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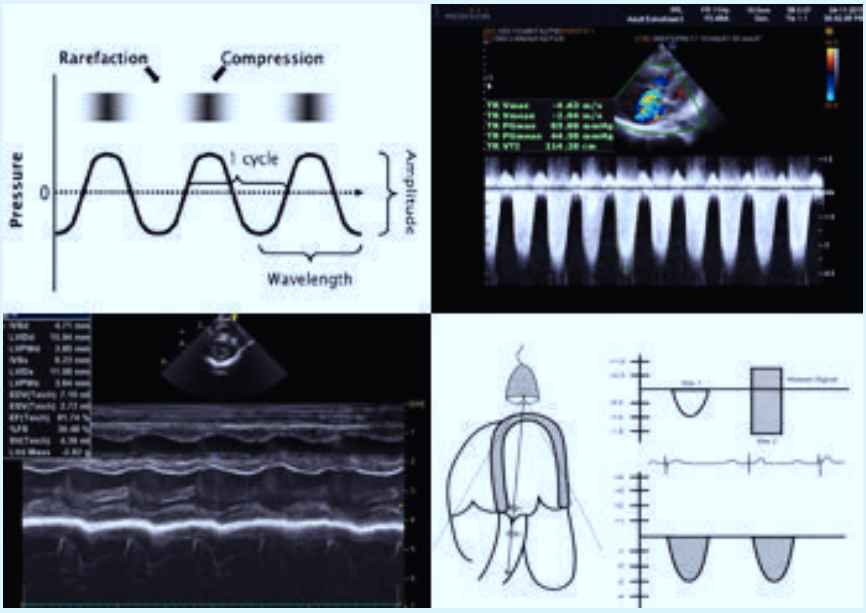

Editorial

"Functional Echocardiography in Neonate"

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EDITORIAL

Functional Echocardiography in Neonate

Manzoor Hussain

Introduction

In neonate cardiovascular vulnerability such as incomplete myocardial development,presence of foetal shunts, changes in systemic and pulmonary vascular resistance and complex haemodynamic changes that take place during transition to extrauterine life have limited clinical manifestations. Despite progressive technological advances, haemodynamic monitoring in newborns is still based on assessment of continuous heart rate, blood pressure, acid base status, urine output and capillary refill time.[1]These measures provide important and useful information to the clinician. Clinical assessment and the classic parameters mentioned before to elucidate the underlying pathophysiology in haemodynamic disturbances can sometime lead to incorrect assumptions and therapeutic decisions, which may even cause harm.[2]Sometimes the clinical signs provide limited insight into the adequacy of systemic blood flow and organ perfusion. Situations in which serial assessment is needed to evaluate response to treatment or the haemodynamic changes that take place during transition from foetal to postnatal circulation, it is important to consider that these changes can be very different from what might be assumed clinically based on conventional assessment.[1]These variables related in varying degrees to tissue perfusion, which is the key haemodynamic parameter, and for which an adequate monitoring method has yet to be developed.[3]

Enhanced cardiovascular imaging and hemodynamic evaluation offers novel insights regarding the contribution of the ductus arteriosus, myocardial performance and pulmonary hemodynamics to ongoing clinical instability. In addition, it allows more accurate delineation of the nature of the underlying disease process and facilitates the evaluation of response to therapeutic intervention.[4]

Functional echocardiography (FnEcho) or point of care echocardiography (PCEcho) or targeted neonatal echocardiography (TNE) depending on the terminology suggested by different authors, is being introduced progressively in neonatal intensive care units (NICU) as a tool to help guide treatment choices.[5]The term functional echocardiography have been introduced to describe the echocardiography as an adjunct in clinical assessment of the hemodynamic status in neonate. It may be defined as "The bedside use of echocardiography to longitudinally assess myocardial function, systemic and pulmonary blood flow, intracardiac and extracardiac shunts, organ blood flow, and tissue perfusion". FnEcho is commonly used to assess haemodynamic status during the transition from foetal to postnatal circulation in the extremely premature neonate, to assess for the presence and significance of PDA, to determine the underlying pathophysiology in patients with haemodynamic instability, and in neonates with high oxygen requirements.[6]It can provide non invasive information on the underlying CVS pathology causing hemodynamic instability and response to treatment.

Purpose of FnEcho in neonatology

There is a wealth of hemodynamic information that can be derived by functional echocardiography. Hemodynamics are variable between individual babies and also within the same baby with time.Without echocardiography there will be guessing the hemodynamics which may be wrong some times.FnEcho must be used as an adjunct to clinical assessment and not as a substitute for assessment by a cardiologist, as their purposes are different and complementary. The neonatologist can use FnEcho to obtain information about haemodynamic function in real time and to make longitudinal assessments as needed. It has shown a

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positive impact on the management of adult patients.There is some evidence which show a positive effect in the management ofneonate.[7]

The increasing availability of echocardiography, with miniaturization of the technology, has resulted in more widespread use of echocardiography in NICUs around the world. Increasingly neonatal intensivists are developing echocardiographic skills. They are able to do more systematic serial studies than cardiologist working outside NICU. Infants without any clinical suspicion of CHD the first echocardiographic study must be a comprehensive examination assessing structure and function.

Conclusion

Functional echocardiography offers evaluation of cardiac performance and systemic hemodynamics to characterize acute physiology, identify the exact nature of cardiovascular compromise and guide therapeutic decisions in neonate.

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SPECIAL ARTICLE

An Overview of Primary Immunodeficiency

Nazia Hossain

Primary immunodeficiency disorder (PID) result from defects in immune system development and/or function. It is more frequent than previously believed. The estimated prevalence of PID is 1 in 1200 with the exception of IgA deficiency (prevalence= 1 in 300-500)[1].PIDs are distinct from secondary immunodeficiency which occurs due to other causes, such as viral or bacterial infections, malnutrition, or treatment with immunosuppressive drugs. The presentation of PIDs is highly variable. Most disorders involve increased susceptibility to infection. Several lists of warning signs of PID are established.

The Jeffrey Modell Foundations' 10 warning signs of immune deficiency.[2]

1. ≥ 8 new ear infections within 1 year.
2. ≥ 2 serious sinus infections within 1 year.
3. ≥ 2 months on antibiotics with little effect.
4. ≥ 2 pneumonias within 1 year.
5. Failure of an infant to gain weight or grow normally.
6. Recurrent, deep skin or organ abscesses.
7. Persistent thrush in mouth or elsewhere on skin, after age 1.
8. Need for intravenous antibiotics to clear infections.
9. ≥ 2 deep-seated infections.
10. A family history of PID.

Classifications

PIDs are broadly classified as adaptive or innate immunity. Adaptive immunity is further classified into T cells and B cells immunity. Innate immunity comprises of numerous cells and proteins that are involved in the innate immune response including phagocytes (neutrophils and macrophages), dendritic cells, and complement proteins. Classification of PIDs with examples and clinical presentations are enlisted below.[3,4]

General Screening and Evaluation

The initial evaluation of immunodeficiency includes a thorough history, physical examination and detailed family history.

Infections

Detail history of infections is important. History regarding the type of infection, site of infection, frequency of infection, severity of infections, the pathogenicity of an infectious agent, infections with unusual pathogen, such as atypical mycobacteria, toxoplasma,nocardiaetc and concomitant presence of noninfectious and non-immune conditions including severe allergy, autoimmunity, malignancies, Down syndrome, muscular dystrophy, or various congenital heart defects.

Family History

A positive family history is highly suggestive of PID.

Clinical presentations

Evaluation of immune function should be done in those patients who have clinical manifestations of immune disorder and in those with a positive family history of infant death or a known immunodeficiency disorder, unusual, chronic, or recurrent infections such as (1) 1 or more systemic bacterial infections (sepsis, meningitis);(2) 2 or more serious respiratory or documented bacterial infections(cellulitis, abscesses, draining otitis media, pneumonia, lymphadenitis) within 1 year; (3) serious infections occurring at unusual sites (liver, brain abscess); (4) infections with unusual pathogens (Pneumocystis jiroveci,Aspergillus,Serratiamarcescens, Nocardia, Burkholderiacep acia); and (5) infections with common childhood pathogens but of unusual severity.[5]

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Disorders of innate immunity

Phagocyte defects • Chronic granulomatous disease • Hyper IgE syndrome • Leukocyte adhesion deficiency	Severe infection; abscesses with granuloma formationChronic dermatitis; recurrent, severe lung infections; skin infections; bone fragility; failure to shed primary teethRecurrent, severe bacterial infections; poor wound healing; delayed separation of the umbilical cord
Complement defects	
Deficiency in early complement pathway components (C1q, C1r, C2, C4)	SLE–like syndrome, rheumatoid disease, multiple autoimmune diseases, infections
Deficiency in late complement pathway components (C5, C6, C7, C8, C9)	Neisseria infections, SLE-like syndrome
C3 and regulatory components	Recurrent infections with encapsulated bacteria

Disorders of adaptive immunity

T-cell (cellular) immunodeficiency	Atypical mycobacterial and salmonella infectionsMucocutaneous candidiasis (thrush) and autoimmune endocrinopathy
B-cell (antibody-mediated) immunodeficiency XLA CVID Selective IgA deficiency Specific antibody deficiency IgG subclass deficiency	Recurrent sinopulmonary infections with encapsulated bacteria Autoimmune disease and increased risk of malignancy in CVID
CID Wiskott-Aldrich syndrome	Thrombocytopenia with bleeding and bruising; eczema; recurrent bacterial and viral infections; autoimmune disease
Ataxia telangiectasia	Chronic Sino-pulmonary disease; cerebellar ataxia (difficulty with control of movement); small, dilated blood vessels of the eyes and skin; malignancy
DiGeorge syndrome	Hypoparathyroidism; seizures; cardiac abnormalities; abnormal facies; infection
SCID	Severe, recurrent opportunistic infections; failure to thrive; diarrhea; rash

Investigations

The broad categories of immunodeficiency are listed below: (1) Neutrophil disorders (2) Antibody deficiency (3) Complement deficiency (4) T cell dysfunction. Its difficult to choose an investigation for evaluation of immune system. The investigations are largely guided by the clinical presentation of the patient, the suspected immune defect and the results of initial laboratory evaluation.

The most useful first-line immunological investigations include a complete blood count with a differential count, lymphocyte subset analysis, serum immunoglobulin levels and Nitroblue Tetrazolium test (NBT). The panel of antibodies used for these purpose includes CD3, CD4, CD8, CD56/16, CD19 and HLA-DR. It is aimed at measuring the absolute and relative number of : B cells (CD19+), T cells (CD3+), T-helper cells (Th, CD3+/CD4+), T-cytotoxic cells (Tc, CD3+/CD8+), Natural Killer (NK) cells (CD3-/CD56+/CD16+), and Activated T cells (CD3+/HLA-DR+).

It is very important to note that the total lymphocyte numbers and T lymphocyte subsets are age-dependent. Its markedly increased in newborns and young infants and decreasing with age. In infants

below 4 months of age, a CD4 count of <1000/mm3 is generally associated with impaired cellular immunity, whereas the corresponding value is <500/mm3 in children over 2 years of age and in adults[6]. Immunosuppressive therapies like steroids also significantly alter the values of T and B cell subsets and should be interpreted carefully.

The results of the initial tests usually give an important clue to the underlying immune defect. Patients with low T cell counts are likely to have combined T and B cell defects (CID). Patients with low or absent B cell and low Immunoglobulin levels with normal T cell fall in the category of predominantly antibody deficiency. Patients with abnormal neutrophil count or abnormal neutrophil function suggest defects in the phagocytic system. However, under these broad categories, there are many subcategories or genetic defects and advanced laboratory tests will be needed to come to a specific diagnosis.

Screening laboratory tests

Complete Blood Count, Differential, and Erythrocyte Sedimentation Rate

Absolute lymphocyte count (normal result rules against T-cell defect)

Absolute neutrophil count (normal result rules against congenital or acquired neutropenia)

Platelet count (normal result excludes Wiskott-Aldrich syndrome)

Howell-Jolly bodies (absence rules against asplenia)

Erythrocyte sedimentation rate (normal result indicates chronic bacterial or fungal infection unlikely)

Screening Tests for B-Cell Defects

Immunoglobulin (Ig) A measurement; if abnormal, IgG and IgM measurement

Antibody titers to blood group substances, tetanus, diphtheria, *Haemophilusinfluenzae*, and pneumococcus.

Screening Tests for T-Cell Defects

Absolute lymphocyte count (normal result indicates T-cell defect unlikely)

Flow cytometry to examine for the presence of naïve T cells (CD3+CD45RA+ cells)

Screening Tests for Phagocytic Cell Defects

Absolute neutrophil count, Respiratory burst assay

Screening Test for Complement Deficiency

CH50

Conclusion

Diagnosis of PID requires expertise in clinical and laboratory evaluation.Wide range of investigations are available for evaluation of immune system which help in the diagnosis of PIDs. Knowledge of clinical presentation of these disorders, correct interpretation of initial results, immune-phenotyping of lymphocytes is essential for choosing the appropriate test for specific diagnosis. Treatment of PID is challenging. SCID is a pediatric emergency which requires definitive therapy (e.g., BMT, HSCT) as soon as possible. B-cell or antibody-deficiency disorders are the most common types of PIDs. The mainstay of treatment for patients with these disorders is Immunoglobulin replacement therapy. Patients with innate immunodeficiency disorders often present with unusual or difficult to eradicate infections. Treatment varies depending on the type of defect (e.g., phagocyte disorder or complement deficiency), but may involve antifungal and antibiotic prophylaxis, cytokine replacement, vaccinations and BMT.

In our setting recognizing a case of PID is Important to ensure timely referral and early treatment of the patients.We need to create awareness about these disorders.

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ORIGINAL ARTICLE

Emergence of Antibiotic Resistance in Intensive Care Unit: Experience of Dhaka Shishu (Children) Hospital Pediatric Cardiac Intensive Care Unit

Mohammad Abdullah Al Mamun[1], Manzoor Hussain[2], Rezoana Rima[3], Abdul Jabbar[4], Nawshika Sharmin Echo[5]

Abstract

Background: *Antibiotics are the most common therapies administered in the intensive care unit (ICU) setting. The rapid emergence and dissemination of antimicrobial resistant microorganisms in ICUs worldwide constitutes to be a serious problem now a day.*

Objectives*: This study was aimed to investigate the initial antibiotics used before ICU admission, pathogen distribution and antimicrobial susceptibility among the congenital heart disease (CHD) children admitted to ICU.*

Methods*: This prospective study was conducted in Pediatric Cardiac Intensive Care Unit (PCICU) of Dhaka Shishu (Children) Hospital from June 2015 to May 2016. Patients having cardiac problems from all over the country were transferred for medical management during the study period was enrolled. Blood, urine and tracheal aspirate were sent when infection was suspected. Antibiotics used before PCICU admission was noted. Data were collected and analyzed by using SPSS version 17.*

Result: *During the study period total 305 patients were admitted and almost all received broad spectrum antibiotics including third generation cephalosporins (36.8%), carbepenem (17.7%) even piperacillin (3.3%) and colistin (8.4%) before admission in PCICU. Organisms were isolated in 10.82% cases and majority were gram negative (Acinatobactor 42.4%, Klebsiella 21.2%, and Pseudomonas 24.2%). Multi drug resistant (MDR) Acinatobacter was found in 90.99% cases and 9.09% was pan drug resistant. Acinatobacters were resistant to conventional antibiotics, even resistant to piperacillin in 85.7% and carbapenem in 78.6% cases. Klebsiella, Pseudomonas and E. Coli was also found resistant to commonly used antibiotics. They also showed higher resistant to piperacillin and carbapenema. Staphylococcus showed 100% resistant to ampicillin, 50% to gentamicin, ceftazidime, ceftriaxone and amikacin. Mortality was significantly higher among MDR cases ($p<0.05$).*

Conclusion: *There is emergence of multidrug resistant organisms in PCICU with very few options to treat which may be related to inappropriate use of antibiotics. To combat and to reduce the mortality judicious use of antibiotic is essential.*

Kew wards: *Antibiotic resistant, ICU.*

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Introduction

Introduction of antibiotics into clinical practice in the 1940's can be considered as one of the most important therapeutic developments in the history of medicine. Over the years antibiotics have brought many serious infectious diseases under control and have saved millions of lives. But these gains are now seriously jeopardized by the emergence and spread of resistant bacteria. In 1945, Fleming the discoverer of penicillin, warned the medical community that our abuses of penicillin would surely lead to an inexorable rise in resistance, which ultimately would prove fatal for our patients.[1] 'In such cases', he said, 'the thoughtless person playing with penicillin is morally responsible for the death of the man who finally succumbs to infection with the penicillin-resistant organism. I hope this evil can be averted'.[1] Sadly we have not learned from our past. Millions of kilograms of antibiotics are exposed to our environment every year.[2] This staggering degree of environmental contamination has, predictably, led to an inexorable rise in resistance rates.[3]Antibiotic resistance is defined as the ability of a specific bacterium to survive in the presence of an antibiotic that was originally effective to treat infections caused by the bacterium.[4]

ICUs worldwide are faced with increasingly rapid emergence and spread of antibiotic resistant bacteria. Antibiotic resistance in the ICUs has made treating infections very difficult, and in some cases impossible. It has emerged as an important variable influencing patient mortality and overall resource use in the ICU setting.Antimicrobial resistance has emerged as an important factor in predicting outcomes and overall resource use after infections in intensive care units. Globally ICUs are encountering emergence and spread of antibioticresistant pathogens and for some pathogens there are few therapeutic options available.[5] Between 5% and 15% of hospital in-patients develop an infection during their admission.[6] In addition, critically ill patients in an intensive care unit (ICU) are 5-10 times more likely to acquire a nosocomial infection than those in general wards.[7] Although the incidence varies with geographical location, type of ICU, patient population and local infection control practices, at any one time up to 20% of ICU patients may have a nosocomial infection.[8] Such infections prolong the duration of mechanical ventilation and length of ICU stay[9,10] and impose a significant economic burden.[11] Optimal antibiotic use is crucial in the critical care setting, especially in an era of rising antibiotic resistance and lack of new antimicrobial development.[12,13]

Study results indicate that 30% to 60% of antibiotics prescribed in ICUs are unnecessary, inappropriate, or suboptimal.[14] Overprescribing and misprescribing antibiotics are undoubtedly contributing to the growing challenges posed by antibiotic-resistant bacteria, and epidemiological studies have clearly demonstrated direct relationships between antibiotic consumption and the emergence and dissemination of resistant strains in hospitals and ICUs.[15]ICU patients are particularly at risk of developing infections with multidrug-resistant (MDR) organisms, which are more prevalent in this environment.Epidemiological studies reported Methicillin-resistant *Staph aureus* (MRSA) and Vancomycin-resistant *Enterococcus* (VRE) in ICU setting.[16] The global spread of carbapenem-resistant *Enterobacteriaceae* (CRE) has become a major challenge.[17] Infections with CRE organisms that are multidrug-resistant or pan-drug-resistant are difficult to treat which are more prevalent in ICUs[18] and severe infections with CRE have significant morbidity, mortality, and health-care costs.[19]

Though antibiotic resistance is widespread and affects the entire world's population, the effects of antimicrobial resistance are even more significant in lower and middle-income countries.In a developing country like Bangladesh, practitioners should be made aware of the importance of combination therapy in the treatment of certain infections so that the chance of resistance development can be ameliorated to the most possible extent. Use of antibiotics in 7 community hospitals of Bangladesh demonstrated that 62% patients were given antibiotics without any clinical evidence of infection.[20] Nearly three quarter of private practitioners of Bangladesh use at least one antibiotic and many of them don't have any indication.[21] Therefore, this study aimed to investigate the initial antibiotics used before ICU admission, pathogen distribution and antimicrobial susceptibility among the CHD children admitted to ICU.

