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Editorial

"Congenital Haemolytic Anaemia: A Preventable Havoc of Bangadesh"

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DHAKA SHISHU (CHILDREN) HOSPITAL JOURNAL

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EDITORIAL

Congenital Haemolytic Anaemia: A Preventable Havoc of Bangadesh

Md. Selimuzzaman

Haemoglobinopathies & Thalassaemia are common variety of haemolytic anaemia throughout the world. These are the inherited genetic disorder of Haemoglobin and varies in different population groups in the world. World Health Organization (WHO) estimates that at least 6.5% of the world populations are carriers of different inherited disorders of haemoglobin. Abnormal haemoglobin, called haemoglobin E which is quite common in Bangladesh has also world wide carriers of 53 millions[1]. A conservative World Health report estimates that 3% are carriers of â thalassaemia and 4% are carriers of Hb E in Bangladesh and affected birth per thousand of b thalassaemia is 0.106 & 0.300 of Hb E-β thalassaemia[2]

Thalassaemia major & sever variety of Hb E-β Thalassaemia patients need frequent blood transfusions about every 2-5 weeks interval. Thalassaemia intermedia patients need blood transfusion at various interval. As a result a good percentage of blood is utilized by them, which is a major burden to the blood banks and transfusions centers of the country. Blood transfusion itself has many complications like transmission of infectious agents e.g. H1V, HCV, HBV and Trypanoma pallidum etc, and toxicities due to iron overload. Iron chelating agents are costly and beyond reach of majority of the thalassaemic patients. So management of thalassaemic patients by blood transfusion and iron chelation is a major financial burden for the affected family as well as for the society and nation. Though the bone marrow transplantation is currently the only curative therapy[3, 4], which is very expensive & the facility is limited only in some highly experienced centers in abroad.

Under-transfused or non-transfused patients are suffered from growth failure, developed various complications like huge hepato-splenomegaly with hypersplenism, bony deformities & pathological fracture, endocrinopathies, cholelithiasis, leg ulcer and heart failure etc which leads to early death.

So the medical researchers of different developed countries are seeking the alternative treatment modalities like drugs which may raise the haemoglobin level and thereby need of blood transfusion can be stopped or reduced in the management of thalassaemias. Reactivation of gamma chain synthesis is now considered as the most tangible approach to improve the clinical severity of the inherited β globin chain defects. The beneficial effects may be obtained by several mechanisms: in β thalassaemia, the additional gamma-chains bind to ± chains remaining in excess because of absence of their normal partners (the b globin chains), and not only neutralize the deleterious consequences of their intracellular precipitation but they add also some functional haemoglobin (HbF) into almost empty erythroid precursors and red-cells of patients. As a result, ineffective erythropoiesis may decrease and the red cell of the patients will survive longer in the circulation[5,6]. Reactivation of gamma-chain synthesis has been observed in several conditions, including intake of various chemicals and drugs. These drugs act either by promoting the transcription of gamma-mRNA molecule[7] or by recruiting into cycle a population of erythroid progenitors, in which the gamma to beta-chain synthesis switch has not been turned off completely.

There are a series of clinical trials in the U.S.A which confirmed that administration of hydroxyurea (HU) to patients with sickle cell disease resulted in an increase of foetal haemoglobin (HbF) synthesis to levels several-fold higher than their baseline values & associated with some clinical improvement in most cases[9-12]. Researchers in different centers

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have introduced hydroxyurea 25 years ago for the treatment of Myeloproliferative disorders, which is still most easy to handle medication because it's toxicity (marrow suppression) is rapidly reversible[13]. Recently it has been reported that virtually 14 patients with sickle cell beta thalassaemia treated with hydroxyurea had increase in HbF levels[14]. Since then there have been many studies conducted on the patients of thalassaemia major & intermedia to see the effectiveness of hydroxyurea with many reports of success[15-26]. Except few cases, therapy lead to lower and even no need of blood transfusion in the management of thalassaemic patients. Others reported few adverse effects such as reversible myelo-suppression, headache, hyper pigmentation, nausea etc, which can be managed by withdrawing the drug temporarily[22-27.] So use of Hydroxyurea is a revolutionary treatment modality of Hereditary haemolytic anaemia like thalassaemia and haemoglobinopathies.

Considering the life-long sufferings of the patients along with their families, prevention of born of thalassaemic baby by pre & post marital genetic counseling and Prenatal diagnosis is the most appropriate & time demanded approach. Several countries like Cyprus prevent the born of thalassaemic baby by genetic counseling and Prenatal diagnosis of thalassaemia. So for implementation of effective prevention program universal carrier screening of general populations should be the first step. Then pre marital counseling and post marital genetic counseling should be the next step. Premarietal and post marietal proper counseling and publicity regarding the consequence and genetic basis of congenital Haemolytic anaemia by different medias and awareness build up methods shoud be implicated to prevent the havoc of this morbid condition.

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SPECIAL ARTICLE

Formalin in Food: Venom in Disguise of Ambrosia

Probir Kumar Sarkar

Introduction

Adulteration of food with toxic chemicals harmful to health has reached an epidemic proportion in Bangladesh. The newspapers have dubbed it as the 'silent killer'. It is very difficult to find a sector of food industry which is free of adulteration. From raw vegetable and fruits to milk and milk products to fish, meat and processed food–every food item is contaminated. Almost every day in the news papers, newer and newer methods of adulterating newer and newer types of foods are reported. Carbide, formalin, textile colours, artificial sweeteners, DDT, urea etc. are used rampantly for this purpose.[1] Contamination of foods with toxic chemicals pose a serious threat to public health in our country due to poor health literacy and awareness.[2] All incidents of food adulteration are united by a common and noble motive-the reduction of post-harvest loss. In 2009, the Food and Agriculture Organization estimated that 40-50 per cent of the global crop of fruit and vegetables is lost annually to spoilage or waste. In a world where hunger is still commonplace, the scale of this loss is concerning.[3]

Epidemiology

According to WHO (World Health Organization), an estimated 2.2 million people are killed annually due to food-borne and water-borne diseases throughout the world, of them 1.9 million are children. In another report of FAO (Food and Agriculture Organisation), it is found that approximately 45 million people in Bangladesh suffer from food poisoning or some kind of food-borne diseases throughout the year and the number could be even higher provided there is a household survey in the country.[4] In absence of authentic database in Bangladesh, reliable estimation of actual health hazard due to food contamination is not available. However, from newspaper reporting, public opinion and situational analysis, it may easily be presumed that this vicious issue has become very acute and is generating a deadly consequence for us. More than 76 percent food items on the market were found adulterated in a random survey by Public Health Laboratory of Dhaka City Corporation in 2004. Non-government development organization RDRS put the proportion at more than 90 percent referring to test results of government laboratories published in newspapers, while the officials and researchers present at the said it is 70 percent.[6]

Formaldehyde, Formalin & Para formaldehyde

Formaldehyde

Formaldehyde is HCHO or CH_2O, the simplest aldehyde. The chemical compound formaldehyde, is a gas with a strong pungent smell. It has a boiling point of -21°C (262 K). The word formaldehyde is always reserved for the gas itself. It is never applied to solutions of the gas. Formaldehyde readily results from the incomplete combustion of carbon-containing materials. It may be found in the smoke from forest fires, in automobile exhaust, and in tobacco smoke. In the atmosphere, formaldehyde is produced by the action of sunlight and oxygen on atmospheric methane and other hydrocarbons. Small amounts of formaldehyde are produced as a metabolic byproduct in most organisms, including humans.

Formaldehyde is a colorless, flammable gas used is an important industrial chemical to manufacture building materials and to produce many household products. It is used in pressed wood products such as particleboard, plywood, and fiberboard, glues and adhesives, permanent press fabrics, paper product coatings, and certain insulation materials. In addition, formaldehyde is commonly used as an industrial fungicide, germicide, and disinfectant, and as a preservative in mortuaries and medical laboratories.

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Formalin

Solutions of formaldehyde gas dissolved in water are called formalin. This name is used regardless of how much of the gas is dissolved, and it contains no information nor inference about the concentration. To specify the concentration of the formaldehyde gas in the water a convention is applied based on the saturated solution being called 100% formalin rather than giving the concentration of formaldehyde directly. Formaldehyde dissolves into water to 37% w/v. This solution is variously called 100% formalin, strong formalin, concentrated formalin, or saturated formalin. The first expression, 100% formalin, is clearest, but the others will be understood and are frequently used.

When diluting formalin solutions, the final concentration is expressed based on the 100% formalin reference. In other words 10% formalin is a 1:10 dilution of 100% formalin, *i.e.* it is 10 mL of 100% formalin plus 90 mL water, or equivalent volumes. The terminology 10% formalin is most commonly used. However, the expression 4% formaldehyde is sometimes encountered. This expression is based on the actual formaldehyde content of the solution. It is less common than10% formalin, but the terms are equivalent and refer to the same thing.

Formalin is a chemical used for preserving dead bodies in hospital mortuaries and dissection room in medical colleges, fixation of biopsy sample in medical examinations, and for disinfection of hospital rooms, operation theatres and few surgical instruments. But this formalin is now used unethically for preserving fruits. Formalin delays decomposition of fruits, so most of the venders use formalin. It is heard that fruits especially mangoes and litchis are sprayed with formalin when they are on trees. The widespread use of formalin, in preservation of fruit is posing a threat to public health. The chemical used as a solution in water

keeps fruit apparently fresh and makes fruits like mangoes attractive. In our country presence of formalin has already been detected in fruits like apples, bananas, grapes, mangoes and even maltas.

Para formaldehyde

Taking advantage of loopholes in the existing laws, a section of traders are importing chemicals like para-formaldehyde that can be used as a substitute for formalin. Para-formaldehyde is used as an industrial raw material. There is no legal barrier for import of this substance. It is a colourless chemical substance commonly used to preserve food for longer time. When it is mixed with food in an excess amount, the chemical is converted into more rigid substance that gives the lasting rigidity of the food for long term preservation.We all are concerned about formalin use in food but to what extent or level formalin is harmful is not yet reported in Bangladesh. WHO says fruits and vegetables typically contain 3-60 µg (microgram) formaldehyde per kg, milk and milk products about 1mg, meat and fish 6-20 mg and shell fish 1-100 mg. The daily intake of formalin is difficult to evaluate, but a rough estimate from the available data is in the range of 1.5-14 mg a day for an average adult. A BRAC study says there is a certain amount of formaldehyde in the human body which is vital for metabolism. If consumed within the permissible limit, it transforms into less toxic formic acid and gets out of the body through urine. A part of formaldehyde also transforms into CO2 and gets out through the respiratory system.

Formalin is such a harmful chemical that the handlers of them are not safe. It has a bad effect on eyes and nose and eyes are most sensitive to exposure. The eyes, nose and throat are irritated by formaldehyde vapors at level as low as about 0.3 part formaldehyde per million parts of air (0.3 parts per million, or 0.3 ppm). Multiple exposures of (5-30 ppm) and higher can trigger or aggravate asthma symptoms. Formalin is highly toxic to all animals, regardless of method of intake. Ingestion of as little as 30ml (1oz.) of a solution containing 37% formaldehyde has been reported to cause death in an adult human. Formalin is a strong corrosive and its ingestion can immediately cause severe injury to upper GI tract. Within the circulation it is converted to formic acid, increases the acidity of blood and cause shortness of breath. Fruits and fishes dipped in formalin are harmful to health. The ingestion of formaldehyde over a prolonged period can cause respiratory, digestive, cardiac, nephrological and neurological problems along with cancer.

In 1987, the U.S. Environmental Protection Agency (EPA) classified formaldehyde as a probable human carcinogen under conditions of unusually high or prolonged exposure. Since that time, some studies

of industrial workers have suggested that formaldehyde exposure is associated with nasal cancer and nasopharyngeal cancer, and possibly with leukemia. In 1995, the International Agency for Research on Cancer (IARC) concluded that formaldehyde is a probable human carcinogen.

Horrifying food adulteration vs food safety situation in Bangladesh

The voracious demon of food contamination has already devoured the consumers of Bangladesh to a great extent. From babyfood to adult foodstuffs, either at breakfast or lunchtime or even at dinner, whether inside our sweet home or at restaurants outside home, no food item is free from contamination.

The Constitution of the Peoples' Republic of Bangladesh ensures food, nutrition and improved public health (Art. 15 & 18) for its citizens. Apart from the Constitutional provisions, there are a number of legislations for controlling food standard.[4] Some important Legislations are:

1. The Consumer Right Protection Act, 2009.
2. The Bangladesh Pure Food Ordinance, 1959.
3. The Iodine Deficiency Disorders (IDD) Prevention Act, 1989.
4. Fish and Fish Product (Inspection and Quality Control) Rules, 1997.
5. The Pesticide Ordinance, 1971.
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7. Marine Fisheries Ordinance 1983 and Rules, 1983.
8. The Bangladesh Standards and Testing Institution Ordinance, 1985.
9. The Bangladesh Pure Food (Amendment) Act, 2005.
10. The Smoking and Tobacco Products Usage (Control) Act, 2005.
11. The Penal Code, 1860.
12. The Narcotics (Control) Act, 1990.
13. The Trade Marks Act, 2009.

Notwithstanding all these, the food safety situation in Bangladesh is very much unstable.

Legal Provisions under "Formalin Control Bill, 2015"

The parliament Monday, 16/02/2015, passed the "Formalin Control Bill, 2015" with a provision of life-term imprisonment as the maximum punishment, and an additional Tk20 lakh fine, but no less than Tk5lakh, for importing, producing, or hoarding formalin without license.

According to the act, for violating the terms and conditions of the license, a trader will get a maximum of seven years imprisonment, but not less than three years, or pay a Tk5 lakh fine, but not less than Tk2 lakhs, or both.

In addition, for selling or using formalin without a license, he or she will be awarded maximum two years' imprisonment, but not less than six months, and fined Tk4 lakh, but not less than Tk1 lakh, or both.[7]

How do you recognize a formalin free fruit?

A fresh fruit is always firm or soft on touch. Its skin shows natural look which changes day by day. A fruit dipped in formalin solution feels hard on touch. Colour of the fruits skin becomes dull and will not change over time. Usually the smell of fruits attract many insects. So, fresh fruits are surrounded by many fruit loving insects. But fruits with formalin are free from flies, bees, ants or any other fruit loving insects. So, before you buy fruits watch for these scenarios.

Tips to Remove Formalin from Fruits

Fruits can be preserved for a long time by using formalin. If you suspect that the fruits you bought contains formalin, you must sink it under salty water for at least 1 hour. After that wash them with normal fresh water. Then, the formalin will be eliminated and you can take those fruits without any doubt. This process **removes 95% formali**n from fruits.

Tips to Remove Formalin from Fishes:

If you suspect that your fish has formalin or might have formalin, sink those fishes under salty-water for one hour. It will eliminateabout 60% formalin. But, If you sink it under salt-water for one and half hour, 90% formalin would be eliminated. Again, if you sink the fishes under vinegar mixed water [10-20% vinegar:80% water], **100% formalin elimination** may be guaranteed.

Conclusion: We, the people of Bangladesh, neither want to embrace premature death nor want to get older quickly. It is our statutory right, both as a human being and a citizen of the country, to possess and enjoy a sound health surrounded by hygienic

atmosphere. But the atrocity of food contamination has reached to such a height that it is quite impossible for us to believe the maxim, "we eat to live." It is like taking venom in disguise of ambrosia. Commitment from the political leaders to wage a sustained campaign against these perpetrators of heinous crime to establish our fundamental right and to have safe nutritious food. For this to achieve, relentless enforcement of existing laws with the execution of highest penalty possible, awareness-building campaign among consumers, promotion of ethical practices among the business community with active involvement of the business leaders, and capacity development of public health labs to test food items for adulteration on the spot are needed. The consumer rights groups should be more vocal and play active role in developing a mass campaign/ movement in the country.

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ORIGINAL ARTICLE

Electrophysiological Findings of Children Presented with Neuromuscular Disorder

Mustafa Mahbub[1], Selina Hosna Banu[2], AZM Moshiul Azam[3], S. Chandra Majumder[4], Naila Zaman Khan[5]

Abstract

Background: *Neuromuscular disease includes disorders of spinal motor neuron, spinal nerves and muscle and can be acquired or hereditary. Neurophysiological investigations like EMG and NCV are important tools for diagnosis.*

Objective : *To distinguish between the disorders of anterior horn cells, peripheral nerves and muscles and to relate neurophysiological abnormalities to the clinical context.*

Method : *Thirty (37) children with neuromuscular disorders were seen from Feb. 2010 to Feb. 2015. Consanguinity, history of perinatal insult and important clinical feature were recorded. Serum Creatinine Phosphokinase (CPK), Electromyography (EMG), Nerve Conduction Velocity (NCV) suggested for all and muscle biopsy for selected cases. EMG & NCV was done in the Neurophysiology Lab of Bangladesh Protibondhi Foundation by trained personnel.*

Result : *EMG and NCV was done in all 37 children. According to the findings of EMG 13 (35%) were suggestive of myogenic disorder, 15 (40%) were neurogenic disorder, 1 (3%) was mixed neurogenic disorder and 8 (22%) was normal. Clinical diagnosis of 37 children was, Spinal Muscular Atrophy (SMA) 12 (32%), Muscular Dystrophy in 8 (22%) cases. Myopathy in 7 (20%), Hereditary Motor & Sensory Neuropathy (HMSN) in 5 (14%) and Paraplegia in 3 (8%). Of the 16 children with clinically myogenic disorders, 13(81%) cases were compatible with electrophysiological findings. Of the 20 with neurogenic disorders, 15 (75%) were compatible with the electrophysiological findings.*

Conclusion : *In most of the cases EMG and NCV findings were in favor of the clinical diagnosis It is necessary to supplement clinical examination by the study of electrical activity in nerve and muscle to validate the diagnosis and for future reference during follow up visits..*

Key words: *Neuromuscular disorders; Myogenic; Neurogenic; EMG; NCV*

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Introduction

The term Neuromuscular Disorder (ND) is used to describe any disease with the primary pathology arising in the lower motor tract and impacting on the functioning of muscles. This large collection of disorders encompasses disease of the anterior horn cells, peripheral nerves, neuromuscular junction, and the muscles themselves.[1]

Spinal muscular atrophy (SMA), an autosomal recessive motor neuron disorder, is the most common hereditary cause of death in infants.[2] SMA is caused by functional loss of the *survival motor neuron*. In patients with SMA, needle electromyography (EMG) demonstrates changes of fibrillation potentials (denoting active denervation) and enlarged motor unit action potentials with neurogenic recruitment.[3-4] *Muscle biopsy is not necessary for the diagnosis of SMA when clinical and EMG data are characteristic, and confirmation is best provided by genetic testing.*[5]

The term myopathy covers the entire spectrum of diseases of muscle and implies that the disorder does not involve the central nervous system or other portions of the peripheral motor unit, including the anterior horn cell, peripheral nerve, or neuromuscular junction.[6]

Mitochondrial myopathies are caused by mutations in mitochondrial DNA (mtDNA) or nuclear DNA and have heterogeneous clinical manifestations. Electromyography may show both neurogenic and myopathic features.[7]

In Hereditary motor sensory neuropathy (HMSN) both motor and sensory nerve conduction velocities (NCVs) are greatly reduced. EMG and muscle biopsy are not usually required for diagnosis.[8]

Myasthenia gravis (MG) is an autoimmune disease of the neuromuscular junction. Neurophysiological investigations may show a decrement in the amplitude of muscle action potentials in response to repeated nerve stimulation.[9]

Evaluation of a neuromuscular disorder begins with the clinical history and examination and is supplemented by electromyography (EMG); nerve conduction studies, neuromuscular junction studies, and concentric needle EMG, muscle biopsy, and other laboratory tests.[10-11]

Electrodiagnostic studies are recommended if the diagnosis remains unclear after initial diagnostic testing and a careful history and physical examination.[12]

EMG can distinguish myopathic from neurogenic muscle wasting and weakness. It can detect abnormalities such as chronic denervation or fasciculations in clinically normal muscle.[13] It cannot diagnose particular myopathies whose characterization is made histologically or by immunochemistry. It may be able to determine only that there is a myopathic process but little further.[14]

The aim of this retrospective study is to assess the diagnostic value of EMG and NCV in children and to determine the concordance of the suspected clinical diagnosis and the findings of electrodiagnostic examination.

Methods

The study represents a retrospective analysis of clinical diagnosis and neurophysiological findings of 37 children and adolescents who were admitted or referred to the Department of Paediatric Neuroscience of Dhaka Shishu (Children) Hospital from Feb 2010 to Feb 2015 whose age ranged from 1 month to 15 years and who were advised for EMG & NCV.

CPK, EMG and NCV suggested for all and muscle biopsy for selected cases . Genetic study was not done due to unavailability. EMG and NCV was done in Bangladesh Protibondhi Foundation by trained person. Data of all 37 patients were documented and subsequently catagorized as either compatible or noncompatible with the clinical diagnosis of the patient.

All examinations were performed only after obtaining informed parental consent and, in most cases, in the presence of the parents.

Results

A total of 37 patients age ranging from 1 month to 15 years were eligible for enrollement into the present analysis. Of which 16 (43%) were from the age group 5–15 years and 24 (65%) were male. Consanguinity was present in 8 (22%) patients and history of perinatal asphyxia in 4 (11%) (Table I).

Hypotonia is an important clinical sign of neuromuscular disease and in this study more than half of the cases 21 (57%) presented with hypotonia. Delayed motor development was the second common (46%) presentation. Recurrent Respiratory Tract

Infection (RTI) is a common presentation among Spinal Muscular Atrophy (SMA) and 5 patients presented with recurrant RTI. (Table II). Deterioration of motor function was found in 11 (30%) cases.

