98	99	99	99	98	98	99	99	99
Myanmar	88	93	93	93	87	85	90	90	86	85	85	90	90	90	87	82	87	88	88	84
Indonesia	80	78	80	80	81	65	62	62	62	64	72	67	66	65	69	76	74	75	74	80
Thailand	99	99	99	99	99	99	99	99	99	99	99	99	99	99	99	98	98	98	98	98
Bhutan	99	94	96	95	95	96	93	91	95	97	96	93	92	95	97	99	94	95	95	95
Timor-Leste	85	71	71	68	71	79	72	72	67	67	79	78	72	66	66	73	70	66	62	62
SEAR	87	87	87	88	88	75	75	74	75	75	74	74	74	74	74	77	78	77	77	78

Source: WHO/UNICEF estimates, 2013

The local health official responsible for disease surveillance activities is called the Disease Surveillance Focal Person (DSFP). The DSFP is the Civil Surgeon (CS) for district, Chief Health Officer (CHO) for City Corporation, Upazila Health & Family Planning Officer (UH&FPO) for Upazila and Municipal Medical Officer (MMO) for Municipality. If MMO post is lying vacant then UH&FPO of respective Upazila acts as DSFP for that municipality. The DSFP is responsible for managing all disease surveillance activities in his/her assigned geographic area. To assist DSFP in carrying out his/her surveillance responsibilities, Local Surveillance Officer (LSO) who would be specifically responsible for implementing surveillance activities including case investigation, outbreak investigations, case or outbreak response immunization and report to DSFP. The LSO for district is Medical Officer-CS (MOCS), for City Corporation is Health Officer/ Assistant Health Officer/Zonal Medical Officer, for Upazila is MO-MCH/MO-DC and for Municipalities is Municipal Medical Officer (MMO). Hospital Surveillance Officer (HSO) has to facilitate and coordinate surveillance activities in Hospital, should be designated by the Director/Superintendent of the Hospital. HSO is responsible for managing hospital surveillance system and for preparing and submitting AFP and EPI Diseases Weekly Line Listing Form for Hospitals and Upazila Health Complexes to DSFP. For case-based surveillance HSO is responsible for notification, initiate case investigation, ensure sample collection, storage and sending of specimen to National Polio and Measles Laboratory (NPML). WHO Bangladesh has assigned Surveillance Medical Officer (SMO) and Divisional Coordinator (DC) in district and division respectively to work in close collaboration with Government of Bangladesh (GoB) counterpart to support surveillance activities at field level. SMOs are primarily responsible for providing technical support, supervise and monitor entire process of surveillance.

Case definition of Acute Flaccid Paralysis (AFP) is any child less than 15 years of age with acute and rapid progression from weakness to paralysis, is sudden onset, flaccid and the paralysis is not present since birth or is not a result of an injury or paralysis of any age diagnosed as Polio by clinician. All health facilities and private practitioners should admit cases of AFP (both polio and non-polio) to the hospital and immediately report the case to the DSFP in their area. The DSFP will send the LSO to investigate the case within 48 hours of notification and take appropriate actions. The SMO also have to investigate/reinvestigate the case. If the case is a resident of or travel to (within 30 days before or after

onset of paralysis) different upazila, municipality or city corporation, the local DSFP should notify the corresponding DSFP to conduct additional case finding and outbreak response immunization and to perform a 60+ day follow up examination of the case.[18,19]

AFP case investigation and response

The DSFP and LSO will perform the following steps after receiving notification of a suspected AFP case.

1. Assign a case identification number
2. Mobilize all members of the investigation team
3. Investigate the suspected AFP case within 48 hours of report and fill up the AFP case investigation form
4. Collect two stool specimens and send to NPML at the IPH, Dhaka together with filled up investigation form for AFP
5. Record the required information in the AFP line listing form
6. Search for additional cases which may have occurred during the previous 6 months and conduct Outbreak Response Immunization (ORI) near the site where the case was believed to have been infected
7. For cases without adequate stool sample, or cases with stool report of non polio enterovirus or vaccine virus, conduct follow-up examination 60-90 days after paralysis onset and submit completed 60+ day follow-up examination form to EPI Headquarter.
8. For cases without adequate stool sample and 60+ day follow-up with residual paralysis or follow-up not done due to death or lost to follow-up, and additional information form along with all medical record should be sent to EPI HQ for Expert Review Committee (ERC) to classify the case.

In AFP cases adequate stool means that two stool specimens are collected at least 24 hours apart and within 14 days of onset of paralysis and fulfill all of the following criteria: sufficient in amount (at least 8 grams), preserved and transported maintaining cold chain, specimens are not dried out on arrival to NPML, no leakage from the containers and must arrive to NPML within 72 hours of collection.[5, 19]

Discussion

Global Vaccine Action Plan (GVAP) is a roadmap to prevent millions of deaths through more equitable access to vaccines. Countries are aiming to achieve vaccination coverage of e" 90% nationally and e" 80% in every district by 2020. While the GVAP should accelerate control of all vaccine preventable diseases, polio eradication is set as the first milestone. Overall, since the Global Polio Eradication Initiative (GPEI) was launched the number of cases has fallen by over 99% since 1988 from an estimated 350000 cases in 125 endemic countries to 650 cases in 2011, 223 cases in 2012 and 416 cases in 2013 in three endemic countries Afghanistan, Pakistan and Nigeria. Of the 3 strains of wild poliovirus, wild poliovirus type 2 was eradicated in 1999 and case numbers of wild poliovirus type 3 are down to the lowest-ever levels with no cases reported since November 2012 from Nigeria. National valid vaccination coverage in Bangladesh increased from 52% in 1991 to 82% in 2014. Whereas in India the national valid vaccine coverage was 56% in 1990 and 74% in 2012 and In Pakistan, fully immunization coverage in 2010 was only 50%.[22] The global coverage of infants with three doses of polio vaccine was 83% in 2011 & 2012 and 84% in 2013 whereas in our country OPV3 coverage increased from only 16% in 1988, 74% in 1991 to 92% in 2013, in a period of intense polio eradication activity and comparable to first world countries. The number of AFP cases reported in Bangladesh and India since 2000 showed Bangladesh is maintaining a high quality AFP surveillance.[24, 25]