Materials and Methods

This prospective study was conducted in PCICU of Dhaka Shishu (Children) Hospital from June 2015 to May 2016. Patients having cardiac problems

transferred for medical management during the study period was enrolled. Relevant history were taken and recorded. Blood, urine, CSF and tracheal aspirate were sent when infection was suspected. Antibiotics used before PCICU admission was noted. Patients were followed up and outcome was noted. Data were collected in a preset questionnaire and was analyzed by using SPSS version 17.

Results

During the study period total 305 patients were admitted and commonest problems during admission were heart failure (22.29%), pneumonia (17.05%) and sepsis (15.74%) [Table-I].

Table I

Presenting problems during admission in PCICU (multiple responses)

Admitting Problem	Number (%)
Heart Failure	68(22.29%)
Pneumonia	52(17.05%)
Cyanotic Spell	20(6.56%)
Shock	28(9.18%)
Sepsis	48(15.74%)
Metabolic Acidosis	91(29.84%)
Respiratory Acidosis	37(12.13%)
Renal Failure	12(3.93%)
Arrhythmia	6(1.97%)
Anemia	15(4.92%)
Duct dependent pulmonary circulation	10(3.28%)
Duct dependent systemic circulation	7(2.29%)
Others	55(18.03%)

Almost all received broad spectrum antibiotics including third generation cephalosporins (36.8%), carbepenem (17.7%) even piperacillin (3.3%) and colistin (8.4%) before admission in PCICU (Fig.-1).

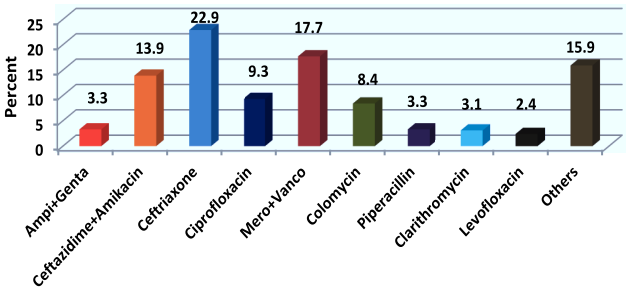

Fig 1 *Pattern of antibiotic before PCICU admission*

Organisms were isolated in 33(10.82%) cases. Most isolates recovered from respiratory specimens (57.58%) followed by blood (30.30%) and urine (12.12%). Majority were gram negative (Acinatobactor 42.4%, Klebsiella 21.2%, and Pseudomonas 24.2%) [Fig.2].

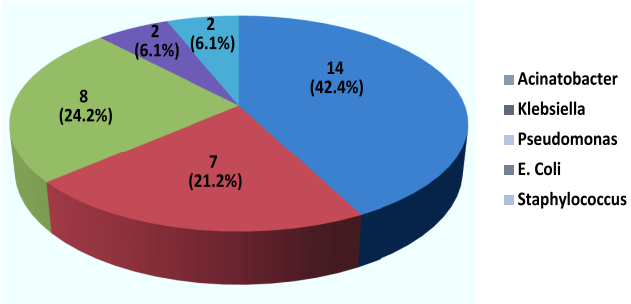

Fig 2 *Pattern of organisms isolated (n=33)*

Among the Acinatobacter multi drug resistant was found in 90.99% cases and 9.09% were pan drug resistant. Acinatobacters were resistant to conventional antibiotics, even it was resistant to piperacillin in 85.7% and carbapenem in 78.6% cases (Fig.-3).

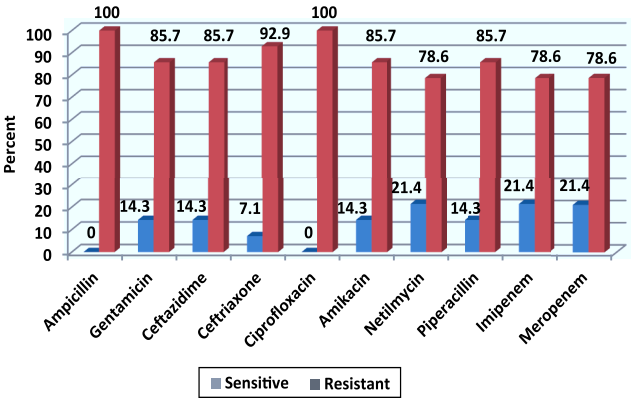

Fig 3 *Sensitivity pattern of Acinetobacter (n=14)*

Klebsiella was also found resistant to commonly used antibiotics. It was resistant to piperacillin and carbapenem in 57.1% cases each (Fig.-4).

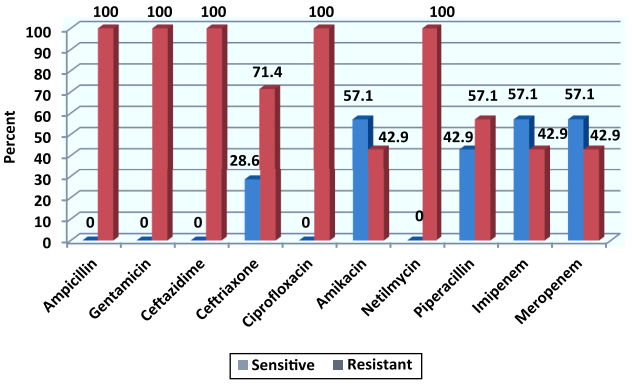

Fig 4 *Sensitivity pattern of Klebsiella (n=7)*

Pseudomonas was resistant to almost all antibiotics even piperacillin and carbapenem were resistant in 87.5% cases (Fig.5).

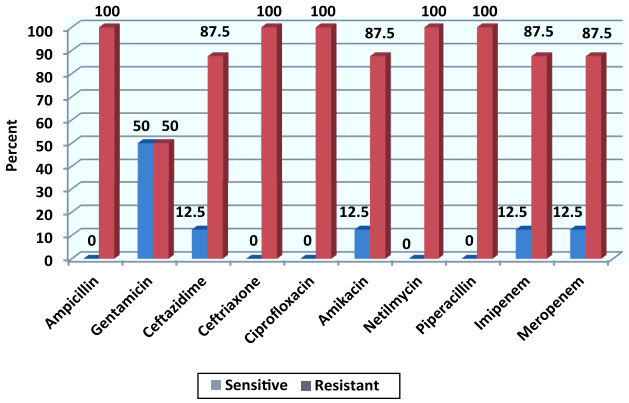

Fig 5 *Sensitivity pattern of Pseudomonas (n=8)*

E. Coli was resistant to all conventional antibiotics. It only showed 50% sensitive to piperacillin and carbapenem (Fig.-6).

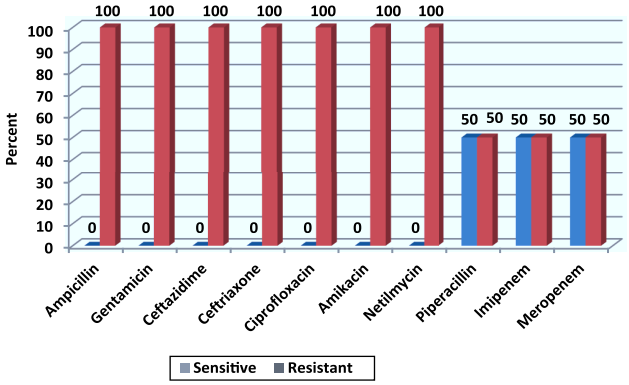

Fig 6 *Sensitivity pattern of E. Coli (n=2)*

Staphylococcus showed 100% resistant to ampicillin, 50% to gentamicin, flucloxacillin, ceftazidime, ceftriaxone and amikacin. It is sensitive to ciprofloxacin, netilmycin, vancomycin and carbapenem (Fig.7).

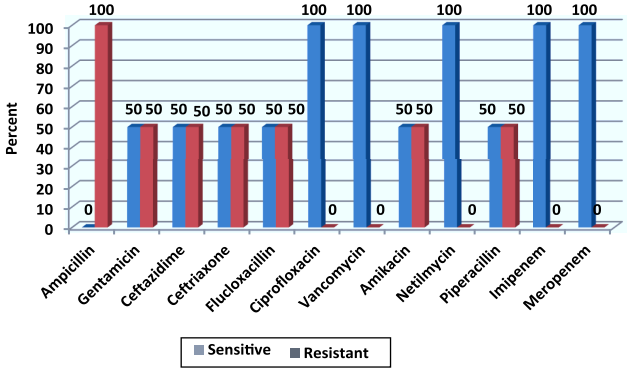

Fig 7 *Sensitivity pattern of Staphylococcus (n=2)*

MDR resistant organisms were isolated in 30 cases and mortality was significantly higher among the MDR resistant cases ($p<0.05$) [Table-II].

Table II
Relation between MDR resistant organisms and outcome

	Survived	Died	p value
Organism isolated	13	17	0.000
Organism not isolated	220	60	

Discussion

Children with left-right shunt are prone to being complicated with recurrent respiratory infections owing to increased blood flow in pulmonary circulation. Besides, CHD children are vulnerable to nosocomial infections because of developmental retardation, low immunity, long-term use of antibiotics and ventilator-assisted breathing.[22] Studies found high incidence of culture-proven sepsis in infants with CHD.[23]

In this study organisms were isolated in 10.82% cases. Most isolates recovered from the respiratory specimen (57.58%) followed by the blood (30.30%) and urine. These findings correlated with the results reported in a study by Saeed et al[16]. The most common isolates observed in this study are Acinetobacter, Klebsiella, Pseudomonas, E. Coli and Staphylococcus. Saeed et al[16] also found similar results in their study. The incidence of Gram-positive and Gram-negative organisms in this study is 6.1% and 93.9% respectively. Lee et al[24] found the incidence of Gram positive and Gram negative in 30% to 47% and 40% to 48% respectively. Khan et al[25] found 15% and 85% respectively in their study.

In this study, all Gram positive isolates are found sensitive to vancomycin contrary to 15.5 % resistant reported by Ashour et al[26] and comparable with Khan et al[25]. Among Gram-negative pathogens; MDR Acinetobacter, carbapenem resistant Pseudomonas and Klebsiella are of great concern. Acinetobacters are the most common pathogens isolated from ICUs in recent time. In this study Acinetobacter accounted 42.4% of all isolates and out of these 90.99% found to be MDR and 9.09% were found pan drug-resistant. This rate is higher than those of previous reports of 58% by Horan TC at al[27]. Acinetobacter is an increasingly infectious threat although not the most

virulent gram-negative pathogen. Cisneros et al[28] shown that Acinetobacter isolates, usually acquired in the ICU, are multidrug resistantand may cause severe infections associated with a high mortality rate. It is an important source of nosocomial septicemia, pneumonia, and urinary tract infections.[29] The emerging pan drug-resistant Acinetobacter warns us that antibiotic resistance can become a serious problem. Because of emergence of multidrug-resistance and pan drug-resistance associated with Acinetobacter, the role of preventing spread of this pathogen to other patients is paramount. Centers for Disease Control and Prevention (CDC) infection control recommendations indicate that hospitals with increased rates of multidrug-resistant Acinetobacter should take more aggressive infection control measures to control and prevent further nosocomial transmission.[30] During the recent years multidrug-resistant isolates have increased, in many cases, these multidrug-resistant isolates are resistant to third generation cephalosporins and carbapenems.[27] Amyes et al[31] concluded that this may be as a result of the extensive use of broad-spectrum antibiotics. In this study broad spectrum antibiotics were used in all cases before PCICU admission and a large number of patient got carbapenem, piperacillin and even colomycin before PCICU admission.

Klebsiella is also a common isolates from ICUs. The incidence is 21.2% in this study is lower than previous reports from Khan et al[25]. Carbapenems are the treatment of choice for serious infections due to Klebsiella. Consequently, there is intensive use of carbapenems as first choice antibiotics for these organisms, resulting in the emergence of carbapenem-resistant isolates and leaving at best only two therapeutic options: colistin and tygecycline.[32] But tygecycline is contraindicated in children younger than 8 years. Carbapenem is resistant to Klebsiella in 57.1% cases in this study which is very alarming. This study found the resistance rates of Pseudomonas to imipenem, Ciprofloxacin, and Ceftazidime in 87.5%, 100%, 87.5% respectively. These findings are much higher than the data reported by Saeed et al[16]. Possible reasons for high resistance rate for carbapanem and other antimicrobial agents in Pseudomonas include more critically ill patients being referred from local hospitals and use of broad spectrum antibiotics before ICU admission. It has been reported that MDR strains of Pseudomonas associated with higher mortality, secondary bacteremia, increase in the length of hospital stay, and a considerable increase in cost.[33] The increasing resistance rates of Pseudomonas strains to several antibiotics are expanding globally. In the United States, 37% of the isolates were found resistant to ciprofloxacin, 32% to imipenem, and 22% to ceftazidime.[34] Reports from ICUs of Europe are even worse, because from 1990 to 1999, resistance to aminoglycosides reached 37% to 70%, ceftazidime reached 57%, piperacillin-tazobactam reached 53%, ciprofloxacin reached 56%, and imipenem reached 52%.[35] In this study Pseudomonas resistant to ciprofloxacin in 100%, ceftazidime in 87.5%, piperacillin in 100% and carbapenem in 87.5% cases. In fact, this study shows much higher resistance rates. Reports from other countries have also shown high antimicrobial resistance rates in ICU patients.[36] Report shows that use of inappropriate antimicrobials has led to the emergenceof MDR species, which are extremely difficult to treat.[37]

Findings of this study suggest a possibility of high resistance rates, may be due to inappropriate, uncontrolled empiric therapy. This justifies the need for establishing prompt infection control strategies in hospitals with special consideration in ICU areas. This single center study data may not reflect antibiotic susceptibility of the ICUs from whole of the country. A multi-center study among children with CHD are advised to find and compare the pattern of antibiotics used before ICU admission, pathogen distribution and antimicrobial susceptibility.

Conclusion

There is emergence of multidrug resistant organisms in PCICU with very few options to treat which may be related to inappropriate use of antibiotics. To combat and to reduce the mortality judicious use of antibiotic is essential.