Table I
Socio demographic status (n= 37)

Age	Number (%)
< 1 year	08 (22)
1- <5 years	13 (35)
5 – 15 years	16 (43)
Sex :	
Male	24 (65)
Female	13 (35)
Consanguinity	
Present	08 (22)
Absent	29 (78)
Perinatal asphyxia	
Present	04 (11)
Absent	33 (89)

Table II
Clinical presentation of the patients :(n=37)

Clinical features	Number (%)
Hypotonia	21 (57)
Delayed motor dev.	17 (46)
Deterioration of motor function	11 (30)
Frequent fall during walking	05 (14)
Recurrent RTI	05 (14)

Clinically 12 (32%) cases were diagnosed as SMA and 8 (22%) cases were muscular dystrophy. Myopathies other than muscular dystrophy were 7 (20%) and hereditary motor and sensory neuropathy were 5 (14%). The clinical spectrum of 16 children with myogenic disorder and 20 cases of neurogenic disorders is shown in table-3. Among the myogenic disorders 8 were muscular dystrophy, 7 were myopathy and 1 was mitochondrial myopathy. Among the neurogenic disorders, SMA was the commonest. HMSN cases were 5 and paraplegia were 3. One was neuromuscular junction disorder (myesthenia gravis).

Serum CPK level was done and results found normal in 19 (53%) cases. Higher level of CPK(>1000U/L) found in 11 (27%) cases. Serum CPK level was found consistently elevated in muscular dystrophy.

Table III
Clinical diagnosis (n=37)

Diagnosis	Number (%)
Myogenic : 16	
Muscular dystrophy	08 (22)
Myopathies	07 (20)
Mitochondrial myopathy	01 (03)
Neurogenic : 20	
Spinal muscular atrophy (SMA)	12 (32)
HMSN	05 (14)
Paraplegia	03 (08)
Junction disorder : 01	
Myesthenia gravis	01 (03)
Total	37 (100%)

Electromyographic (EMG) finding shows myogenic response in 13 (35%) cases and Neurogenic response in 15 (40%), normal record observed in 8 (22%) cases and 1 record shows mixed response. NCV was not recordable in 16 (45%) cases, no abnormality found in 12 (33%) cases. Motor and sensory conduction defects found in 9 cases (Table IV).

Table IV
Electrophysiologic (EMG / NCV) finding (n=37)

Electromyographic (EMG) Findings	Number (%)
Myogenic	13 (35)
Neurogenic	15 (40)
No abnormality	08 (22)
Mixed	01 (03)
Nerve Conduction Velocity (NCV) findings.	
Not recordable	16 (45)
No abnormality	12 (33)
Slow sensory conduction	04 (11)
Low amplitude motor	04 (08)
Low amplitude sensory	01 (03)

Clinical diagnosis of myogenic disorder was 16 and 13 (81%) was compatible with the electrodiagnosis (EMG/NCV). So compatibility was 81% for myogenic disorder.

Clinical diagnosis of neurogenic disorder was 20 and 15 (75%) was compatible with electrodiagnosis . So for neurogenic disorder 75% was compatible.

With the total 37 children, compatibility between Electrodiagnostic result and clinical diagnosis was in 28 (76%) cases.

Table IV
Compatibility of EMG / NCV results with Clinical diagnosis(n=37)

Clinical subgroup	No. of cases	Number (%)
Compatible with Diagnosis		
Myogenic	16	13 (81%)
Neurogenic	20	15 (75%)
Junction disorder	01	00
Total	37	28 (76%)

Discussion

The present analysis demonstrates that neurophysiological tests are important diagnostic tools to assist in the diagnosis of most NMDs. despite the increasing availability of molecular genetic testing.[15-16]

Among the clinically diagnosed cases, myopathy including muscular dystrophy was the most common(41%) and SMA (32%) was the second common disorder. EMG finding were compatible with clinical diagnosis of myopathic diseases in 13 (81%) out of 16 cases. Among the clinically diagnosed neurogenic diseases, 15 (75%) of total 20 cases were compatible with neurophysiological findings.

In a review of 4 retrospective studies of the diagnostic accuracy of EMG in infants with generalized muscle hypotonia ("floppy infants") came to the conclusion that a high rate of concordance exists between clinical diagnosis and the neurophysiologic examination in peripheral neurogenic diseases, whereas in myopathies false-negative results occurred in 50% to 75%. [17] In Another study shows patients with infantile spinal muscular atrophy had neurogenic changes on muscle biopsy consistent with the clinical diagnosis. In 13 (65%) of 20 patients with spinal muscular atrophy, the electromyogram met all the criteria for this diagnosis and thus was a good predictor of the final diagnosis.[18]

David and Jones found a high concordance rate of EMG with neurogenic disorders like SMA (88% to 93%) but a low concordance rate with myopathic disorders (31% to 50%) in very young children.[19] Russell et al. (1992) published a retrospective study reporting on 79 infants with generalized muscle hypotonia. They described consistent neurophysiological findings in 69% of all patients studied, whereas compatible EMG results could be identified in only 25% of patients with congenital myopathies. Serum CPK level was found consistently elevated in DMD. Electromyography (EMG) shows characteristic myopathic features but is not specific for DMD**.** No evidence of denervation is found. Motor and sensory nerve conduction velocities were normal.[20] In our study 5 patients are clinically diagnosed as HMSN and 3 (60%) of them are compatible with electrodiagnosis. Study of Feasby shows 17 of the 36 children of parents with HMSN 1, had slowed motor conduction velocities and clinical signs. A positive diagnosis based on clinical and electrophysiological criteria.[21]

NCV studies are of considerable value in the initial categorization of Charcot-Marie- Tooth disease into different subtypes. Although there is some overlap, motor conduction velocities in both HMSN Ia and both are greatly slowed and sensory conduction is impaired.[22]

Very few publications are available on procedural problems of EMG examination in pediatric patients. Hays and colleagues have addressed the problem of pain and stress in young patients and gave suggestions for optimization of the procedures.[23]

Conclusion

This study shows that in most of the cases EMG and NCV studies were in favour of the clinical diagnosis. In the evaluation of neuromuscular disorders, EMG and NCV are very useful in establishing or excluding a diagnosis of SMA, myopathy and other peripheral neuropathies and should be conducted as routine procedures

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ORIGINAL ARTICLE

Screening for Retinopathy of Prematurity in Neonatal Unit – An Experience of A Tertiary Care Hospital in Bangladesh

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Abstract

Background: *Retinopathy of prematurity (ROP) is a leading cause of childhood preventable blindness. Improved survival of preterm neonates has increased the incidence of retinopathy of prematurity (ROP).*

Objective: *To determine the incidence of retinopathy of prematurity (ROP) in Neonatal Unit of a Dhaka Shishu (Children) Hospital (DSH) and assess the treatment requirements of these cases.*

Methods: *A ROP prospective screening survey was performed enrolling preterm neonates with a gestational age of 34 weeks or less and a birth weight of 1800 gram or less admitted to the SCABU and NICU of Dhaka (Shishu) Children Hospital from July 2013 to July 2014. Retinal evaluation was done by indirect ophthalmoscopy and ROP was classified as type 1, type 2, APROP (Aggressive posterior ROP) and retinal detachment (RD) groups. Infants who were found type 1 ROP, APROP and RD were assigned for treatment.*

Results: *A total of 100 babies retinal evaluation were done. Among them 35 babies 70 eyes (35%) were found to have ROP (27 eyes 13.5% type1, 4 eyes 2.0% APROP, 5 eyes 2.5% retinal detachment and 34 eyes 17.0% were type 2). During the first screening 9 eyes had type 1, 52 eyes had type2, 4 eyes had APROP and 5 eyes were found to have retinal detachment. In the subsequent follow up another 18 eyes progressed to type 1 ROP from the type 2 group. In regards to treatment, 19 (52.8%) eye received laser, 10 (27.8%) eyes had received both laser and intra vitreal avastin, 2 eyes (2.6%) has got only intra vitreal avastin and 5 (13.9%) were advised for surgery.*

Conclusion: *The incidence of ROP is high in premature infants and more common in babies with gestational age less than 30 wks. Management of treatable ROP is also a time demanding issue.*

Key words: *Retinopathy of prematurity, ROP, prematurity, incidence, treatment, Bangladesh*

Introduction

Retinopathy of prematurity (ROP) is a disease of low birth weight and premature infants, in which the retinal blood vessels fail to develop properly. This may result in rapidly progressive ocular abnormalities and causing childhood blindness from retinal detachment, macular dragging, strabismus and refractive error.[1-4] With recent advances of care of very low birth weight infants, ROP is a serious problem among newborn babies. ROP may resolve without treatment by itself or can cause complications like moderate to severe visual

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impairments.[5, 6] Preventive measurements are the best treatment, if disease occurs; it should be follow up very closely. The reported incidence of ROP in different regions of the world may varies from 10 to 46% among the low birth weight premature infants.[7-9] It seems that the incidence of this disease is quite high in premature infants in many countries.[10] Today, the survival rates for premature infants with low birth weight are improved. The prevention of disabling the disease is highly significant.[11] Several investigations have been carried out to follow up parents, meticulous neonatal care; screening and early treatment can reduce disability from this disease.[10, 12]

Earlier the Cryotherapy for Retinopathy of Prematurity (CRYOROP) demonstrated the decrease of incidence of adverse structural outcome and severe visual loss by 50% and latter on laser photocoagulation showed significantly better structural outcomes and visual function than cryotherapy. At present anti vascular endothelial growth factors (Anti-VEGF) is also found an effective modality of treatment.[13, 14]

Children of premature deliveries and low birth weights do not born with ROP. We know the natural history of ROP and we have effective treatment to prevent blindness from it. As such, ROP screening is now recommended by many international bodies.[15] Once upon a time ROP was the disease of developed countries but at present with the improvement of neonatal care in the developing countries most of the premature and low birth weight babies survived causing the risk of developing ROP and hence childhood blindness.

Despite its importance, very little data regarding the incidence as well as treatment requirements are available for future planning. The goals of this article are to report the incidence of ROP in a tertiary neonatal care center and to determine treatable cases to aware the health care professionals to address this issue in Bangladesh. We believe that this study would give clinical information and resources needed to combat the upcoming epidemic of ROP in the country.

Materials and methods

As part of the continuous ROP screening program at the neonatal Intensive care unit (NICU) and SCABU of Dhaka Shishu (Children) Hospital, we reported here those from July 2013 to July 2014 on first 100 babies, with a gestational age of 34 weeks or less and birth weight of 1800 gram or less. Babies with gestational age >34 weeks or birth weight >1800 gms were excluded from the study. Retinal evaluation was done by a ROP screening group headed by Dr. Dipak Kumar Nag, Department of Vitreo -Retina of National Institute of Ophthalmology and Hospital. ROP screening was done using indirect ophthalmoscope and 20D condensing lens after dilatation of commercially available eye drop which contained 0.8% tropicamide and 5.0% phenyleprine.. ROP was classified as type 1(Severe form, needed treatment), type 2 (Mild form) and APROP (Aggressive posterior ROP) groups. Infants who were found type 1 ROP assigned for laser therapy. In case of APROP where laser can be applied satisfactorily was given laser, otherwise laser and intravitreal avastin both were given simultaneously. However in some situation where pupil was not well dilated or fundus could not be visualized clearly due to vitreous haziness or in most posterior situations, only intravitreal avastin was given as a rescue treatment. In cases with stage 4b and 5, vitrectomy was advised. First screening was done within the 30 days of birth but those came after that were also included in the study. Laser (double frequency Nd:YAG) and intravitreal injection (0.0625 mg Bivacizumab) was given as treatment according to indication mentioned earlier in the retina operation theater of NIO under surface anesthesia (oxybuprocaine 0.4%) in presence of anesthesiologist or neonatologist if required. After laser a combination eye drop dexamethasone 0.1 % and tobramycin 0.3% and after intravitreal injection only tobramycin 0.3 % were given for 7 days. Follow up was done on next day and 7 days after to see any adverse effect. Patients then followed up four weekly upto 40 weeks. Treatment outcome defined as good when on indirect ophthalmoscopy retina appeared stable, no sign of active disease and child can follow the optokinatic dram. Data was collected in a pre validated data sheet, zone and stages was drawn with colour pencil.

Results

A total of 100 babies retinal evaluation were done. Among them 35 babies (Fig 1) 70 eyes (35%) were found to have ROP (27 eyes 13.5% type1, 4 eyes 2.0% APROP, 5 eyes 2.5% retinal detachment and 34 eyes 17.0% were type 2). Table I shows the incidence of Retinopathy of prematurity according to gestational age. It is observed that who born ≤28 weeks were at greater risk to develop ROP, 10 out of 11 (90.9%) and risk reduced to 14.3% (3 out of 21) if babies born > 32 weeks.

Table I
Retinopathy of prematurity according to gestational age

GA (weeks)	Total Patients	ROP Patients	No ROP
≤28	11	10 (90.9%)	01 (09.1%)
29-30	38	15 (39.5%)	23 (60.5%)
31-32	30	7 (23.3%)	23 (76.7%)
>32 -34	21		

During the first screening 9 eyes had type 1, 52 eyes had type 2, 4 eyes had APROP and 5 eyes were found to have retinal detachment. In the subsequent follow up another 18 eyes progressed to type 1 ROP from the type 2 group (Fig 2).

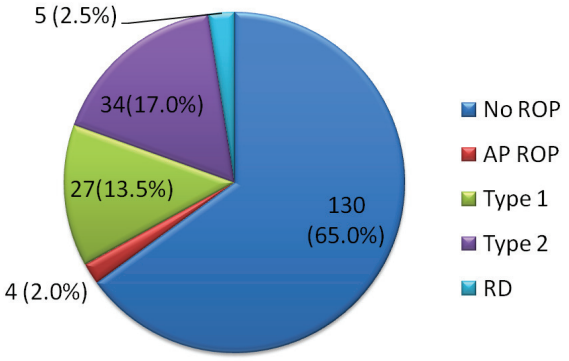

Fig 1 *Pie chart of ROP and no ROP among the screened babies.*

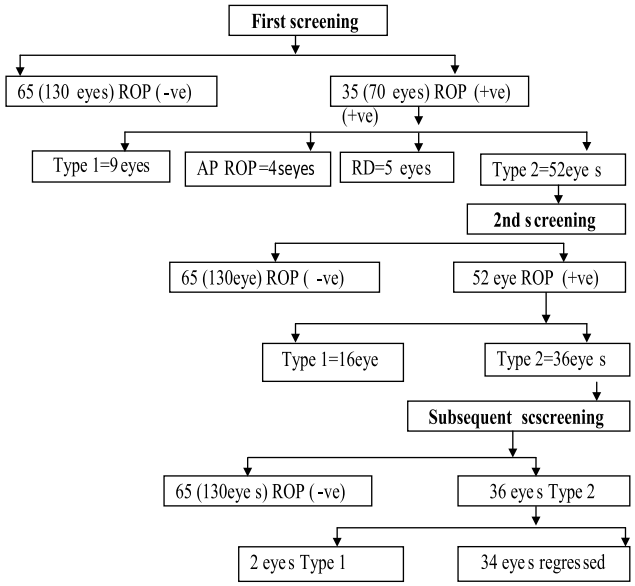

Fig 2 *Flowchart of Retinopathy of prematurity screening.*

Table II shows the incidence of retinopathy of prematurity according to the birth weight. It has been observed that all babies <1000g had ROP and the risk declined to approximately half (44.4%) if the birth weight was between 1000g to 1499g, and it was further reduced to nearly one tenth (11.8%) when the birth weight e" 1500g. Figure 3: depicted the bar diagram according to ROP/ no ROP according to birth weight.

Table II
Retinopathy of prematurity according to birth weight

Birth wt (gm)	N	ROP (%)	No ROP (%)
<1000	03	3 (100.0%)	00 (0.0%)
1000-1499	63	28 (44.4%)	35 (55.6%)
1500- 1750	34	4 (11.8%)	30 (88.2%)

In regards to treatment, 19 (52.8%) eye received laser, 10 (27.8%) eyes had received both laser and intravitreal bivacizumab, 2 eyes (2.6%) has got only intra vitreal bivacizumab and 5 (13.9%) were advised for surgery Figure 4).

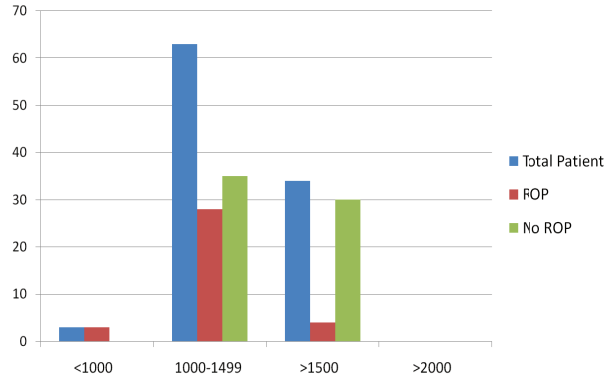

Fig 3 *Bar diagram according to ROP/ no ROP according to birth weight.*

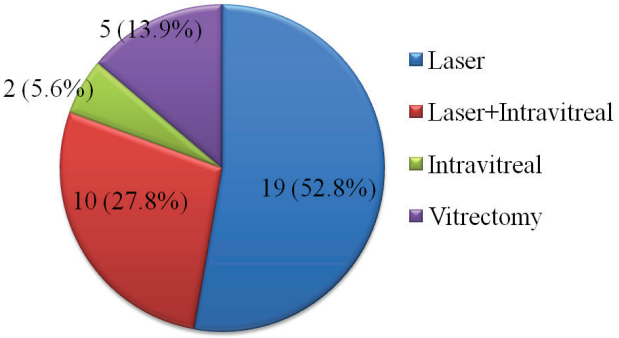

Fig 4 *Pie chart showing various modalities of treatment given for ROP babies*

Table III

Stages, treatment modality and outcome of treated of ROP patients (S=stages of ROP, Z=zone of ROP)

SL	Severity of ROP (Stage, Zone)		Modalities of Treatment				Outcome	
	OD	OS	Laser	Laser/ Intravitreal	Intra-vitreal	PPV	OD	OS
1	S3 Z2plus	S3 Z2 plus		√			GOOD	GOOD
2	S3 Z2 plus	S3 Z2 plus		√			GOOD	GOOD
3	S3 Z2 plus	Iva with VH	√ (Rt.)		√ (Lt.)		Good	Blind
4	S3 Z2 plus	S3 Z2 plus	√				GOOD	GOOD
5	IVb	Iva	√ (Lt.)			not done (Rt.)	Blind	Good
6	IVa	S3 Z2 plus		√		√ (Rt.)	Macular dragging	Good
7	S3 Z2plus	S3 Z2plus	√				Good	good
8	S3 Z1 plus VH	IVb	√ (Rt.)			√ (Lt.)	Macular dragging	blind
9	A-P	A-P with VH	√ (Rt.)		√(Lt.)		Blind	Blind
10	S3 Z2	S3 Z2		√			Good	Good
11	S3 Z2 plus	S3 Z2 plus	√				Good	good
12	S3 Z2 plus	S3 Z2 plus	√				Good	good
13	AP	AP	√				BLIND	BLIND
14	S3 Z2 plus	S3 Z2 plus	√				GOOD	GOOD
15	S2 Z2 plus	S2 Z2 plus	√				Good	Good
16	S1 Z2 plus	S1 Z2 plus	√				Good	Good
17	S2 Z2 plus	S2 Z2 plus		√			Good	Good
18	S3 Z2 plus	S3 Z2 plus	√				Good	Good

Table III showed the Stages, zones, treatment modality and outcome of treated of ROP patient's upto forty weeks of follow up. Laser showed the effective choice of treatment where it can be given satisfactorily (among 19 eyes (52.8%), one eye got macular dragging, 2 eyes got blind). Combined treatment of laser and intravitreal bivacizumab showed promising results (out of 10 eyes (27.8%), only one eye got macular dragging), On the other hand, only intravitreal bivacizumab and pars plana vitrectomy did not show good results in our study.

Discussion

Screening of premature low birth weight infants for retinopathy of prematurity is being carried out as a routine procedure in NICU and SCABU of Dhaka Shishu (Children) Hospital by the ROP team, National Institute of Ophthalmology since late 2013. We reported here result of the first 100 screened babies for the incidence of ROP and their treatment requirements. We have included the babies who were less than 34 weeks of gestational age and birth weight less than 1800 grams after a consensus meeting with the neonatologists, pediatric ophthalmologists and retina specialists forum on a strategic workshop on ROP screening held at the Ispahani Islamia Eye Institute & Hospital, Dhaka, Bangladesh in 2013.

Several studies have reported incidence rates ranging from 10% to 46% among low birth weight premature infants.[8-9] In our study have got 35% of the screened infants had ROP. The incidence of ROP was highest among the low gestational age ≤28 (90.9%) which steadily decreased with the increment of such ages. It has also been observed that low birth weight is the other most important risk factor for the development of ROP and found those babies who were <1000 gram had ROP in all of them. The development of ROP reduces with the increases of birth weight.

One of our important finding in this study is that we got most of the babies with ROP in first screening.

That means, although we decided to do first screening within 30 days of birth, many children came after the time frame and as such, we had few babies in advanced stages (2.5%, five eyes with retinal detachment). This could be important news for the neonatologists who are basically the integral part of ROP screening procedure.

Another observation in this study was recognition of aggressive posterior retinopathy of prematurity (APROP) in the Bangladeshi children. There were 2.0% (4 eyes) babies had aggressive form of the disease, an uncommon, rapidly progressing and severe form of ROP. APROP is characterized by its posterior location with prominence of plus disease, does not progress through classic stages from 1 to 3 and neovascularization may be flat and easily overlooked. In our study we did indirect ophthalmoscopy with the relative magnification of a 20 D condensing lens may aid in identifying this type of neovascularization[16].

Treatment was necessary after diagnosis of ROP varies in different literature and found from 1.4% to 10.8%.[17] In this study, there was 18.0% babies (36 eyes) required treatment by different modalities. Why such a large number of babies required treatment is a question indeed. We looked for the answer of this question and assumed that most of the screened babies came to us in advanced stages due to irregularity and missing of follow-up. As per treatment modalities, laser was still remained the best option in the early stage. However, intravitreal bivacizumab and pars plana vitrectomy were disappointing in our setting may be because of the lack of skillness or advanced stage of the disease.