In January 2006 polio importation with P1 serotype occurred in Bangladesh from neighboring state (Uttar Pradesh) of India. After confirmation of polio virus circulation, Bangladesh organized unprecedented rapid response and provided opportunity to all under five years children to receive mOPV (monovalent oral polio vaccine) with 4 rounds in 13th special NIDs and another 2 rounds in 14th NIDs in 2006 with tOPV (trivalent oral polio vaccine). A total of 18 polio cases in 12 districts were identified after importation in 2006. Timely response with very high coverage in all 6 rounds of NIDs, strong routine EPI Programme and special effort to ensure "reaching the unreached" were the interventions for that Bangladesh was able to stop the virus circulation again. The strength of Bangladesh polio eradication programme lies in maintaining high routine coverage, strengthened AFP surveillance, NIDs and

mop-up OPV campaigns. [18, 22, 23] As a result of the outstanding performance in improving the child immunization status' Bangladesh achieved GAVI Alliance Award in 2009 and 2012, which is given as recognition to achieving the Millennium Development Goal (MDG), particularly in reducing child mortality.

Bangladesh along with 10 other countries of WHO South-East-Asia Region was certified polio free on March 27, 2014 by an independent commission under the WHO certification process. Before a region can be certified polio-free, several conditions must be satisfied such as: at least three years of zero confirmed cases due to indigenous wild poliovirus, excellent laboratory based surveillance for poliovirus, demonstrated capacity to detect report and respond to imported cases of poliomyelitis and assurance of safe containment of polioviruses in laboratories (introduced since 2000).[25] On very rare occasions, under certain conditions a strain of poliovirus in OPV may change and revert to a form that may be able to cause paralysis in humans and develop the capacity for sustained circulation of circulating vaccine derived poliovirus (cVDPV). Inactivated polio vaccine (IPV) cannot cause cVDPV and boosts immunity when administered in combination with OPV. Certification of the region comes as countries prepare for the introduction of inactivated polio vaccine (IPV) in routine immunization as part of the eventual phasing out of oral polio vaccines (OPV). More than 120 countries currently use only OPV. These countries will introduce a dose of IPV by the end of 2015 as part of their commitment to the global polio endgame plan which aims to ensure a polio free World by 2018.[26,27]

Conclusion

Immunization is one of the most successful public health initiatives and has been instrumental in eradicating smallpox and nearly eliminating polio. Polio eradication programme is an excellent programme in the history of EPI in Bangladesh, because of intensification of routine EPI, effective surveillance, NIDs, Sub NIDs was very much successful and meticulously performed. This is a momentous victory for the millions of health workers who have worked with governments, NGOs, civil society and international partners to eradicate polio from this region. Now, 80% of the world's population lives in regions certified polio free. Until polio is globally eradicated, all countries are at risk and the regions polio free status remains fragile. High immunization coverage and a sensitive surveillance system are able to detect, identify any importation and guide a programmatic response. Current challenges to the final eradication of paralytic poliomyelitis include the continued transmission of wild polioviruses in endemic reservoirs, re-infection of polio free areas and outbreak due to circulating vaccine derived polioviruses.

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DS (Child) H J 2014; 30 (2) : 152-156

CASE REPORT

Cases of Herbal drug induced Hemorrhagic Cystitis

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Introduction

Herbal remedies are herbs, herbal materials, herbal preparations and finished herbal products, that contain as active ingredients parts of plants, or plant materials, or combinations thereof used to treat a multitude of ailments throughout the world.[1] The Government of Bangladesh has supported and opened ventures in the field of complementary and alternative medicine (CAM) in the last one decade or so, which is a welcome move, since it will promote research and standardization of medications used in CAM. There are a number of persons in the society who are unqualified and/or incompetent to prescribe medicines in any branch of medicine whether it be allopath or homeopathy or branches from CAM, but these faith-healers and quacks are inherently mingled with the society and prescribe medicines injudiciously causing more damage than good. In fact, recent studies have suggested that there has been a rise in usage of herbal medicines especially Chinese and Indian herbs not only in the developing countries but also in the developed world. An oft quoted survey of alternative medicine revealed that 42% Americans used alternative therapies with 12% of these therapies being use of herbal supplements. Moreover, over two-thirds of people using alternative therapies did not report this piece of information to their health care providers.[2] In Bangladesh though there is no statistics but common people are commonly using herbal from traditional healers as they are cheap and taking as an additional off the record medicines. It is a widely known fact and well-corroborated that many herbal medications particularly Chinese and Ayurvedic herbal preparations contain nephrotoxic heavy metals like lead, mercury, cadmium and arsenic.[3] Herbs nephropathy is a established phenomena. Three cases of herbal induced hemorrhagic cystitis are described here.

Case 1

Shohidul Islam, 8yrs old, from Bakulia, Chittagong took herbal in the form of pellets from a kobiraj along with other family members for suspicion of dog bite to one of his elder brother 4 days back. Three hours later he developed gross hematuria and and painful micturition, mixed with clotted blood. He also complained of lower abdominal pain and burning sensation during micturition. So, six hours later of pellets ingestion he got admitted in Pediatric Nephrology ward on 3rd February, 2015. His two other elder brothers also developed hematuria and resolved spontaneously by two days. He had no other relevant history relating to hematuria. There was no remarkable physical findings except supra pubic tenderness. Complete blood count and PBF was normal. Plenty RBC and 12-15/hpf pus cell without any growth in the urine. Renal function and liver function tests were normal. USG KUB revealed hypoechoic area in bladder. He was hydrated adequately and symptoms abated by 4 days. On day 7 urine RME was normal and discharged with advice for follow up after 1 month(Fig.1-4).