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ORIGINAL ARTICLE

Hospital Acquired Diarrhoea in Children: A Study in A Tertiary Care Hospital

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Abstract

Background: *Children hospitalized for non-diarrheal illness can be infected with an enteric pathogen during their hospital stay, which complicates and prolongs the course of illness. Nosocomial diarrhoea are defined as those occurring more than 72 hours after admission to hospital and have been shown to be second only to nosocomial respiratory tract infections in causing morbidity among hospitalized children.*

Objectives: *The aim of the study was to document the rate of hospital acquired diarrhoea, to identify associated risk factors and to observe clinical features.*

Materials and method: *This was a cross-sectional study conducted in the inpatient department of Institute of Child Health and Shishu Sasthya Foundation Hospital, Mirpur-2, over a period of 3 months from 01-10-2012 to 31-12-2012. A total number of two hundred and forty six children admitted with diseases other than diarrhoea in the above mentioned period aged from 1 month to 5 years were consecutively included in the study. During their hospital stay and up to 3 days after discharge, all patients were followed up daily for development of diarrhea. When a patient developed hospital acquired diarrhea, demographic and medical information were recorded after taking informed written consent from guardian.*

Results: *Out of 246 children enrolled, 40 developed diarrhoea 72 hours after admission. So, rate of occurrence of hospital acquired diarrhoea, therefore, was 16.3%. Among the underlying diseases for which patients were admitted initially, respiratory diseases accounted for 18 (45%) which was the highest, followed by meningitis (17.5%). Presence of any diarrheal patient in a bed close to the patient's bed , hand wash by mother during handling baby, bottle feeding and severe malnutrition were found to be statistically significant risk factors (p values 0.02, <0.001, 0.02 and <0.001 respectively) for developing nosocomial diarrhoea. In the present study mean duration of nosocomial diarrhea was only 3 days, the stool was generally watery in nature and patients suffered from milder dehydration.*

Conclusion*: Hospital acquired diarrhoea is not uncommon in hospitalized population, which was an important serious complication found in this study which complicated and prolonged the course of illness.*

Keywords: *Hospital acquired diarrhoea, Rate, Children.*

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Introduction

Children hospitalized for non-diarrheal illness can be infected with an enteric pathogen during their hospital stay, which complicates and prolongs the course of illness. Nosocomial diarrhoea are defined as those occurring more than 72 hours after admission to hospital and have been shown to be second only to nosocomial respiratory tract infections in causing morbidity among hospitalized children.[1] Rotavirus constitutes the single most important cause of acute dehydrating viral gastroenteritis. Some studies have shown that viral agents such as rotavirus, astrovirus, and adenovirus account for a large portion of both community-acquired and hospital-acquired gastroenteritis in hospitalized pediatric patients in developed countries.[2] One in five children admitted into hospital without an enteric infection is at risk of developing a nosocomial gastrointestinal infection, with rotavirus being the most common etiological agent.[1] This infection is more prevalent and intensive during the first two years of life. It is common in the colder months, and oral-faecal contamination is also possible. As the disease provides short-term immunity, recontamination is not uncommon. Spreading of this infection is common in hospitals and childcare centers. Prevalence of hospital-acquired diarrhea was 26.25% which increases the duration of hospitalization and/or re-hospitalization. Regarding the 48-72-hour incubation period of rotavirus, for the assessment of its role on nosocomial infection, it is necessary to examine the child up to 48 hours after discharge from hospital.[3] Nosocomial diarrhoea had less frequency of stools which resulted in mild dehydration had different grades of malnutrition.[4] Transmission of health care-associated pathogens takes place through direct and indirect contact, droplets, air and a common vehicle. Transmission through contaminated health care workers' (HCW) hands is the most common pattern.[5]

Material and Methods

A hospital-based, cross-sectional study was conducted in inpatient department of ICH & SSF hospital, Mirpur-2, Dhaka over a period of 3 months between 01 October 2012 to 31 December 2012. A total number of 246 children admitted with diseases other than gastroenteritis aged from 1 month to 5 years of age of both sexes were consecutively included in the study. The age, sex, nutritional status, date of admission, diagnosis of patient, contact with diarrheal patient and feeding history were recorded on admission. The patients were followed up daily during their hospital stay, especially regarding development of diarrhoea. When they had any complaint of diarrhea after 72 hours of admission, data were collected by reviewing the history, physical and laboratory findings. Data were collected in a structured questionnaire. All the patients in the study group, including those who did not have any diarrhoea, were followed up to 72 hours after discharge over telephone. If any of these patients developed diarrhoea after discharge, they were seen again by the investigator and data were collected. Analysis was performed by using a computer based statistical program SPSS version 22 for windows. Categorical variables were expressed as proportions (percentages) and numerical data were expressed as means (standard deviations). Appropriate statistical tests were done. Tables and figure were constructed according to the finding.

Results

Two hundred and forty six children from 1 month to 5 years of age admitted in the inpatient department of Pediatric Medicine, Institute of Child Health & SSF Hospital, Mirpur for non-diarrhoeal illness enrolled in the study. Among them 40(16.3%) patients developed hospital acquired diarrhea (Figure-1).

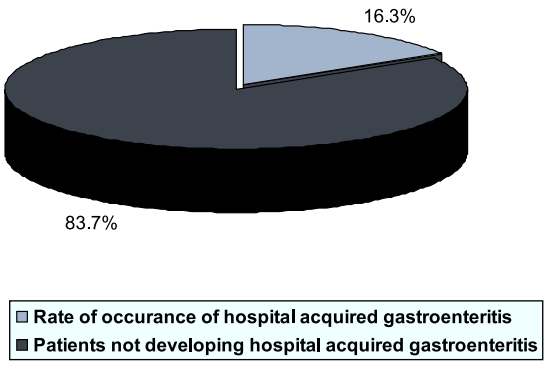

Fig 1 *Percentage of patient who developed hospital acquired gastroenteritis.*

Figure-1 showed out of 246, 40 (16.3%) children developed hospital acquired gastroenteritis. Among 40 patients, 34 patients (85%) were under 2 years

and 6 patients (15%) were between 2-5 years and number of male (65%) was higher than female (35%). The male and female ratio was 1.8:1(Table I & II).

Table I
Distribution of the studied population by age and sex (n=246).

Age (years)	Sex Male	Total Female	No (%)
<24 months	98(39.8%)	42(17.1%)	140 (56.9%)
> 24 months	72(29.3%)	34(13.8%)	106 (43.1%)

Table II
Distribution of patients acquiring nosocomial diarrhoea by age and sex (n=40)

Age (years)	Sex Male	Total Female	No (%)
<24 months	22(55%)	12(30%)	34 (85%)
> 24 months	04(10%)	02(05%)	06 (15%)

Out of 7 patients staying for a longer time (11-14 days) in the hospital, 5 (71.4%) developed nosocomial gastroenteritis (Table III).

Table III
Correlation between duration of hospital stay and occurrence of nosocomial diarrhoea (n=40).

Duration (days)	Total Study population	Patients acquiring nosocomial gastroenteritis	p value
3-5 days	183 (74.4%)	5 (2.7%)	
6-10 days	56 (22.8%)	30 (53.6%)	<0.001[s]
11-14 days	7 (2.8%)	5 (71.4%)	

p value reached form Chi-square test, s = Significant

Table IV shows distribution of patients with nosocomial diarrhoea according to diagnosis at admission. Among the underlying diseases for which patients were admitted initially, pneumonia accounted for 18 (45%) which was the highest, followed by meningitis 7 (17.5%).

Table IV
Distribution of the patients with nosocomial diarrhoea according to diagnosis on admission (n=40).

Diagnosis on admission	Frequency	Percent
Bronchopneumonia	18	45.0
Meningitis	7	17.5
SAM	5	12.5
Febrile Convulsion	4	10
CP with pneumonia	4	10
UTI	2	5

Presence of any diarrheal patient in a bed closed to the patient's bed just beside, hand wash by mother during handling baby, bottle feeding and severe malnutrition were found to be statistically significant risk factors (p values 0.02, <0.001, 0.02 and <0.001 respectively) for developing nosocomial gastroenteritis (Table V & VI).

Table V
Distribution of the studied patients according by risk factor (n=246)

History	Patients developed nosocomial diarrhoea (n=40) No. (%)	Patients not acquiring nosocomial diarrhoea (n=206) No. (%)	χ^2 value	p value
History of rotavirus vaccination				
Yes	8(20.0%)	47 (22.8%)	0.15	0.69[ns]
No	32(80.0%)	159(77.2%)		
Bottle feeding				
Yes	23(57.5%)	78(37.9%)	5.34	0.02*
No	17(42.5%)	128(62.1%)		
Presence of any diarrhoeal patient beside bed				
Yes	16(40.0%)	46(22.3%)	5.55	0.02*
No	24(60.0%)	160(77.7%)		
Hand wash by mother during handling baby				
Yes	10(25.0%)	112(54.4%)	11.56	<0.001*
No	30(75.0%)	94(45.6%)		
Hand wash by medical personnel during handling				
Yes	34(85.0%)	178(86.4%)	0.06	0.81[ns]
No	6(15.0%)	28(13.6%)		
Sharing same bathroom with diarrhoeal patients				
Yes	31(77.5%)	180(87.4%)	2.68	0.10[ns]
No	9(22.5%)	26(12.6%)		

p value measured by Chi-square test
ns = Not significant * = Significant

Table VI
Distribution of the study population by nutritional status (n=246)

Nutritional status (Gomez classification)	Patients developed nosocomial gastroenteritis (n=40) No. (%)	Patients not acquiring nosomocomial gastroenteritis (n=206) No. (%)	χ^2 value	P value
Well nourished (90-110%)	14(5.7%)	89(36.2%)	0.93	0.335^{ns}
1st degree malnutrition (75-89%)	10(4.1%)	68(27.6%)	0.99	0.319^{ns}
2nd degree malnutrition (60-74%)	7(2.8%)	40(16.3%)	0.08	0.777^{ns}
3rd degree malnutrition (< 60%)	9(3.7%)	9(3.7%)	16.24	<0.001*

In the present study nosocomial diarrhea was generally watery in nature and patients suffered from milder dehydration (Table VII). Table VII showed that clinical manifestation of nosocomial diarrhoea, most of the patients, 30 (75%) had less frequency of stool and watery (87.5%) stool with milder (90%) dehydration. Table-8 showed stool R/M/E report which demonstrates pus cell in 11 (27.5%) patients, macrophage in 9 (22.5%) patients and antibiotics were prescribed accordingly in 9 patients with invasive feature.

Table VII
Distribution of the patients with nosocomial diarrhoea according to clinical features (n=40).

Clinical features	Frequency	Percentage (%)
Frequency of stool		
< 10 times/day	30	75.0
> 10 times / day	10	25.0
Stool character		
Watery	35	87.5
Mixed with mucus	5	12.5
Vomiting		
Present	23	57.5
Absent	17	42.5
Fever > 39^{0}C		
Present	9	22.5
Absent	31	77.5
Abdominal pain		
Present	3	7.5
Absent	37	92.5
Abdominal distention		
Present	5	12.5
Absent	35	87.5
Dehydration		
Mild	36	90.0
Moderate	4	10.0

Table VIII
Distribution of the patients acquiring nosocomial diarrhoea by findings in stool R/E (n=40)

Report	Frequency	Percent
Pus cell		
< 10	8	20.0
> 10	3	7.5
No pus cell	29	72.5
RBC		
Absent	36	90.0
Present	4	10.0
Macrophage		
Present	9	22.5
Absent	31	77.5

Discussion

This study was carried out with the aim to measure the rate of hospital acquired diarrhoea in children. The result of the current study demonstrated the rate of occurrence of hospital acquired diarrhoea in children was 16.3 %.(Figure-1).

In South India, the prevalence of hospital acquired diarrhoea was 20.1%.[1] Dutta et al. (1992) found a prevalence of hospital acquired diarrhoea was 19% in a study conducted in a pediatric hospital in Calcutta. In another study in the USA, approximately 27% of children acquired rotavirus while hospitalized for disease other than gastroenteritis.[6] Hospital acquired diarrhoea constituted one-fifth of the diarrheal diseases among hospitalized children in United Kingdom.[7] Prevalence of hospital acquired diarrhoea was reported to be 26.3% in Iran, 27.7%

in Italy, 14.6% in Australia and 19.4 % in France.[3] The result of above studies are somehow similar to the findings of present study.

In present study, majority of the patients were under 2 years of age. Out of forty, 34 patients (85%) were under 2 years and 6 (15%) were between 2-5 years. The percentage of male (65%) was higher than female (35%).The male: female ratio was 1.8:1. Cunliffe et al. (2010) reported that median age of the patients in case of hospital acquired gastroenteritis was 12 months which was consistent with present study. (Table II).

In the present study, relation between duration of hospital stay and occurrence of nosocomial diarrhoea showed that 71.4% infection occurred if duration was more than 10 days. The increased incidence in these patients may be due to prolonged exposure due to prolonged hospital stay which has been documented as significant risk factor ($p<0.001$) (Table-3). Kamalaratnam et al. (2001) reported that 14.5% affected if duration of hospital stay was up to 7 days, 21% affected if duration was 8-14 days, 44.5% affected if duration was 15-21 days. Martin and co-workers in 2001 showed that hospital acquired diarrhoea was mildest in Austria but occurred within the shortest median duration of hospitalization (4 days vs. 5 and 7 in Germany and Switzerland, respectively). In the study of Kordidarian, Kelishadi and Arjmandfar (2007) mean duration of hospitalization of patients acquiring nosocomial gastroenteritis was 11 days. Cunliffe et al. (2010) stated that two thirds of infections occurred at least 1 week after hospital admission.

In this study, only 20% of patients were vaccinated against rotavirus which was statistically not significant (p value-0.69) as a risk factor (Table-5). But, Anderson et al. (2011) stated that rotavirus vaccine decrease the number of community acquired rotavirus infection, causing reduced the exposure of other hospitalized children to rotavirus, thus decreasing hospital acquired rotavirus gastroenteritis. It means that community implementation of rotavirus vaccination dramatically decreases the substantial burden of hospital acquired rotavirus infection which was not consistent with the present study.

In the present study majority 57.5% of the infected patient had history of bottle feeding in comparison to only 27.3% in Iran according to Kordidarian, Kelishadi and Arjmandfar (2007). Previous study showed no effect of bottle feeding on this prevalence but in present study it is a statistically significant risk factor (p value-0.02) as similar to study by Ghenghesh et al. (2008), who stated that 50% of affected children were bottle fed.

In the present study 40% cases had diarrheal patients beside the bed which was a statistically significant risk factor (p value-0.02) and 77.5% patients were sharing the same bathroom with diarrheal patient for washing, toileting but was statistically not significant (p value-0.10). In present study, presence of diarrheal patients beside beds also a significant risk factor (P value-0.02) which was also consistent with the study of Sherchen et al. (2011). (Table-V).

Hand washing were not done by mothers during handling in 75% of cases in comparison to 85% of medical personnel were practicing hand wash (Table-5). So, hand washing by mothers during handling the baby is an important risk factor (p value-<0.001) in acquiring hospital acquired diarrhoea (Table-IV). Alcohol based hand rub may be superior to traditional hand washing as it requires less time, acts faster (Pittet, 2009). Dutta et al. (1992) found that mother had little knowledge of personal hygiene but were primarily responsible for nursing sick children and contaminated their hands, food and drinks and transmitted infection to their children.

Cunliffe et al. (2010) stated that hand washing has reduced the rate for nosocomial infection. Diarrheal patients brought organism in hospital and helped spread via mothers. Fomites and environmental surface may also have important role (Dutta et al.1992). Cross infection through contamination of hands is probably the most common transmission route.[8]

Among the patients with nosocomial gastroenteritis, severe acute malnutrition was statistically significant risk factor in our study (Table-V). Dutta et al. (1992) stated that children with severe malnutrition acquire infection easily due to their depressed immunity, which is probably the reason of high infection rate in the malnourished patients in the present study.

Diagnosis of the patient during admission who developed hospital acquired diarrhoea revealed that pnumonia accounted for 45% followed by 30% with meningitis (Table-IV). Present study result was almost similar to Kamalaratnam et al. (2001) who

reported that respiratory disease accounted for 45 % of the admissions followed by 28.9% neurological diseases. Sherchan et al. (2011)[9] reported that 33.3% were suffering from pneumonia. This picture also reflected the pattern of diseases other than diarrhea for which children were admitted in our hospitals.

In this study, most (90%) of patients have mild dehydration similar to the study done by Dutta et al. (1992), who stated that 82.8% patients with nosocomial gastroenteritis had mild dehydration.

In the present study, 75% patients with hospital acquired diarrhoea had less frequency of stool, 87.5% have watery stool, 57.5% had vomiting, 22.5 % had fever. Sherchan et al. (2011) reported in their study nosocomial gastroenteritis had milder dehydration lasting for 4 days similar to present study. Kamalaratnam et al. (2001) reported that only 10% hade vomiting and 5% with fever which was not consistent with present study.

In the current study, in stool R/M/E pus cell was found in 11(77.5%) patients and macrophage in 9 (22.5%) patients and antibiotic were given accordingly in these 9 patients with invasive diarrhea (Table-IV). Every patient was treated with ORS to correct dehydration. All the patients but one improved. Only one patient died of complications of severe acute malnutrition.

Conclusion

Hospital acquired diarrhoea is not uncommon in hospitalized population. About one in six (16.3%) children developed nosocomial diarrhea in this study which is complicated and prolonged the course of illness. The longer duration of hospital stay, diarrheal patient in a bed beside the patient's bed, no hand wash by mother during handling baby, bottle feeding and severe malnutrition were found to be statistically significant risk factors in present study.