Conclusions

The observed incidence of retinopathy of prematurity is high among the infants with very low birth weight. The development of ROP was inversely proportional to the weight and gestational age at birth.

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ORIGINAL ARTICLE

Clinical Presentation and Outcome of Children with Henoch-Schönlein Purpura in a Tertiary Care Hospital

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Abstract

Background: *Henoch-Schönlein purpura (HSP) is an inflammatory disorder characterized by a generalized vasculitis involving the small vessels of the skin, GI tract, kidneys, joints, and, rarely, the lungs and CNS. It is the most common vasculitis in children, twice as common in boys, peaks during the winter months and is often preceded by an upper respiratory tract infection. Despite much research, the cause is unknown.*

Objective: *The aim of this research is to study the clinical characteristics, diagnosis, prognosis and joint and kidney involvement in children with Henoch Schonlein Purpura in order to expand our knowledge about the disease.*

Methods: *This retrospective study was conducted in Dhaka Shishu Hospital & Bangladesh Institute of Child Health, Dhaka between July 2012 to June 2014 on 54 children admitted with HSP. The diagnosis of HSP was based on purpura, acute arthritis or acute arthralgia, accompanied by abdominal pain, histopathologically confirmed proliferative glomerulonephritis and renal involvement. Children with HSP less than 14 years of age, without any history/evidence of allergic or hematological disorders, systemic lupus erythematosus, renal or any other immunological disorders, and active infections (such as, tuberculosis, hepatitis B and other contagious diseases) were included in the study.*

Results: *Majority (63%) of the children was above 5 years old with mean age being 6 years (range: 1-10 years). Males outnumbered females by 3:2. The children with HSP invariably presented with skin rash (100%) followed by joint swelling (48.1%), arthralgia (44.4%), abdominal pain (44.4%), nausea/vomiting (40.7%), arthritis (37%) and GI bleeding (37%). The next common manifestations were acute nephritis (22.2%), proteinuria (14.8%), hematuria (11.1%), nephrotic syndrome (22.2%) and fever (22.2%). Thigh was the predominant site of rash (92.6%) followed by waist & hip (63%), foot & calf (59.3%), upper limb (29.6%) and abdomen (22.2%). Knee and ankle were frequently the affected joints. Elbow was less commonly affected. The mean ALT and AST were within normal range. The kidney function was also normal. Following interventions none of the patients had skin rash, arthralgia, joint swelling, nausea/vomiting, abdominal pain. Occult blood test was negative in all cases. The mean values of*

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serum ALT, AST, creatinine and total count of WBC and platelet were all within normal range. Serum ALT, AST after intervention reduced significantly following intervention ($p < 0.001$). Serum creatinine also reduced ($p = 0.021$). Total count of WBC and platelet count also dramatically dropped following intervention ($p < 0.001$).

Conclusion: *The patients of Henoch–Schönlein purpura presents diversly but skin rashes present in all patieint. It is diagnosed soley by clinical pesentation as no definite diagnostic tools are available and HSP bears good prognosis.*

Key words: *Henoch–Schönlein purpura, clinical presentation, outcome etc.*

Introduction

Henoch-Schönlein purpura (HSP) is the commonest systemic vasculitis of childhood typically presenting with a palpable purpuric rash and frequently involving the renal system. The reported incidence ranges from 10–20 cases per 100,000 children per year.[1] The estimated annual incidence of HSP in China is 14.06 cases per 100,000 children[2] with an increasing trend observed over successive years. However, this rising trend has recently tapered, possibly due to changes in social, economic, health, and environmental conditions.[3] The disease can present at any age, but 75% of the patients are under 8 years and 90% under 10 years of age[4-6] with mean age of the patients being 6 years. In some series, boys are affected more than girls.[7] Generally the prognosis is good with the exception of those with significant renal involvement.[8]

The disease was first recognized in 1801 by Heberden and was first described its association with arthritis by Schonlein in 1837.[9] It is a systemic vasculitic disease affecting mainly the small vessels of skin, joints, gastrointestinal tract, and kidneys. The typical clinical characteristics involve the triad of palpable purpura, abdominal pain and arthritis. The incidence of joint involvement in HSP patients could be as high as 78%,[10] which is the second most common feature after dermal manifestations.[11] Joint manifestations in HSP tend to be neglected due to their mild nature. The exact etiology of the disease is unclear. However, certain factors like infections (mainly upper respiratory infection), drugs, food, insect bites and vaccination are considered triggering factors for HSP. Physical conditions, such as exposure to cold are also known to be environmental triggers for the disease onset. The pathogenesis of HSP is related to aberrant deposition of IgA-containing immune complexes,[12] which typically affects skin, gut, joints and glomeruli. Isolated microscopic hematuria and minimal proteinuria are common occurrences in children, with nephrotic syndrome and renal dysfunction also being observed occasionally. The prognosis is, to a large extent, dependent on the severity of renal involvement.[7,13,14]

Of the complications encountered, progressive renal function impairment and bowel perforation are not uncommon, but central nervous system involvement is rare. The occurrence of purpura, which is non-thrombocytopenic, is the essential element for the diagnosis of HSP. The purpura is often located on lower extremities and buttocks.[15] HSP, in general, is considered benign and self-limited and the treatment is supportive. Moreover, atypical cases are liable to be misdiagnosed and mistreated. So investigation of every potential case and assessment of renal involvement in these patients are important for the successful management of HSP. To expand our knowledge about HSP, we retrospectively reviewed the clinical characteristics, prognosis and joint and kidney involvement in HSP patients.

Materials and methods

This retrospective study was conducted in Dhaka Shishu Hospital, Dhaka over a period of 2 years between July 2012 to June 2014 on children admitted with HSP and were treated completely up to recovery. In this study definition of HSP had been adopted from the European League Against Rheumatism (EULAR) endorsed consensus criteria for HSP classification.[10] In this study HSP is defined by purpura, acute arthritis or acute arthralgia, accompanied by: abdominal pain (diffuse colicky pain with or without gastrointestinal bleeding and emesis, histopathologically confirmed proliferative glomerulonephritis with predominant IgA deposit or typically leucocytoclastic vasculitis with predominant IgA deposit, renal involvement as evidenced by proteinuria or hematuria. Children with HSP below the age of 14 years, without any history or evidence of allergic or hematological disorders, systemic lupus

erythematosus, renal or any other immunological disorders, and active infections (such as, tuberculosis, hepatitis B and other contagious diseases) were included in the study. These cases are diagnosed based on their specific clinical and laboratory criteria. However, patients with incomplete information, or patients unable to comply with the treatment or patients with pre-existing severe heart, liver, lung, kidney or other systemic diseases were excluded from the study.

Proteinuria is defined as urine albumin > 30 mg/dl of urine or albumin > 4mg/m^2/h or urinary albumin/creatinine ratio on a spot morning sample of >0.2.[16] Arthritis was defined as arthralgia with limited movement or joint swelling. Arthralgia was defined as joint pain without restricted movement of joint or swelling. Approval for the study was obtained from the Ethical Review Committee of the Hospital. Previous infection, special food, vaccination, insect bite, and accident were considered as the triggering/precipitating factors and were specially looked for, if they happened in 2 weeks before HSP onset. Preceding infection was self reported. Microscopic hematuria was defined as more than 5 RBCs per high power field in the sediment from 10 ml of centrifuged freshly voided urine, while gross hematuria was defined as blood in the urine seen with the naked eye.[17] Rash location means parts of the body where purpura was mainly concentrated. Elevated ESR was defined when ESR was > 20 mm/hour; increased ASO titer meant when the titer increased > 300 IU/mm.

The statistical analyses were performed using computer software SPSS (Statistical Package for Social Sciences), version 17 and test statistics used to analyse the data were Chi-square (χ^2) Test, Unpaired t-Test. While categorical data were compared between groups using Chi-square (χ^2) or Fisher's Exact Test, as appropriate, changes in continuous variables following intervention were evaluated using Unpaired t-Test. The level of significance was set at 5% and $p < 0.05$ was considered significant.

Results

Majority (63%) of the children was above 5 years old with mean age being 6 years. The youngest and the oldest children were 1 and 10 years old respectively. Male was predominant with male to female ratio 3:2 (Table I). The children with HSP invariably presented with skin rash (100%) followed by joint swelling (48.1%), arthralgia (44.4%), abdominal pain (44.4%), nausea/vomiting (40.7%), arthritis (37%) and GI bleeding (37%). The next common manifestations were acute nephritis (22.2%), proteinuria (14.8%), hematuria (11.1%), nephrotic syndrome (22.2%) and fever (22.2%). The less common manifestations were scrotal swelling, seizure, pulmonary haemorrhage (Figure 1). Thigh was the predominant site of rash (92.6%) followed by waist & hip (63%), foot & calf (59.3%), upper limb (29.6%) and abdomen (22.2%) (Figure 1I). Knee and ankle were the frequently affected joints (37% each). Elbow was less commonly affected (18.5%). Metacarpo-phalangeal and wrist joints were least affected (Fig 3). Pertinent haematological and biochemical findings of the patients are illustrated in Table II. The categorical variables are presented as frequency and corresponding percentage and quantitative variables are presented as mean and standard deviations (SD) from the mean. The mean ALT and AST were within normal physiological range. The kidney function was also normal as indicated by serum creatinine (mean serum creatinine 0.74 mg/dl) (Table III).

Outcome variables show that none of the patients had skin rash, arthralgia, joint swelling, nausea/vomiting, abdominal pain. Occult blood test was found negative in all cases. The mean values of serum ALT, AST, creatinine and total count of WBC and platelet were all within normal range (Table II). Comparison of serum ALT, AST (liver function test variables) before and after intervention shows that they reduced significantly following intervention ($p < 0.001$). Serum creatinine also reduced ($p = 0.021$). Total count of WBC and platelet count also dramatically dropped following intervention ($p < 0.001$) (Table IV).

Table I
Distribution of the children by demographic characteristics (n = 54)

Demography	Frequency	Percentage
Age (yrs)		
≤ 5	20	37.0
> 5	34	63.0
Sex		
Male	32	59.3
Female	22	40.7

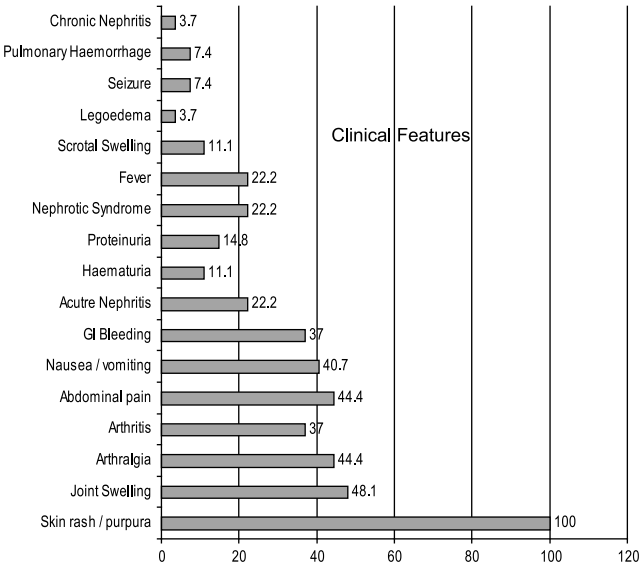

Fig 1 *Distribution of children by their clinical features*

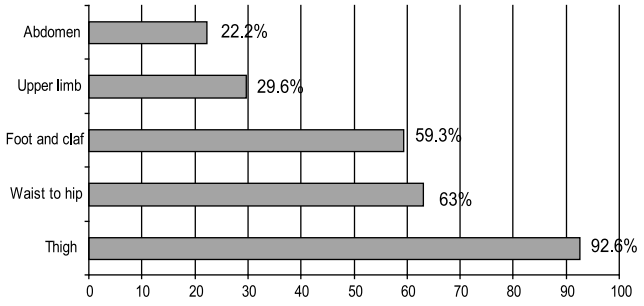

Fig 2 *Distribution of children by location of rash*

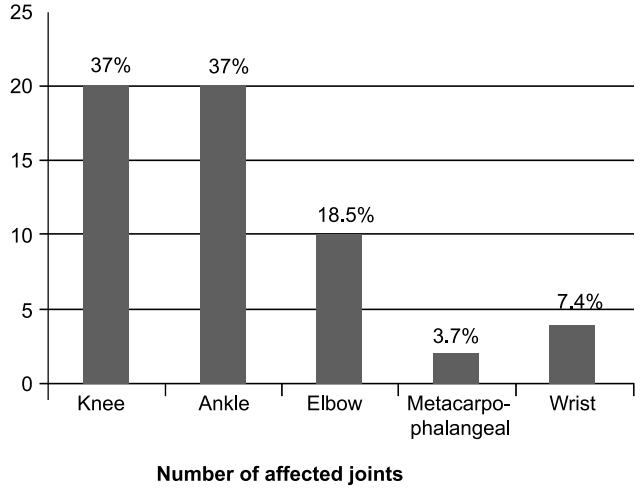

Fig 3 *Distribution of children by affected joints (n = 54*

Table II
Distribution of children by laboratory test findings (n = 54)

Laboratory test	Mean ± SD
Platelet count (per cu-mm)	398148 ± 15089
Clotting time (sec)	6.22 ± 0.96
Bleeding time (sec)	3.55 ± 0.88
Anti-Streptolysin O titres (units/mL)	231.8 ± 58.1
Serum C3 (mg/dL)	1.00 ± 0.01
Serum CRP (mg/dL)	44.66 ± 13.14
ESR (mm at the end 1st hour)	63.44 ± 13.7
Total count of WBC (per cu-mm)	14519 ± 1518
Differential Count of WBC (%)	
Neutrophil (%)	76.7
Lymphocyte (%)	17.9
Monocyte (%)	2.6
Eosinophil (%)	2.5
Basophil (%)	0.14

Table III
Changes in liver and kidney functions and haematological variables

Variables	Group		p-value
	Before intervention (n = 54)	After intervention (n = 54)	
Serum ALT (IU/L)	43.0 ± 6.7	37.7 ± 9.7	<0.001
Serum AST (IU/L)	37.9 ± 6.5	34.8 ± 8.6	0.021
Serum creatinine (mg/dl)	0.74 ± 0.16	0.65 ± 0.19	0.002
Total count of WBC (per cu-mm)	14519 ± 1518	9292 ± 1239	<0.001
Platelet count (per cu-mm)	398148 ± 15089	165000 ± 22445	<0.001

Discussion

In the present study, nearly two-thirds of the cases of HSP occurred after 5 years of age with mean age of occurrence being 6 years. A male preponderance was also observed in our study with male-to-female ratio being 3:2. Studies have shown that school-age children are more often affected (mean age-incidence being 6 years) than preschool children, and the disease is more prevalent in boys than in girls consistent with these demographic features of children with HSP.[5-7] In contrast Narchi showed that HSP can present at any age, but is most common in children under five.[8] The disease has been reported to occur most frequently at age of 4-7.[18,19]

Although most studies have shown a male preponderance,[18-22] but there are reports where greater number of females have been found to be affected.[5,23] The higher incidence of HSP in boys could be explained by their increased exposure to various allergens and a higher chance of contacting infection, (for boys are generally more active than the girls in this age-group). Infection has been previously reported as the major predisposing factor for HSP.[6,18,19] Most of the cases being reported in autumn, winter, fall and spring.[24] We did not analyse the seasonal variation in the incidence of the disease. Wang[24] reported 90% of the children with HSP developed skin manifestations at the outset. Most commonly, the rash first appeared in the lower limbs and foot and gradually spread over to other limbs. In our study as well, over 90% of the children had rash in their thighs. In previous studies, rash has been reported to be occurring mainly in lower limbs and buttocks.[25] Half of the children in the present study had joint involvement (either joint swelling or arthralgia) and over one-third had arthritis (both joint swelling and arthralgia). Wang's[24] study demonstrated that varying degrees of joint involvements, which occurred with rash in most patients or after rash with no specific clinical manifestations. Pain, swelling and other symptoms sometimes did not occur simultaneously, mostly occurred as acute arthritis with different nature of pain. Joint symptoms frequently occur in weight bearing large joints with knee and ankle joints being most affected ones. Abdominal pain, vomiting and gastrointestinal bleeding are the most common symptoms in patients with HSP[7,19,20,21,23] which bear consistency with findings of our study. The reported incidence of gastrointestinal symptoms could be as high as 34-75%. However, some reports have indicated gastrointestinal bleeding as the most common symptom[19,23] while some others have reported pain to be the most common symptom.[19,21]Wang[24] reported 56% of the patients had gastrointestinal symptoms, with abdominal pain being the most common, followed by vomiting and gastrointestinal bleeding. In this study abdominal pain, nausea, vomiting and GI bleeding were 44.4%, 40.7% and 37% respectively. The diagnosis of HSP is usually straightforward in children presenting with skin purpura or rash followed by GI symptoms and joint involvement. However, some patients might present with atypical manifestations leading to a misdiagnosis.

Wang[24] found 11% of children to present with abdominal pain or arthralgia as the initial symptoms. Previous reports[10,20,21] indicate that 15-25% of patients may present with joint symptoms one week prior to the rash. Ten to 20% of these patients have been reported to present with abdominal pain two weeks prior to the appearance of rash. Our experience suggests that if children with abdominal pain or arthralgia are admitted and develop rash a few days later, the diagnosis of HSP should be considered. Thus, it is important for the health care professionals to have adequate knowledge about variable presentation of HSP so as to avoid unnecessary invasive procedures in such cases.

Renal function is a key determinant of prognosis in HSP patients. In our study 6 (11.1%) children had haematuria, which in other studies were found ranging from 20 - 54%.[19,26-28] Although the exact mechanism of pathogenesis is not clear, previous studies have implicated IgA-containing immune complex deposition in glomerular basement membrane.[13] The main pathological changes include messangial proliferative changes, with varying degrees of segmental necrosis and glomerular crescent formation.[29] Earlier studies have shown that HSP nephritis (HSPN) is mostly seen within 1 month, with some cases occurring within 6 months, and a few cases appearing after 1 year. Among these cases, 1-2% of patients may develop irreversible kidney damage.[30] In Wang's study,[24] 76% cases developed HSPN within 1 month, with most occurring within 2 weeks. No cases of end-stage renal disease was observed during the 2-year follow up period indicating that the prognosis for HSPN was good in this study.[14,18,19]

Conclusion

The patients of Henoch–Schönlein purpura presents diversly but skin rashes present in all patieint. It is diagnosed soley by clinical pesentation as no definite diagnostic tools are available and HSP bears good prognosis. As we did not have follow up data, the comment on long-term outcome of these patients is left pending.

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ORIGINAL ARTICLE

Role of RBC Indices in Screening of Thalassaemia and other Haemoglobinopathies in Children

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Abstract

Background: *Thalassaemia and haemoglobinopathies are common genetic disorders in Bangladesh. There are expensive tests to diagnose thalassaemia and haemoglobinopathies which are not affordable by majority of our patients. As cellcounter is now widely available this study was undertaken to see the role of RBC indices in suggesting thalassaemia and advising further confirmatory tests like High Performance Liquid Chromatography (HPLC) or haemoglobin electrophoresis.*

Objective: *To observe values of RBC indices as tools for screening of thalassaemia and haemoglobinopathies.*

Methodology: *The retrospective study was carried out in Dhaka Shishu Hospital from November 2011 to November 2013. From the register, 555 subjects were taken as the study population. The study population were diagnosed as Beta thalassaemia major, Haemoglobin E beta thalassaemia, beta thalassaemia trait, haemoglobin E trait, haemoglobin E disease and normal haemoglobin status by HPLC. Their RBC indices were also taken from the register. Data were analyzed by SPSS (version 11.5). Mean values of RBC indices were expressed in different age groups against the diagnosis. Independent sample 't' test was done to show the difference of mean values of RBC indices between the Normal haemoglobin status and thalassaemia or haemoglobinopathies.*

Result: *Mean values of RDW was markedly raised in both beta thalassaemia major and haemoglobin E beta thalassaemia with low mean values of RBC count, MCV and MCH. Mean values of RBC count were significantly high in both beta thalassaemia trait and haemoglobin E trait when compared with control, though mean values of MCV and MCH were low in these groups but not statistically significant when compared with the control.*

Conclusion: *Simple observation of RBC indices can be utilized to screen thalassaemia and haemaglobinopathies. HPLC should be advised for confirmation.*

Key words: *RBC indices, Thalassaemia, haemoglobinopathies, HPLC*

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Introduction

Thalassaemia and haemoglobinopathies are commonest genetic disorders of haemoglobin.[1] Thalasssaemia are characterized by a reduced rate of production of normal haemoglobin due to absent or decrease synthesis of one or more type of polypeptide chain. Haemoglobinopathies are characterized by the production of structurally defective haemoglobin due to abnormalities in the formation of globin moiety of the molecule.[2]

These hereditary disorders are major public health problem in many parts of the world including Bangladesh. The clinical spectrum of the disorders varies from asymptomatic conditions to serious disorders like thalassaemia major that requires regular blood transfusions and extensive medical care. World Health Organization (WHO) figures estimates that 7% of world population is carrier for hemoglobin disorders.[3]

Beta thalassaemia and Hb-E-Beta thalassaemia is common in our country. A conservative world health report has estimated that 3 percent are carriers of Beta thalassaemia and 4 percent carriers Hb-E- Beta thalassaemia (WHO 1994). A recent study on school children in different district of Bangladesh has shown overall prevalence of Beta thalassaemia trait was 4.1 percent and Haemoglobin E trait was 6.1 percent.[4]

Cell counters are now widely used in our country for routine haematological parameters including haemoglobin, total count of WBC, differential count of WBC, platelet count along with RBC indices.