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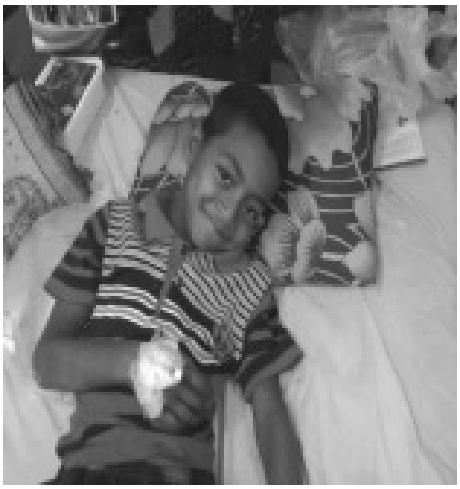

Fig 1 *Shahidul Alam*

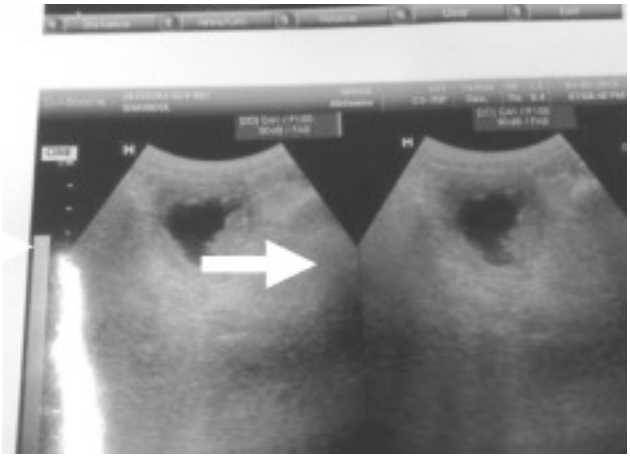

Fig 2 *USG revealed Hypoechoic area in urinary bladder*

Fig 3 *Urine Colour*

Fig 5 *pellets*

Case 2

Sabbir, 4 years old boy from Bakulia, Chittagong took herbal drug in the form of kola pora (In local language Banana is known as Kola and kola pora is Banana impregnated with some unknown substance) on 2nd june, 2014 with the suspicion of dog bite one day back. Two hours later he vomited once and developed lower abdominal pain. He had strong urge for micturition but failed. He failed to pass urine for eight hours and abdomen become more tender. So he was admitted in pediatric nephrology ward, Chittagong Medical College Hospital. He was put on I/V fluid for adequate hydration and then frusemide given. He started to pass urine in drop along with clotted blood and catheterization done. He had no other relevant history relating hematuria or urinary retention. Gradually gross hematuria and dysuria improved and normal urination established by eight days. Complete blood count and PBF was normal. Plenty RBC and 20-30 pus cell / hpf without any growth in the urine. Liver function test and s.electrolytes were normal. USG KUB revealed slightly increased echogenicity of renal parenchyma and hypoechoic area in bladder. Initially s. creatinine was slightly increased (1 mg/dl) then become normal (0.5 mg/dl). He was discharged on day twelve with normal urine RME (Fig 5-9).

Fig 5 *Sabbir*

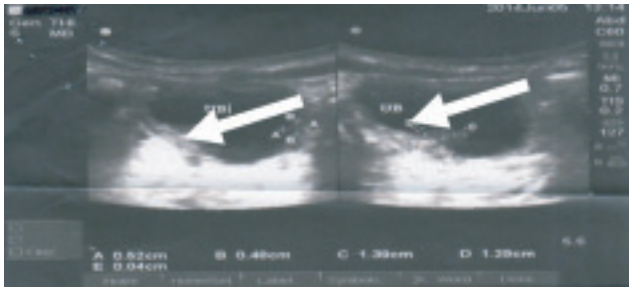

Fig 6 *USG revealed Hypoechoic area in urinary bladder*

Fig 7,8 *Urine Colour Change*

Case 3

Rezaul Azim, 10 years old boy from Banshkhali, Chittagong admitted in pediatric nephrology on 22nd February, 2015 with sudden onset of dysuria and gross hematuria with passage of clotted blood , 4 hours after taking Kola Pora from a kobiraj with the suspicion of dog bite two days back. Initially he went to Upazilla Health Complex and referred immediately to Chittagong Medical College. Prior to this illness he was healthy without any previous history of hematuria. He had no other history related to hematuria. Suprapubic tenderness was the only remarkable physical finding. He was hydrated and sign-symptoms resolved spontaneously by day 5. Complete blood count and PBF was normal. Plenty RBC and 10-15/hpf pus cell without any growth in the urine. Renal function and liver function tests were normal. USG KUB was normal. He was discharged on day 7 with normal urine RME.

Discussion

Hemorrhagic cystitis is a condition characterized by diffuse bleeding from the bladder mucosa due to damage of the bladder transitional epithelium and blood vessels.[4,5] Clinically, it is characterized by the presence of hematuria and irritative voiding symptoms, such as dysuria with frequency, urgency, and suprapubic discomfort. The etiology of hemorrhagic cystitis might be viral (BK virus, adeno virus), bacterial, parasitic, or fungal infections; drugs; radiation; chemicals (aniline or toluidine, insecticides); or rarely idiopathic. Hemorrhagic cystitis occurs in up to 70% of the patients exposed to cyclophosphamide or iphosphamide and in 15% of patients who undergo pelvic irradiation for the treatment of malignancy.[6,7] Other extremely rare reports include associations with food poisoning (Salmonella typhi), prolonged high-altitude air travel (Boon disease) [8,9] and collagen vascular diseases like SLE.[10]

Bright DA et al reported a 3-years old boy with gross hematuria after taking very high dose of amoxicillin suspension without any allergic signs. This child's cystitis cleared rapidly when the drug therapy stopped and the child was hydrated. No sequel were observed.[11] Hemorrhagic cystitis following cephalexin overdose in a child described by Zahra et al.[12] Drug-induced hemorrhagic cystitis are seen both in therapeutic or toxic doses of drugs. Toma Y et al reported a case with gross hematuria, bilateral hydroureteronephrosis when the patient received penicillin G for endocarditis, suggesting hemorrhagic cystitis complicated with urinary tract obstruction.[13] Guyhudson R. and Mark P. described a case of hemorrhagic cystitis associated with risperidone.[14] Cases of hemorrhagic cystitis are also described with ticarcillin, nafcillin, carbenicillin, piperacillin, kanamycin, isoniazid, indomethacin, naproxen, diclofenac, cyclophosphamide, ifosfamide, busulfan, vincristine, tiaprofenic acid, danazol and allopurinol.[8,15,16]