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DS (Child) H J 2016; 32(2) : 90-93

ORIGINAL ARTICLE

Kangaroo Mother Care (KMC): Experience of Dhaka Shishu (Children) Hospital

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Abstract

Background: *KMC is a safe and effective method of caring for low birth-weight (LBW) babies to reduce neonatal morbidity and mortality. At Dhaka Shishu Hospital it was initiated on July, 2013 with some support from WHO. This centre is now serving as a training centre for individuals from various government and non-government canters to implement KMC at their places and helping the government to scale up the program in the country.*

Objectives: *To substantiate the efficiency of KMC for preterm neonates, share the experience and to motivate the health care providers and convince the government to scale-up this simple method in public health facilities of Bangladesh with the necessary skills for KMC practice.*

Methods: *The duration of this study was from July, 2013 to October, 2015. All preterm, birth weight <2000gms, hemodynamically stable babies were offered KMC care. All the babies were monitored and recorded during the hospital stay and followed up to 40 weeks of gestational age. Incidence of complication and their weight gain and outcome were recorded. All data were recorded and statistic analysis was done with SPSS-17 version.*

Results: *During the period from July 2013 to October 2015, total admitted LBW babies were 1062. Among them 288 (27%) babies received KMC. Sixty (21%) cases who got KMC came for their follow up visits and most of them (55 cases, 92%) gained weight. Mean age of starting KMC of babies was 12.52±9.15 days (Minimum age was 1 day and maximum age was 60 days at this age the baby's wt was 1070gms). Mean weight of starting KMC of babies was 1340±283.89gm. Baby's minimum wt of starting KMC was 790gms at 19 days of age & this baby was discharged at 50 days of age and maximum wt of starting KMC was 2000gm. Mean duration of KMC was 6.63±3.77 days. Baby's mean hospital stay was 15.61±10.56 days. Episode of apnea occurred in 32 (11%) cases and sepsis also developed in 32 (11%) cases. Among them 21 babies could restart KMC. The episodes of hypothermia was 29 (10%) in this study. Ninety percent (90%) of KMC were discharged with exclusive breast feeding. The rest received cup feeding along with the breast feeding. Regarding the mortality, out of total 1062 LBW babies, 195(18.4%) died. But out of 288 KMC babies mortality was less (11, 3.8%).*

Conclusion: *This study further substantiated the efficiency of KMC for preterm neonates. The experience of Dhaka Shishu (Children) Hospital in KMC implementation can help the government and non-government organizations to scale up the program in public canters and also in the community.*

Key words: *Kangaroo mother care, KMC, Dhaka Shishu Hospital.*

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Introduction

Bangladesh is one of the ten countries with the highest burden of newborn deaths.[1] Nearly 45% of all newborn deaths are directly related to preterm birth and its complications.[2] To decrease neonatal morbidity and mortality, Kangaroo mother care (KMC) is now considered as the most feasible, readily available, and preferred intervention in developed and developing countries.[3] It is a special way of caring for the preterm or low birth weight infants where baby is kept in skin-to-skin contact with the mother and breastfed exclusively.[4] It is a safe and effective method of caring for low birth-weight (LBW) infants, especially in low-resourced settings.[3] It has also been described as a cost-effective,[5,6] high-impact intervention[7,8] for improving newborn survival. Beneficial physiological and behavioral effects of KMC for the infant are well documented.[9,10] Physiological effects include better thermoregulation, improved cardiorespiratory stability, lower risk of infection and faster growth. Behavioral effects relate to better sleep cycles, less crying and an analgesic effect during painful procedures. Beneficial effects for the mothers include better breastfeeding (increased milk production, exclusivity, duration, early initiation) and psychosocial effects (reduced anxiety, more maternal satisfaction, improved maternal-infant attachment and bonding).[9,10] Although KMC has become widely accepted during the past decade, it remains, according to Lawn and colleagues, 'unavailable at-scale in most low-income countries'.[3]

In Bangladesh, KMC was first started in a missionary Hospital (LAMB) of northern Bangladesh in late nineties. At Dhaka Shishu Hospital it was initiated on July, 2013 with some WHO support and is continuing successfully. The aims of this study are to substantiate the efficiency of KMC for preterm neonates, share the experience and to motivate the health care providers and convince the government to scale-up this simple method in public health facilities of Bangladesh with the necessary skills for KMC practice.

Materials and Methods

KMC has been implemented at neonatology ward of Dhaka Shishu (Children) Hospital (DSH) since July 2013 with some WHO support. The data were compiled from July 2013 upto to October 2015. All preterm babies who fulfilled the inclusion criteria - birth weight <2000gm, hemodynamically stable (RR-30-59/min, HR- 100-160/min, pink in air or with oxygen < 40%), no gross congenital anomaly and no major surgical problem, were offered for KMC management. Mother (or other care giver) who did not agree or otherwise was not fit for KMC, their babies were managed with conventional care.

Mothers who agreed, were trained with KMC position and how they would monitor the baby. During KMC position, baby was kept skin to skin contact with mother bare chest in between the breasts. Baby was remained froglike position, head turned in one side with neck slight extended, wearing front open sleeveless shirt, cap, shocks and a nappy. There was a binder for support the baby around baby and mother.

Three trained nurses, supervised by trained doctors were especially engaged with KMC practice in the neonatology ward. All the babies were monitored (for RR, HR, stability, daily weight, anycomplications-apnea, hypothermia, signs of sepsis, feeding etc) during the hospital stay and followed up to 40 weeks of gestational age. All data were recorded and statistic analysis was done with SPSS-17 version.

Results

During the period from July 2013 to October 2015, total admitted LBW babies were 1062. Among them 288 (27%) babies received KMC. Sixty (21%) cases who got KMC came for their follow up visits and most of them (55 cases, 92%) gained weight. Mean age of starting KMC of babies was 12.52±9.15 days (Minimum age was 1 day & maximum age was 60 days at this age the baby's wt was 1070gm). Mean weight of starting KMC of babies was 1340±283.89gms. Baby's minimum wt of starting KMC was 790gms at 19 days of age & this baby was discharged at 50 days of age and maximum wt of starting KMC was 2000gm. Mean duration of KMC was 6.63±3.77 days. Baby's mean hospital stay was 15.61±10.56 days. Episode of apnea occurred in 32 (11%) cases and sepsis also developed in 32 (11%) cases. Among them 21 babies could restart KMC. Ninety percent (259, 90%) of KMC were discharged with exclusive breast feeding. The rest received cup feeding along with the breast feeding. Regarding the mortality, out of total 1062 LBW babies, 195(18.4%) died. But out of 288 KMC babies mortality was less (11, 3.8 %).

Table I
Distribution of sex of KMC babies

Variables	Case (n=288)
Male	170 (59%)
Female	118(41%)

Table II
Distribution of LBW babies and KMC babies and their courses during this study period

Study period from July 2013 to October 2015	N (%)
Total LBW Babies	1062
Total KMC babies	288 (27%)
Death of LBW	195(18.4%)
Death of KMC babies	11 (3.8 %).
Follow up visit of KMC babies	60 (21%)

Table III
Distribution of the patients according to hospital course of the patients

Episode of apnea	
Yes	32 (11%)
No	256(89%)
Sepsis	
Yes	32(11%)
No	256(89%)
Exclusive breast feeding	
Yes	259(90%)
No	29 (10%)

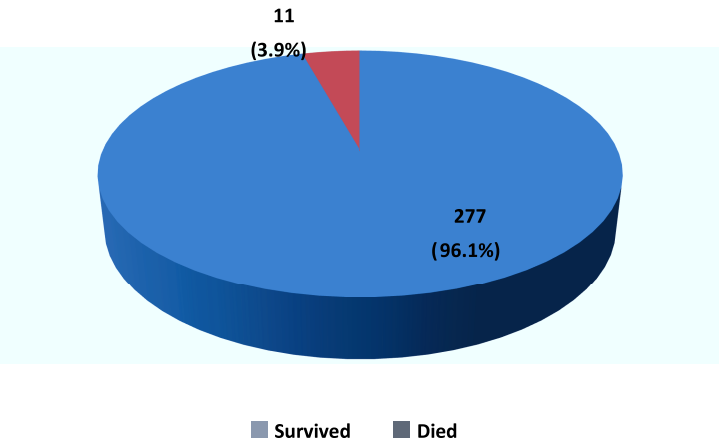

Fig 1 Pie chart shows mortality of KMC Babies

Table IV
Distribution of the patients according to outcome

Outcome	KMC babies (n=288) No. (%)	LBW babies (n=1062) No. (%)	p value
Improved	277(96.1%)	867(82.6%)	0.036
Death	11(3.8 %).	195(18.4%)	

Discussion

This study was conducted at Dhaka shishu (children) hospital from July 2013 to October, 2015. During the period from July 2013 to October 2015, total admitted LBW babies were 1062. Among them 288 (27%) babies received KMC.

Sixty (21%) cases who got KMC came for their follow up visits. Various studies have reported a follow up rate ranging from 64 to 90%.[5,9]In DSH, low follow up visit was mainly because of most of the babies came from peripheral districts in Bangladesh and they did not come this center so easily. Mean age of starting KMC of babies was 12.52±9.15 days (Minimum age was 1 day & maximum age was 60 days. In our center most of the babies were out born and unstable. Initially they might be stabled and then they got KMC, so the time to start KMC for this babies was longer. Mean weight of starting KMC of babies was 1340±283.89gms. Baby's minimum wt of starting KMC was 790gms at 19 days of age & this baby was discharged at 50 days of age with wt 980gm and maximum wt of starting KMC was 2000gm. In this study most of the baby (55 cases, 92%) gained weight. In another study, it was found that KMC babies achieved significantly better growth (KMC; 23.99gms vs Conventional Care; 15.58gms, p<0.0001).[11]Episode of apnea occurred in 32 (11%) cases in this study. Chowdhury et al. also found apnea in their study and episode of apnea was less in KMC group (KMC:2, 8% vs 8, 32%. p= 0.03).[12]

The episodes of hypothermia was 29 (10%) in this study. Several studies showed that incidence of hypothermia were less in KMC group. Cattaneo et al showed in their study that hypothermia was more in babies that did not get KMC (31.5 vs 13.5 episode/ 100 infants).[13] In this study sepsis developed in 32 (11%) cases. Chowdhury et al showed in their study sepsis was more in babies who did not get KMC than who got KMC.[12]

In this study mean duration of KMC was 6.63±3.77 days. Baby's mean hospital stay was 15.61±10.56 days. Chowdhury et al showed less hospital stay in KMC babies in their study and which was statistically significant.[12] But there was no difference in hospital stay between KMC and no-KMC group in the study done by Rao et al (KMC Vs no-KMC: 12.78 days Vs 12.86 days, P=0.929).[11]

Ninety percent (259, 90%) of KMC were discharged with exclusive breast feeding. The rest received cup feeding along with the breast feeding. Ali et al showed higher rate of exclusive breast feeding in their study (KMC: 94.4%, Control 72%, p= 0.002). In one meta-analysis showed increased exclusive breastfeeding (RR 1.50; 95% CI 1.26, 1.78) in KMC group. [14,15]

Regarding the mortality, out of total 1062 LBW babies, 195(18.4%) died. But out of 288 KMC babies mortality was less (11, 3.8 %). Meta-analysis of three RCTs showed a significant reduction in neonatal mortality [relative risk (RR) 0.49, 95% confidence interval (CI) 0.29–0.82] compared with standard care.[16]

Conclusion

This result substantiated the efficiency of KMC for preterm neonates in term of decrease neonatal morbidity and mortality. So the experience of Dhaka Shishu (Children) Hospital in KMC implementation can help the government and non-government organizations to scale up the program in public canters and also in the community.

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ORIGINAL ARTICLE

Clinical Features of Pneumonia Observed in Neonates Admitted in a Tertiary Care Hospital

Nahid Farzana[1], Md. Ruhul Amin[2], Abu Ishaque Khan[3]

Abstract

Introduction: *Neonatal pneumonia is one of the important causes of neonatal morbidity and mortality especially in developing countries like Bangladesh. Diagnosis is difficult as the clinical manifestations are being nonspecific.*

Objectives*: The purpose of the study was to evaluate the clinical features of pneumonia among neonates for early diagnosis, treatment and to reduce the rate of mortality.*

Methodology: *This prospective observational study was conducted in Dhaka Shishu (children) Hospital from April to September 2014. A total of 50 neonates, admitted in the inpatient department were included who fulfilled the inclusion criteria's like having difficult breathing, fast breathing>60 /min, chest indrawing, grunting, cyanosis, cough or fever. Diagnosis was confirmed by Chest X-ray.*

Results: *Study showed that in majority 42 (84%) cases pneumonia was late onset (4-28 days) type..Term neonates 29(58%) were comparatively more affected than preterm 21(42%). Most commonly found clinical feature was difficulty in breathing (respiratory distress) in 44 (88%) cases. Followed by poor feeding 37 (74%), chest-indrawing30 (60%), grunting respiration 9(18%) and cyanosis were found in 7(14%) cases.*

Conclusion: *Respiratory distress was considered as most common clinical feature of neonatal pneumonia.*

Key words*: Pneumonia, Neonate, Respiratory Distress.*

Introduction

Neonatal Pneumonia is the lung infection of a neonate. It is an inflammatory pulmonary process that may originate in the lung or be a focal complication of a systemic process[1]. Definition of pneumonia varies widely. World Health Organization (WHO) has defined pneumonia solely on the basis of clinical findings obtained by inspection and respiratory rate.[2]

Neonatal pneumonia accounts for significant morbidity and mortality especially in developing countries like Bangladesh. It is estimated that pneumonia contributes to between 750,000 and 1.2 million neonatal deaths worldwide annually and neonatal pneumonia accounts for 10% of global child mortality.[3]

Neonatal mortality rate is 24 per 1000 live births in Bangladesh[4], It is estimated that 3.9 million of the 10.8 million deaths in children annually worldwide occur in the first 28days of life andpneumonia incidence still remains very high.[4]

Neonatal pneumonia can be classified as early and late onset [2]. Early onset pneumonia, in general, is defined as a clinical presentation in the first 48 hr up to 1week of life, while late onset neonatal

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pneumonia occurs in the next 3weeks. Intra uterine pneumonia is a subgroup of early onset neonatal pneumonia.[2]

Nissen et al found that tachypnea appears to be the most consistent sign present in 60–89% of cases. Other signs appear to be less reliable and include chest recession (36–91%) , fever (30–56%), inability to feed (43–49%), cyanosis (12–40%) and cough (30–84%).[5] In an Indian journal Misra et al described that Neonatal pneumonia can be suspected in any newborn infant with respiratory distress, the features of which include any of the following: rapid, noisy or difficult breathing, respiratory rate>60 beats/ min, chest retractions, cough and/or grunting. The sensitivity of clinical findings for radio logically diagnosed pneumonia in neonates has been evaluated in developing countries [6,7,8]. According to Stoll BJ in Padiatric Textbook of Nelson Neoatal Pneumonia describe as having : Early Symptoms: Non specific ill looking, lethargy, poor feeding, irritability, cyanosis, temperature instability and respiratory symptoms like grunting, tacchypnea, retraction, flaring of alae nasi, cyanosis, apnoea & progressive respiratory failure. Signs are like dullness to percussion, change in breath sound, and presence of rhonchi. Radiology suggests new infiltrate or effusion[1]. In a study Mathur et al mention that recognized changes on chest radiographs included nodular or coarse patchy infiltrates, diffuse haziness or granularity on air bronchogram, perihilar interstitial streaking and lobar and sub lobar consolidation[9]. With this background this study was conducted to evaluate the important presenting features of pneumonia among neonates admitted in this tertiary hospital.

Methodology

This prospective observational study was conducted in Dhaka Shishu Hospital from April to September 2014. Sampling method was purposive sampling .This study included total 50 neonates with pneumonia who fulfilled the inclusion criteria's admitted in the in-patient department of the hospital during this period. Inclusion criteria's included 0 to 28 days old both term and preterm neonates having cough or fever, rapid or difficult breathing, respiratory rate >60/min, severe chest indrawing, grunting and /or cyanosis. Pneumonia confirmed by Chest X-ray later on. Chest X-ray were read by investigator, a senior radiologist and guide himself. Radiological findings were recorded. After taking written consent from patient's attendant, detail history was taken and physical examination was conducted. The history included name, age, sex, residence, birth weight, gestational age the of neonate and symptoms included cough, difficulty in breathing, grunting, poor feeding. Physical examination findings included temperature, heart rate, respiratory rate, chest indrawing, cyanosis, capillary refill time (CRT) and chest examination findings. A structured questionnaire was used for recording all the information. Data were then analyzed and plotted in graphs and tables.

Results

In this study, 50 neonates were enrolled who diagnosed as pneumonia clinically and confirmed by chest radiology. Among them 8 (16.0%) neonates were between 0-3 days of age and remaining 42(84.0%) were between 4-28 days old.

Table I
Age distribution of neonates (n=50)

Age (days)	Frequency of cases (n=50)	Percentage (%)
0-3	8	16
4-28	42	84
Total	50	100

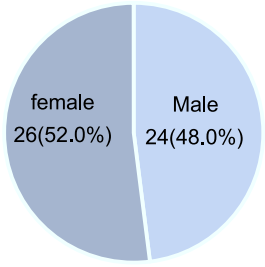

Fig 1 *Sex distribution of study cases (n=50)*

Among the study cases, 24 (48.0%) neonates were male and 26 (52.0%) were female neonate (Fig1).

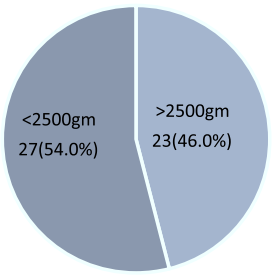

Fig.-2: *Study cases according to birth weight (n=50)*

In this study group, 23(46.0 %) cases had normal birth weight (>2500gm) and 27 (54.0 %) cases were low birth weight(<2500gm) neonate (Fig-2).

Table II
Clinical presentation (symptoms and signs) of study cases (n=50)

Symptoms	Frequency (n=50)	Percentage (%)
Difficulty in breathing (respiratory distress)	44	88
Poor feeding	37	74
Cough	9	18
Physical findings		
Fast breathing (>60/min)	33	66
Chest indrawing	30	60
Grunting respiration	9	18
Central cyanosis	7	14
Hypothermia	7	14

The most common symptom was difficulty in breathing (respirsatory distress) 44(88.0% followed by poor feeding 37 (74%) and cough 9(18%) .The most common physical finding was chest indrawing 30(60%) followed by grunting 9(18%), hypothermia 7(14%) and cyanosis 7(14%) among study neonates (Table II).

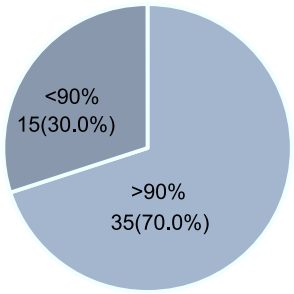

Fig 3 *Oxygen saturation by pulse oxymetry of pneumonia cases on admission*

Among the neonates, 35 (70.0%) neonate had oxygen saturation >90% and 15 (30.0%) had oxygen saturation <90% within 24 hour of hospital admission.