Microcytic hypochromic anaemia is most common in our population.[5] Causes of anaemia mainly include iron deficiency, Haemoglobin disorders like beta thalassaemia major, Hb-E-beta thalassaemia, beta thalassaemia trait, haemoglobin E trait and haemoglobin E disease. To screen and diagnose thalassaemia and haemoglobinopathies RBC indices like total count of RBC, MCV, MCH and RDW can be utilized. Final diagnosis should be made by High Performance Liquid Chromatography or electrophoresis of haemoglobin. Therefore the topic was selected to find out simple observational methods which will be easy to interpret for diagnosis of thalassaemia and haemoglobinopathies by observing cell counter reports at a glance and later on going for confirmatory test. Individuals with RBC indices values like MCV<75 fl, MCH<26 pg are advised for Haemoglobin Electrophoresis or High Perfomance Liquid Chromatography of haemoglobin as part of screening and creating awareness for thalassaemia prevention programme.[6]

High Performance Liquid Chromatography of haemoglobin is a powerful, excellent diagnostic tool for direct identification of different haemoglobin variants with a high degree of precision in the quantification of major and minor, normal and abnormal, haemoglobin fractions.[7]

Normal haemoglobin fractions include: Haemoglobin A (about 95% - 98%), Hb A_2 (about 2% - 3.5%), Hb F (up to 2%) this is the primary haemoglobin produced by the fetus during gestation. Its production usually falls to a low level within a year after birth. Haemoglobin variant include: Haemoglobin E, Haemoglobin S, Haemoglobin D, Haemoglobon C, Haemoglobin lepore etc.[8]

Materials and methods

This retrospective study was conducted in pathology department of Dhaka Shishu Hospital from November 2011 to November 2013. Patients are referred to the department of pathology for the confirmation of diagnosis of thalassaemia and haemoglobinopathies. These patients were advised by different paediatrician, haematologist and clinical pathologist to do High Performance Liquid Chromatography .

For doing the test two ml of blood samples were collected in a vial containing ethylene diamine tetra acetic acid (EDTA) and mixed immediately.

HPLC was done by BIO –RAD D-10™ Dual program for determination of different fractions of haemoglobin level. A value of more than 3.5% of A_2 fraction of hemoglobin was taken as the cut off point for determining the beta thalassemia trait. A_2 peak between 25% -30% was labeled as Haemoglobin E trait. 10% to 90% Haemoglobin F was diagnostic for thalassaemia.[2]

Blood samples were also run in automated hematology analyzer mythic-18 for cell counts and red blood cell indices before doing HPLC. Blood films were reviewed to correlate with HPLC before giving the final diagnosis.

Patients' age, sex, RBC indices and HPLC reports were recorded in the register. From the register total 555 subjects whose haemoglobin level were less than

or equal to 11 gm/dl was taken as the study population. Out of total 555 subjects199 subjects were reported as normal haemoglobin status they were considered as control and 356 subjects were reported as cases of Beta thalassaemia major, Haemoglobin E Beta thalassaemia, beta thalassaemia trait, Haemaoglobin E trait, Haemoglobin E disease. RBC indices of the study populations were also taken from the register. They were divided into 3 groups according to age as RBC indices varies in different age group. Group I: below 1 years, group II: 1 years to 8 years, Group III: 8 years to 16 years. Data were analysed by SPSS (version11.5), mean values of RBC indices were expressed in different age groups against the diagnosis. Independent sample t test was done.

Patient having previous transfusion at least within four months were excluded from the study.

Results

HPLC of haemoglobin reports of 555 subjects were included in the study. Among them total 64.1% have different types of haemoglobinopathies. most common was haemoglobin E beta thalassaemia which was 21.3% ,followed by Beta thalassaemia trait 20.2%,then E trait which was 15%,Beta thalassaemia major4.9%,Haemoglobin E disease was2.7%,35.8% were normal (Table I).

Table I

Result of haemoglobin variant by HPLC (n=555)

Diagnosis	No of subject	Percent
Normal haemoglobin status	199	35.8
Hb-E beta thalassaemia	118	21.3
Beta thalassaemia trait	112	20.2
Haemoglobin E trait	84	15.1
Beta thalassaemia major	27	4.9
Haemoglobin E disease	15	2.7
Total	555	100

According to Age the RBC indices were analyzed against diagnosis, results were expressed as mean±SD (table 2, 3& 4).Mean value of RDW is markedly increased in both thalassaemia major and Hb-E beta thalassaemia along with lower mean values of Hb, MCV, MCH and RBC count. Mean value of RDW is mildly high in other cases along with normal mean value RBC count, lower Hb, MCV and MCH (table II, III & IV).

Table II

RBC indices in normal haemoglobin status infant and infant with thalassaemia and haemoglobinopathies aged below 1 year (group I) (n=145)

Diagnosis	Haemoglobin in gm/dl (Mean±SD)	RBC 10^9/ L (Mean±SD)	MCV Fl (Mean±SD)	MCH Pg (Mean±SD)	RDW (Mean±SD)
N (n=58)	7.99±2.12	4.16±.89	63.17±9.51	19.38±3.90	18.50±3.20
BTT (n=26)	8.25±1.74	4.64±.77	60.81±12.41	19.04±4.09	19.15±3.54
ET (n= 20)	8.22±1.64	4.49±.53	60.00±7.58	18.44±3.01	18.53±2.82
BTM (n=19)	5.65±2.11	2.33±.96	68.18±7.74	26.42±12.54	28.31±4.42
EBT (n=21)	5.77±1.38	3.06±.88	59.81±6.62	19.09±3.28	28.43±3.91
ED (n=1)	8.200	5.59	43.00	15.00	21.00

Normal haemoglobin status, BTT=Beta thalassaemia trait, ET=Haemoglobin E trait, BTM=Beta thalassaemia major, EBT=Haemoglobin E beta thalassaemia, ED=E disease RBC=RBC cout, MCV=Mean corpuscular volume, MCH=Mean corpuscular haemoglobin, RDW=Red cell distribution Width.

Table III

RBC indices in normal haemoglobin status children and children with thalassaemia and haemoglobinopathies aged 1 to 8 years (group II) (n=347)

Diagnosis	Haemoglobin gm/dl (Mean±SD)	RBC 10^9/ L (Mean±SD)	MCV Fl (Mean±SD)	MCH Pg (Mean±SD)	RDW (Mean±SD)
N (n=125)	8.52±2.36	4.27±1.01	66.27±13.00	20.13±5.12	17.85±3.26
BTT (n=77)	9.26±1.59	4.81±1.12	62.98±10.52	20.56±4.02	17.17±3.76
ET (n= 53)	9.64±1.97	4.72±.85	63.81±8.59	20.32±3.68	16.96±3.50
BTM (n=8)	5.19±1.88	2.44±.74	67.75±5.26	21.13±4.26	28.00±2.33
EBT (n=73)	5.83±1.36	3.24±.71	59.19±5.22	18.32±2.46	27.31±3.33
ED (n=11)	8.94±.68	4.89±.47	56.18±3.31	18.18±1.33	17.36±2.35

N=Normal haemoglobin status, BTT=Beta thalassaemia trait, ET=Haemoglobin E trait, BTM=Beta thalassaemia major, EBT=Haemoglobin E beta thalassaemia, ED=E disease RBC=RBC cout, MCV=Mean corpuscular volume, MCH=Mean corpuscular haemoglobin, RDW=Red cell distribution Width.

Table IV

RBC indices in normal haemoglobin status children and children with thalassaemia and haemoglobinopathies aged 8 to 16 years (group III)(n=63)

Diagnosis	Haemoglobin gm/dl (Mean±SD)	RBC 10^9/L (Mean±SD)	MCV Fl (Mean±SD)	MCH Pg (Mean±SD)	RDW (Mean±SD)
N(n=16)	9.96 ±2.70	4.24±.66	75.62±13.06	23.38±4.81	14.90±2.98
BTT (n=9)	10.11±1.19	5.09±.74	63.11±13.18	20.22±4.44	16.56±4.48
E T (n= 11)	10.70±1.81	5.00±.90	68.90±7.80	22.10±2.47	14.70±2.06
E BT (n=24)	4.94±1.81	2.78±1.01	57.50±8.10	18.04±3.40	26.90±3.19
ED (n=3)	7.63±4.91	4.14±2.73	57.00±1.00	18.67±1.53	20.63±8.99

N= Normal haemoglobin status, BTT=Beta thalassaemia trait, ET=Haemoglobin E trait, BTM=Beta thalassaemia major, EBT=Haemoglobin E beta thalassaemia, ED=E disease RBC=RBC cout, MCV=Mean corpuscular volume, MCH=Mean corpuscular haemoglobin, RDW=Red cell distribution Width.

RBC count and Hb were significantly low (p value<.001) and RDW was significantly high (p value <.001) in both beta thalassaemia major and haemoglobin E beta thalasssaemia in all groups (table 5,6). MCV and MCH values were significantly low in group II and group III haemoglobin E beta thalassaemia (p value<.001) and they were also significantly low in group I beta thalassaemia major (p value<0.05) ((table 5,6).

RBC count was significantly high in all groups of beta thalassaemia trait and haemoglobin E trait (p value<0.02). MCV is significantly low in group III beta thalassaemia trait (p value<0.03).Although in this study RDW was higher than normal reference range in both normal and beta thalassaemia trait, but it was lower than the normal in group II beta thalassaemia trait,(p value<0.01) (Table 7,8).

Table V

Comparison of RBC indices between Normal Haemoglobin status and beta thalassaemia major patients

		Normal haemoglobin status	Beta thalassaemia major	Mean Difference	Level of Significance (p vlue)
Group I	Total RBC count10^9/L	4.16±.89	2.33±.96	1.83	<.001***
	Haemoglobingm/dl	7.99±2.12	5.65±2.11	2.34	<.001***
	MCV fl	63.17±9.51	68.18±7.74	2.41	<.05 *
	MCH pg	19.38±3.90	26.42±12.54	4.25	.001**
	RDW	18.50±3.20	28.43±3.91	9.82	<.001***
Group II	Total RBC count10^9/L	4.27±1.01	2.44±.74	1.84	<.001***
	Haemoglobingm/dl	8.52±2.36	5.19±1.88	3.34	<.001***
	MCV	66.27±13.00	67.75±5.26	1.47	.75
	MCH	20.13±5.12	21.13±4.26	1.00	.59
	RDW	17.85±3.26	28.00±2.33	10.15	<.001***

p value <0.001=***
p value <0.01 =**
p value<0.05 = *
No beta thalassaemia Major patients were diagnosed in Group III

Table VI

Comparison of RBC indices between normal haemoglobin status children and haemoglobin E beta thalassaemia patients

		Normal	Haemoglobin E beta thalassaemia	Mean Difference	Level of Significance (p vlue)
Group I	Total RBC count10^9/L	4.16±.89	3.06±.88	1.09	<.001***
	Haemoglobingm/dl	7.99±2.12	5.77±1.38	2.22	<.001***
	MCV fl	63.17±9.51	59.81±6.62	3.63	.140
	MCH pg	19.38±3.90	19.09±3.28	0.28	.767
	RDW	18.50±3.20	28.43±3.91	9.93	<.001***
Group II	Total RBC count10^9/L	4.27±1.01	2.78±1.01	1.03	<.001***
	Haemoglobingm/dl	8.52±2.36	5.83±1.36	2.69	<.001***
	MCV	66.27±13.00	59.19±5.22	7.08	<.001***
	MCH	20.13±5.12	18.04±3.40	1.81	<.001***
	RDW	17.85±3.26	27.31±3.33	9.45	<.001***
Group III	Total RBC count10^9/L	4.24±.66	2.78±1.01	1.46	<.001***
	Haemoglobingm/dl	9.96 ±2.70	4.94±1.81	5.06	<.001***
	MCV	75.62±13.06	59.19±5.22	18.13	<.001***
	MCH	23.38±4.81	18.04±3.40	5.33	<.001***
	RDW	14.90±2.98	27.31±3.33	12.01	<.001***

p value <0.001=***
p value <0.01 =**
p value<0.05 = *

Table VIII
Comparison of RBC indices between normal haemoglobin status children and beta thalassaemia traits

		Normal Haemoglobin study (Mean±SD)	Beta thalassaemia trait (Mean±SD)	Mean difference	Level of significance (p value)
Group I	Total RBC count10^9/L	4.16±.89	4.64±.77	.48407	.02*
	Haemoglobingm/dl	7.99±2.12	8.52±1.78	.26131	.58
	MCV fl	63.17±9.52	60.18±12.41	2.3640	.34
	MCH pg	19.37±3.90	19.03±4.09	.9234	.93
	RDW	18.5±3.2	19.15±3.54	.78098	.78
Group II	Total RBC count10^9/L	4.27±1.01	4.81±1.12	.38443	.006**
	Haemoglobingm/dl	8.52±2.36	9.26±1.59	.65840	.034*
	MCV fl	66.28±13.00	64.11± 11.45	2.17015	.23
	MCH pg	20.13±5.12	20.18±4.02	.05880	.93
	RDW	17.85±3.26	17.17±3.76	1.17194	.012*
Group III	Total RBC count10^9/L	4.24±.66	5.09±.74	.85049	.007**
	Haemoglobingm/dl	9.96±2.70	10.11±1.18	.14861	.87
	MCV fl	75.62±13.06	63.11±13.18	12.51589	.03*
	MCH pg	23.38±4.81	20.22±4.44	3.15278	.12
	RDW	14.90±2.98	16.56±4.47	1.65556	.27

p value <0.001=***
p value <0.01 =**
p value<0.05 = *

Table VIII
Comparison of RBC indices in normal haemoglobin status children and haemoglobin-E traits

		Normal Haemoglobin study (Mean±SD)	Haemoglobin E- trait (Mean±SD)	Mean difference	Level of significance (p value)
Group I	Total RBC count109/L	4.16±.89	4.50±.53	.33707	.05*
	Haemoglobingm/dl	7.99±2.12	8.21±1.64	.22362	.67
	MCV fl	63.17±9.52	60.00±7.58	3.17241	.14
	MCH pg	19.37±3.90	19.03±4.09	.9234	.93
	RDW	18.50±3.2	19.42±3.54	.95941	..271
Group II	Total RBC count109/L	4.27±1.01	4.72±.85	..43726	.004**
	Haemoglobingm/dl	8.52±2.36	9.26±1.59	.65840	.03*
	MCV fl	66.28±13.00	64.11± 11.45	2.17015	.23
	MCH pg	20.13±5.12	20.18±4.02	.05880	.93
	RDW	17.85±3.26	17.17±3.76	1.17194	.01**
Group III	Total RBC count109/L	4.24±.66	5.00±.90	.76037	.02*
	Haemoglobingm/dl	9.96±2.70	10.70±1.81	.7375	.40
	MCV fl	75.62±13.06	68.90±7.79	6.725	.11
	MCH pg	23.38±4.81	22.10±2.47	1.275	.38
	RDW	14.90±2.97	14.70±2.06	.2000	.84

p value <0.01 =**
p value<0.05 = *

Discussion

Thalassaemia is an emerging health problem in developing countries like Bangladesh. As a result of reduction of deaths from infectious disesese and improved status of nutrition increasing number of children are now attending hospital with genetic or heriditary disorders like thalassaemia. This study was performed to get an easily performed, available and cheap screening procedure for thalassaemia and haemoglobinopathies This study reveals 21.3% of Hb E beta thalassaemia, 4.9% of Beta thalassaemia major, 20.2% of beta thalassaemia trait and 15.1% of haemoglobin E trait out of 555 anaemic patients. Haemoglobin E beta thalassaemia is the most common haemoglobinopathy in our country.Waqar et all repoted in a study in 2005 that expected birth of Haemoglobin E beta thalassaemia in Bangladesh is 6,443and Beta thalassaemia major is 1044 in every year.[4]

It is important to recognize haemoglobin disorders to give treatment of thalassaemia patients, to detect traits and also for genetic counseling. Again it is important to differentiate between thalassaemia and haemoglobinopathiesn specially their carrier states from iron deficiency anaemia which is a very common cause of anaemia in our country.[9]There are expensive tests to diagnose thalassaemia and other haemoglobinopathies which are not affordable by majority of our patients. As haematology cell counter is now widely available this study was under taken to see the role of RBC indices in suggesting thalassaemia and advising further confirmatory tests like HPLC.

Different formulas have been setup with RBC indices for screening of thalassaemia. But the formulas are not 100% sensitive and specific and are complicated.[10]

In simple observation our study revealed mean value of RDW is markedly increased in both thalassaemia major and Hb E beta thalassaemia along with lower mean values of Hb, MCV, MCH and RBC count.

Mean value of RDW is mildly high along with normal mean value RBC count, lower Hb, MCV and MCH in the normal, beta thalassaemia trait, haemoglobin E trait and E disease which was not consistant with study of Burdick et al in 2009. They have described traits with mildly low Hb, MCV,MCH, high RBC count, normal RDW.[11] In our study anaemic patient were chosen. Therefore mildly increased RDW is probably due to coexistence of iron deficiency anaemia which is common in our country. To get more conclusive result iron profile were needed.

In this study RBC count and Hb was significantly low (p value <.001) and RDW was significantly high (p value <.001) in both beta thalassaemia major and haemoglobin E beta thalasssaemia in all groups.MCV and MCH were also significantly low (p value <0.05) in group I beta thalassaemia major and group II and group III haemoglobin E beta thalassaemia (table 5,6).This study also consistant with the study Baruah MK et all in 2014 who had repoted low level RBC count, Hb, MCV and MCH and high RDW in both beta thlassaemia major and haemoglobin E beta thalassaemia.[12]

RBC count was significantly high in all groups of beta thalassaemia trait and haemoglobin E trait (p value<.05).MCV is significantly low in group III beta thalassaemia trait (p value <0.02).In this study RDW is high in both normal and beta thalassaemia trait and interestingly RDW was higher in normal than group III beta thalassaemia trait it (p value<0.01) (table 7, 8).We have taken anaemic patients only and in our population iron deficiency is the most common cause of anaemia. RDW is mildly high in control group probably due to iron deficiency anaemia as RDW is mildly high in the normal anaemic patients.[13]

The most widely used cut-off values of MCV and MCH for detecting thalassaemia traits are 79 fl and 27pg, respectively. Values below these may indicate ±- or ²-thalassaemia traits or iron deficiency.[14] Owing to a high prevalence of Iron deficiency anaemia in our population, lower cut off values should be considered to increase the sensitivity and specificity of BTT detection. The proposed cut off values based on ROC curve analysis were 71.3 ¼m3 (71.3 fL) for MCV and 22.5 pg for MCH. Lafferty et al have proposed a similar revised cut off values for MCV and MCH, which is based on ROC curve results.[15]

Conclusion

RBC indices can be utilized to screen thalassaemia and other haemoglobinopathies. RDW are markedly raised in both Beta thalassaemia major and haemoglobin E beta thalassaemia with low HB, RBC count, MCV and MCH. RBC count is high in both beta thalassaemia trait and haemoglobin E trait with low MCV and MCH.

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ORIGINAL ARTICLE

Thoracotomy for the Treatment of Empyema Thoracis at the Fibrinopurulent Stage in Children

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Abstract

Background: *Paediatric empyema is increasing in incidence and continues to be a serious problem.But optimal management of empyema remains still controversial.*

Objective: To determine the effectiveness of thoracotomy in the management of empyema thoracis at the fibrinopurulent stage.

Methods: *A prospective study was done on 16 cases of empyema up to 14 years of age treated in the department of Pulmonology of Dhaka Shishu(Chidren)Hospital, from May 2014 to April 2015. Diagnosis of empyema was confirmed by thoracocentesis. All the children were treated with parenteral antibiotics and tube thoracostomy was done immediately after diagnosis. However, patients with extensive pleural involvement underwent formal decortication.*

Results: *Total 16 cases were included in the study. Male sex predominance was seen. The most common age group affected was 1-5 years. Most common presenting complaints were fever (100%), respiratory distress (81.3%) and cough (75%). More than 87.5% of the children were presented with >7 days of illness and found to have advanced stage of disease. The majority of the pleural collections were on the right pleural space. All children were treated with parental antibiotics and tube thoracostomy. Out of these, 7 patients had adequate drainage of their empyema corresponding to a success rate of 43.8%. In the remaining 56.3% of cases (9 patients) required open decortications. In all of the children, empyema was resolved after treatment.*

Conclusion: Tube thoracostomy should be done in all patients regardless of the stage as this leads to a reduction in septic load. In a developing country, decortication remains a safe procedure in the management of empyema thorasis.

Keywords: *Thoracotomy, Empyema, Tube thoracostomy*

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Introduction

Pleural empyema continues to be a serious problem despite recent advances in management.[1] Empyema thoracis is defined as the presence of pus in the pleural space.[2] Empyema develops as a complication of bacterial pneumonia in 0.6 - 3% of hospital admissions but small pleural effusions may be present in up to 40% of bacterial pneumonias.[3-6] Three stages of evolution have been described for empyema. The early exudative stage (stage I) usually lasts 3–5 days and is characterized by the presence of sterile effusions. The fibrinopurulent stage (stage II) occurs 7-10 days after the onset of the illness with eventual pus formation and deposition of fibrin on both visceral and parietal pleurae as well as tendency toward septum formation and loculation of the effusion. The last (organizing) stage takes place after about 2–3 weeks of illness and is characterized by thickened and non-elastic intrapleural membranes and poor lung compliancev.[7] It is an advanced parapneumonic effusion. While most cases would respond to antibiotic therapy, needle aspiration, fibrinolytics and intercostals drainage (ICD), few cases requires further surgical management.[8] The type of drainage depends on the stage of the effusion.[9-10] At the acute stage, closed chest tube drainage is indicated; at the fibrinopurulent stage, removal of the pleural content by mini-thoracotomy or thoracoscopy, together with subsequent closed pleural drainage, is indicated; at the organized stage, thoracotomy or open drainage by thoracostomy is indicated.[9] The objective of this study was to determine the efficacy of thoracotomy (for decortication) in the management of a significant number of children with empyema thoracis at the fibrinopurulent stage.