Three cases described here have taken herbal drugs from quacks and two to four hours after ingestion they developed gross hematuria, dysuria, passage of clotted blood during micturition with suprapubic pain. All the features resolved by four to eight days. All were hydrated properly. Case 2 also treated with frusemide and needed catheterization. Before taking herbal they were healthy. Interesting observation in case 1 is other 2 sibs also developed gross hematuria after taking same herbal at the same time and resolved spontaneously by two days. So they did not seek any medical attention. There is a strong belief that this herbal induced hematuria is expected and this hematuria is nothing but the blood containing infective substances developed after dog bite will be cleared through urine making the blood pure. Some samples were collected and analyzed in Dept. of Biochemistry & Molecular Biology, University of Chittagong. Analysis revealed presence of 1. Djenkolic acid: S,S2 -methylenebiscysteine 2R)-2-Amino-3-[{(2R)-2-amino-3-hydroxy-3-oxopropyl} sulfanylmethylsulfanyl] propanoic acid mainly 2. Turpentine: Oil like fluid obtained by the distillation of plant resin , 3. methyl parathion,& oxalic acid. Djenkolic acid (or sometimes jengkolic acid) is a sulfur-containing non-protein amino acid naturally found in djenkol beans of the South-East Asian legumes jengkol (*Archidendron jiringa*). Djenkolism is considered an uncommon but important cause of acute kidney injury in tropical Asia. Many articles revealed male predominance (70%) , symptom onset occurred between 2 hours–4 days after ingestion (usually 2-12 hours). Major presenting signs and symptoms were: abdominal/loin/colicky pain, 70%; dysuria, 66%; oligouria, 59%; hematuria, 55%; and hypertension, 36%. The amino acid precipitates into crystals which cause mechanical irritation of the renal tubule and urinary tract, Crystals may lacerate renal tissue and cause bleeding, or in some cases obstruction with sludge necessitates passage of an urethral catheter or stent. H'ng et al found in ultrasonogram increased echogenicity; prominent pyramids; no hydronephrosis.[17-23]

Most relevant data on CAM-induced nephrotoxicity come from individual case reports. It is often impossible to prove a definitive cause-and-effect relationship. In these cases presence of Djenkolic acid in the collected samples, USG findings of the Kidney and urinary bladder and the resolution of the symptoms soon after the discontinuation of the herbal product indicate nephrotoxicity and hemorrhagic cystitis. Fibrosing interstitial nephritis was observed with Chinese herb nephropathy.[24]

Conclusion

These three cases are the little reflection of our society. It is nothing but the misbelieve, misconception and inadequate knowledge of our peoples and faulty procedure of production of herbal remedies by the village quacks, so, we recommends not to use any herbs other then prescribed by the qualified physician and matters should be taken in to consideration by our Government and media also.

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CASE REPORT

DiGeorge Syndrome presenting as neonatal seizure due to hypocalcaemia - A Case Report

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Abstract

DiGeorge Syndrome is the most common microdeletion syndrome, first described by Dr. Angelo D. George, characterized by facial dysmorphism, congenital heart disease, hypocalcaemia, hypoparathyroidism, thymic aplasia & immunodeficiency due to T cell abnormality. Neonatal hypocalcaemia is one of the common presentation of DiGeorge Syndrome, which can be transient, persistent or even latent. Neonatal seizure due to hypocalcaemia is frequently seen in paediatric wards. These cases should be thoroughly screened so that we can diagnose & manage them early. Here we described one case who presented with neonatal seizure, having facial dysmorphism, hypoparathyroidism, congenital heart disease, absent thymus and ectopic kidney. Later, microdeletion of 22q was detected by fluorescence in situ hybridization. DiGeorge syndrome should be seen as the severe end of the clinical spectrum embraced by the acronym CATCH 22 Syndrome; cardiac defects, abnormal facies, thymic hypoplasia, cleft palate, and hypocalcaemia resulting from 22q11 deletion.

Key words: *DiGeorge Syndrome, Neonatal seizure, Hypocalcaemia*

Introduction

DiGeorge syndrome (DGS) was first described by Paediatric endocrinologist Angelo D. George in 1965.[1,2] Later 22q11 microdeletion was identified as the cause.[3,4,5] Phenotypic features of DiGeorge Syndrome can be described by the acronym CATCH 22; cardiac defect, abnormal facies, thymic hypoplasia, cleft palate and hypocalcaemia resulting from 22q deletion.[6,7] It was also called 3rd & 4th pharyngeal pouch syndrome. Due to defective development of 3rd & 4th pharyngeal pouch, there is malformation of thymus & parathyroid gland. The frequent association of conotruncal anomaly can be explained by the close proximity of the aortic arch & 3rd & 4th pharyngeal pouch during fetal life.[8,9] Neonatal hypocalcaemia is one of the common presentation of DiGeorge syndrome. Hypoparathyroidism can be transient with spontaneous resolution or persistent or even latent.[10,11] Hypoparathyroidism is classically a transient feature in the neonatal period and more characteristic of the DiGeorge syndrome subgroup of 22q11 deletion syndrome.[12]

The etiology of DiGeorge syndrome is presumed to be heterogeneous, with reported cases demonstrating autosomal dominant, autosomal recessive, X-linked chromosomal modes of inheritance. Approximately 15%-20% of patients with DiGeorge syndrome have chromosomal

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abnormalities. Since the original report of DiGeorge in 1965, a total of 47 patients have been described with congenital absence or hypoplasia of the thymus and parathyroid glands. However, there is no single universally recognized definition of syndrome that bears his name. This problem was discussed in 1977 by Lischner who suggested three categories: a general third and fourth pharyngeal pouch syndrome, and complete and partial DiGeorge syndromes. Thymic deficiency may be associated with parathyroid deficiency with or without congenital heart disease and dysmorphism.[13]

Investigations consisted of a detailed clinical history enquiring into symptoms of hypocalcaemia, blood sampling for measurements of serum concentrations of calcium, parathyroid hormone, phosphate, magnesium and alkaline phosphate and a urine sample for estimation of the calcium: creatinine ratio.[14] Patients with 22q11 DiGeorge syndrome have an immune defect caused by thymic hypoplasia, thymic T cell diversity[15] and output is reduced with reduced absolute numbers of native CD3CD45RA[16] and regulatory CD3CD4CD25 T cells.[17] B cells can also be affected[18] with a tendency for immunoglobulin deficiencies.[19-21] These alterations are not severe, but could at least partly explain an increased frequency of autoimmune disorders. Autoimmunity against the parathyroid is rare and reports are scarce. Moreover, both blocking and stimulating antibodies against the calcium sensing receptor have been reported,[22,23] the latter giving rise to hypoparathyroidism. Recently, a novel parathyroid autoantigen NACHT leucine-rich-repeat protein 5 (NALP5) was reported in patients with autoimmune polyendocrine syndrome type 1 (APS1).[24] Whether these autoantibodies are involved in DiGeorge syndrome is not known.