Discussion

This research was conducted in Dhaka Shishu(Children) Hospital included total 50 neonates with pneumonia showed 42 (84.0%) neonates were between 4-28 days of age and 4 (16.0%) were 0-3 days old. There is a study in Bangladesh found that out of 115 neonate, 11(9.6%) were 0-7 days old , 8-28 days old were 104(90.4%) and the mean age was 16.2 days[10] and findings are nearly similar to present study. Another study in USA showed that median age of presentation of pneumonia was 18.9 days [11]. In ourstudy, female neonates 26(52%) were more affected than male 24(48%). A study in Dhakafound that male neonate was more affected than female.[10] In Dhaka Medical College hospital, a study reported that male neonate were more than female.[12]

In the present study, neonate with low birth weight had pneumonia more 27(54%) than the babies who had normal birth weight. In Bangladesh another study reported that newborn suffering from pneumonia had mean birth weight of 2870gm, which is dissimilar to the present study.[10]

Diagnosis of neonatal pneumonia is mainly dependent on clinical presentations and physical findings. The symptoms differ widely between individuals with pneumonia.[13]

In our research work, majority 44(88%) of neonates were presented with difficulty in breathing. Other sign symptoms were poor feeding37 (74.0%), fast breathing 33(66.0%), chest indrawing 30(60.0%), grunting respiration 9(18.0%), cough 9(18.0%), hypothermia 7(14%) and central cyanosis7(14%). Singi and singi described that neonatal pneumonia was the cause of respiratory distress in 68.7% cases[8]. The results of present are comparable with a study in Bangladesh in which the presenting features of neonatal pneumonia cases were mostly rapid noisy or difficult breathing (92.17%), lethargy (86.08%), cough (85.22%), cyanosis (26.95%), grunting (20%), hyperthermia (12.17%).[10] This study is comparable with a study in India which reported that respiratory distress is the most common presenting feature of neonatal pneumonia and 68% of respiratory distress were found to be due to pneumonia.[14]

Falah et al reported that commonest cause of respiratory distress in full term newly born babies were transient tachypnea of newborn TTN (41.8%), followed by neonatal pulmonary infection(17.8%), respiratory distress syndrome RDS (13.1%) and meconium aspiration syndrome (13.1%).[15]

The results of our study also showed that 20 (40.0%.) neonates were seriously ill having cyanosis and grunting. About two third of study neonates had oxygen saturation >90% and rests had<90%. Duke et al[2] commented that using oxygen on the basis of objective evidence of hypoxemia has the potential for large reduction in neonatal mortality [2]. In Papua New Guinea it was found that improving neonatal care by oxygen supplementation along with other supportive care, case fatality from pneumonia was more than 50% lower during 30 months after the intervention compared with the 30 months before.[16]

So the study concluded that difficulty in breathing was the most common presenting feature and chest indrawing was the most common physical sign of pneumonia among neonates.

Conclusion

Difficulty in breathing (respiratory distress) was the most common presenting feature followed by poor feeding and cough among neonatal pneumonia cases. Chest indrawing was the most common physical finding followed by grunting respiration and central cyanosis .

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ORIGINAL ARTICLE

Correlation of Blood Gas Status with the Mortality of Neonates Admitted in ICU

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Abstract

Objective: *To study the correlation between blood gas status and mortality of neonates admitted in ICU.*

Methods: *This observational study was carried out at the ICU of Dhaka Shishu (Children) Hospital (DSH) from January 2014 to July 2014. Total 121 neonates were enrolled according to inclusion criteria and analyzed their blood gas status which were correlated with the mortality of neonates.*

Results: *Perinatal asphyxia was common disorder with the highest mortality in neonate followed by sepsis and pneumonia. Significant association between mortality with lower pH, $PC0_2$ and higher base deficit was observed. Metabolic acidosis was the most common acid-base disorder.*

Conclusion: *Low pH, $PC0_2$ & more base excess are predictor of mortality in this group of neonate. Initial acid-base derangement significantly correlates with the mortality of critically ill neonates requiring ICU care.*

Keywords: *Blood gas analysis, mortality, neonate*

Introduction

Understanding of hemoglobin-oxygen interactions and gas exchange provide cornerstone for clinical success to neonatal care. Critically ill neonate commonly have acid-base disorder, a valuable asset to a pediatrician about patient assessment, therapeutic decision and prognostication.[1] Blood gas measurements permitted the diagnosis of metabolic and respiratory acidosis associated with birth process and with postnatal adaptation to air breathing.[1-3] The cardiovascular system undergoes changes after birth just as dramatic with conversion from parallel to two circulations, respiratory gas exchange and formerly placental function, must be established by the lungs within minutes. Therefore, frequent and serious difficulties in cardio-respiratory adaptation in perinatal and neonatal periods are not surprising.[4] Blood gas analysis provides pH, $PC0_2$ from which ($HC0_3^-$) and base excess (BE) can be derived.[5-8] Moreover, it is easily understandable and widely used at the bed side management.[9] This traditional approaches to analysis of acid-base status adapted

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from Handerson–Hasselbach equation mathematically links the variables of pH, $PC0_2$ and bicarbonate concentration ($HC0_3^-$).[10] The $PC0_2$ concentration in a given patient reflects the balance between metabolic production of $C0_2$ and excretion by ventilation. The normal range of $PC0_2$ after the first hours of life can be considered 35 - 45 mmHg, desirable $C0_2$ values for a specific situation may be either higher or lower $PC0_2$ elevation of 10 mmHg decreases pH by 0.08 while $PC0_2$ decrease of 10mm Hg, increase pH by 0.08.[11,12] Marked structural and functional difference in children in comparison to adults, i.e. , children have narrow distal airways, so atelectasis develop quickly resulting in rapid-onset of hypercarbia and hypoxia. Chest wall is compliant and respiration is less efficient; the respiratory center is immature, hypoxia and hypercarbia lead to decreased respiratory drive. In addition they have reactive vascular bed to maintain their blood pressure until late, so one cannot rely on hypotension to diagnose shock as in adults. [13] Hence blood gases provide essential information on acid-base status in critically ill neonates and predict their mortality. Perinatal asphyxia and neonatal sepsis both are common occurrence in neonate and major health problems in Bangladesh like other developing countries and devastating cause of mortality. The acid-base abnormalities are common in perinatal asphyxia and neonatal sepsis, need more vigorous measures to reduce their mortality in an emergency situation. Perinatal asphyxia occurs when there is inadequate placental gas exchange to meet ongoing tissue needs for oxygen consumption and $C0_2$ elimination. The combination of lactic acidosis, product of anaerobic metabolism and $C0_2$ accumulation results in a mixed acidosis. It results most commonly from a drop in maternal blood pressure or some other substantial interference with blood flow to the infant's brain during delivery. This can occur due to inadequate circulation or perfusion, impaired respiratory effort, or inadequate ventilation.[14] An infant suffering from severe perinatal asphyxia usually has cyanosis, less perfusion, poor responsiveness, reduce muscle tone and poor respiratory effort as reflected in low APGAR score (5- minute). Extreme degrees of asphyxia can cause cardiac arrest and death. There has been a scientific debate whether newborn infants with asphyxia should be resuscitated with 100% oxygen or normal air.[15] It has been demonstrated that high concentrations of oxygen lead to generation of oxygen free radicals, which have a role in reperfusion injury after asphyxia.[16] Temperature affects pH, $PC0_2$ and $P0_2$.[11] In neonatal sepsis, unstable temperature and less tissue perfusion leading to derangement of acid-base balance. This study was carried out in neonates with various ailments attending ICU at a tertiary care hospital of Dhaka, Bangladesh. The objective was to study acid-base status in common neonatal disease such as perinatal asphyxia, sepsis etc in neonates.

Materials and Methods

This observational study was conducted at ICU, Dhaka Shishu (Children) Hospital during the period of January 2014 to July 2014. For each neonate, a detailed from the mother or other care-giver was recorded in a preset questionnaire. Maternal history included antenatal care, prolonged rupture of the membranes (>12 hours before delivery was considered), prolonged second stage of labour, gestational age was determined from maternal records, time of first cry or breathing immediately after birth, apnoea/cyanosis, convulsion, reluctant to feed and bleeding manifestation were recorded along with particulars of the neonates. Total 161 neonates admitted during this period among these 40 were excluded from this study due to any congenital anomaly, severely jaundiced due to blood group incompatibilities or received LAMA (Left against medical advice). Before enrollment parent of each child was given a detail explanation about the nature and purpose of the study. The study was started after obtained ethical clearance by Bangladesh Institute of Child Health, Dhaka Shishu Hospital. 121 neonates were analyzed for the blood gas status as well as baseline investigation as part of management. With all aseptic precaution blood sample was obtained in the disposable syringe. Blood gas analyzer (Gastal-600) based on the principle of potentiometry analyzed pH, $PC0_2$ by respective electrodes. Base excess (BE) and ($HC0_3^-$) were calculated parameters from pH and $PC0_2$ were provided by the analyzer.

Results

In this study, 121 neonates (0 - 28 days), median age was 7 days. Eighty four neonates were male and thirty seven were female, ratio 2.27:1.

Table I
Blood gas parameters in perinatal asphyxia and sepsis (Initial)

	PNA (n=43) Mean ±SD	Sepsis (n=39) Mean ±SD	P* value
pH	7.33 ± 0.12	7.38± 0.12	0.042^{s}
$PC0_2$ (mm of Hg)	32.67± 15.74	29.85 ± 11.71	0.364^{ns}
$HC0_3$ (mmol/L)	16.83 ± 4.91	19.31± 10.09	0.155^{ns}
Base Excess(mmol/L)	-7.14 ± 5.17	-8.3 ±17.55	0.681^{ns}

*****Unpaired t-test

This study gives a comparative observation of blood gas status in major diagnosed pathological conditions (perinatal asphyxia and sepsis) among neonates. Here initial pH was found less in perinatal asphyxia than sepsis patients which was statistically significant (Table I). But no statistical significant difference of blood gas status between perinatal asphyxia and sepsis before death / discharge (Table II).

Table II
Blood gas parameters in perinatal asphyxia and sepsis (before death / discharge)

	PNA (n=43) Mean ±SD	Sepsis (n=39)Mean ±SD	P* value
pH	7.32 ± 0.14	7.33± 0.22	0.808^{ns}
$PC0_2$ (mm of Hg)	37.57± 12.71	34.96 ± 16.58	0.417^{ns}
$HC0_3$ (mmol/L)	24.14 ± 8.21	26.03± 11.82	0.265^{ns}
Base Excess(mmol/L)	-8.35 ±11.69	-6.21 ±9.42	0.369^{ns}

*Unpaired t-test

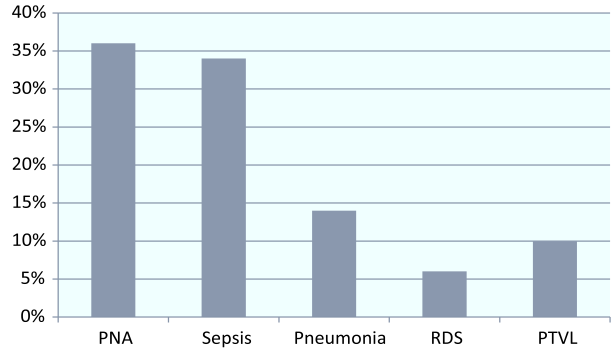

Fig 1 *Mortality of disease profile among this group of neonate*

This study gives initial observation of blood gas status in perinatal asphyxia and sepsis among survivors and non-survivors. Non- Survivors had less pH and more base excess level than survivors which were statistically significant (Table III). There is also statistical significant difference of blood gas status in perinatal asphyxia and sepsis among survivors and non-survivors after death / discharge. Non-survivors had less pH, $HC0_3$, $PC0_2$ and more base excess level than survivors which were statistically significant (Table IV).

Table III
Acid-base parameters in Survivors and Non-survivors (Initial)

	Survivors (n =71) Mean ± SD	Non-Survivors (n =50) Mean ± SDMean ± SD	P* value
pH	7.36 ± 0.1	7.3 ± 0.19	0.011^{s}
$PC0_2$ (mm of Hg)	31.69 ± 11.54	33.63 ± 17.48	0.466^{ns}
$HC0_3$ (mmo1/L)	18.03 ± 6.59	17.95 ± 10.4	0.961^{ns}
Base Excess	-4.3 ± 6.88	-10.74 ±15.89	0.004^{s}

*****Unpaired t-test

Table IV
Acid base parameters in Survivors and Non-Survivors (before death / discharge)

	Survivors (n =71) Mean ± SD	Non- survivors(n =50) Mean ± SD	P* value
pH	7.4 ± 0.07	7.21 ± 0.22	0.001[s]
$PC0_2$ (mm of Hg)	41.41 ± 13.23	26.39 ± 12.12	0.007[s]
$HC0_3$ (mmo1/L)	28.21 ±9.37	18.71 ± 8.34	0.013[s]
Base Excess	-3.82 ±4.51	-13.21 ±12.4	0.001[s]

*Unpaired t-test

Discussion

The study was carried out on the basis of neonates suffering from a wide variety of ailments attending ICU care. The selection was unbiased. Preponderance of males in this age group suffering from perinatal asphyxia, in accordance with the epidemiological pattern having the highest mortality (Fig.1) was observed. The data may therefore, be generalized on a population of sick neonates seeking ICU care.

Arterial blood gas (ABG) sampling represents the gold standard method for acquiring patients acid-base status. The acid-base status in major pathological disorders such as perinatal asphyxia and sepsis occurring in neonates is discussed as follows. In this study lower mean pH was found in perinatal asphyxia. This is not surprisingly as various studies, show the same results[17,18] Palsdottir K et al. evaluated the association between lower umbilical artery pH, more base deficit, and the development of hypoxic ischemic encephalopathy.[19] The majority of neonates with death had an arterial pH <7.00, so this would have had to occur in the majority of babies termed as acidosis paradox.[20] Acid-base disorders in critically ill neonatal ICU patients and predicting survival by the presence of deranged acid-base variables.[21] In this study lower mean pH in non-survivors was around 7. Goodwin TM et al.[22] stated with worsening acidosis, mortality increases. They found that at pH<7.00 mortality occurs in 12%, 33% with cord pH<6.9, 60% with pH <6.8, 80% with pH <6.7. No infant was live born with pH <6.6.[22] Lekhwani S et al[23], & Goldaber et al.[24] showed significant correlation was found between outcome & critical value of pH <7.2 were associated with increase patient mortality. In sepsis, metabolic acidosis was found to be compensated by respiratory alkalosis. In this study low $PC0_2$ & $HC0_3$ were statistically significant in non-survivors compared with survivors. $PC0_2$ provides the most accurate determinations of alveolar ventilation.[11] $P0_2$ and $Sa0_2$ provide important information about oxygenation , but must be combined with other clinical and laboratory profile to asses a comprehensive picture. $Pa0_2$ values vary considerably throughout the day in sick neonates.

Hence 0_2 supplement much variable in aspect of general condition and different entity. Patient with anaemia may have normal saturation because of cardiac compensation.[11] Pulse oximetry measures peripheral 0_2 saturation ($Sa0_2$) not $Pa0_2$ and this is relatively insensitive to detecting hyperoxaemia. This is particularly important in the small premature baby. Values of $pa0_2$ and $Sa0_2$ may be lower in premature caused by reduced lung function.[12] This study has shown that metabolic acidosis (BE <5mmol/L) is one of the most frequent acid-base disorder occurring in neonates, similar to various studies (Lekhwani S et al.).[23] which remains a powerful marker of poor prognosis in critically ill patients.[24] Consequently, the management of acid-base disorder always demands precise diagnosis and treatment of the underlying disease, it requires steps to combat the deviation to reduce the mortality.[25] Nana W et al.[26] showed low pH and high base deficit alone or in combination reflect an impaired condition e.g. , bad outcome parameter at birth. Similar to the present study, lower pH and higher base excess in non-survivors compared with survivors both initial and before death/discharge.

Conclusion

Blood gas status helpful in explaining of mortality in sick neonate. Low pH, low $PC0_2$ & more base excess

are predictor of mortality in this group of neonate. Initial acid-base derangement significantly correlates with the ultimate outcome of critically ill neonates requiring total ICU care to reduce their mortality.

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ORIGINAL ARTICLE

The Influence of Family History and Atopy of Asthma in Occurrence of Pediatric Asthma: A Single Center Experience

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Abstract

Background: *Asthma is a common disorder with increasing prevalence in children. World Health organization (WHO) estimates that approximately 500,000 annual hospitalizations in individuals aged 18 y or younger) are due to asthma. However, data on the influence of family history as well as atopy in developing childhood asthma in developing including Bangladesh is scarce.*

Objective: *This study attempts to analyze the clinical records of 100 pediatric asthma patients with variable family history and personal history of atopic disease.*

Methods: *It was a retrospective study that was conducted in the department of Pediatric Respiratory Medicine (Pulmonology), Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh from May 2016 to May 2017. We retrospectively analyzed the 100 cases between 2 years to 12 years of age visited in our outpatient and asthma clinic during study period.*

Results: *Out of 100 children of asthma, 29 (29%) were between 2 to 5 year, 48 (48%) between 5-8 years, 23 (23%) more than 8 years. The proportion of male was higher than female. Of the hundred children, 63% were found to have a positive family history of atopy and 37% did not have any family history, and 51% were found to have a positive family history of bronchial asthma, and 12% have a family history of allergic rhinitis, dermatitis or conjunctivitis. Out of the 63 (63%) children with family history of bronchial asthma, 44 (86%) had the positive parental history (35%) had maternal history, 51% had paternal history), 14% children had a positive history in grandparents. Also 17 (17%) children had a positive family history of allergic rhinitis, 57 (57%) children had personal history of atopy.*

Conclusion: *The results of our study further underscore the clinical importance of assessing and intervening in the family relational processes during treating children with asthma.*

Keywords*: Bronchial Asthma, Atopy.*

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Introduction

Asthma is a chronic inflammatory disorder characterized with the intermittent andvariable periods of airway obstruction. The pathophysiology of asthma involves chronic inflammation, airway hyper responsiveness, bronchoconstriction, swelling of the airways and mucus obstruction. Several risk factors for asthma have been identified including, skin test reactivity to allergens, atopic dermatitis, and family history.[1-4] Researchers are continually investigating the association between family history and childhood asthma.[5-10] More recently studies have focused on the examination of family history of asthma as an explanatory variable for the rising rates of asthma. Research to identify family risk has focused on parental influence, specifically birth order, genetic predisposition, and maternal asthma.[5-6,11-16] Study results examining asthma family risk have been inconclusive with some pointing to a maternal link and others a paternal link, while others have not found an association between asthma and family history.[13-15] Thus, this study attempts to analyze the clinical records of 100 pediatric asthma patients with variable family history and personal history of atopic disease to understand the impact of family history and atopy on childhood asthma.