Materials and Methods

This prospective study comprised of 16 patients up to 14 years of age, treated in the department of Pulmonology unit of Dhaka Shishu Hospital, from May 2014 to April 2015. Aspiration of pus from the pleural space was the inclusion criteria; patients with tubercular empyema were excluded. The diagnosis of empyema was made by presenting symptoms and signs, laboratory studies such as complete blood count, Gram stain and culture of pleural pus, blood culture, chest radiographs and ultrasonography. Computed tomography (CT) scan chest was done whenever required. After diagnostic thoracocentesis and obtaining appropriate cultures, parenteral antibiotics were started and tube thoracostomy was done immediately after diagnosis. Antibiotics were changed if clinical response was inadequate. Surgery was considered after failed tube drainage (TD). However, patients with extensive pleural involvement underwent formal decortication. All information were recorded in pre-tested semi-structured questionnaire. Ethical clearance was taken from institutional ethical committee. Treatment protocol was followed according to BTS guidelines. Closed thoracostomy was carried out with a straight chest tube (size according to age), attached to a water seal system. Successful closed tube drainage was evidenced by improvement in clinical and radiological status within 48 to 72 hours. Continuous drainage was maintained until daily fluid output dropped to below 50ml and improvement in the chest radiograph were noted. The chest tube was removed within 7days when lung expansion was evident on X-ray. Decortication was performed if there was a stage II to III empyema (fibrinopurulent and organized stage) and if patients did not improve after tube thoracostomy. For surgery, patients were referred to National Institute of Chest Disease Hospital (NIDCH) and to a private clinic also. Surgical decortications were done in most of the cases.

Results

Age distribution of cases, 5 (31.25%) were within 1 year, 8(50%) were between 1 to 5 years, 2(12.5%) were 6 to 10years, 1(6.25%) was above 10 years of age (Table-I).

Table- I
Distribution of study population according to Age (n=16)

Age (years)	Number	Percentage
< 1	5	31.25
1-5	8	50
6-10	2	12.5
> 10	1	6.25
Total	16	100

There was a male preponderance. Male were 62.5% and female were 37.5% (Fig 1).

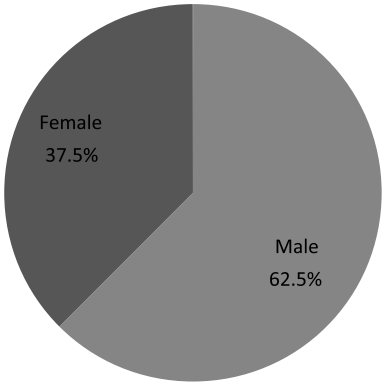

Fig 1 *Sex distribution of the studied children*

All of the patients had received all of standard vaccinations according to age (100%). The most common symptom was fever in 16 patients (100%) followed by respiratory distress in 13 patients (81.3%) and cough in 12 patients (75%) (Table II).

Table II
Presenting symptoms of studied children

Presenting symptoms	No of the patients	Percentage
Fever	16	100
Respiratory distress	13	81.3
Cough	12	75

Duration of fever was less than 1week in 2 (12.5%) of patients, 1-2 weeks in 4 (25%) of patients and >2 weeks in 10 (62.5%) of patients (Table III).

Table III
Duration of fever in studied children

Clinical signs	Number	Percentage
<7 days	02	12.5
8-15 days	04	25
16-30 days	10	62.5

Right sided empyema (12 patients, 75%) was more common than left sided (4 patients, 25%). (Table IV). In CXR pneumothorax and collapse-consolidation were also found.

Table IV
Site of pleural effusion among study population (n=35)

Involvement	Number	Percentage
Right side	12	75
Left side	04	25

Regarding the radiological tests performed in order to diagnose and confirm the fibrinopurulent stage of empyema, 16 children (100%) underwent chest X-ray, 11 (68.8%) underwent ultrasound and 9 (56.3%) underwent CT. Preoperative chest tube drainage was performed in all of the patients in this study. Of those, 10 patients were referred to surgeon as there was no improvement and among them 9 (56.2%) required thoracotomy. (Table V).

Table V
Treatment of studied children

Treatment	Number	Percentage
Antibiotic	16	100
Chest drain+Antibiotic	0 7	43.8
Surgery	09	56.2

Discussion

In our study a total of 16 pediatric patients were included. Male sex predominance was seen. The most common age group affected was 1-5 years. B P Kuti[11] found that infants were more likely to develop effusions than older children. Another study also found that parapneumonic effusions were more common in boys than girls and most frequently encountered in infants and young children.[12] Patients presented most commonly with fever, respiratory distress and cough. Duration of the illness and stage of the disease were significantly correlated.

We observed that more than 87.5% of the children presented with more than 7 days of illness and found to have advanced stage of disease. Byington et al[13] also demonstrated that children with empyema had prolonged fever (Q7 days). One possible explanation for this finding is that children with empyema were diagnosed after a prolonged illness and were therefore more likely to develop this complication.[14] Timely institution of proper management prevents the need for any surgical intervention and avoids

long-term morbid complications.[15] It is noteworthy that the majority of the pleural collections were on the right pleural space. This is in agreement with reports by Gomez-Go et al[16] and Baranwal et al[17] among children in Nepal. The high incidence of right-sided pleural fluid collections may be related to the fact that the right main bronchus is shorter, wider and straighter in comparison to the left, facilitating the descent of the infection.[18-21] In this study all the patients had evidence of fluid on chest X-ray. Ultrasound was used in 11 of the children. Chest CT was used in only 9 children to evaluate loculation, marked thickenings of pleura with encasement of lung. The recommendation to use chest CT in children with empyema should be made with great caution, since the test usually requires sedation or general anesthesia and exposes the child to high doses of radiation.[22] The optimal treatment of children with empyema remains controversial. The different modalities that are used when the child remains febrile despite adequate antibiotic treatment include chest drain with or without fibrinolysis or surgery (including VATS).[14] In our study, initially tube thoracostomy was done in all the patients. Out of these, 7 patients had adequate drainage of their empyema corresponding to a success rate of 43.8%. This is likely to be explained by the fact that most of our patients present late with the empyema in fibrinopurulent stage. Despite the expected low success rate for tube thoracostomy in the treatment of late empyema, it remains a first line therapy to decrease the severity of pleural sepsis until further therapy can be instituted.[23] In this study the patients were discharged on an average of 7-10 days after tube insertion and the patients with unresolving empyema were prepared for decortication. In the remaining 56.3% of cases, open decortication was electively done after stabilizing the patient's hemodynamics status. Decortication represents the most invasive treatment for organized empyema cavities. Decortication allows a more rapid recovery with a decreased number of chest tube days, decreased length of hospital stay and success rate.[23] Open decortication still remains the gold standard procedure for managing chronic empyema thoracis. All the patients were successfully treated and the success was gauged by lung expansion and general well-being of the patient. The patients were discharged after 10-12 days postoperatively. There was no mortality in this study. In a recent series from Great Ormond Street, later chest drain insertion (8.1 vs 6.3 days after effusion detected) was associated with a trend towards requirement for surgical drainage.[24] Hoff et al[25], in a series of 61 children, reported that resolution of the disease process was more prolonged in patients managed by chest tube alone (16.8 days in hospital) than resolution after thoracotomy (6.7 days, P <0.001). Carey et al[26], reported a series of 22 children with empyema referred to a paediatric cardiothoracic unit. Those children who had immediate thoracotomy (18 cases) were afebrile and had their chest tubes removed by 2 days. Their mean hospital stay was 4 days. The authors suggested that early thoracotomy remains the benchmark treatment.

A similar case series of 44 children undergoing thoracotomy[27] also revealed very short duration of fever (mean 1 day) and an average of 3 days until chest tube removal. In our study the number of sample size was small in relation to huge number of population. It was a single center study. Intrapleural fibrinolytics were not advocated for lysis of the fibrinious strands which may help to avoid surgery.

Conclusion

Tube thoracostomy should be done in all patients regardless of the stage as this leads to a reduction in septic load. In a developing country where expensive therapy like fibrinolytics and VATS is not freely available, decortication remains a safe procedure in the management of empyema thorasis.

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ORIGINAL ARTICLE

Outcome of Infants of Diabetic Mothers Admitted in CMH, Dhaka

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Abstract

Background: *There is a high prevalence of Diabetes Mellitus (DM) in Bangladesh. Gestational DM (GDM) carries very high risks for the mother and the child. In different studies, there are diversity of neonatal outcomes due to GDM. So, main aim of this study is to observe the outcome of infants of diabetic mothers (IDMs) admitted to Combined Military Hospital (CMH), Dhaka.*

Objective: *To determine the outcome of infants of diabetic mothers (IDMs) admitted in CMH, Dhaka.*

Methodology: *This cross sectional observational study was carried out in Combined Military Hospital (CMH), Dhaka from January 2015 to December 2015. All infants born to diabetic mothers and presented within 24 hours to the neonatal unit, CMH Dhaka were included in the study. All the babies were kept to the neonatal intensive care unit (NICU) for observation. Maternal history was obtained from all included patients and a detailed physical examination was performed. Those having any maternal risk factor or neonatal complication during observation were admitted to NICU for further investigations. All admitted babies were screened for pathological, biochemical and other complications. Outcome of IDMs and relative frequencies of various complications were evaluated. Results were analyzed using statistical package for social sciences (SPSS) version 17.*

Results: *A total number of 102 consecutive cases of IDMs were included in the study. Out of diabetic mothers, seventy-two (70.6%) were multigravida and thirty (29.4%) were primigravida, 35.3% mothers had H/O abortion or still birth previously, 2.9% had polyhydramnios and 16.6% had preeclampsia. Ninety-one (89.2%) mothers delivered babies by cesarean section (LUCS) and 11 (10.8%) had vaginal delivery (NVD). Ninety-six (94.1%) mothers had gestational diabetes mellitus (GDM) whereas six (5.9%) had pre-conceptional DM. Median age of the diabetic mothers was 27 years. The youngest diabetic mother was 20 and the eldest was 40 years old. In most of the cases (98%) blood sugar level was controlled and it was mostly by dietary advice (57.9%). Only 5 mothers (4.9%) had to take both Insulin and oral hypoglycemic agents and out of them 2 cases had uncontrolled DM till delivery. The male infants of diabetic mothers in this study were 57.3%. Most of the babies (82.4%) were delivered at term, 88 (86.3%) cases were admitted to the hospital due to various complications and 46 (45%) cases had hospital stay for 4-7 days. 96.1% cases were discharged with advice and the mortality rate was 3.9%. Neonatal jaundice (24.5%) was found to be the most common complication followed by prematurity (17.6%), large for gestational age (15.68%) and congenital anomaly (13.7%). Only seven (6.86%) babies were macrosomic and nine (8.8%) were hypoglycemic. Among admitted IDMs (n=88), 13 (14.7%) babies had hypocalcemia, 4 (4.5%) had hypomagnesemia and 7 (7.9%) had polycythemia.*

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Conclusion: *This study reveals the high occurrence of different complications in newborns, born to diabetic mothers. Neonatal jaundice, prematurity, large for gestational age, hypocalcemia and congenital anomaly were the commonest complications. Lower rate of macrosomia and hypoglycemia in comparison to other studies may reflect the effect of good glycemic control and regular antenatal check up of GDM mothers. Most of the GDM mothers of this study had good glycemic control with dietary advice only. Preeclampsia was the commonest comorbidity in them.*

Key wards: *Infants, Diabtic mother, CMH*

Introduction

Diabetes Mellitus is a syndrome of diverse genetic, environmental and pathogenic origin characterized by hyperglycemia resulting from impaired insulin secretion and/or effectiveness.[1] Gestational diabetes mellitus (GDM) is defined as 'glucose intolerance of variable severity with onset or first recognition during pregnancy.[2]

There is a high prevalence of GDM in Bangladesh. It varies from 6.7% to 12.9% in different Bangladeshi studies.[3-5] GDM carries very high risks for mother and child. Infants of diabetic mother (IDMs) have a three to fivefold increased risk of having congenital malformations.[6] These anomalies include mostly cardiac and skeletal defects.[7] Poor peri-conceptional glycaemic control causes the increased risk of congenital malformations that are associated with GDM.[8]

GDM causes increased rate of perinatal mortality. GDM is also associated with a significantly higher risk of stillbirth. Congenital malformations contribute to stillbirths but even when these are excluded there is still an increased prevalence. The underlying pathological mechanism is unclear; however suboptimal glycaemic control is implicated.[8]

Premature delivery and very low birth weight (VLBW) is common in pregnancies complicated by maternal diabetes. Again Insulin deficiency in utero causes many infants of diabetic mothers to be small for their gestational age.[9] Fetal growth is often disrupted in diabetic pregnancy, with both the extremes of macrosomia and fetal growth restriction. Spontaneous preterm labour is increased in GDM and potentially relates to fetal hyperglycaemia and diuresis driven polyhydramnios. Even in premature infants the risk of shoulder dystocia and its attendant risk of hypoxia, brachial plexus injury and trauma are increased in diabetic pregnancy due to altered neonatal body composition. Risk is further increased if there is concomitant macrosomia.[8]

IDMs have a 47% risk of significant hypoglycaemia, 22% risk of hypocalcaemia, 19% risk of hyperbilirubinemia, 34% risk of polycythaemia, 6-9% incidence of major congenital anomalies(congenital heart disease, central nervous system & vertebral anomalies), 64% risk of respiratory distress syndrome, 28% risk of macrosomia & 30% risk of cardiomegaly.[10]

Nevertheless, in different studies, there are diversity of neonatal outcomes due to GDM. This study was attempted to observe the clinical outcome of infants of diabetic mothers admitted to CMH, Dhaka so that prompt management could be carried out after admission thereby preventing complications. A good fetal outcome depends on regular antenatal follow-up and maintenance of good glycemic control throughout pregnancy in GDM mothers. These babies should be delivered at hospitals where special neonatal care is available for management of high risks babies to reduce the morbidity and mortality. All diabetic women should have planned pregnancy and proper antenatal care in order to maintain strict glycaemic control, to have a satisfactory outcome in infants of diabetic mothers.

Methods

This cross sectional observational study was carried out in Combined Military Hospital (CMH), Dhaka from January 2015 to December 2015. All infants born to diabetic mothers and presented within 24 hours to the neonatal unit, CMH Dhaka were included in the study. Infants of Diabetic Mothers presented to neonatal unit after 24 hours of delivery were excluded from the study. All the babies were kept to the NICU for observation. Maternal history was obtained from all included patients and a detailed physical examination was performed. Those having any maternal risk factor or neonatal complication during observation (e.g hypoglycemia within 2 hrs of birth, prematurity(<36 wk), low birth weight(<2.5

kg), poor feeding, lethargy, convulsion, RDS, MAS, birth trauma or apparent congenital malformation) were admitted to NICU. Serial capillary blood glucose level was measured by glucometer at 0-1 hr of age before first oral feeding, 2 hrs after first feeding, at 6 hours of age and at 12 hrs of age in all the babies. Estimation of peripheral venous blood glucose level was done for further confirmation of diagnosis in suspected cases of hypoglycemia. Laboratory tests for complete blood count (CBC), serum electrolyte, serum calcium and serum magnesium were observed routinely in all admitted patients. Chest X-ray and echocardiography were done in each of the IDMs to identify congenital heart diseases (CHD). Other investigations like serum bilirubin or imaging like USG was done according to specific co-morbidity. Infants whose birth weights were at least 4000g regardless of gestational age were defined as macrosomic, while those who weighed less than 2500 g were defined as low birth weight. Hypoglycaemia was defined as blood glucose concentrations <2.2 mmol/l, polycythaemia was defined as a peripheral venous hematocrit greater than 0.65 or hemoglobin >22 gm%, hypocalcaemia was defined by total serum calcium values < 8 mg/dL in term and <7 mg/dl in preterm infant, hypomagnesemia was defined when serum magnesium level was lower than 1.6 mg/dl. Outcome of IDMs and relative frequencies of various complications were evaluated. Due to very short number of pre-conceptional DM, the difference of outcome of this with GDM was not analyzed. Again laboratory profile of all babies could add more in the finding of outcome of IDMs. Results were analyzed using statistical package for social sciences (SPSS) version 17. Ethical issues were addressed duely.[11-13]

Results

A total number of 102 *consecutive cases of* infants of diabetic mothers were included in the study. Out of diabetic mothers, seventy-two (70.6%) were multigravida and thirty (29.4%) were primigravida, 35.3% mothers had H/O abortion or still birth previously, 2.9% had polyhydramnios and 16.6% had preeclampsia. Ninety-one (89.2%) mothers delivered babies by cesarean section (LUCS) and 11 (10.8%) had vaginal delivery (NVD). (Table I)

Table I
Profile of mothers of infants included in the study (n=102)

Profile	Number	Percent(%)
Parity		
Primi	30	29.4
Multi	72	70.6
Total	102	100
H/O abortion/still birth		
Present	36	35.3
Absent	66	64.7
Total	102	100
H/O polyhydramnios		
Present	3	2.9
Absent	99	97.1
Total	102	100
H/O preeclampsia		
Present	17	16.6
Absent	85	83.4
Total	102	100
Mode of delivery		
NVD	11	10.8
LUCS	91	89.2
Total	102	100

Ninety-six (94.1%) mothers had gestational diabetes mellitus (GDM) whereas six (5.9%) had pre-conceptional DM. Median age of the diabetic mothers was 27 years. The youngest diabetic mother was 20 and the eldest was 40 years old with a mean of 27.39± 4.24years. Diagnosis of GDM was in 38 cases at 1st trimester, 37 cases at 2nd trimester and 27 cases at 3rd trimester. In most of the GDM cases (98%) blood sugar level was controlled and it was mostly by dietary advice (57.9%) followed by Insulin (19.6%) and oral hypoglycemic agent Metformine (17.6%). Only 5 mothers (4.9%) had to take both Insulin and oral hypoglycemic agents and out of them 2 cases had uncontrolled DM till delivery. Most of the mothers (62.7%) had no co-morbidity and preeclampsia was the commonest (16.6%) co-morbidity followed by hypertension (HTN) and hypothyroidism (8.9%). (Table II).

Table II
Status of Diabetes Mellitus (DM) (n=102)

Charecteristics	Number	Percent(%)
Type of DM		
GDM	96	94.1
Pre conceptional DM	6	5.9
Total	102	100
Diagnosis at pregnancy		
1st trimester	38	37.3
2nd trimester	27	26.5
3rd trimester	37	36.2
Total	102	100
Control of DM		
Controlled	100	98
Uncontrolled	2	2
Total	102	100
Way of control		
Oral Metformine	18	17.6
Insulin	20	19.6
Metformine+Insulin	5	4.9
Diet	59	57.9
Total	102	100
Maternal co morbidity		
No	64	62.7
HTN	9	8.9
Hypothyroidism	9	8.9
Preeclampsia	17	16.6
*Others	3	2.9
Total	102	100

*Others- subfertility, hyperthyroidism

Of the IDMs, 57.3% were males and 42.7% were females with M: F ratio of 1.3:1. The mean birth weight was 2.97 kg±0.69 (1.10 – 4.20 kg). Among them 7 (6.9%) were macrosomic. Most of the babies (82.4%) were delivered at term, 88 (86.3%) cases were admitted to the hospital due to various complications and 46 (45%) cases had hospital stay for 4-7 days. The mean duration of hospital stay was 6.22 days±5.3 (1 – 36 days). 96.1% cases were discharged with advice and the mortality rate was 3.9%. (Table III).

Table III
Profile of infants of diabetic mothers included in the study (n=102)

Profile	Number	Percent(%)
Gestational age		
Term	84	82.4
Preterm	18	17.6
Total	102	100
Sex		
Male	59	57.3
Female	43	42.7
Total	102	100
Birthweight		
<2.5 kg	20	19.6
2.5-3.99	75	73.5
>4	7	6.9
Total	102	100
Admission		
Admitted	88	86.3
Not admitted	14	13.7
Total	102	100
Hospital stay (days)		
≤3	32	31.4
4-7	46	45.0
>7	24	23.6
Total	102	100
Mode of Discharge		
Discharge with advice	98	96.1
*Death	4	3.9
Total	102	100

* Causes of death 1 each number were severe perinatal asphyxia, multiple congenital anomaly, preterm LBW with respiratory distress syndrome and meconium aspiration syndrome.

Neonatal jaundice (24.5%) was found to be the most common complication followed by prematurity (17.6%), congenital anomaly (13.7%), large for gestational age (15.68%), small for gestational age (8.9%), hypoglycaemia (8.8%), neonatal convulsion (7.8%), transient tachypnea of newborn (5.9%), meconium aspiration syndrome (5.9%), birth asphyxia (5.9%), respiratory distress syndrome (2.9%), birth injury (1%) and dyselectrolytemia (5.8%). (Table IV).

Among admitted IDMs (n=88), 13 (14.7%) babies had hypocalcemia, 4 (4.5%) had hypomagnesemia and 7 (7.9%) had polycythemia. (Table IV) The mean Hemoglobin % was 18.18±6.7 gm%, mean total WBC count was 17.77±7.7x10^9/mm^3, mean platelet count was 196.72±108.8 x10^9/mm^3, mean serum creatinine was 0.77 ±0.34 mmol/l, mean RBS at 0 hr was 3.51±1.2 mmol/l, at 2 hrs was 4.19±1.4 mmol/l, at 6 hrs was 4.48±1.12 mmol/l and at 12 hrs was 4.52±0.87 mmol/l. (Table V)

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Table IV
Complication of IDM babies

Complications	N	Number	Percent(%)
Macrosomia	*102*	*7*	6.86
LGA*	*102*	16	15.68
SGA*	*102*	9	8.9
Prematurity	*102*	18	17.6
TTN*	*102*	*6*	5.9
MAS*	*102*	*6*	5.9
RDS*	*102*	*3*	2.9
Birthinjury	*102*	1	1.0
Neonatal jaundice	*102*	25	24.5
Neonatal convulsion	*102*	8	7.8
Congenital Anomaly	*102*	14	13.7
Hypoglycemia	102	9	8.8
Hypocalcemia	88	13	14.7
Hypomagnesemia	88	4	4.5
Polycythemia	88	7	7.9
Dyselectrolytemia**	88	8	9.1
Sepsis	*102*	9	8.8
Birth asphyxia	*102*	6	5.9

*LGA=large for gestational age, SGA=small for gestational age, TTN= transient tachypnea of newborn, MAS=Meconium Aspiration Syndrome, RDS=Respiratory distress syndrome.
**Dyselectrolytemia- Hypernatremia (n=3), hyponatremia (n=1), hyperkalemia (n=2), hypokalemia (n=2).