DiGeorge Association (DGA) is also known to be associated with several recognizable syndromes, such as Zellweger syndrome, teratogenic exposures (alcohol and retinoic acid), and chromosome abnormalities, primarily monosomy 22q11 (Lammer and Opitz 1986). In 1981, de la Chapelle et al. reported familial DGA associated with an unbalanced 20;22 translocation producing monosomy for 22q11 (de la Chapelle et al.1981). This association of DGA and monosomy 22q11 was confirmed by Kelley et al. (1982), who reported three of 14 patients with DGA and monosomy 22q11 due to unbalanced translocations involving chromosomes 3, 10, and 20. These cases were all identified as gross translocations after routine chromosome analysis and suggested the possibility that analogous to the situation in Prader-Willi syndrome (Ledbetter et al. 1982), small interstitial deletions of 22q11 might be present in some patients, but some deletions would only be detectable by high-resolution chromosome techniques.[25] The majority of cases with either DiGeorge syndrome or velocardiofacial syndrome are caused by a submicroscopic deletion in chromosome 22ql1 (del22ql1).[26] Since the advent of a routine diagnostic test for this microdeletion, the number of patients diagnosed has increased dramatically, including many patients with either mild features or non-specific presenting symptoms. The del22ql1 occurs much more frequently than previously thought, but precise incidence figures are not known. Wilson et al found a del22ql1 in approximately 5% of children with a congenital heart defect (CHD), and therefore an estimated incidence of at least 1/4000 live births. A more direct way is to determine the annual incidence of cases with a del22ql1, in a well-defined region, with a known number of births. In a region in southern France, with an annual birth rate of approximately 23 000, Du Montcel et al found 1/9700 as a minimum incidence of the del22ql1 associated with the typical clinical picture.[27]

Here we report one case presenting with neonatal hypocalcaemia, having dysmorphic facies, congenital heart disease, hypoparathyroism, absent thymus and ectopic kidney. Later FISH detected deletion of TUPLE 1 region of 22q.

Case report

A one and half month old male child got admitted in Dhaka Shishu (Children) Hospital with the complaints of recurrent generalized tonic seizure from 8th day of life. There were episodes of tonic rigidity, fisting of hands and retraction of head lasting for couple of minutes at first, but later became recurrent and continued for prolonged period (Fig. 1). He was well in between seizures. For these he was admitted in a private clinic and treated with injectable phenobarbitone, injectable calcium glunconate irregularly and perenteral different

broadspectrum antibiotics for one month and seven days without any significant improvement, so parents brought him to our hospital for further evaluation and better management.

Fig 1 *Age : 1 months 25 days*

The baby was delivered at term by LUCS and there was no perinatal adverse event and baby cried just after birth. His mother was otherwise healthy throughout her pregnancy period. He is the first issue of a young couple and there was no family history of such illness. He was exclusively on breast fed and not yet vaccinated.

On examination, the baby was alert, active, mildly pale, anterior fontanel open but not bulged. Anthropometrically the boy was normal (weight 2.9 kg, length-52 cm, OFC- 35.5cm). His heart rate-136 beats /m, respiratory rate-28/m, temperature - normal. He had low set ears, small oral cavity, fish mouth, micrognathia. Apex beat was located in left 5th intercostal space just medial to the mid clavicular line. There is a systolic murmur best heard over the left lower sternal border, with grade 3/6, without any radiation.The baby was not cyanosed and he has no organomegaly. Other systemic examinations reveal normal findings.

Complete blood count, serum electrolytes, RBS, serum calcium done. Serum Ca was found reduced (1.5mmol/l), but others within normal limit. Serum Magnesium (1.4 mg/dl), Serum total Protein (73.6 gm/dl, and albumin (30gm/dl) also within normal limit. Chest X-ray was done which revealed absent thymic shadow with normal findings in chest (Fig.2).

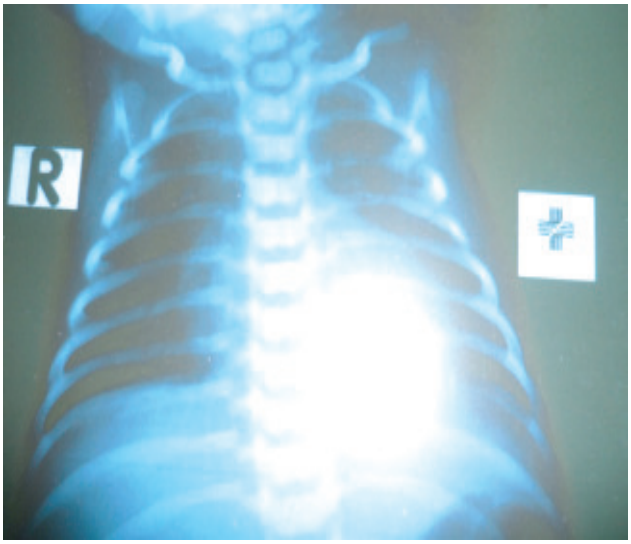

Fig 2 *Chest Xray showing absent thymus*

DiGeorge Syndrome was suspected and some more investigations were done. Serum parathormone was found 3.6 pg/ml (normal-9-80 pg/ml).

Echocardiography revealed large ASD, multiple small VSD, mild TR, mild LPA & RPA origin stenosis.

USG of KUB region revealed a very small hypoplastic ectopic position of left kidney. FISH was advised which showed deletion of TUPLE 1 region of chromosome 22q- that is positive for DiGeorge Syndrome (Fig.3).