Materials and Methods

A retrospective study was conducted in the department of Pediatric Respiratory Medicine (Pulmonology), Dhaka Shishu (Children) Hospital, Dhaka, Bangladesh between May 2016 and May 2017. We retrospectively analyzed the 100 cases between 2 years to 12 years of age visited in our outpatient and asthma clinic during study period. Enrolled patients were diagnosed clinically and consent was taken from parents before enrolment. Data for all patients regarding age at diagnoses, family history of asthma and other atopic diseases, personal history of atopy were taken.

Results

Out of 100 children of asthma, 29% between 2 to 5 year, 48% between 5-8 years,23% more than 8 years (Table-1). The proportion of male (76%) children was a higher than female (24%) children (Fig I).

Of the hundred children, 63% were found to have a positive family history of atopy and 37% did not have any family history (Table II), and 51% were found to have a positive family history of bronchial asthma, and 12% have a family history of allergic rhinitis, dermatitis or conjunctivitis. Out of the 63% with family history of bronchial asthma, 86% of the children had positive parental history of bronchial asthma (35% had maternal history, 51% had paternal history), 14% children had a positive history in grandparents. Also 17% children had a positive family history of allergic rhinitis (Table IV). 57% children had personal history of atopy (Table III).

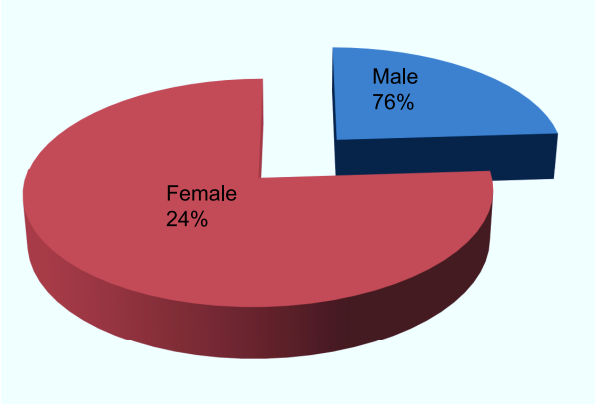

Fig 1 *Pie chart showing the sex distribution of the study patients*

Table I
Age distribution of the study patients (n=200)

Age (years)	Frequency	Percent (%)
2 to 5 year	58	(29%)
5 to 8 year	96	(48%)
More than 8 year	46	(23%)

Table II
Distribution of cases based on family history (n=100)

Family History of Atopy	Percentage of children
Present	63
Absent	37

Table III
Distribution of cases based on personal history of atopy (n=100)

Personal History of Atopy	Percentage of children
Present	57
Absent	43

Table IV
Distribution of family history positive cases(n=200)

Characteristics	Number	Percentage
Family history of	51	51
Bronchial asthma:		
Father	26	50.98
Mother	18	35.29
Grand parent	7	13.72
Family history	12	
Other Atopic disease:		
Father	7	58.33
Mother	3	25
Both	2	16.66

Discussion

The results of this study demonstrate that majority (48%) of the children diagnosed to have bronchial asthma belonged to the age group of 5-8 years, that is in school going age group. Only 29% had bronchial asthma in 2 to less than 5 years age group. The reported prevalence of asthma increased among 6-11-year-old children between the first (1971 to 1974) and second (1976 to 1980) National Health and Nutrition Examination Surveys in United States.[17] In children aged 6–7 years, the prevalence of asthma ever ranged from 4.1–26.9%, and the prevalence of wheezing in the last 12 months ranged from 8.6–32.1%.[18] A survey conducted in 106 centres in 56 countries among children of 13–14 years of age and in 66 centres in 37 countries in children of age 6–7 years of age reported to have had asthma at some time in their lives increased by 0.28% per year in the 13–14 year age group and by 0.18% per year in the 6–7 year age group.[19]

In our analyses, asthma was more common among male children, which is in agreement with other studies,[20,21,22] although, in some instances we did not find any significant difference between males and females.[21]

In our study, children with positive family history of asthma were more likely to develop asthma, which is similar to results of other studies.[22,23] Of the hundred children, more than half of children had personal history of atopy (Table III), whereas almost two-thirds had family history of bronchial asthma, and 86% of the children had positive parental history of bronchial asthma (35% had maternal history, 51% had paternal history), lowest percentage of them had a positive history in grandparents and a positive family history of allergic rhinitis (Table IV). This distribution was also consistent with 17% children had a positive family history of allergic rhinitis (Table IV). This study demonstrates that history of asthma in first degree relatives influence the level of hyper responsiveness at early age.[22,23] This is not a surprising observation, however, further research is warranted to better understand the influence of grandparental asthma status on child's asthma.

Conclusion

In conclusion, our study findings re-emphasize the clinical importance of assessing and intervening the family relational processes during treating children with asthma. As we advance our understanding, we will gain better insight into where and how to intervene to improve asthma outcomes by promulgating further prospective multi-centre research.

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ORIGINAL ARTICLE

Grading of Perinatal Asphyxia by Clinical Parametrs and Its Correlation with Outcome

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Abstract

Background*: Perinatal asphyxia is an important cause of neonatal mortality, morbidity and disability in many countries including Bangladesh.*

Objective*: To categorize the asphyxiated babies by a new scoring system to reduce morbidity & mortality, to anticipate future neurological handicap and thereby to determine the efficacy of this scoring system to predict their future outcome.*

Methods: *A prospective study was conducted in neonatal care unit of Dhaka Shishu Hospital from July 2005 to June 2006. A thorough history and physical examination were carried out and a simple scoring system was designed based on 12 historical & clinical criteria. Each criteria was given scores of 0 ,1, 2.(Table-I).Total scores were 0 – 24****. Scores <12 was mild perinatal asphyxia (PA), 12-18 was moderate (PA) and >18 was severe (PA)****. They were followed up carefully to find out a short hospital outcome. After discharge from hospital babies were followed up at 3 months of age to find out any growth & developmental delay or any neurological deficit.*

Results: *In this study total 97 patients were enrolled. Of 97 patients, 20 died & 77 patients came for follow at 3 months. According to scoring system, 34 were mild PA with scores <12, 53 were moderate with scores 12-18 and 10 were severe PA with scores >18. Male babies were more frequently affected than female ones. Primigravidas were more likely to have asphyxiated babies than multigravidas. Mothers without antenatal checkup had significantly higher risk to develop perinatal asphyxia. Maximum deliveries, though took place in clinic or hospital and were conducted by doctors & nurses, APGAR scores were not recorded in most of the cases. Resuscitation was not adequate in most of the cases (72%). Statistical analysis revealed insignificant results (p >0.05). Among the mild PA cases 32 (94.4%) recovered fully & 2 (5.9%) died. In moderate PA, 40 (75.5%) survived & 13(24.5%) died. Among the survived moderate PA cases 27(67.5%) were normal & 13 (32.5%) developed neurological deficit at 3 months. Of 10 severe PA cases, 5 (50%) survived & 5 (50%) died. Only 1 (20%) case was normal & 4 (80%) developed complication at 3 months follow up. Analysis of outcome revealed statistically significant difference (p<0.05) between mild Vs moderate & mild Vs severe PA but insignificant difference (> 0.05) moderate Vs severe cases.*

Conclusion: *This proposed scoring system may be helpful in diagnosis and management of asphyxiated babies and will allow for reasonably accurate prognostication regarding the probability of future handicap.*

Keyword: *Perinatal asphyxia, Hypoxic- ischaemic encephalopathy, Neurological deficit.*

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Introduction

Despite advances in perinatal & obstetric care, perinatal asphyxia is still the most important cause of brain injury in newborn.[1] Perinatal asphyxia refers to a combination of hypoxia, hypercarbia & metabolic acidosis as a consequences of occlusion of umbilical vessels or interference with placental perfusion in fetal life and/ or due to lack of effective breathing after birth.[2] It is a major cause of preventable mortality among the newborn in developing countries like Bangladesh. It is estimated that about 7 million perinatal death death occur each year, mostly in developing countries.[3] Nearly 3-6 million newborns suffer moderate to severe birth asphyxia with at least 800,000 dying & at least equal number developing sequelae.[4] The incidence of PA is about 1-1.5% in most centre in USA and is usually related to gestational age and birth weight, accounting for 20% of perinatal death.[5] The overall incidence of PA is about 2-9% in developing countries.[6] Studies in Bangladesh have been showed that 7-8% of rural and 9-12% of urban newborn babies are born with moderate to severe birth asphyxia, more than 150,000 newborns are born asphyxiated in Bangladesh every year.[7] In Bangladesh infant mortality is 51 per 1000 live birth, of which about 2/3rd is due to high neonatal mortality rate which is 48/1000 live birth.[8] It is one of the highest not only with respect to global figure but also the Asian country like Srilanka. A hospital based study in Bangladesh showed that 39% of the neonatal death is due to perinatal asphyxia.[9] Another hospital based study showed that there is an increasing trend of admission in neonatal ward with perinatal asphyxia as high as 40% of total admission despite improved obstetrical care in the recent years at urban & periurban areas of Dhaka city.[10] Among the survivors, the long term sequelae including mental deficiency & cerebral palsy is about 12-15%.[11] These mentally handicapped children become the ultimate burden to the family as well as to the society & the nation. Hence prevention of perinatal asphyxia as well as their appropriate management should be integral part of the health program. There are some old methods of assessment of asphyxiated babies known as APGAR Score & of limited value particularly for the TBA who conduct about 80% of the total birth in Bangladesh. There are some recent studies that have poor correlation between APGAR score and mental prognosis.[12] About 90% of the deliveries in Bangladesh take place at home, those occurring in clinics/ hospital, APGAR Scores are rarely recorded. Though recorded in most centers, it is recorded at 1 & 5 minutes after birth. APGAR score at 1 & 5 minutes have poor correlation with future neurological outcome. Clinical assessment of degree of HIE by Sarnat & sarnat staging is a better predictor of outcome but may not become obvious until 12-36 hours after birth and HIE staging require both clinical & EEG parameters.[12] In our country it is not feasible to do EEG in every patients which is expensive. We have to search for better predictors of neurological handicap in survivors of PA depending on the available history & clinical findings on presentation.

Therefore we designed a new scoring system depending purely on history and clinical findings Therefore we designed a new scoring system depending purely on history and clinical findings without any laboratory data. As such study has not been done in Bangladesh, we tried to see how far our clinical prediction correlated with the progress and outcome of the patients and thereby tried to validate the scoring system we designed. Again validation of this scoring system is very difficult to perform by using modern technological investigations like EEG, CT Scan, MRI. As this investigations are costly for the patients considering the socioeconomic condition & also may give inconclusive results about the ultimate outcome of the patients. Clinical follow up results at 3 months of age will be used in particular to correlate with the initial findings of mild, moderate & severe PA with proposed scoring system. If statistical analysis shows significant correlation with the scores and outcome at 3 month, this study will proved to be worthwhile for assessment of birth asphyxia and further studies for evaluation of this newly scoring system.

Materials & Methods

This was a prospective study conducted in neonatal care unit of Dhaka Shishu hospital from july 2005 to June 2006.Newborn admitted in DSH with gestational age 37 weeks and within 48 hours of delivery with H/O delayed cry or failure to breath spontaneously immediately after birth are included in this study. Neonates less than 37 weeks and more than 48 hours age, having s/s of RDS, septicaemia & congenital anomalies were excluded from this study. Informed consent from parents and permission of ethical review committee of Bangladesh Institute of

Child Health was taken. Detailed history regarding antenatal, natal & postnatal period were taken from parents. Thorough examination of all neonates was done. A simple scoring system was designed based on 12 historical & clinical criteria. Each criteria was given scores of 0,1,2.(Table-I). Total scores were 0-24.

All babies were investigated and managed with conventional management as far as possible & indicated. They were followed up carefully to find out a short hospital outcome. After discharge from hospital babies were followed up at 3 months of age to find out any growth & developmental delay or any neurological deficit. Regarding growth assessment- Weight, length & OFC were recorded. Neurodevelopmental assessment were done by using developmental domain like-gross motor, fine motor and vision, hearing, cognition, speech and primitive reflexes. Data entry and statistical analysis was done by using SPSS 11 version. Comparative analysis was done between mild Vs moderate, mild Vs severe & moderate Vs severe PA to determine statistically significant difference. Z test, Chisquare test & correlation coefficient were done for comparative analysis.

Table I
The proposed clinical scoring system

	2	1	0
1. Cry/breathing	Did not cry within 30 mins.	Cried after 5 mins but less than 30 mins.	Cried within 5 mins.
2. Color.	Blue or pale	Body pink, limbs blue	Pink all over
3. Movement of body	Absent	Some movement	Active movements
4.Resuscitation tried	Bag and mask ventilation/Mouth to mouth breathing	O2 inhalation, OP suction/ slapping at back	No resuscitation needed
5. Level of consciousness	Stuporous/ comatose	Lethargic	Well, alert
6.Activity and tone	Nil	Minimal (occasional) spontaneous activity.	Have spontaneous activity (flexion)
7. Active convulsion	Present- frequent convulsion	Occasional	Nil
8. Respond to stimuli	None	Some response	Present
9. Heart rate	Very feeble(<60/mins)	Bradycardia (60-100/mins)	Normal(>100/mins)
10. Respiration	Periodic/apnoea/severe grunting	Spontaneous respiration with some difficulty	Spontaneous and good respiration
11. Injuries	Obvious injuries like subaponeurotic hemorrhage, bulged fontanela due to IVH,large ecchymosis over face etc.	Minimal injury like abrasion, cephalhematoma.	No injury
12. Primitive reflexes	Absent	Weak	Normal

Babies were graded as- mild PA with scores <12, moderate PA with scores 12 -18 and severe PA with scores >18.

Results

Total 112 patients were studied. Among them, 15 patients were dropped out. The rest 97 patients were the study population. Of 97 patients, 20 died & 77 patients came for follow at 3 months of age.

Table II

Socio- demographic characteristics and clinical parameters of study population

	Number	Percentage	
Residence			
Rural area	52	53.6	
Urban area	45	46.4	
Parity			
Primaepara	65	67	
Multipara	32	33	
Sex			
Male	60	61.9	
Female	37	38.1	
Antenatal Checkup			
Regular	54	55.7	P<0.001
Irregular	38	39.3	highly significant
Nill	5	5.2	Z" test
Place of Delivery			
Clinic	49	50.5	
Home	28	28.9	
Hospital	20	20.6	
Mode of Delivery			
Vaginal	76	78.4	
LUCS	21	21.6	
APGAR score at 5mins			
0-3	9	32.14	
4-6	12	42.86	
7-10	7	25	
Resuscitation at birth			
Resuscitation tried	69	71.1	
Mouth to mouth breathing	30	43.5	
O_2 inhalation/OP suction/positioning/tactile stimulation	50	72.5	
Slapping at back	20	29	
Bag & mask ventilation	8	11.6	
Endotracheal intubation	2	2.9	

Table III

Distribution of time required to tolerate feed, for convulsion remission and duration of hospital stay of the infants (n=97)

Feeding tolerated (days)	Mild	Moderate	Severe	Total
Mean ± SD	2.3±0.79	3.5±2.46	6.8±1.30	3.2±2.18
Range(min, max)	1-5	6-8	8-12	1-12
Time taken for convulsion Remission (hours)				
Mean ± SD	46.4±19.17	83.3±49.87	120±58.79	75.6±48.09
Range (min, max)	24-72	24-240	48-168	24-240
Duration of hospital stay (days)				
Mean ± SD	7.6±3.44	13.3±5.52	19.6±2.70	11.3±5.76
Range (min, max)	3-12	13-17	17-24	3-24

Table IV

Causes of death in different grades of PA (n=20)

Causes of	Mild		Moderate		Severe	
Death	n	%	n	%	n	%
Cardio respiratory failure due to recurrent apnea	0	0.0	10	76.9	5	100.0
Septicemia	2	100.0	2	15.4	0	0.0
DIC	0	0.0	1	7.7	0	0.0

Table V

Distribution of infants by neurological deficit at three month age follow-up in different grades of PA (n=77).