Table V
Laboratory profile of admitted IDM patients (n=88)

Parameter	Mean± SD	Median	Minimum	Maximum
Hemoglobin%	18.18±6.7	*20.00*	10.50	25.00
Total WBC/mm^3	17.77±7.7x10^9	16.45 x10^9	5 x10^9	28 x10^9
Platelet Count/mm^3	196.72±108.8 x10^9	202x10^9	10x10^9	493x10^9
Serum Creatinine (mmol/l)	0.77 ±0.34	*0.*70	0.40	1.90
Serum Calcium (mmol/l)	8.7±3.1	8.80	5.00	10.80
Serum Magnesium (mmol/l)	1.73±0.74	1.90	1.00	3.0
RBS at 0 hr (mmol/l)	3.51±1.2	3.35	1.40	10.10
RBS at 2 hrs (mmol/l)	4.19±1.4	4.20	2.30	16.40
RBS at 6 hrs (mmol/l)	4.48±1.12	4.55	2.30	9.80
RBS at 12 hrs (mmol/l)	4.52±0.87	4.60	2.10	8.40

Discussion

There is a high prevalence of GDM in Bangladesh. It varies from 6.7% to 12.9% in different Bangladeshi studies.[3-5] In this study, the total number of IDMs was 102. Out of diabetic mothers, most (70.6%) were multigravida which is similar to a study of Nigeria.[14] In this study, 35.3% mothers had H/O abortion or still birth previously, 2.9% had polyhydramnios, 16.6% had preeclampsia which were almost similar to other studies.[15] The rate of LUCS in our study was 89.2% which is higher than the study from Netherland (45.2%) and Karachi (55%) but correlated

well with other national and international data.[14-17] Reasons for primary LUCS in our study were mostly fetal distress, pre-eclampsia, maternal hypertension, macrosomia and breech presentation. Reasons for a secondary LUCS were failed induction or obstructed labour and fetal distress.

Most of the diabetic mothers (94.1%) had gestational diabetes mellitus (GDM) in our study. GDM was higher than pre-conceptional DM in two other Bangladeshi studies.[17,18] Median age of the diabetic mothers was 27 years. The youngest diabetic mother was 20 and the eldest was 40 years old with a mean of 27.39± 4.24 years which is almost similar to a Nigerian study.[14]

Diagnosis of GDM was in 38 cases at 1st trimester, 37 cases at 2nd trimester and 27 cases at 3rd trimester. In most of the GDM cases (98%) blood sugar level was controlled and it was mostly by dietary advice (57.9%) followed by Insulin (19.6%) and oral hypoglycemic agent (OHA) Metformine (17.6%). Only 5 mothers (4.9%) had to take both Insulin and oral hypoglycemic agents and out of them 2 cases had uncontrolled DM till delivery. Among diabetic mothers of an Indian hospital 48.4% mothers had to take medication to control DM during pregnancy. Among drug users, 50.7% mothers received OHA and 49.3% received insulin to control blood glucose, 2.9% mothers had to take both OHA and Insulin to control DM in that study.[19]

Maternal morbidities like polyhydramnios, pre-eclampsia, infections and maternal mortality were observed more in GDM mothers in a Bangladeshi study.[4] But in our study, most of the mothers (62.7%) had no co-morbidity probably due to regular antenatal check up and strong management protocol of CMH Dhaka. Preeclampsia was the commonest co-morbidity (16.6%) among all in this study.

Of the IDMs of our study, males outnumbered females with an M: F ratio of 1.3:1 which is in accordance to some international studies.[20] The mean birth weight of the IDMs was 2.97 kg±0.69 (1.10 – 4.20 kg). Among them 7 (6.9%) were macrosomic. The mean birth weight was higher (4.14 kg ± 0.838) with 61.7% macrosomia in a study of Nigeria.[14] Mean birth weight and rate of macrosomia were also higher in two Bangladeshi studies, whereas in a study of India macrosomia was found in 3.2% cases and the mean birth weight was 2962.9 ± 505.9 gm.[4, 19, 21] Macrosomia remains an important complication of the diabetic pregnancies contributing heavily to birth injuries and asphyxia. It is in part related to maternal glucose control.[14] The lower rate of macrosomia in this study may therefore reflect strict glycaemic control in the mothers.

IDMs may need to be delivered prematurely due to maternal or fetal problems. Again increased prevalence of pre term low birth weight in IDMs is due to placental vascular insufficiency. Preterm LBW was higher in some national and international studies.[4, 22] But most of the babies (82.4%) in our study were delivered at term like another Indian study.[23] In this study, 86.3% cases were admitted to the hospital due to various complications and 46 (45%) cases had hospital stay for 4-7 days. The mean duration of hospital stay was 6.22 days±5.3 (1 – 36 days) which goes with the result of an international study.[14]

Despite improvement in diabetic care, the perinatal mortality still remains four times higher than in infants of nondiabetic women. Predominant causes of mortality are congenital anomaly, birth trauma, respiratory distress syndrome, prematurity and unexplained still birth.[24] In our study, the mortality rate of IDMs was 3.9% which is lower than a study of Pakistan (4.7%) and higher than another study of USA (2.5%).[20, 25] Causes of death 1 each number in this study were severe perinatal asphyxia, multiple congenital anomaly, preterm LBW with respiratory distress syndrome and meconium aspiration syndrome.

GDM is one of the important risk factors for perinatal and infant morbidity and mortality.[4] In this study, neonatal jaundice (24.5%) was found to be the most common complication which was in accordance with other studies.[22, 26, 27] Hyperbilirubinemia is common in IDM due to release of bilirubin from increased red cell mass, especially in association with polycythemia.[28] The rate of polycythemia (6.9%) in our study did not correlate with rate of clinical jaundice as PCV was checked in 88 admitted patients out of 102 patients.

Other complications in our study were prematurity (17.6%), congenital anomaly (13.7%), large for gestational age (15.68%), small for gestational age (8.9%), hypoglycaemia (8.8%), neonatal convulsion (7.8%), transient tachypnea of newborn (5.9%), MAS (5.9%), birth asphyxia (5.9%), RDS (2.9%), birth injury- Erb palsy (1%) and dyselectrolytemia (5.8%). (Table IV)

Infants of diabetic mothers are known to be at high risk for hypoglycemia. Maternal hyperglycemia leads to foetal hyperglycaemia, stimulating the foetal pancreas to synthesize excessive insulin. With separation of the placenta at birth, there is a sudden interruption of glucose infusion to the neonate without a proportional effect on hyperinsulinemia. Thus hypoglycaemia develops within the first hours of birth which is a marker of poor glycaemic control in the mother.[14] Seizures, coma, and long-term brain damage may occur if neonatal hypoglycemia is unrecognized and untreated. Both frequent examination for the clinical signs of symptomatic hypoglycemia and serial blood glucose measurements for several hours after birth are therefore recommended to detect the patient with asymptomatic hypoglycemia.[29] Although hypoglycemia was found in only 8.8% cases of our study, it was the commonest neonatal problem with very high rate (23-55%) in different international studies.[14, 20, 27]

Birth asphyxia (BA) is also a vital complication in IDMs that occurs as a result of multiple factors: maternal hypertension with resultant reduction of placental blood flow, premature labour, fetal macrosomia and maternal hyperglycaemia within 6 to 8 hours preceding delivery ,which supposedly reduces placental blood flow.[30] The higher rate of BA in different studies (17%-21%) does not correlate with our study (5.9%), probably due to better glycemic control of mothers in our study.[18, 21, 22]

Large for gestational age was found to be 35% in an Indian study and 45.2% in a study of USA both of which are higher than in our study (15.68%).[19, 25] Respiratory distress was noted in 16 (34.0%) cases with transient tachypnoea of the new born in 62.5%, congenital pneumonia in 31.3% and RDS in 6.3% cases in a Nigerian study and TTN with MAS comprised 14.9% cases of respiratory problem in a study of Pakistan which are dissimilar to ours.[14, 20] The congenital anomalies (13.7%) in our study were Hirschsprung disease, multiple congenital anomaly including polydactyly, cleft palate & preauricular skin tag) and congenital heart disease (n=11). The rate was higher than in two other Bangladeshi studies (5.7% and 10.7% respectively).[17, 18] The higher rate of congenital anomaly in this study mostly is contributed by cardiac anomaly as neonatal echocardiography by pediatric cardiologist in suspected cases of CHD and IDMs, is a very common practice in CMH, Dhaka. Birth injuries were seen in 14% cases in a study done by Hussain et al and 2.5% cases in another study by Thomas et al which contradicts with our study where the rate was only 1%.[19, 20]

Among admitted IDMs (n=88) of our study, 13 (14.7%) babies had hypocalcemia, 4 (4.5%) had hypomagnesemia and 7 (6.9%) had polycythemia. This finding supports the experience and observations of other workers.[14,20,23,27] The mean Hemoglobin % was 18.18±6.7 gm%, mean total WBC count was $17.77\pm7.7x10^9$ /mm^3, mean platelet count was $196.72\pm108.8\ x10^9/mm^3$, mean serum creatinine was 0.77 ±0.34 mmol/l, mean RBS at 0 hr was 3.51±1.2 mmol/l, at 2 hrs was 4.19±1.4 mmol/l, at 6 hrs was 4.48±1.12 mmol/l and at 12 hrs was 4.52±0.87 mmol/l. Table V. Significant leukocytosis was found in IDMs-AGA babies and significant increase in band count was observed in IDMs-LGA babies in a study conducted by Mimouni et al.[31] Polycythemia may be observed in IDM due to increased erythropoiesis triggered by chronic fetal hypoxia and thrombocytopenia and hypocalcemia occurs probably due to functional hypoparathyroidism.[32] Hypomagnesemia in IDMs may be related to maternal hypomagnesemia, neonatal hyperphosphatemia, neonatal hypocalcemia and functional hypoparathyroidism.[33]

According to WHO the diabetic population will increase until the year 2025 and the major part of this numerical increase will occur in developing countries. There are more women than men with diabetes. This report supports the earlier prediction of the epidemic nature of diabetes in the world during the first quarter of the 21st century. Worldwide surveillance of diabetes and its effect on newborns is a necessary first step toward its prevention and control, which is now recognized as an urgent priority.[34]

Conclusion

This study revealed neonatal jaundice, prematurity, large for gestational age, hypocalcemia and congenital anomaly were the commonest complications of IDM and preeclampsia was the commonest comorbidity in GDM patients. Lower rate of macrosomia and hypoglycemia in comparison to other studies may reflect the effect of good glycemic control and regular antenatal check up of GDM

mothers. Most of the GDM mothers of this study had good glycemic control with dietary advice only.

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ORIGINAL ARTICLE

PATIO Repair in Solitary Urethrocutaneous Fistula : Experience of Dhaka Shishu (Children) Hospital

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Abstract

Background: *The commonest complication following hypospadias repair is occurrence of urethrocutaneous fistula. A variety of surgical techniques have been described in literature and it is accepted that no single technique is suitable or effective for all patients.*

Objective*: A novel technique has been described for repairing penile urethrocutaneous fistula: the PATIO (preserve the tract and turn it inside out) repair. We report our experience with this technique in managing solitary urethrocutaneous fistula following primary hypospadias repair.*

Methodology*: A total of 42 male children with urethrocutaneous fistula were included in the study from July 2014 to December 2015. The inclusion criterion was solitary fistula of <4mm widest diameter.*

Results*: The mean age of patients was 68.57±25.96 months. Operation time, length of hospital stay and operation cost were 24.95±2.78 minutes, 2.14±0.36 days and 3625.71±215.14 taka respectively. No recurrence of fistula was noted.*

Conclusion: *The PATIO technique is simple, easy to perform, can be done with short operative time and short hospital stay, with low morbidity, and is reliable in treating solitary urethrocutaneous fistula <4 mm in size.*

Key Words: *Hypospadias, Urethrocutaneous fistula, PATIO*

Introduction

Hypospadias is a developmental anomaly characterized by a urethral meatus that opens onto the ventral surface of penis from glans to the scrotum or even in the perineum. It is one of the commonest congenital abnormalities of male genitalia that occurs 1 in 125 live male births.[1] A poor cosmetic result is the most common complication, often related to irregular and asymmetric scars with skin blobs and an excess of ventral skin.[2] Urethrocutaneous (UC) fistulae after hypospadias surgery have been a serious problem for patients and surgeons since repair was first attempted.[3] Although developments in technique have improved the outcome, making fistula formation an uncommon event, there is still a small incidence even

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in the best of hands.[4] In fact currently UC fistula formation rate is between 10-20 % for most one stage hypospadias repair.[1] Usually fistula can be seen as soon as diverting catheter is remove. Many factors may cause fistula formation. These include distal stricture, failure to add appropriate second layer and tension with coverage.[5] Location of fistula varies but is often found proximal to the glans corona. More than half of the fistula closes spontaneously and minimum delay of 6 months is required before deciding on a surgical closure.[6] This is the minimum time (6 months) required for complete wound healing and to allow for full resolution of scar tissue.[7] A combination of fistula and urethral stenosis is common, and therefore the distal urethra needs to be checked before deciding on a fistula closure.[6] This is important because any such stricture leads to recurrence of fistula.[7]

Delicate tissue handling, inversion of the urethral mucosa after excising the epithelialized tract of the fistula, a multilayer repair with well vascularized tissues, avoiding overlapping sutures and non absorbable or thick suture materials, a tension free closure, use of optical magnification and needle point diathermy for coagulation are currently considered mandatory.[8]

The closure of the UC fistula is a challenging problem. Several procedures have been used for closure of fistula, including simple closure and complex operations according to the site and size of the fistula. Simple closure is technically easy, but results are less than promising. Recurrence rate quoted to be as high as 29% after fistula repair.[9]

During the last four years, a method of UC fistula repair, based on preserve the tract and turn it inside out (PATIO) repair, in which UC fistula tract is mobilized down to the urethra by sharp dissection after a circumferential incision around the skin opening and keep the fistula tract inverted inside the urethra to create a flap valve inside the urethral lumen. This technique in UC fistula repair significantly reduces recurrence.[10]

Material and methods

Children with urethrocutaneous fistulae following hypospadias repair formed study population from July 2014 to December 2015 admitted in Dhaka Shishu (Children) Hospital. All children were examined in detail, to note the number, site and size of the fistulae. Children with a solitary coronal/ penile urethrocutaneous fistula of less than 4 mm maximum diameter were included in the study. Repair of the fistula was planned at least 12 weeks after the previous surgery.

The PATIO technique - The UC fistula tract is mobilized down to the urethra by sharp dissection after a circumferential incision around the skin opening (Fig 1a). Meticulous dissection is important to prevent the formation of a hole in the tract that might invalidate the technique. A 2/0 nylon suture is passed down the tract and brought out through the external urinary meatus. A fine polyglactin suture is then passed through the tip of the fistula tract and tied to the nylon, leaving a length of polyglactin suture sufficient to allow it to be pulled out of the tip of the urethra. As the nylon is pulled out of the urethra the fistula tract is pulled inside out into the lumen of the urethra (Fig 1b). The end of the polyglactin suture is sutured to the tip of the external urinary meatus to keep the fistula tract inverted (Fig 1c). The subcutaneous tissue and skin are then closed using fine polyglactin. The children received both preoperative and postoperative antibiotics.

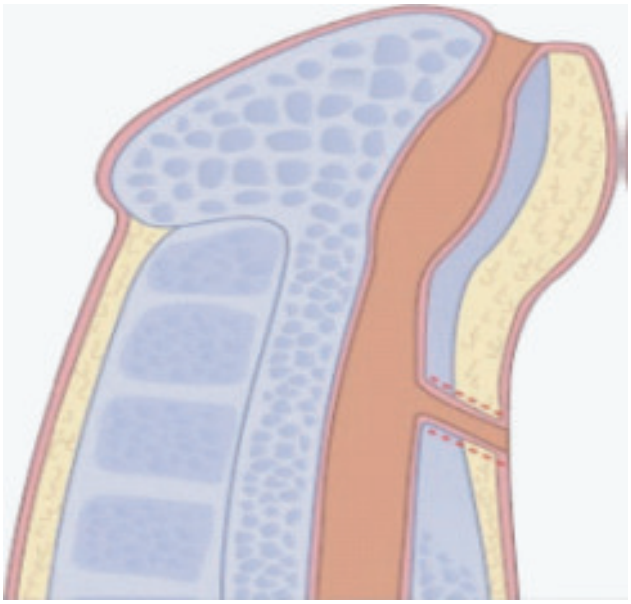

Fig 1a *First step of PATIO repair*

The fistula tract is mobilized down to the urethra using a circumferential incision around the cutaneous opening of the fistula.

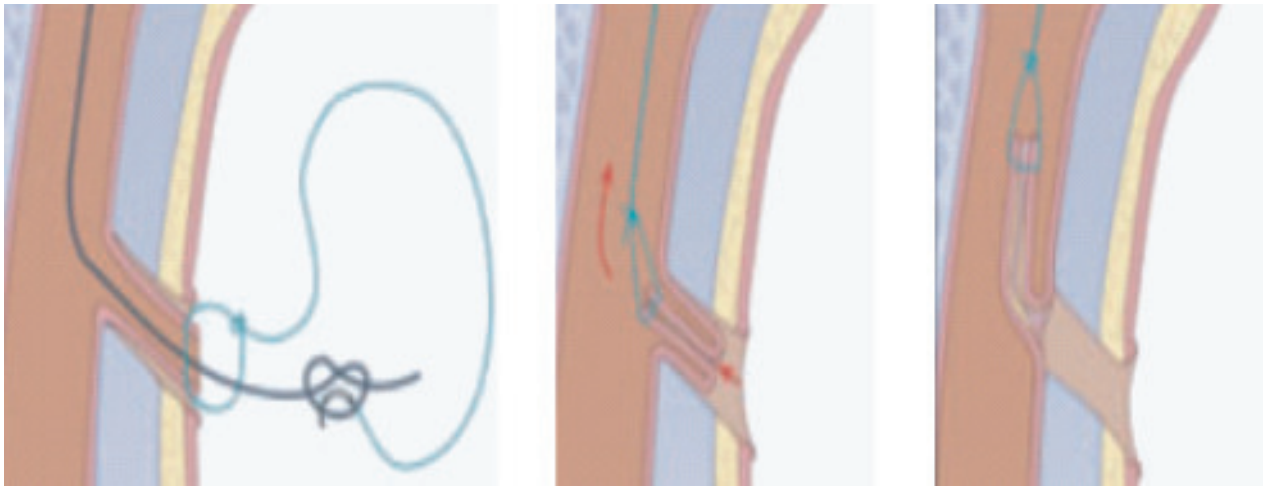

Fig 1b *Second step of PATIO repair*

A nylon suture is fed through the fistula tract and brought out through the external urinary meatus. A fine polyglactin suture is passed through the tip of the fistula tract after leaving sufficient length to allow it to be pulled out through the tip of the urethra. Traction on the suture inverts the fistula tract so it lies insideout in the urethral lumen.

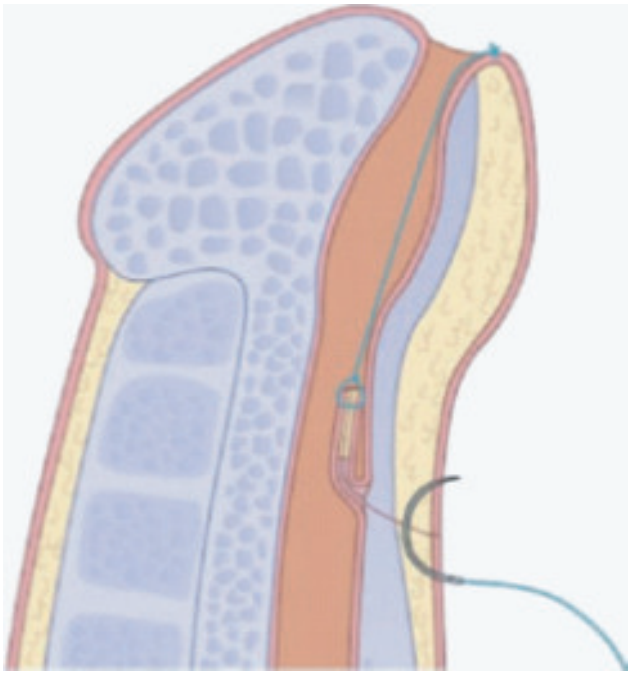

Fig 1c *Third step of PATIO repair*

The polyglactin suture, running through the tip of the fistula is secured to the tip of the external urinary meatus. The skin and subcutaneous tissues are closed with fine polyglactin suture. No suture is used on the urethra.

Results

All operations were successful and with no complications. All the UC fistulae remained healed with mean (range) follow-up of 18 months. Mean age of participants was 68.57±25.96 months where the range was from 30 to 132 months. The mean operation time was 24.95±2.78 minutes. The mean length of hospital stay 2.14±0.36 days. The mean operation cost including suture material, IV canula, gloves, medicine, bed rent etc were 3625.71±215.14 taka. None of the patients developed postoperative complications.

All children voided well after surgery. None of the children needed postoperative analgesia and could be managed with mild sedation only. The polyglactin sure fixed to the glans fell off by itself in 14-19 days.