Probe used	Total metaphases Analysed	Metaphases showing Normal signals 2 orange signals 2 green signal	Metaphases showing Abnormal signals 1 orange signals 2 green signals
1/ SI DiGeorge VCFS Vysis probe kit	20	-	30

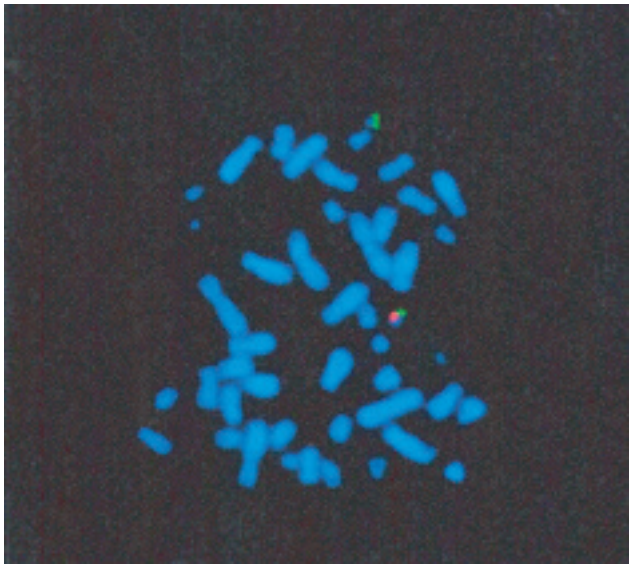

Fig 3 *FISH Result*

We managed the case with calcium and calcitriol and improved dramatically.

Fig 4 *Age of the child: 18 months*

Discussion

Congenital absence of the thymus and parathyroid glands has for many years, been known to be a cause of neonatal hypocalcaemia and tetany.[7] The association with cardiovascular malformations was first noted by Lobdell[8] and by Farber and Vawter.[9] DiGeorge[3] described the clinical spectrum and emphasized the deficit of thymic-dependent immunity. Though the anomaly has been reported as the III-IV pharyngeal pouch syndrome[10], the term DiGeorge syndrome is now widely used. A critical review of the terminology and a classification have been presented by Lischner.[11] DiGeorge Syndrome is the most common microdeletion syndrome having incidence of 1:4000.[11,12] Mode of presentation has wide variation.[15,17] In our case the baby had neonatal hypocalcaemia with hypoparathyroidism, facial dysmorphism, congenital heart disease, absent thymus and ectopic kidney. Later 22q deletion was detected by FISH.

In DiGeorge syndrome 3rd & 4th pharyngeal pouch development is affected. So they may have absent thymus & hypoparathyroidism. Neonatal hypocalcaemia is one of the common presentation.[10,11] Sometimes it is transient & there is spontaneous resolution, as in our case.The baby had neonatal hypocalcaemia but symptom free for the last 13 months (Fig.-4).

Ryan and colleagues reported hypocalcaemia in 60% of subjects with 22q11 deletion syndrome, mostly in the neonatal period, but some in childhood; one patient was diagnosed at aged 18 years. The natural history of hypocalcaemia remains poorly understood or defined. It has been shown to be both latent and overt in children and adolescents with 22q11 deletion syndrome. Adachi and colleagues, in reviewing their population of patients with hypoparathyroidism, found 10 of 14 children to have 22q11 microdeletion with an age of diagnosis of hypoparathyroidism between 9 days and 13 years.[16] K. Lima et al found hypoparathyroidism in 28 (47%) patients in a cross sectional study on 59 patient of DiGeorge syndrome, of them 15 (25%) had neonatal hypocalcaemia.[15] Mc. Donald et al reported hypocalcaemia in 77 (49%) of 158 patients with a confirmed deletion of 22q11.[22] S. Hieronimus et al showed parathyroid dysfunction in 50% of the patients, 6 patients were diagnosed with overt hypoparathyroidism and hypocalcaemia manifested by seizure & laryngeal stridor in infancy

(n-4), in adolescence (n-2). One patient had transient neonatal hypoparathyroidism & one patient had latent hypoparathyroidism.[17]

Hypoparathyroidism classically transient in neonatal period in DiGeorge Syndrome but can present in late childhood or even in adulthood. Persistent as well as latent hypoparathyroidism also seen.[18,19,20] Sometimes there is recurrence of hypoparathyroidism, precipitated by infections, pregnancy or surgery.[11] Cardiac abnormality & immunodeficiency are recognized association of DiGeorge syndrome.[13] So it should be kept in mind during overwhelming infection or surgery. Due to varying presentation and severity, the diagnosis of chromosome 22q11 deletion syndrome is still often delayed. Increased awareness and knowledge among the many specialists such as endocrinologists, who may encounter these patients is needed to reduce the diagnostic delay and provide optimal clinical care. The gene TUPLE1 (TUP-like enhancer of split gene-1; 600237) reported by Halford et al. (1993) is an attractive candidate for the central features of the syndrome. This putative transcription factor shows homology to the yeast transcription factor TUP, and to Drosophila enhancer of split. It contains 4 WD40 domains and shows evidence of expression at the critical period of development in the outflow tract of the heart and the neural crest derived aspects of the face and upper thorax. The gene localizes to the critical DiGeorge region but was not disrupted by the translocation breakpoint described by Augusseau et al. (1986). The possibility of this being a contiguous gene syndrome remains.

Conclusion

Neonatal seizure is very common in neonatal wards and hypocalcaemia is not uncommon in neonate, whereas physical appearance and clinical presentation of DiGeorge Syndrome has wide variation. Therefore any patient of neonatal tonic seizure, having hypocalcaemia, should be screened properly. Early diagnosis of this syndrome can help in the management of cardiac, endocrine, immunological or psychiatric problems associated with this patient.

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DS (Child) H J 2014; 30 (2) : 163-164

ABSTRACT FROM CURRENT LITERATURE

Perinatal Asphyxia with Hyperoxemia within the First Hour of Life Is Associated with Moderate to Severe Hypoxic-Ischemic Encephalopathy

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J Pediatr 2013;163:949-54

Objective: To determine whether early hyperoxemia in neonates with severe perinatal acidemia is associated with the development of hypoxic-ischemic encephalopathy (HIE).