Impairments at 3	Mild		Moderate		Severe		Total	
Month follow up	n	%	n	%	n	%	n	%
Normal	32	100.0	27	67.5	1	20.0	60	77.9
Gross motor- neck control	11	27.5	3	60.0	14	18.2		
Cognition – social smile	3	7.5	3	60.0	6	7.8		
Vision- No fix and follow object	5	12.5	2	40.0	7	9.1		
Fine motor- can't reach out object and hold object	-	-	8	20.0	1	20.0	9	11.7
Hearing respond to sound	-	-	4	10.0	2	40.0	6	7.8
Muscle tone increased	-	-	11	27.5	3	60.0	14	18.2
Reflexes Exaggerated	-	-	6	15.0	2	40.0	8	10.4
Convulsion	-	-	2	5.0	0	0.0	2	2.6
Total	32	100.0	40	100.0	5	100.0	77	100.0

Table VI

Distribution of neurodevelopment outcome of infants with PA at 3 months follow up (n=77)

PA	n%	Normal		Neurological deficit		P value	
		N	%	n	%		
Mild	32100.0	32	100	0	0.0	<0.001	< (Mild Vs Moderate)
Moderate	40	100.0	27	67.5	13	32.5	<0.001[2] [2](Mild Vs Severe)
Severe	5100.0	1	20.0	4	80.0	0.059[3]	[3](Moderate Vs severe)
Total	77	100.0	60	100	17	100.0	

p value reached from chi square test

Table VII

Relationship of clinical findings with neurodevelopmental outcome at three months

Findings	Normal (n=60)	Abnormal (n=17)	Chi	df	P value
Cry/breating cried within 5 minutes	5.(8.3)	0(0.0)	6.566	2	0.038*
cried between 10 to 29 minutes	18(30.0)	1(5.9)			
did not cry within 30 minutes	37(61.7)	16(94.1)			
Color pink all over	1(1.7)	0(0.0)	10.316	2	0.005***
body pink, limbs blue	36(60.0)	3(17.6)			
Blue or pale	23(38.3)	14(82.4)			
Movement of Infants					
Active movement	9(15.0)	1.(5.9)	29.862	2	0.001***
Some movement	46(76.7)	4(23.5)			
Absent	5(8.3)	12(70.6)			
Resuscitation Tried					
No resuscitation needed	13(21.7)	6(35.3)	1.703	2	0.426
Mouth to mouth breathing & others	45(75.0)	10(58.8)			
like 02 inhalation					
Bag & mask ventilation/intubations	2(3.3)	1(5.9)			
Level of consciousness					
Well, alert	19(31.7)	0(0.0)	18.407	2	0.001***
Lethargic	39(65.0)	11(64.7)			
Stuporous/comatose	2(3.3)	6(35.3)			
Activity and Tone					
Had spontaneous activity (flexion)	7(11.7)	0(0.0)	22.873	2	0.001***
Minimal (occasional) spontaneous activity	43(71.7)	4(23.5)			
Nil	10(16.7)	13(76.5)			
Active Convulsion					
Nil	22(36.7)	0(0.0)	16.061	2	0.001***
Occasional	20(33.3)	3(17.6)			
Present-frequent convulsion	18(30.0)	14(82.4)			
Respond to Stimuli					
Present	9(15.0)	1(5.9)	34.407	2	0.001***
Some response	46(7.7)	3(17.6)			
None	5(8.3)	13(76.5)			
Heart Rate					
Normal	52(86.7)	15(88.2)	0.028	1	0.0865
Bradycardia	8(13.3)	2(11.8)			
Respiration					
Spontaneous and good respiration	13(21.7)	0(0.0)	5.136	1	0.0766
Spontaneous respiration with some	30(50.0)	9(52.9)			
difficulty-grunting					
Periodic/apenea/severe grunting	17(28.3)	8(47.1)			
Injuries					
No injuries	33(55.0)	9(52.9)	0.484	2	0.784
Minimal injury like abrasion	23(38.3)	6(35.3)			
haemorrhage, bulged fontanel due to IVH,					
Primitive reflexes					
Normal	4(6.7)	0(0.0)	28.981	1	0.001***
Weak	45(75.0)	2(11.8)			
Absent	11(18.3)	15(88.2)			

p value reached from chi square test Highly significant at p<0.001*** level. Significant at p<0.05* level Nonsignificant at p>0.05 level

In this table it is shown that all the clinical finding are significantly ($p<0.05$) related with 3 months outcomes except resuscitation tried, heart rate, respiration and injuries, which are not significantly ($p>0.05$) related with 3 months outcome.

Discussion

Perinatal asphyxia is a leading cause of neonatal mortality and morbidity in developing countries including Bangladesh.[1] In our country in 2000 neonatal mortality rate is 42/1000 live birth and about 39% of total neonatal mortality is due to perinatal asphyxia.[9] This study was designed to categorize the asphyxiated babies by using a simple scoring system based on 12 historical and clinical criteria. Each of the criteria given scores- 0, 1, 2 (Table I). Grading was done as mild, moderate and severe PA. In this study total 97 neonates with PA were included. The male to female ratio is approximately 2:1. Similar male preponderance is also noted in other studies.[13-15] Parity is an important factor as newborn of primipara had higher incidence of perinatal asphyxia than multipara that is consistant with other studies.[7,16] Mothers without antenatal checkup had significantly higher risk of development of perintal asphyxia. In our country, most of the deliveries are conducted at home. In this study though majority were hospital/ clinic deliveries, among them majority of the deliveries first tried at home and then went to hospital when labour was obstructed. So babies suffered from prolonged period of intrapartum asphyxia. Though maximum deliveries took place in hospital and majority were conducted by doctors & nurses, the APGAR score was not recorded in most cases. Resuscitation majority was done by O_2 inhalation / Op suction/ tactile stimulation in 72% cases, by mouth to mouth breathing in 43.5%, bag and mask ventilation in only 11,6% cases in this study. In 28.9% cases no resuscitation was tried at all. Statistical analysis regarding measures tried for resuscitation revealed insignificant ($P>0.05$) results. In our country resuscitative measures in most centre are not adequate. Basic equipment for resuscitation and skilled personnel attending the delivery are not available. According to scoring system, 34 were mild PA with score <12, 53 were moderate PA with score 12-18 and 10 were severe PA having score >18. Among the mild PA, 32 (94.4%) recovered without any complication and 2 (5.9%) died because they develop septicemia due to nosocomial infection. In moderate PA, 40(75.5%) survived and 13(24.5%) died. Among the survived group of moderate PA, 27 (67.5%) were completely normal & 13 (32.5%) developed neurological deficit at 3 months follow up. Among 10 severe perinatal asphyxia cases, 5(50%) survived & 5 (50%) died. Only 20% baby was normal & 4 (80%) babies developed complications at 3 months follow up. Analysis of outcome revealed statistically significant ($p<0.05$) difference between mild vs moderate & mild vs severe perinatal asphyxia but insignificant difference ($p> 0.05$) between moderate vs severe cases. The rate of mortality from PA in this study correlates with other studies.[4,17]

The mean days of tolerance to feed in mild PA case were less than those of moderate & severe cases. There is a significant positive correlation between clinical score of asphyxiated babies & duration of tolerance to feed. Higher the score of babies , more time needed to tolerate feeding. This intolerance to initial feed is due to ischaemia of gutwall. Time taken for convulsion remission in mild PA was 46.4 # 19.17 hr, in moderate PA was 83.3 # 49.87 hrs and in severe PA it was 120# 58.79 hrs. Among the survivors, mean duration of hospital stay in mild PA was7.6 # 3.4 days, in moderate PA was 13.3 # 5.52 days and in severe cases 19.6# 2.7 days. The cause of increased hospital stay is multifactorial. Because of severity of degree of asphyxia insult, there is development of multisystem failure particularly brain, heart, ,liver, kidney, bowel and bone marrow resulting from hypoxia ischaemia, Because of multiorgan dysfunction, moderate & severely asphyxiated babies required prolonged period for recovery. This findings were similar to other studies reported previously.[7,17]

Among the survivors, 94.1% of mild PA recovered fully without any long term sequelae like developmental delay, vision or hearing impairement. 67.5% of moderate cases recovered fully without any sequelae, 32,5% developed different types of impairment at 3 months of age. So, there was statistically significant difference between fully recovered cases with mild vs moderate PA ($P<0.001$). Similarly comparison between moderate & severe PA showed that 20% with full recovery & 80% developed different types of impairment at 3 months follow up in severe PA. Comparison between mild & severe cases showed that there was significantly higher risk of development of long term sequelae in severely asphyxiated babies in comparison to mild

groups whereas difference between moderate & severe cases, who recovered, the result was statistically insignificant (P >0.05). These result was comparable with other studies who did grading by APGAR score & HIE staging.[14,18,19]

In recent studies mortality due to PA had come down considerably in developing countries. In this study total 20.6% of asphyxiated babies expired. This result is comparable to recently published results. Bhuiyan S J 1996 showed 44% in his study. Higher mortality was also observed in other studies.[17] This study showed 5.9% in mild PA, 24.5% in moderate and 50% mortality in severe PA. Most of the expired patients in this study were in severe group (50%) & most of the recovered patients were in mild & moderate groups. This result was consistent with other studies.[18,19] Similarly Finer MN et al found 74% in severe, 26% in moderate and no mortality in mild PA.[14] This indicates as the degree of asphyxia increases, the mortality increases. Therefore, this proposed scoring system may help us in diagnosis and management of asphyxiated babies and will allow for reasonably accurate prognostication regarding the probability of future handicap. Early recognition and more aggressive therapy for severe cases may reduce the mortality and morbidity of this condition.

In this study, FU was done at 3 months of age to identify patients who are at risk to have neurodevelopmental impairment and who need special care or early intervention. Most common impairment are gross motor delay & increased tone followed by fine motor or vision impairment, impairment of hearing & cognition. Many studies have been carried out to prove importance of early intervention.[20-22]

Conclusion

From this study it can be concluded that this new scoring system may be convenient, easier &effective in classifying asphyxiated babies in different groups. Early recognition & more aggressive supportive management of groups, who are at risk of developing future neurological handicap, will reduce the mortality & morbidity of this condition. This scoring system may also be helpful to the physicians, who are managing asphyxiated babies in different hospital & also health workers in their management, follow up and counseling of parents.

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ORIGINAL ARTICLE

Immediate Outcome of Acute Leukemia Following Induction Chemotherapy in Relation to Clinical and Laboratory Profile

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Abstract

Background*: Acute lymphoblastic leukaemia (ALL) is the most common paediatric malignancy. It represents 25% of all childhood cancers and approximately 75% of all cases of childhood leukaemia.*

Objectives: *Study objective was to see the bone marrow remission pattern at the end of induction therapy in paediatric ALL and AML patients.*

Methods*: It was an observational study and conducted at Paediatric Haematology and Oncology Department, Dhaka Shishu Hospital, July 2013 to June 2014. Thirty pediatric ALL patients and 10 AML patients were included in the study. Diagnosis was based on history, examination findings, peripheral blood film and bone marrow study. According to UK ALL 2003 protocol all patients were given 4-drug induction therapy, i.e., vincristine, prednisolone, L-asparagenase and daunomycin and for AML '3+7' regimen given for 2 cycles. Bone marrow study was repeated at day 28 of induction therapy and remission pattern was seen.*

Results*: Out of 40 Patients, 27(67.5%) were males. Age range was between 1–12 years (Mean 5.4 years). Bone Marrow study was done in 40(100%) patients. At day 28 of induction therapy, 24 (60%) patients went into complete remission (<5% blast cells in bone marrow), 10 (25%) into partial remission (5–25% blast cells in bone marrow). Total six (15%) patients,3 from each group (ALL and AML) died due to febrile neutropenia and sepsis during the course of induction therapy.*

Conclusion*: Outcome of ALL after induction therapy using modified 'UK ALL-99' regime in this study was below the anticipated response rates of developed countries, but in case of AML outcome of induction therapy using 2 cycles of '3+7' regime (with cytarabin and daunomycin), was not satisfactory. The outcome was affected by age and sex of the patient, initial WBC and Platelet count and blast cells in the bone marrow during diagnosis.*

Keywords*: Acute Leukemia, induction therapy chemotherapy*

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Introduction

Acute leukemia is the most common pediatric malignancy, comprising approximately 25% of all childhood cancers.[1] Of the acute leukemias, acute lymphoblastic leukemia (ALL) occurs five times more commonly than acute myeloid leukemia (AML). Acute lymphoblasti leukemia (ALL) accounts for about 77% of cases of childhood leukemia, acute myelogenous leukemia (AML) for about 11%.[2] A sharp peak of ALL incidence is observed at 2–5 years of age.[3] There has been a gradual increase in the incidence of ALL in the past 25 years due to more occurrence and better reporting.[4] At the same time with advent of modern chemotherapy and radiation therapy current event free survival (EFS) rates for ALL are approximately 80%.[5-8] Survival rates for ALL have improved dramatically since the 1980s.[9-11] AML accounts for approximately 20% of acute leukaemia in children compared to 80% in adults.[12] The incidence of AML has been reported to vary in different geographical regions. Highest rates of childhood AML have been reported in Asia and the lowest in North America and India.[13] AML in both children and adults requires intensive induction therapy for achieving a remission and further post remission therapy for durable long-term survival. The ultimate intensity has been achieved by administering myeloablative chemotherapy and/or radiation followed by bone marrow transplantation (BMT). Overall survival (OS) rates have improved over the past three decades for children with AML, with 5-year survival rates now in the 55% to 65%.[14-17] Overall rates of induction of remission are approximately 85% to 90%, and event-free survival (EFS) rates from the time of diagnosis are in the 45% to 55%.[14-17] Advances have occurred as a result of the optimal utilization of chemotherapeutic agents, improved antimicrobial supports and specialized nursing care.[18] But there is still lack of enough data from the developing world regarding the incidence, prognosis and comparison of survival with developed countries.[19-20]

Materials and methods

This was a prospective study done in Dhaka Shishu(Children) Hospital, a tertiary care paediatric Hospital in Bangladesh conducted from July 2013 to June 2014. Children who were admitted in different wards in Dhaka Shishu (Children) Hospital, age 1 year to 12 years and diagnosed as acute leukemia(ALL/AML) by CBC and bone marrow study were included and relapse acute leukemia patients who received chemotherapy previously and acute leukemia patients who were given chemotherapy elsewhere and age >12 years. After confirmation counseling was done regarding treatment, cost of the treatment, outcome and complications. When the parents had given written consent for treatment then they were included in this study. Before starting treatment liver function test, renal function test, uric acid, CXR and CSF analysis were done. All informations from each patient and their investigation findings were recorded in the case record form. Patients were followed up regularly. For ALL patients bone marrow study was done after induction therapy become complete and result was recorded in record form. For ALL induction was given with weekly vincristine, intrathecal MTX, daunomycin and L-asparaginase 9 doses, prednisolone and allopurinol(UK ALL-99). For AML induction was given with cytarabin for 7 days and daunomycin for 3 days ('3+7' regime). For first 2 cycles Intra thecal was given. In case of AML M_3 all trans retinoic acid 45 mg/m^2 body surface area also given along with chemotherapy. Both ALL and AML total duration of induction was 4 weeks. In case of AML duration of each induction period was 7 days. Two cycles of chemotherapy 14 days apart were given in induction of remission. Other supportive measures like antibiotics, transfusion of blood products etc. were used when needed. During induction chemotherapy weekly CBC, LFT and RFT were done for assessment and monitoring. The results were recorded in the record forms. Written approval was taken from the concerned authority and the departments with due procedure. The ethical clearance was taken from the ethical committee of Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital to perform the investigations and study, as well. The aim and objectives of the study along with its procedure and benefits were explained to all enrolled patient's parents or to the responsible attendants. Informed verbal consent were taken from the parents during data collection. Privacy and secrecy were maintained during the procedure. Patient's identity also kept confidential. Data were Collected & checked for completeness and correctness. Chi square test and t test were applied to find out the significance. Association between risk factors and outcome were detected by univariate analysis. P value <0.05 were accepted as level of statistical significance. Analysis were done by employing SPSS Version 15 software programme.

Results

Total 40 patients of acute leukaemia of both sexes who were admitted to Dhaka Shishu Hospital during the study period, were taken as study sample before starting the chemotherapy.

Table I
Age distribution of study cases (n=40)

Age	ALL (n-30)	AML (n-10)	Total (n-40)
< 2 years	4(13.33%)	2(20%)	6(15%)
2 to <5 year	15(30%)	5(50%)	20(50%)
5 to <10 years	6(20%)	2(20%)	8(20%)
10 years and above	5(16.66%)	1(10%)	6(15%)
Total	30(100%)	10(100%)	40(100%)

Among all 40 cases 28(70%) were 2 to 10 years age group.

Table II
Gender distribution of study cases (n=40)

Gender	ALL (n-30)	AML (n-10)	Total (n-40)
Male	19(63.33%)	8(80%)	27(67.5%)
Female	11(36.7%)	2(20%)	13(32.5%)
Total	30(100%)	10(100%)	40(100%)

Among all 40 patients, 27(67.5%) male & 13(32.5%) female acute leukemia patients, indicate male predominance. Male: Female ratio=2.07:1.

Table III
Clinical features and findings of study cases (n=40)

Clinical features and findings	Number of patient		Total
	ALL (n-30)	AML (n-10)	
Fever during admission	30(100%)	10(100%)	40(100%)
Bony tenderness	15(50%)	8(80%)	23(57.5%)
Bleeding	20(66.66%)	10(100%)	30(75%)
Lymphadenopahy	20(66.66%)	5(50%)	25(62.5%)
Splenomegaly(2 cm or more)	22(73.33%)	10(100%)	32(80%)
Hepatomegaly(2 cm or more)	20(66.66%)	8(80%)	28(70%)
CXR PulmonaryInfection	10(33.33%)	4(40%)	14(35%)
Mediastinal mass	3(10%)	0	3(7.5%)

Among all 40 patients, fever present in all patients(100%), bone pain present in 57.5% cases, bleeding present in 75% cases, Lymphadenopahy present in 62.5% cases, Splenomegaly present in 80% cases, Hepatomegaly present in 70% cases, Pulmonary infection present in 35% cases and mediastinal mass in 7.5% cases.

Table IV
Hemoglobin (Hb) concentration among study cases during admission

Hb%	Number of patient		Total
	ALL (n-30)	AML(n-10)	
< 6 gm/dl	16(50%)	6(60%)	22(55%)
6-10 gm/dl	10(33.33%)	2(20%)	12(30%)
>10 gm/dl	04(12.5%)	2(20%)	6(17.5%)
Total	30(100%)	10(100%)	40(100%)

In this study majority patients 22(55%) having Hb% less than 6 gm% due to bone marrow suppression by disease process.