Table I
Operation time (n=42)

Operation time	Mean±SD
In minutes	24.9±52.78

Table II
Length of hospital stay (n=42)

Length of hospital stay	Mean±SD
In days	2.14±0.36

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Table III
Operation cost (n=42)

Operation cost	Mean±SD
In taka	3625.71±215.14

Discussion

The modern surgical repair hypospadias requires an experienced and dedicated surgeon, be they a pediatric urologist/surgeon, a plastic surgeon, or an adult reconstructive surgeon. With advances in surgical techniques and suture materials, and use of oftical magnification and microsurgical instrumentation, hypospadias repair has developed into a safe and reliable procedure, with very high reported success rate.[2] The fistula formation after hypospadias repair continues to be a frustrating complication, thus surgeons have evaluated their techniques, as well as the possible underlying causes that may put the patients at risk of a postoperative fistula.[11]

Fistula formation is the commonest complication after hypospadias repair.[12] The cause of fistula remains less known although it is likely that local infection, local ischaemia, inadequate procedure, poor tissue handling, distal obstruction due to distal stenosis or encrustration with severity of hypospadias has significant impact on the outcome of the primary hypospadias repair.[13] Surgery for hypospadias fistulas has remained a challenge for the treating surgeons and several surgical procedures have been described each claiming good results. With refined surgical techniques, fine suture materials, and special dressings, the results of surgery after hypospadias repair have improved significantly. Distal narrowing and infection are important factors to determine the surgical outcome. Several procedures have been used for closure of fistula, including simple closure and complex operations according to the site and size of the fistula.[12]

The penile skin advancement flap with dartos interposition technique was very successful in both primary fistula repair, and in a patient who had multiple previous operations.[14]

On the other hand, the PATIO technique is easy to perform and can be done as a day-case with no need for urethral catheterization. It does not preclude the use of other techniques to minimize the risk of recurrence, but so far these have not been necessary.[10] The PATIO repair is simple and easy to perform, with low morbidity, and is reliable in treating solitary urethrocutaneous fistula < 4mm in size.[2]

In this study, the mean age of the participants was 68.57±25.96 months. When studies were conducted regarding PATIO repair the researcher found the mean age of the participants was 53 months[2]. In the present study, the mean age of patients was higher than studies done abroad may be due to the fact that people living in high socio-economic condition are more aware of their health. In the present study, 26 (61.90%) patients had anterior hypospadias. On the other hand 16 (38.09%) patients had middle hypospadias. No patient was found with posterior hypospadias. This result was consistent with the result where the author showed that 50% of the total hypospadias was anterior hypospadias and 30% of the total hypospadias was middle hypospadias.[1] But this study showed dissimilarity with the study which was conducted in BSMMU where the researcher found 36.84% participants had anterior hypospadias, 21.05% had middle hypospadias and 47.06% had posterior hypospadias.[15] The possible explanation of the fact that, the researcher took participants with large UC fistula which was mainly found in middle and posterior hypospadias.

While looking for fistula site, it was found that majority 76.19% (n=32) of the UC fistulae were found coronally. After that, 14.29% (n=6) of the UC fistulae were found sub-coronally and 9.5% (n=4) of the UC fistulae were found in mid-penile region. A study was conducted in Egypt to evaluate the results of post-hypospadias urethral fistula repair where 34.29% UC fistulae were found coronally and 37.14% of the UC fistulae were found in mid-penile region.[11] The dissimilarity of the result might be due to the fact that, in that study the researcher did not exclude the patients who had UC fistulae more than 4 mm of size where as in the present study, patients with UC fistulae more than 4 mm in size were excluded purposively. This study also did not match with the study of Neilson et al. where 50% UC fistula were found coronally.[14] In that study, the researcher also did not exclude patients with UC fistulae more than 4 mm in size.

In this study only those patients were taken who had penile surgery at least 6 months ago so that any

local inflammation could resolve completely. The mean duration of time between the primary penile surgery and fistula repair was 13.055.97 months. When studies were conducted in India, mean duration of time between the primary penile surgery and fistula repair was found 11 months which also matches the current study.[2]

The surgical outcomes of the procedure were measured which included operation time, hospital stay, complications and cost of the procedures. The mean operation time was 24.952.78 minutes. Nerli et al. found the mean operation time for PATIO surgery was 22 minutes which was quite similar to the current study.[2]

It is not easy for a child to stay in the hospital with a catheter for almost a week. Patient underwent PATIO technique, had to stay in the hospital without catheter for 2.14±0.36 days. Generally in PATIO technique, patients were discharged from hospital in the 1st post operative day (POD), but parents of six patients wanted to stay for one day more for the sake of the patient's comfort. So, they were discharged on the 2nd POD

On follow up for 6 months, no patients developed wound infection. This result may be due to the fact that the prophylactic antibiotic was given and it was continued post-operatively upto 6th post-operative day.

No patient had recurrence of fistula formation. Similar result also found where solitary UC fistula was managed by PATIO repair.[2] All patients had normal urinary flow within six months follow up. Similar result also found where solitary UC fistula was managed by PATIO repair.[2]

Absence of recurrence of fistula is an indicator of success of fistula operation. In this study, the success rate was 100%.

In the current study, the total operation cost of the procedure was calculated. It was found 3625.71± 215.14 taka. No literature was found the operation cost in this procedures. But in this study, operation cost was compared as Bangladesh is a developing country and many people belong to low socioeconomic status.

Conclusion

Urethrocutaneous(UC) fistula is a very common complication of hypospadias repair. The PATIO technique for repair of UC fistula following hypospadias repair is simple, easy to perform, can be done with short operative time, less cost and short hospital stay with 100% success rate. So, PATIO repair can be a better alternative than others procedure for Urethrocutaneous fistula.

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REVIEW ARTICLE

Nutritional Support to the Children with Cancer

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Abstract

Malnutrition is common in cancer children. Nutritional support is an important part of the medical treatment inn cancer inn children. Nutrition related problems like cancer cachexia, wasting and sarcopenia are related but can be distinct from one another. Risk factors are to be known, discussed and identified. Nutritional status are clinically assessed by history, physical examination and anthropometric measurements. Laboratory investigations like albumin and pre-albumin also are of great help. The method of nutritional support chosen is based on the clinical assessment and the child's nutritional requirements. The cancer affected child can be supported by oral enteral or parenteral feeds as required.

Introduction

It is a common finding to get malnutrition in cancer children.[1-6] There are lot of controversies surrounding prognostic significance of malnutrition in cancer affected children.[7-9] Nutritional support is an important component of medical treatment in cancer.[10,11] That obviously guided care providers to appropriately support the under-nutrition in cancer affected children. Therefore, customized nutritional intervention is required right from the diagnosis, through to the end of treatment depending on the condition that varies from patient to patient. Each and every newly diagnosed child with cancer requires a systematic, comprehensive enquiry of his/her nutrition status, with regular reassessments.[12] The frequent use of complementary and alternative dietary supplements also signifies the importance that families attach to nutritional therapy.[13,14] In this context it is very crucial to review the definitions, epidemiology, etiology and practical therapy of nutritional problems of the paediatric patients with cancers.

Definitions and detections

Cancer Cachexia: Cachexia is defined as a severe state of malnutrition characterized by anorexia, weight loss, muscle wasting, and anemia.[9,15] Roubenoff proposed that the terms wasting, cachexia and sarcopenia be considered as three distinctly defined entities.

Wasting is defined as involuntary weight loss and is found in patients with anorexia nervosa, cancer, advanced HIV infections, and marasmus. Cachexia, in contrast, is defined as involuntary loss of fat-free mass in the setting of minimal or no overall weight loss. Reduction of lean body mass has important functional and prognostic significance. Sarcopenia refers to the involuntary loss of muscle mass that occurs with aging.[16,17] There are no disease process where malnutrition is advantageous to the host.[18] Malnutrition to Paediatric and adult patients with cancer has been associated with intolerance to chemotherapy and increased mortality rates.[7,19] Early recognition of the patient at risk for malnutrition can obviate the need for more aggressive nutritional support subsequently in the patient's course.[17,20] Therefore, the topic was selected here to review for discussion.

Risk factors for malnutrition in paediatric patients with cancer

In Paediatric cancers there are some who are in high nutritional risks. These are advanced diseases during

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initial intense treatment like unfavourable histology Wilms' Tumor, Stages III and IV Neuroblastoma, advanced stage Rhabdomyosarcoma, advanced stage Ewing Sarcoma, some Non Hodgkin's Lymphoma, tumors of the Head and Neck (eg Nasopharyngeal Carcinoma), Acute MyeloblasticLeukemia, some Poor prognosis Acute Lymphoblastic Leukemia, Acute Lymphoblastic Leukemias during induction, multiple relapse Leukemia, Medulloblastoma and other high grade tumors, Stem Cell Transplantation, especially with graft versus host disease

Low nutritional risks are Good Prognosis Acute Lymphoblastic Leukemia, nonmetastatic solid tumors, advanced diseases in remission during maintenance treatment.[21]

Clinical Assessment of Nutritional status

The assessment of a child with cancer includes standard elements of a nutritional evaluation: history of present and past illness, review of dietary intake, physical examination and anthropometric measurements. Attention should also be directed to the significance of body composition changes as well as review of pertinent laboratory measures.

Although malnutrition is a common complication of Paediatric cancer and its treatment, firm criteria defining this state are not universally used. The children oncology group nutritional committee has established categories of nutritional status and an algorithm for nutritional intervention based on body mass index (BMI), weight for length or height.[1] Arm Anthropometric measurements have been shown to be a more sensitive indicator of malnutrition among children with cancer than BMI.[22,23] Although triceps skin fold measurement is recommended for the assessment of nutritional status in cancer patients, yet a COG survey revealed that only 5% of the institutions resorted to the measurement.[24] Laboratory investigations like serum albumin and prealbumin are commonly used to assess the nutritional status of cancer children.[25] There are reports of limitations and lack of correlation with other indices of nutritional status.[26,27] But there are others to argue favouring prealbumin measurements in patients with Acute Lymphoblastic Leukemia (ALL) or solid tumors.[23,28,29] Subtle changes in micronutrients and metabolism may occur even in the absence of deviations from normal in height and weight. Low plasma 1,25 OH D3 levels have been demonstrated in children with ALL at diagnosis, consistent with the effect of leukemiais Vitamin D metabolism and bone turn over.[30] Low levels of antioxidant nutrients, including vitamins A, C, E, as well as zinc and selenium, have also been observed in ALL patients at diagnosis and during treatment.[31] All of these facts and factors deserve additional study related to the prevalence and consequences of micronutrient deficiencies in children with cancer.

Measures of body composition

Anthropometric measurements are subjects to get influenced depending on technique, inaccuracy of equipment, lack of patient cooperation, and discrepancies between weight and protein energy reserves. Physiologically, lean body mass is the metabolically active component of the body. Therefore, it should be preferable to characterize weight by some measures of lean body mass to estimate the need more precisely for assessing the response to nutritional intervention.[32]

Bioelectric Impedance (BIA) is an available technique that relies on the principle of fat-free mass conducts an electrical charge faster than fat mass. Because fat-free mass are composed of water and ions that are good conductors of electrical charges. Lean body mass therefore has lower resistance to current. Cell membrane capacitance also can be measured by BIA. Cell membrane capacitance and resistance both together can be used to estimate total body water. Then, it is also possible to measure reliably the fat-free mass is calculated. The method is inexpensive, increasingly available as well as reliable for the purpose.[33,34] DXA scan is another to measure the lean body mass, fat mass and bone mineral density.[35]

Nutrition Intervention Technique

The method of nutrition support chosen is based on the clinical assessment and the child's nutrient requirements.[36]Some children may require minor alterations to their oral diet; others may require specialized enteral or parenteral support. There is substantial evidence that enteral support is a less expensive, safer, and effective way of nourishing the child with cancer than parenteral nutrition.[37] Patients and their family members should of course be included in the decision of nutrition options, with accurate depiction of the risks and benefits of the possible methods of nutrition support given the patient's current situation. Severe metabolic complications may be avoided by the slow advancement of macronutrients over a period of days

to weeks as well as close laboratory monitoring of electrolytes, glucose and minerals.

Oral feeding: Modifications to oral diet for Paediatric oncology patients include reduced bacteria,[38] texture changes, adjustments to electrolyte or mineral content, and calorie supplementation. Although the efficacy of low bacteria dies to reduce infection has not been proven, some centres continue to use them routinely, particularly in the stem cell transplant setting. General principles of cautious food safety should be followed for any immunocompromised child. That is described as below.

Good hand washing should be practised before and after preparing meal. The food should not be shared with anyone else. Foods from street vendors, salad bars, shared bins of foods inn grocery stores must be avoided. Raw foods should be washed prior to eating. Meat should be cooked very well. Raw eggs must be avoided. Foods should be kept at below 40 F or more than 140 F to minimize growth of bacteria. To avoid cross contamination all preparation items should be thoroughly cleaned before and after use. Refrigerated leftovers of more than 3 days must not be given to cancer patients.[39] Children with mucositis often better tolerate a soft diet. A diet high in magnesium or potassium may be useful for the child with excessive urinary losses of minerals because of chemotherapies or antibiotics. Calorie supplementation may be required to assist with weight gain or weight maintenance during cancer treatment. This can be accomplished with usual foods, or in combination with commercial supplemental drinks or in combination or calorie additives. Techniques for increasing oral energy intake are described in below.

Since these children with cancers suffer from loss of appetite small frequent feeding like 6 to 8 feeds per day should be practised. These boys should be encouraged to take energy dense beverages between meals. They should be offered favourite nutritious foods during treatment free period.

When nausea and vomiting are problems feed the child 3 to 4 hours before therapy that typically are emetics. Small amounts of cool foods should be offered to them. They should be encouraged slow eating. Foods with strong odour should be avoided. Clear liquids should be offered between meals. Covered cups and straws can be used to facilitate sipping.

For the cancer patients with mouth sores, soft or pureed bland liquids should be served. In these cases to moisten foods butter, gravy, sauce or salad dressings can be added. Highly seasoned or hard rough foods should be avoided.

As because the cancer children does have altered taste perception stronger seasonings should be used avoiding excessively sweet foods. Salty foods and new flavours of foods can be used.[39]

If the children are unable to meet their nutrient needs orally, tube feedings should be considered in order to maintain the nutritional status of the patient. In these children Nasogastric tube can be used in addition to their willingly oral feeding.[40] If enteral feed is compared with parenteral feeding the cheap, easy set up and less incidence of cholestasis are the advantages in favour of enteral feeding. Many often, per cutaneous gastrostomy tubes can be a valuable option.[41]

- It is important to mention here that nutritionally complete formulas for oral or parenteral feeding are available. Intact protein yielding 1 Kcal/ml is tolerated by most of the Paediatric patients. Rarely, special formulas for tube feeding are indicated. Formulas with elemental (free amino acids) or semi-elemental (small peptides) proteins are used in case of allergies and intolerance. Medium chain triglycerides are also used in many formulas used for patients with fat malabsorption. (Nestle Nutrition, Abbott Nutrition, Nutritia North America).

When the gastrointestinal tract is non-functional or unavailable, nutrients may be infused via Central Venous Catheters. Parenteral nutrition has been widely used in the oncology population due to the cytotoxic effects of many treatment regimens. Many chemotherapy agents commonly cause some degree of nausea and vomiting. Radiation therapy when directed to gastrointestinal organ can cause cell damage impairing GI function and absorption. High dose chemotherapy regimens and Total Body Irradiation, used in preparation for stem cell transplantation, may cause a severe mucositis and gastroenteritis. These make significant oral or enteral intake difficult for these patients to achieve for many weeks. Gastrointestinal Graft Versus Host disease, a complication of allogenic stem cell transplantation, causes impaired absorption of nutrients, either because of anorexia and diminished

oral intake in its mildest cases, or as profuse, bloody diarrhoea in its more severe cases. When indicated PN goals should be based on estimated requirements for age and nutritional assessment. Fluid requirements and venous access must also be considered in formulating the PN prescriptions. Electrolytes, Paediatric multi vitamins and trace elements are required according to usual needs.

The risks of PN can be significant, and include infections, hepatotoxicity, suppression of oral intake and metabolic abnormalities. Most children undergoing aggressive cancer treatment will require indwelling central venous catheters for chemotherapies, but the use of PN has be associated with a 2.4 fold increase in the risk of infection in children receiving chemotherapy who have central access devices inn place.[42]

Many of the medicines used in oncology can cause liver injury. The use of PN, singly or in combination with these medicines, may cause biliary dysfunctions or steatosis.[43] The use of intravenous omega 3 fatty acids in the treatment of PN associated liver disease as been described I infants with short bowel syndrome. Another potential risk of PN administration is the generation of peroxide compounds, which may have harmful effects in neonates and others with immune dysfunction and/ or reduced antioxidant defences.[44] Covering PN bags and intravenous tubing with opaque plastic coloring may reduce this effect.[45] PN can also cause early satiety and decreased oral intake.[46] Nausea and vomiting have been linked with children receiving PN at home.[47] Metabolic derangements are also associated with PN. Over- or under- hydration, electrolyte imbalance, hyperglycemia, and hypoglycaemia are among the most common concerns.[48]

Antioxidants, those chemicals nutrients that help prevent the accumulation of highly reactive oxygen species, are thought to stave off the adverse effects of cancer treatment, aid the anticancer effects of conventional therapy, and prevent second malignancies.[49] Clearly, vitamins have a critical role in both enteral and parenteral nutritional intervention. Research suggested that vitamins may be linked to the prevention of certain childhood cancers and the decrease off certain adverse effects of chemotherapy.[50] Prenatal maternal multivitamin use has been connected to a reduction in the risk of neuroblastoma.[51] Protective effects of Iron or folate during pregnancy has been linked with reduction of ALL.[52] Increased Vit E intake at 3 months post chemotherapy offers a protective effect against infection, while beta carotene intake at 6 months decreases toxicity.[53] Inn a cohort of children with Down Syndrome, a decreased risk of leukemia was observed with maternal use of periconceptional vitamins.[54]

The guidelines have also been determined for the cancer survivors also. To achieve the fitness level healthy weight has been described and advice has been given to be active each day within personal limitations. Variety of whole grains, fruits and vegetables have been advised each day. Three to four servings of high calcium foods need to be consumed. Diet should be selected low in saturated fat and cholesterol. Sugary foods and beverages should be limited. Salt should be restricted sensibly.[55]

In conclusion, the nutritional assessment is an integral part of management of cancer children. In doing that the health personals need to be focused in assessing the status of nutrition of the patient physically, anthropometric measurements and with some laboratory supports very much available and affordable. Utmost care must be given in selecting foods for the patients, in preparing and maintaining hygiene of foods for the cancer ridden children. The appropriate protocols are already standardized and authorized by different internationally recognized organization. The most important thing is to follow the norms and regulations with appropriate recommended measures.

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DS (Child) H J 2015; 31(2) 133-135

CASE REPORT

A Female Adolescent with Bronchiectasis due to Cystic Fibrosis

Mohammed Rizwanul Ahsan[1], Hossain Shahid Kamrul Alam[2], Afroza Islam[3], A.B.M Mahfuj Hasan Al- Mamun[3]

Introduction

Bronchiectasis is a disease characterized by irreversible abnormal dilatation & anatomic distortion of the bronchial tree, likely represents a common and stage of a member of non-specific and unrelated antecedent events. Its incidence has been decreasing overall in developing countries. Females are affected more frequently than males.[1] Cystic fibrosis is the most common causes of bronchiectasis in children & young adults.[2] Pneumonia and tuberculosis, other causes of bronchiectasis are concomitant or subsequent infection with agents such as histoplasmosis, viruses & certain fungi, foreign body aspiration, cystic fibrosis, congenital absence of supportive airway cartilage (kartagener's syndrome), immunodeficiencies (IgA), asthma & middle lobe syndrome.[3]

Bronchiectasis findings are non specific. Most commonly crackles, are non-specific & may occur 73% of patients[4], ronchi, scattered wheezing approximately one third of patients, wheezing may be due to airflow obstruction from secretion, destruction of the bronchial tree lending to airway collapsibility or a concomitant condition.[2,4] Digital clubbing is an inconsistent finding in approximately 2-3% of patient.[4] Cyanosis & plethora are rare findings secondary to polycythaemia from chronic hypoxia, wasting, weight loss are suggestive of advanced disease but are not diagnostic of bronchiectasis. In severe cases, findings are consistent with corpulmonale ultimately lead progressive respiratory failure.[5] Sputum analysis may be used to further strengthen clinical suspicion, specially CT scanning, then may be used to confirm the diagnosis, once the diagnosis confirmed, additional laboratory testing may be careful to determined the underlying cause. The choice of laboratory test may vary & should be tailored to the individual patient & clinical situation. However, high reduction CT (HRCT) scanning is the criterion standard for the diagnosis of bronchiectasis.[6,7,8] CT sensitivity & specificity reportedly are 84-97% & 82-99% respectively.[9] Pneumonectomy is the treatment of choice for varying stage of lung disease with bronchiectasis and causes low mortality & morbidity.[10]

Case Report

Arcepa, a 12 years old girl, weight 25kg hailing from Madaripur presented with fever for 10 days , cough for 7 days & respiratory distress for 3 days. Fever was low grade, associated with productive cough, with profuse sputum which was deep yelowish and mucoid in nature and increased at morning but never blood mixed. She had sufferred from recurrent attacks of Respiratory Tract Infection (RTI) manifested by fever, cough & respiratory distress since 5 years of age. She had no history of contact with tuberculous patient. She was on herbal medicine & took some medications along with inhaler by village quack but never hospitalized. For the last 3 days she developed severe respiratory distress & admitted in DSH.