Study: design We identified 120 infants at $36 weeks gestational age with perinatal acidosis born at Parkland Hospital who qualified for a screening neurologic exam for cooling therapy. Based on a PaO2 measurement during the first hour of life, the cohort was divided into infants with hyperoxemia (PaO2 >100 mmHg) and those without hyperoxemia (PaO2 #100 mmHg).The rate of moderate-severe encephalopathy was compared between the groups using c2 analysis, as well as multiple logistic regression, taking into account baseline characteristics and confounding variables.

Results: Thirty-six infants (30%) had an initial PaO2 >100 mmHg. Infants with and without hyperoxemia had similar baseline maternal and infant characteristics. Infants with hyperoxemia had a higher incidence of HIE than those without hyperoxemia (58% vs 27%; P = .003). Admission hyperoxemia was associated with a higher risk of HIE (OR, 4; 95% CI, 1.4-10.5; adjusted P = .01). Among the neonates with moderate-severe HIE during the first 6 hours of life, those with hyperoxemia had a higher incidence of abnormal brain magnetic resonance imaging results, consistent with hypoxic ischemic injury, compared with those without hyperoxemia (79% vs 33%; P = .015).

Conclusion: In neonates with perinatal acidemia, admission hyperoxemia is associated with a higher incidence of HIE. Among neonates with HIE, admission hyperoxemia is associated with abnormal brain magnetic resonance imaging findings. The judicious use of oxygen during and after resuscitation is warranted.

Risk Factors for Febrile Status Epilepticus: A Case-Control Study

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J Pediatr 2013;163:1147-51

Objective: To identify risk factors for developing a first febrile status epilepticus (FSE) among children with a first febrile seizure (FS).

Study design: Cases were children with a first FS that was FSE drawn from the Consequences of Prolonged Febrile Seizures in Childhood and Columbia cohorts. Controls were children with a first simple FS and separately, children with a first complex FS that was not FSE. Identical questionnaires were administered to family members of the 3 cohorts. Magnetic resonance imaging protocol and readings were consistent across cohorts, and seizure phenomenology was assessed by the same physicians. Risk factors were analyzed using logistic regression.

Results: Compared with children with simple FS, FSE was associated with younger age, lower temperature, longer duration (1-24 hours) of recognized temperature before FS, female sex, structural temporal lobe abnormalities, and first-degree family history of FS. Compared with children with other complex FS, FSE was associated with low temperature and longer duration (1-24 hours) of temperature recognition before FS. Risk factors for complex FS that was not FSE were similar in magnitude to those for FSE but only younger age was significant.

Conclusions: Among children with a first FS, FSE appears to be due to a combination of lower seizure threshold (younger age and lower temperatures) and impaired regulation of seizure duration. Clinicians evaluating FS should be aware of these factors as many episodes of FSE go unnoticed. Further work is needed to develop strategies to prevent FSE

Long Duration of Hyperglycemia in the First 96 Hours of Life Is Associated with Severe Intraventricular Hemorrhage in Preterm Infants

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J Pediatr 2013;163:388-93

Objective: To assess the association between severe intraventricular hemorrhage (IVH) and blood glucose variables during the first 96 hours of life in preterm infants.

Study design: Preterm infants with IVH grade 3-4 (n = 70) were compared with matched infants of similar gestational age and birth weight, but with no IVH (n = 108). Studied variables included the frequency and duration of hyper/hypoglycemic (>6.9/ <3.3 mmol/L, respectively) events, the extreme slope of an event evolution, the maximal glucose value observed, and the "hyper/hypoglycemic index" representing a weighted average of the hyper/ hypoglycemic amplitude.

Results: The IVH group had significantly more hyperglycemic events (2.9 _ 1.7 vs 2.4 _ 1.8 events, P < .05) with longer duration (22.2 _ 14.2 vs 14.1 _ 12.5 hours, P < .001) and a higher hyperglycemic index (1.0_0.9 vs 1.4_1.0, P = .003) compared with the non- IVH controls. Respiratory distress syndrome, hypotension, and thrombocytopenia increased the adjusted OR for IVH. Hypoglycemia was not independently associated with IVH. Conversely, the increase in hyperglycemic duration was most prominently increasing the aOR for severe IVH (OR = 10.33, 95% CI = 10.0-10.6, P = .033).

Conclusion: Longer duration of hyperglycemia in the first 96 hours of life was most strongly associated with severe IVH in preterm infants. Consequently, interventional studies to determine the selective effect of continuous control of long-lasting hyperglycemia by appropriate and timed insulin treatment on the incidence of severe IVH are warranted.

Long-Term Neurodevelopmental Outcome with Hypoxic-Ischemic Encephalopathy

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J Pediatr 2013;163:454-9

Objectives: To determine the long-term neurodevelopmental outcome for children after hypoxic-ischemic encephalopathy (HIE) without major disability, and to examine neonatal injury patterns detected on cerebral magnetic resonance imaging (MRI) in relation to later deficits.

Study design: Prospectively enrolled children with HIE and neonatal cerebral MRI data (n = 68) were examined at a mean age of 11.2 years (range, 8.2-15.7 years). Eleven children had a major disability (ie, cerebral palsy or mental retardation). Brain injury was scored according to the region and extent of injury.

Results: Children without major disability (n = 57) had lower full-scale and performance IQ scores compared with norms (P = .02 and .01, respectively), and the proportion of children with an IQ <85 was higher than expected (P = .04). Motor performance on the Zurich Neuromotor Assessment was affected in the pure motor, adaptive fine motor, and gross motor domains, as well as in the movement quality domain (all P< .001). Watershed injury pattern on neonatal MRI correlated with full-scale and verbal IQ scores (P=.006 and <.001, respectively), but neonatal MRI pattern did not correlate with motor performance in children without major disability.

Conclusion: Children who sustained neonatal HIE without major disability are at increased risk for long-term intellectual, verbal, and motor deficits. The severity of watershed injury is correlated with later intellectual performance. Long-term follow-up examinations are necessary for early detection of neurodevelopmental impairment and early initiation of adequate therapies.