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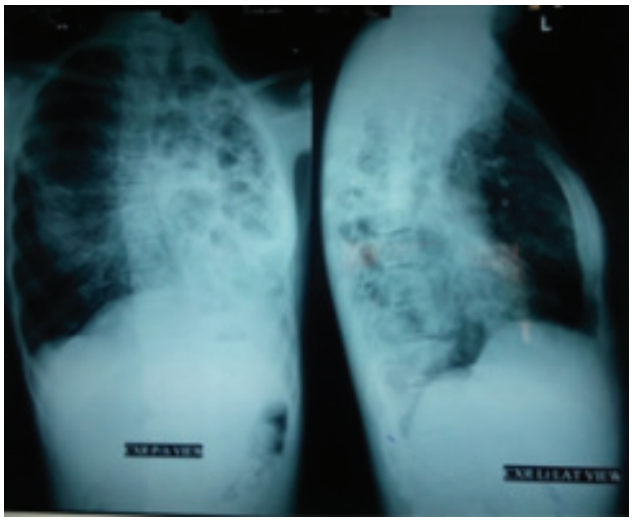

Fig 1 *X-Ray Chest A/P & Lt. Lateral view*

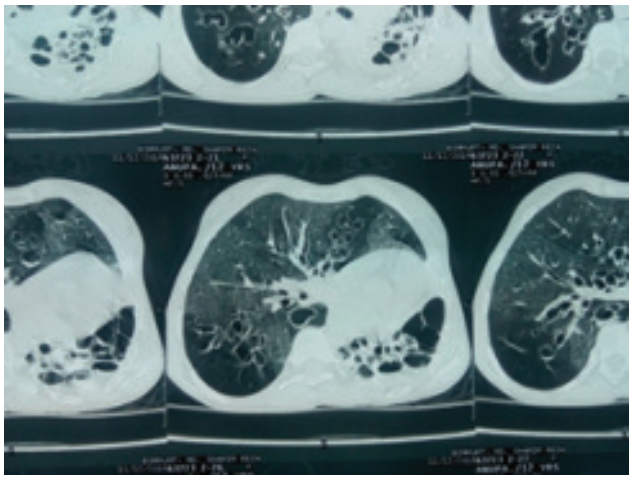

Fig 2 *CT Scan of Chest*

Clinically Arcepa was dyspnoic, acyanotic, mildly anaemic, febrile (temp-100°F), R/R 40 breaths/min, generalized clubbing present. There was no lymphadenopathy. Respiratory system examination revealed chest movement & expansibility reduced on left side, trachea shifted to left, woody dullness on percussion present on left side & vocal fremitus was increased on left side of the chest. Breath sound bronchial on left side & course crepitation in both lung fields. Lung function test was normal. On laboratory findings complete blood count showed neutrophilic lecucytosis, Blood culture no growth, sputum examination no AFB found. Montaux test was 00 mm, sweat chloride test 1st sample 70mmol/L, 2nd sample-90.6mmol/L both were positive, chest x-ray showed multiple ring like shadow throughout the left lung field, there was difuse patchy opacities present on the left lower lung field and hyperinflation of the right lung, On HRCT of chest complete collapse of left lung is noted and mediastinal is shifted towards left. Herniation (retrocardiac & retrosternal) of right lung is also seen. Multiple thick walled dilated bronchi are noted in almost all segment of both lung fields, some of having mucus plug with ground glass opacities interspersed within air trapping in all segment of right lung. With the above findings bilateral bronchiectasis with collapse of left lung due to cystic fibrosis was diagnosed. Initially the patient was managed with parental broad spectrum antibiotic for 14 days, antipyretic, nebulization with acetylcysteine, broncho-dilator, steroid, chest physiotherapy with postural drainage. Patient was referred to paediatric thoracic surgeon for pnecomonectomy, but patient is not fit for pneumonectomy. She was advised for continuing conservative management for 42 days then follow up.

Discussion

Bronchiectasis are cough & daily mucopurulent sputum production, often lasting months to years. Blood streaked sputum on haemoptysis may result airway damage associated with acute infection, less specific symptoms include dyspnea, puritic chest pain, wheezing, fever, weakness & weight loose. A rare veriant known as dry bronchiectasis manifest as episode haemoptysis with little-to-no sputum production usually in a sequel of TB & is found in upper lobes. Patient may report repetitive pulmonary infection that require antibiotic over several years, a single episodic of severe infection often in childhood, may result bronchiectasis.[11]

Our patient represent a classical case of bronchiectasis due to cystic fibrosis. Our patient having 7 years of repeated pulmonary infection, fever, cough, mucoid sputum production & dyoponea. Chronic productive cough up to 98% patient.[12] Dyspnea may occur in 72% patient a 2006 review reported a rate of 62%.[4] Wheezing, & plethoric chest pain is on intermittent finding occurring in 19-46% patient.[4] Weight lose may occur, fever may occur if acute infection, urinary incontinence occur more frequently in women with bronchiatasis versus age-matched controls (47% VS 12%).[13] The prevalence of bronchiectasis has declined in developed countries with improved health care & the availability of suitable antibiotics. It continuous to be an important

problem in developing countries because of increased prevalence of tuberculosis, pneumonia & other childhood infections. The majority of cases present in a late stage of the disease, where the definite etiology is difficult to establish, due to prolonged history of recurrent infection & inadequate medical treatment. In a series of 166 patients who underwent pnecomonectomy, the indication in 158 was bronchiectasis with failure of medical treatment.[14] The management of bronchiectasis has been changed over the last faw decades from surgical resection to a more conservative approach.[15,16] It has been suggested that if aggressive conservative management in the form of chest physiotherapy, postural drainage, prophylactic antibiotics & treatment of primary cause is instituted the dilatation of bronchi may be reversed. Those children who have lots of mucoid secretion, the lung tissue may be damage, conservative treatment is the treatment of choice. The morbidity & mortality rates of bronchiectasis surgery are within acceptable ranges. Most of the children benefit from surgery, especially when total escision is accomplished. Pneumonectomy is well tolerated in children without increasing morbidity & mortality. Therefore, pneumonectomy may be preferred instead of leaving residual disease when bronchiectasis in unilateral.[17]

Conclusion

Surgical treatment of bronchiectasis poses a great challenge & has to be multidisiciplinary. Bilateral bronchiectasis due to cystic fibrosis is a uncommon condition and early diagnosis & treatment by resection of the affected segment may help in alleviation of symptoms & avoidance of complication.

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CASE REPORT

Familial Hypercholesterolemia

Abu Sayed Munsi[1], Md. Jahangir Alam[2], Abu Sayeed[3], Manzoor Hussain[4]

Introduction

High cholesterol concentration in the blood is caused by an inherited genetic defect known as familial hypercholesterolaemia (FH). Familial hypercholesterolemia is a single gene disorder. It is a rare defect of lipid metabolism characterized by markedly elevated level of serum cholesterol with normal triglyceride. There is mutation in the LDLR gene located on chromosome19[1-3] and is associated with elevated plasma low density lipoprotein cholesterol in blood.[4] Familial hypercholesterolemia is of 2 types, heterozygous FH and homozygous FH. A raised cholesterol concentration in the blood is present from birth and may lead to early development of atherosclerosis and coronary heart disease.

The disease shows an autosomal dominant pattern of inheritance, being transmitted from generation to generation in such a way that siblings and children of a person with FH have a 50% risk of inheriting FH. Most people with FH have inherited a defective gene for FH from only one parent and are therefore heterozygous. Rarely, a person will inherit a genetic defect from both parents and will have homozygous FH or compound heterozygous FH. The prevalence of heterozygous FH in the UK population is estimated to be 1 in 500, which means that approximately 110,000 people are affected. The elevated serum cholesterol concentration that characterizes heterozygous FH leads to a greater than 50% risk of coronary heart disease in men by the age of 50 years and at least 30% in women by the age of 60 years. Homozygous FH is rare, with symptoms appearing in childhood, and is associated with early death from coronary heart disease. Homozygous type FH, both LDLR alleles are defective due to mutation and has a prevalence of approximately one case per one million.[5]

Case report

Sadia afrin a nine years old girl, 3rd issue of consanguineous parents presented with the complaints of white skin lesion over back of elbow joint, front of ankle joint, back of wrist, hands and other parts of the body since birth. She was delivered by LUCS at term and developed jaundice at 3rd day of her age. Phototherapy given for 8-10 days. Mother noticed that one skin spot was present at ankle since birth. As spot at ankle increasing day by day, She visited to a private clinic and referred her to BSMMU where she was treated with Cholestyramine ½ sachet once daily and Nicotinic acid ½ tab thrice daily for 6 months. As the skin lesion was increasing day by day, atovastatin 10 mg once daily started at 7 years of her age without significant improvement.. Her maternal grandfather died at 47 years of his age due to heart attack. So she was admitted in Dhaka Shishu Hospital for further evaluation and management.

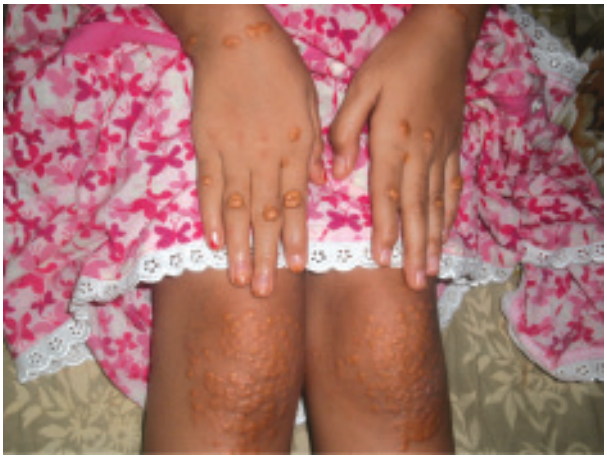

Fig 1 *Patient with xanthomas on knee joint and back of hand*

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General examination revealed multiple soft subcutaneous tissue swelling over her back of hand, wrist, elbow, ankle and front of knee joint which was suggestive of xanthomas. Her weight 23 kg and height 125 cm. Her body mass index 14 kg/m^2. Systemic Examination revealed a soft systolic murmur at mitral area that radiates towards left axilla. Lipid profile was grossly deranged for patient and parents. Her fasting lipid profile revealed total cholesterol was 674 mg/dl, Low density lipoprotein (LDL) was 595 mg/dl, High density lipoprotein was 33 mg/dl, Triglycerides 110 mg/dl. Her father and mother had high concentration of total and LDL cholesterol while high density lipoprotein cholesterol and triglyceride were normal. We treated the patient with tab. Rosovastatin 10 mg twice daily, Cholestyramine 1 sachet thrice daily and tab. Nicoson (Nicotinic acid) 1 tab thrice daily. After 1 month of treatment, fasting lipid profile done which revealed total cholesterol was 650 mg/dl, Low density lipoprotein (LDL) was 585 mg/dl, High density lipoprotein was 34 mg/dl, Triglycerides 112 mg/dl. Echocardiography of the patient showed mild MR.

Discussion:

Familial hypercholesterolemia (FH) is an autosomal dominant inherited lipid disorder that causes marked elevation of serum total cholesterol and low density lipoprotein cholesterol. The primary defect is a mutation for the receptor for plasma low density lipoprotein in the hepatocytes which is the primary determinant of hepatic low density lipoprotein uptake. So excess low density lipoprotein accumulation occurs in the body tissue. In homozygous familial hypercholesterolemia individual the consequence is severe. Atherosclerosis begins before puberty and are at risk for early coronary events and sudden death [6-9]. The diagnosis of familial hypercholesterolemia is based primarily on the family history, clinical examination which revealed xanthoma and investigation finding of serum total cholesterol and low density lipoprotein elevated in the absence of secondary causes of hypercholesterolemia. The definitive diagnosis can be made only with gene or receptor analysis. The overall goal of treatment is to lower the risk for atherosclerotic heart disease by lowering the LDL cholesterol levels in the blood stream. Atherosclerosis is a condition in which fatty material collects along the walls of arteries. This fatty material thickens, hardens, and may eventually block the arteries. Atherosclerosis happens when fat and cholesterol and other substances build up in the arteries and form a hardened material called plaque. The plaque deposits make the arteries less flexible and more difficult for blood to flow leading to heart attack and stroke. The first step in treatment for an individual who has heterozygous familial hypercholesterolemia is changing the diet to reduce the total amount of fat eaten to 30 percent of the total daily calories. This can be done by limiting the amount of beef and pork in the diet; cutting out butter, whole milk and fatty cheeses as well as some oils like coconut and palm oils; and eliminating egg yolks, organ meats and other sources of saturated fat from animals. Dietary counseling is often recommended to help people to make these changes in their eating habits. Exercise, especially to lose weight, may also help in lowering cholesterol levels. Drug therapy is usually necessary in combination with diet, weight loss, and exercise, as these interventions may not be able to lower cholesterol levels alone. There are a number of cholesterol-lowering medications that are currently used. The first and more effective choice of drugs called "statins." Other drugs that may be used in combination with or instead of the statins are: bile acid sequestrant resins (for example, cholestyramine), ezetemibe, nicotinic acid (niacin), gemfibrozil, and fenofibrate. Individuals who have homozygous familial hypercholesterolemia need more aggressive therapies to treat their significantly elevated levels of cholesterol. Often drug therapies are not sufficient to lower LDL cholesterol levels at the desiderated goal and these individuals may require periodical LDL apheresis, a procedure to "clean up" LDL from the blood stream, or highly invasive surgery such as a liver transplantation is an effective treatment option in this disorder as liver is the most important tissue for removing circulating low density lipoprotein.

Conclusion

Familial hypercholesterolemia is a genetic disorder. Lipid profile and vital organs should be investigated in any patient presented with xenthoma, and all the relatives in the family should be screened for dyslipidemia.

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ABSTRACT FROM CURRENT LITERATURE

Anemia among children and adolescents in a rural area

Ivan Riyanto Widjaja, Felix Firyanto Widjaja, Lucyana Alim Santoso, Erick Wonggokusuma, Oktaviati

[Paediatr Indones. 2014;54:88-93].

Background: Anemia in children and adolescents affects growth and development. It is a preventable disease, but unfortunately is often ignored until the symptoms occur. There have been limited reports on the prevalence of anemia in children and adolescents in Indonesia, especially from rural areas.

Objective: To describe the prevalence of anemia in children and adolescents in district ofMalinau, a rural area in East Kalimantan Province.

Methods: This cross-sectional study was done in June 2010 using laboratory records between July 2009 to January 2010. Laboratory records of patients aged between 6 months and 18 years which investigated were complete blood count (CBC) from ambulatory, inpatient, and emergency care ofMalinau Public Hospital in East Kalimantan. Mentzer and England & Fraser indices were used to differentiate iron deficiency anemia (IDA) and thalassemia among microcytic hypochromic anemic patients.

Results: This study involved 709 laboratory records. Prevalence of anemia was 53.9% (95% CI 50.2% to 57.5%). The prevalence of IDA among age groups were as follows: 29.4% (95% CI 24.3 to 34.5%) in 6-59 months group, 16% (95% CI 11 to 21 %) in 5-11.9 years, and 15.2% (95% CI 10.2 to 20.2%) in 12-18 years. Children aged 6-59 months tended to have more anemia than those aged 5-11.9 years (OR 2.184, 95% CI 1.398 to 3.413) or aged 12-18 years (OR 2.319, 95% CI 1.464 to 3.674).

Conclusion: The prevalence of anemia in children and adolescents of the Malinau Regency is 53.9% (95% CI 50.2 to 57.5%), quite similar to that of other developing countries. A government program to overcome anemia is recommended, not only for pregnant women, but also for children and adolescents.

Reducing dyspeptic symptoms in children: proton pump inhibitor vs. HZ receptor antagonist

Tien Budi Febriani, Titis Widowati, Mohammad Juffrie

[Paediatr Indones. 2014;54:198-201.].

Background: Dyspepsia is known as a leading cause of upper gastrointestinal tract morbidity. If left untreated, dyspepsia may become chronic. Dyspeptic symptoms manifest as epigastric pain, heartburn, nausea, hematemesis, or melena. Experimental studies have shown that omeprazole is more effective at reducing heartburn than ranitidine in adults. However, there have been few studies comparing the effects of proton pump inhibitors to Hz receptor antagonists for reducing dyspeptic symptoms in children.

Objective: To compare the effect of omeprazole with ranitidine for reducing dyspeptic symptoms.

Methods: We performed a double-blind randomized controlled trial (RCT) at Sardjito Hospital and three community health centers in the Sleman District from June to November 2012. We recruited children aged 3-18 years with dyspepsia. Subjects were allocated into two groups using block randomization: the proton pump inhibitor (omeprazole) and the Hz receptor antagonist (ranitidine) groups. According to the groups, either omeprazole (0.4-0.8 mg/kg/dose) or ranitidine (2-4 mg/kg/dose), respectively, were taken twice daily for 5 days. Dyspepsia was clinically diagnosed using the new Rome III criteria. Both groups were monitored for 5 days to assess for a reduction of dyspeptic symptoms.

Results: Significantly more subjects in the omeprazole group recovered from dyspeptic symptoms than in the ranitidine group (RR= 4.87; 95%CI 1.5 to 15.3; P=0.005).

Conclusion: Omeprazole was 4.87 (95% CI 1.5 to 15.3) times better than ranitidine in reducing dyspeptic symptoms on children aged 3-18 years with dyspepsia.

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Folic acid and acute diarrhea in children

Ade Amelia, Atan Baas Sinuhaji,Supriatmo

[Paediatrlndones. 2014;54:273-9].

Background: Diarrhea has been a health problem in children under five year old. Although the mortality caused by acute diarrhea has fallen worldwide, the mortality has increased in developing countries, such as Indonesia.

Objective: To assess the effect of folic acid in reducing the severity of acute diarrhea in children.

Methods This study was a single-blind, randomized control trial in children with diarrhea aged six months to five years at a local goverment clinic in the Secanggang District, Langkat Regency, North Sumatera Province from August 2009 until January 2010. Subjects were recruited by consecutive sampling then randomized into two groups. Of the 112 children who participated, 56 children received oral folic acid and 56 children received placebo, 1 capsule per day for five days. The statistical analyses used were the independent T-test and Chi square test with 95% confidence intervals (95% Cl) and P values < 0.05 considered to be statistically significant.

Results: There were significant differences between the folic acid and placebo groups with regards to stool consistency (P=0.02), diarrheal volume on the second day [147.52 vs. 303.21 ml., respectively, (P=0.001)], frequency of diarrhea on the third day [1.9 vs 2.8 episodes, respectively, (P= 0.001)], duration of initial treatment to recovery [91.3 vs. 117.9 hours, respectively, (P =0.001) and the total duration between initial symptoms and recovery [123.6 vs. 147.4 hours, respectively, (P = 0.001)].

Conclusion: Oral folic acid is clinically beneficial for reducing the severity of acute diarrhea in children under five year old.

Serum transaminase levels and dengue shock syndrome in children

YogaPutra, Bagus Ngurah Putu Arhana, Ida Safitri, Raka Widiana

[Paediatr lndones. 2014;54:181,5].

Background Clinical and biochemical impacts on liver dysfunction, as manifested by an increase in serum transaminase levels, are common in dengue infection. However, an association of elevated serum transaminase and dengue shock syndrome (DSS) has not been well-established.

Objective: To assess for an association between serum transaminase levels and the presence of DSS in children.

Methods: A nested, case control study was conducted on children aged 1 month to 12 years admitted to Sanglah Hospital who were diagnosed with dengue infection. Baseline characteristics and serum transaminase levels were recorded. Patients who were included in the study were observed for the presence of DSS. Those who had DSS were selected as cases, and those who did not develop DSS were selected as controls. Data was analyzed using bivariate and multivariate methods with 95% confidence intervals and P value <0.05 was considered as statistically significant.

Results: Ninety-four children were involeved, 4 7 children in the case group and the other 4 7 were in the control group. Baseline characteristics of the subjects were similar between the case and control groups. Serum aspartate transaminase (AST) level of 2:: 128 U/L and alanine transaminase (ALT) of 2::40 U/L were associated with DSS (OR 10; 95%CI 2.3 to 44.4; P=0.002) and (OR 7.3; 95%CI 1.6 to 32.9; P=0.009), respectively.

Conclusion: Elevated AST and ALT levels were associated with an increased risk of DSS in children with dengue infection.

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DSH NEWS

Launching ceremony on introduction of PCV and IPV in routine EPI, inaugurated by our honourable minister, Ministry of Health and family welfare, Mohammed Nasim MP along with Honourable Director of DSH Professor Manzoor Hussain, Honourable Direcor General of Health Services, Professor Dr. Kazi Din Mohammad Nurul Hoque to reduce the burden of invasive pneumococcal disease and to eradicate the poliomyelitis from our country.

Discussion of donation, Rotary Club of Dhaka Royal on 29.11.2015

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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.

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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.

Contact Person : Prof MAK Azad Chowdhury
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Students Qualified from Bangladesh Institute of Child Health

Undergoing Courses of BICH

Institution	Courses
Bangabandhu Sheikh Mujib Medical University	MD(Paediatric)
	MD (Neonatology)
	MD (Nephrology)
	DCH
Bangladesh Collage of Physicians and Surgeons (BCPS)	MS (Paediatric Surgery) FCPS (Paediatric) FCPS (Neonatology) FCPS (Haemato-Oncology)
Dhaka University	BSc (Health Technology)

Students Qualified From BICH Till January 2015

Name of Courses	Number
DCH	327
MD (Paediatrics)	95
MS (Paediatrics)	86
FCPS (Paediatrics)	22
MD (Neonatology)	12
MD (Paediatric Nephrology)	4
Total	**546**

Foreign Students Qualified From Bich Till January 2013

Country of Origin	Course	Number
Nepal	DCH	23
	MS(Paed. Surgery)	2
	MD(Paed)	1
India	MD(Paed)	1
Iran	DCH	1
Iraq	DCH	1
Somalia	DCH	1
Sudan	DCH	1
Total		**31**

Present Students January 2015

Name of Courses		Number of Students
DCH		14
MD (Paediatrics)	Part-I	13
MD (Paediatrics)	Part-II	8
MD (Paediatrics)	Final Part	2
MS (Paediatrics)	Part-I	6
MS (Paediatrics)	Part-II	2
MS (Paediatrics)	Final Part	6
FCPS (Paediatrics)	Part-II	2
FCPS	(Paediatric Nephrology)	1
Total		**54**

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Seminar/Symposium & CME/CPD programs held at BICH (July to December, 2015)

Date	Topic	Presenter
August, 2015	Perinatal Pulmonary Hypertension of Newborn	Department of Paediatric Cardiology
8 August 2015	Probiotic :	Department of Paediatric Gastroenterology, Hepatology and Nutrition
6 September 2015	Kawasaki Disease:	Department of Paediatric Rheumatology
20 December 2015	Care in Paediatric Nephrology :	Department of Paediatric Nephrology