DSH NEWS

A meeting of Dhaka Shishu (Children) Hospital Board of Trust held on 20/12/2014 chaired by National Professor Dr. Sahela Khatun, Honourable Chairman, Management Board, Dhaka Shishu (Children) Hospital along with Honorable members of the trustee (From Left) National Professor MR Khan, Mr. Kazi Akramuddin Ahmed, President, FBCCI & Chairman, Standard Bank limited, Prof. Nazmun Nahar, DG, BIRDEM General Hospital, Dr. Md. Shafiqur Rahman, Prof. Dr. Md. Abdul Aziz, Prof. Dr. Maniruzzaman Bhuiyan, Dr. Md. Nazrul Islam, Deputy secretary(Admin), Department of finance, Ministry of finance, Prof. Samir Kumar Shaha, Prof. Md. Sharfuddin Ahmed and Member secretary of Board of trust and honourable Director, Dhaka Shishu (Children) Hospital, Professor Manzoor Hussain.

Celebration of World Pneumonia Day on 12th April 2014 with rally started from Dhaka Shishu Hospital compoud with our honourable Acadenic Director Professor M.A.K. Azad Chowdhury, Prof. Md. Ruhul Amin, Prof. Samir Kumar Saha, Prof. A.S.M. Nawshad Uddin Ahmed, Prof. Mahbubul Hoque and Doctors & Sisters of Dhaka Shishu (Children) Hospital.

BICH NEWS

BICH is the academic wing of Dhaka Shishu Hospital. It was established in 30th January, 1983. It is affiliated with Dhaka University, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bangladesh College of Physicians and Surgeons (BCPS). It has been conducting different courses e.g. DCH, FCPS, MD Paediatrics, MS Paediatric surgery & B.Sc in Health technology. It also conduct different sub-specialty courses e.g. FCPS Neonatology, FCPS Haemato-oncology, FCPS Nephrology, MD Neonatology, MD Haemato-oncology and MD Nephrology. It conducts 3 months certificate course in Paediatrics and 15 days Intensive course for MCPS. It organizes IMCI training and Palli Shishu Rural Health Training. Apart from this, the Institute also run its regular academic activities. It has established Basic Science Department since 2006.

Diploma course of paediatric nursing has started from 1st January 2012 and Diploma in paediatric physiotherapy under process.

Library facilities

The library of BICH has a rich collection of updated medical texts and reference books and reputed Medical Journals of home and abroad. BICH has introduced Broad Band facilities which are open to all students, teachers/ consultants of hospital for 24 hours. Facilities of library are also improved by HINARI. Students can download 2230 Medical Journals & more than 50 Paediatric Journal.

Present News

A newly formed classroom in BICH has been named as Prof. Sultan Ahmed Chowdhury as a tribute to First Honarary Director of Dhaka Shishu Hospital.

DS (Child) H J 2014; 30(2) : 167

Postgraduate courses/training in paediatrics and child health

1. FCPS in paediatrics : Twice in a year, in the months of January and July.
2. Recognized center by BCPS for training in FCPS (Paeditric surgery) .
3. Recognized centre for course and training in different subspeciality as: Neonatology,pediatric Nephrology, paediatric haematology and Onchology, paediatric pulmonology and paediatric Neuroscience.
3. MD/MS in paediatrics : Part I: In the month of January every year; 2nd and 3rd parts twice every year.
4. DCH course : Once in a year in the month of July.
5. Three months certificate course : The institute every year runs 3 months certificate course on paediatrics for general practitioners & other post graduate candidates e.g. MCPS.
   (Ist August – 31st October)
6. Training programme on IMCI (Integrated management of childhood illness), Essential Newborn Care for doctors and nurses. KMC (Kangaroo Mother Care) traing, ETAT (Emmergency Triage, Assessment and Treatment) training.

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DS (Child) H J 2014; 30(2) : 168

Students Qualified from Bangladesh Institute of Child Health

Undergoing Courses of BICH

Institution	Courses
University	MD (Paediatric) MD (Neonatology) MD (Nephrology) DCH MS (Paediatric Surgery)
Bangladesh Collage of Physicians and Surgeons (BCPS)	FCPS (Paediatric) FCPS (Neonatology) FCPS (Haemato-Oncology) FCPS (Paed. Neurology & Development)
Dhaka University	BSc (Health Technology)

Students Qualified From BICH till June 2014

Name of Courses	Number
DCH	312
MD (Paediatrics)	81
MS (Paediatrics)	76
FCPS (Paediatrics)	20
MD (Neonatology)	9
MD (Paediatric Nephrology)	2
Total	500

Foreign Students Qualified From Bich Till July 2013

Country of Origin	Course	Number
Nepal	DCH	23
	MS (Paed. Surgery)	3
	MD (Paed)	1
India	MD(Paed)	1
Iran	DCH	1
Iraq	DCH	1
Somalia	DCH	1
Sudan	DCH	1
Total		**32**

Present Students

Name of Courses		Number of Students
DCH		14
MD (Paediatrics)	Part-I	13
MD (Paediatrics)	Part-II	
MD (Paediatrics)	Final Part	
MS (Paediatrics)	Part-I	6
MS (Paediatrics)	Part-II	
MS (Paediatrics)	Final Part	
FCPS (Paediatrics)	Part-II	4
FCPS	(Paediatric Nephrology)	1
Total		**38**

Seminar/Symposium & CME/CPD programs held at BICH (July to December, 2014)

Date	Topic	Presenter
24/08/2014	Cerebrovascular Disorders in	Department of Paediatric Neuroscience Children (MU-3), Dhaka Shishu (Children) Hospital
28/09/2014	Sleep in Paediatric Practice	Department of Paediatric Respiratory Medicine Pulmonology (MU-5), Dhaka Shishu (Children) Hospital
25/12/2014	Pediatric Advanced Life Support	American Association of Paediatrics (AAP), American Heart Association (AHA), BMA North America (BMANA), Paediatric Educational Development Society International (PEDS), Bangladesh Society of Paediatric Critical Carte (BSPCC), Bangladesh Institute of Child Health (BICH) and Dhaka Shishu (Children) Hospital.
24/12/2014 to 27/12/2014	Pediatric Advanced Life Support (PALS) & Advanced Pediatric Life Support (APLS)	American Association of Paediatrics (AAP) American Heart Association (AHA), BMA North America (BMANA), Bnagladesh Society of Pediatric Critical Care (BSPCC) and Bnagladesh Institute of Child Health (BICH) and Dhaka Shishu (Children) Hospital.