Table V
Total Leucocyte count in study cases during diagnosis

Total Leucocyte count	Frequency ALL (n=30)	AML (n=10)	Total
$<10\times10^9$/L	21(70%)	5(20%)	26(65%)
10×10^9/L to 50×10^9/L	7(23.33%)	2(20 %)	9(22.5 %)
$> 50\times10^9$/L	2(6.7%)	3(30 %)	5(12.5 %)
Total number of patients	30(100%)	10(100%)	40(100%)

Most commonly TC of WBC was $<10\times10^9$/L in 26(65%) cases at diagnosis, marked leucocytosis ($>50\times10^9$/L)was found only in 5(12.5%) cases.

Table VI
Platelet count of study cases during admission (n=40)

Platelate count	Number of patient		Total
	ALL (n=30)	AML (n=10)	
<100×10^9/L	20(66.67%)	7(70%)	27(67.5%)
≥100×10^9/L	10(33.33 %)	3(30%)	13(32.5%)
Total	30(100%)	10(100%)	40(100%)

In most cases (67.5%) platelate count were <100×10^9/L,among them 20 were ALL and 7(70%) were AML.10 patients (33.33%) and 3 patients(30%), ALL and AML respectively, were found to have platelet count at or above 100×10^9/L.

Table VII
Bone marrow finding of study cases at diagnosis

ALL (n=30)		AML (n=10)	
Morphology (FAB type)	Number	Morphology (FAB type)	Number
L1	22(73.33%)	M1	3(30%)
L2	8(26.7%)	M2	5(50%)
L3	0	M3	2(20%)
Total	30(100%)	Total	10(100%)

Majority of ALL were FAB type L1(73.33%). In case of AML majority(50%) were FAB type M2.

Table VIII
Bone marrow remission pattern after 28 days of induction therapy(n=40)

Remission pattern	No. of Patients		Total
	ALL(n=30)	AML(n=10)	
Complete Remission	23 (76.67%)	1(10%)	24(60%)
Partial Remission	4 (13.33%)	6(60%)	10(25%)
Total patients	27(90%)	7(70%)	34(85%)

Most of the ALL (76.67%) showed complete remission after 28 days of induction therapy. In case of AML six (60%)out of total 7 had partial remission at the end of induction chemotherapy. A total of 6 patients,3 of ALL and 3 of AML, expired during the period of induction.

Table IX
Comparison of outcome of ALL cases with favorable and unfavorable features

Variable	Criteria	Total no of patients (n-27)	No of pt. in Remission		P value
Age	<2yr	4(15%)	2(50%)	50% vs 96%	.035*
	>2yr	23(85%)	22(96%)		
Sex	Male	17(63%)	16(94%)	94% vs 70%	.019*
	Female	10(37 %)	7(70%)		
Lymphadenopathy	Present	18(67%)	14(78%)	78% vs 100%	.49
	Absent	9(33%)	9(100%)		
Hepatomegaly	Present	17(63%)	15(88%)	88% vs 90%	.085
	Absent	10(37%)	9(90%)		
Splenomegaly	Present	20(74%)	19(95%)	95% vs 71%	.45
	Absent	7(26%)	5(71%)		
Mediastinal mass	Present	3(11%)	1(33.33%)	33% vs 96%	.262
	Absent	24(89%)	23(96%)		
WBC count	<50×10^9/L	25(93%)	22(88%)	88% vs 100%	.007*
	>50×10^9/L	2(7%)	2(100%)		
Hb level	<6 gr/dl	14(52%)	13(93%)	81% vs 79%	.073
	>6 gr/dl	13(48%)	11(85%)		
Platelate count	<100×10^9/L	18(67%)	15(83%)	83% vs 100%	.038*
	>100×10^9/L	9(33.33%)	9(100%)		
FAB for ALL	L1	21(78%)	18(86%)	86% vs 100%	.107
	L2	6(22%)	6(100%)		
Blast % in BM	≤90%	8(30%)	5(63%)	63% vs 100 %	.013*
	>90%	19(70%)	19(100%)		

* =P value <.05 is significant. Statistical significance on achievement of CR was found for age, sex, WBC and PLT count and percentage of blast in the bone marrow. **Note**-Among 30 cases of ALL,3 died during induction chemotherapy, so result for 27 cases given.

Discussion

Among all 40 cases, 28(70%) were within 2 to 10 years age group(table-1). In all age group male were more than female (Table 2). Male to female ratio were 2.07:1.Male preponderance in this group were due to more occurrence of acute leukemia in male.[2] Similar male preponderance also observed in the study in Malaysia[21]they found 54.44% male in their study. Fever were found in all 40 cases(100%). Previous study showed fever in ALL 93.33%[22] and 74%[23] in AML patients, which is co-insides with our study. Bony tenderness were present in 23 (57.5%) case and absent in 15 (37.5%), which coincide with previous study in Bangladesh where it was 65.6%[24]., but in western study it was 25%.[2]

Bleeding manifestation were present in 30(75%) case only. Our result is similar with previous study which was 33%.[25] Bleeding sites involved mostly in the gum & skin in about 17(42.5%) it is always secondary to severe thrombocytopenia, caused by marrow failure. Pallor was present in 100% of case but severity varied. Anaemia was due to marrow failure which was almost due to direct reduction in stem cells and may associated with ineffective erythropoiesis, but it was 60% in western children.[2] Lymphadenopathy was present in 25(62.5%) & absent in 15(37.5%) patients. In majority of the patients cervical lymph nodes were involved in 13 (32.5%) others were generalized (27.5%) which coincide with Western study where lymphadenopathy was in 35 to 54% cases.[2]

Splenomegaly was found in 32(80%) cases,which was higher then previous study, where it was 50%.[2] Hepatomegaly found 28(70%) cases, it was more then previous study, where it was found 48 to 56%.[2]

We found pulmonary infection in 14(35%)cases of acute leukemia, which was not coincide with previous study where it was 52.5%.[26]Mediastinal mass found only in 3(7.5%) cases of ALL, which coincide with previous study where it was 10-15%.[27] Our majority patients of ALL was ALL L1,22(73.33%) and majority patient of AML was M2(50%),our result coincide with previous results.[28,29] MRC UK ALL X study showed that 2–3% all patients will die during induction or in remission, most frequently due to leucostasis, bleeding or opportunistic infections such as gram-negative septicaemia and pneumocystis carinii pneumonia.[30] In our study higher incidence of deaths, i.e., 10% during induction was observed as compared to above studies, i.e., 2–3%. All of these 3 (10%) patients expired due to severe sepsis in spite of good antibiotic coverage. In these patients infection site were lower respiratory tract in 1 and urinary tract in 1 patient and 1 patient septicemia.

Improved supportive care has decreased the mortality rate during induction therapy to approximately 3% or less.[31] But in spite of adequate supportive care and use of appropriate antibiotics, there is higher incidence of mortality in our patients, i.e., 10%. This may be due to (a) delayed referral to tertiary care centre (b) complications of disease at the time of presentation (c) poor nutritional status (d) 4-drug induction therapy including daunomycin and (e) higher incidence of nosocomial/community acquired infection. In our study of AML, we found high death rate (30%). Due to more infection during induction or less supportive care. Similar result were found in previous study.[32-33] The standard induction therapy used in this study resulted in a response rates slightly below the anticipated response rates of developed countries which may be due to less prolongation of duration of therapy, poor supports especially during the period of pancytopenia, lack of molecular prognostic markers identification and advanced treatment options or due to little modification of the original protocol. Our study revealed age >2years, female sex, high platelet count (e"100×10^9/L),WBC <50000/cumm and blast cells d"90% in bone marrow during diagnosis affects the induction therapy, our result is similar with previous study.[33]

Conclusion

Majority of ALL showed encouraging outcome at the end of induction chemotherapy using modified 'UK ALL-99'regime. In case of AML outcome of induction therapy using 2 cycles of '3+7' regime (with cytarabin and daunomycin),was not satisfactory. The outcome was affected by age and gender of the patient. Initial WBC and Platelet count and blast cells in the bone marrow at diagnosis were also found to have significant effect on the outcome at the end of induction therapy.

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REVIEW ARTICLE

Utility of Targeted /Functional Neonatal Echocardiogram to Enhance Cardiovascular Care: An Update

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Abstract

Cardiovascular assessment of critically ill neonate using monitoring of blood pressure (BP) or poorly validated clinical signs such as capillary refill time or heart rate alone is insufficient to decide on the most physiologically relevant therapy. Functional echocardiograph is the bedside use of cardiac ultrasound to monitor rapidly changing neonatal hemodynamic status including cardiac function and systemic and pulmonary blood flow in critically ill preterm and term neonates and guide therapeutic decisions. It should be considered an extension of the physical assessment and not a replacement for a complete echocardiography evaluation of cardiac structure. This review examines the potential usefulness of functional echocardiography in different disease states, and how the technology may be introduced safely in the NICU.

Introduction

Newborns in the NICU are unique in that they are in the process of transition from fetal to postnatal circulation. Haemodynamic monitoring in newborns is based on assessment of continuous heart rate, blood pressure (BP), acid base status, urine output and capillary refill time.[1]These measures provide important and useful information to the clinician. Clinical assessment and the classic parameters mentioned to elucidate the underlying pathophysiology in haemodynamic disturbances can sometime lead to incorrect assumptions and therapeutic decisions, which may even cause harm.[2]Functional echocardiography and point-of-care echocardiography have been introduced to describe the use of echocardiography as an adjunct in the clinical assessment of the hemodynamic status in neonates.[1] It identifies the exact nature of cardiovascular compromise and guide therapeutic decisions also facilitates the evaluation of response to therapeutic intervention. The increasing availability of echocardiography, with miniaturization of the technology, has resulted in more widespread use of echocardiography in NICUs around the world.[3]It can provide detailed real time information concerning physiology and hemodynamics leading to rapid identification of the mechanism of circulatory failure in critically ill neonates, resulting in appropriate targeting of therapy.

Evaluation of cardiac output

End-organ perfusion is dependent on systemic blood flow and vascular resistance; therefore, reliance on blood pressure measurements alone provides limited information regarding the adequacy of organ blood

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flow.[4] The poor correlation between blood pressure and systemic flow are important determinants of the likelihood of altered perfusion, and neither should be monitored nor treated in isolation, without consideration of the influence of the other. Serial echocardiography offers the potential of novel insights as to the physiologic nature of the cardiovascular impairment: specifically, whether the concern relates to preload, afterload or myocardial contractility.

Doppler assessment of left (LVO) and right (RVO) ventricular outputs provides additional hemodynamic information regarding the adequacy of blood flow. Assessment of LVO involves measuring the mean velocity of blood flow across the ascending aorta from an apical five-chamber view using PW Doppler and determining the diameter of the aortic root from a parasternal long-axis view using m-mode methods. The area under the wave form of the aortic systolic beat can be used to calculate the velocity time integral (VTI), which is a measure of the distance traveled by blood during a given beat. Multiplying that by the aortic cross-sectional area (AoCSA) derived from Ao CSA = pX aortic diameter2/4gives the stroke volume. LVO can be derived from multiplying stroke volume by heart rate: LVO = (AoCSA X VTI X heart rate)/weight and is expressed in ml/kg/min.Normal values range from 170 to 320 ml/kg/min.[5] Walther et al[6] evaluated cardiac output in normal healthy term & preterm neonates during 1st week of life by pulse Doppler echo-cardiography.They have showed mean cardiac output values (±SD) per kilogram of body weight were 249±34 mL/mm/kg and decreased with advancing birth weight (Table 1). LVO must be used with caution as it may give a falsely reassuring picture of acceptable systemic blood flow in the presence of hemodynamically significant ductusarteriosus (HSDA) specifically, as a high volume left-to-right shunt will lead to increased pulmonary venous return, left heart preload and stroke volume, but at the expense of systemic blood flow. Early measurement of LVO following PDA ligation has been shown to predict late-onset impairment in LV contractility, low systolic arterial pressure and need for cardiotropes.[7]

Table I
Cardiac output of neonates at different birth weight[6]

Birth weight	Cardiac output
<1,500 g	265 ± 32 mL/min/kg
1,500 to 2,500 g	253 ± 34 mL/min/kg
>2,500 g	241 ± 33 mL/min/kg

Measurement of RVO is done using a similar approach described above. The pulmonary artery diameter is best assessed from an oblique long axis parasternal view. The RV VTI is obtained from Doppler interrogation of the same view. RVO reflects blood return from the systemic circulation and, in the absence of a large trans-atrial shunt, is reflects systemic blood flow in infants. However, RVO measurements are confounded by the presence of atrial shunt.Typically the atrial shunts are much smaller than ductal shunts, therefore RVO may be used as an estimation of systemic blood flow.[5]

SVC flow has been proposed to be a better echocardiographic measure of systemic blood flow as it reflects exclusive venous return from the brain and upper body and is untainted by shunts. SVC flow can be assessed using echocardiography.[8] A subcostal approach is used to assess SVC Doppler signals and a high supra- sternal view is used to measure SVC diameter.

The SVC flow was calculated using the following formula: SVC flow = (velocity time integral X(pX(mean SVC diameter2/4) Xheart rate)/body weight. The resulting figure is expressed as ml/kg/min.Normal values 40-120 ml/kg/min in VLBW.As four-fifths of flow in the SVC represents venous return from the head and neck, such measurements may provide novel insights into any association between regional cerebral blood flow and cerebral injury. Reduced flow in the SVC is common in premature infants in the first 24 h, reaching a nadir between 8 and 12h which coincides with increased systemic vascular resistance. Low SVC return is associated with an increased incidence of late intraventricular hemorrhage and may be one factor in the causal pathway of impaired preterm neurodevelopmental outcome.[9-10] However SVC return reflects blood supply to the brain and upper body and therefore no information regarding blood supply to the liver, kidney and gut can be derived. Second, cerebral blood flow is subjected to intrinsic

autoregulatory mechanisms and may not truly reflect cardiac performance.[11] Measurement of SVC diameter beyond 48 h of life is difficult. In addition, the diameter of the vessel varies widely within the cardiac cycle. Therefore a wide margin of error would have resulted from volumetric calculations. Groves et al[12] have also questioned the validity of this measurement due to high interobserver variability.

Inferior Vena Caval (IVC) diameter & variation in IVC provides indirect evidence of intravascular volume which is important for diagnosis of neonatal hypotension & shock. An average size of IVC <8mm in term &<6mm in preterm is considered as rough estimate of hypovolemia. Also more than 50% collapsibility of IVC is suggestive of hypovolemia.

Evaluation of myocardial performance

Systolic performance

Maturational differences make the immature myocardium susceptible to impaired performance. These developmental disadvantages make the neonatal myocardium vulnerable during a hypoxicischemic insult or when subjected to preload or afterload compromise. The evaluation of myocardial contractility is challenging as current methods are load dependent, although serial evaluation may provide valuable insights. The immature neonate is particularly sensitive to sudden changes in afterload.[13] The immediate transitional period after elimination of the placenta from the systemic circulation and following PDA ligation represent clinical situations in which afterload may be playing an important role.

Left ventricular (LV) systolic performance can be assessed by shortening fraction (SF), ejection fraction or the rate-corrected mean velocity of circumferential fibre shortening (mVCFc). SF characterizes LV contractility using m-mode methods from either a long parasternal axis or short axis view of the left ventricle (Fig.-1). It is calculated by measuring left ventricular end-diastolic diameter (LVEDD) and left ventricular end-systolic diameter (LVESD) using m-mode echo and applying the following formula:

SF% = (LVEDD – LVESD) X100/ (LVEDD)

Normal neonatal values for SF% are 28-40%. Shortening fraction is an unreliable measure of systolic LV function in the first few days of life as high right ventricular pressures impair ventricular septal wall movement.[14]

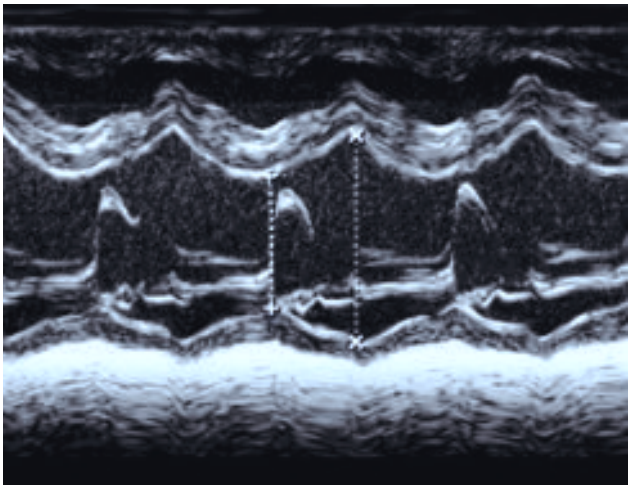


Fig 1 *m-Mode measure of shortening fraction*

LV mean velocity of circumferential fractional shortening (mVCFc) is a preload-independent afterload adjusted measure of LV function. It is determined by the following method[15]:

mVCFc = (LVEDC–LVESC)/(LVEDC X ETc)

Where LVEDC is left ventricular end diastolic circumference, LVESC is left ventricular end-systolic circumference, and ETc is left ventricular ejection time corrected for heart rate (ET/ÖRR interval, where RR is the time between consecutive heart beats).

Diastolic performance

Diastolic performance is altered in the newborn but its relevance to clinical decision-making is not well-appreciated. Diastolic filling is influenced by the compliance of the ventricular wall. In adults and older children, transmitral flow occurs in two phases: an early phase of passive flow during which the majority of the filling occurs and a late atrial contraction phase during which the remaining third of the venous return to the ventricle is delivered. In patients with diastolic dysfunction, the majority of filling occurs during the atrial phase as the stiff ventricular wall prevents passive early flow across the mitral valve. The immature fetal and preterm myocardium is characterized by impaired diastolic function. PW Doppler can be used to examine this biphasic pattern of transmitral flow. First phase is the early wave (E wave) and is a result of passive blood flow across the atrioventricular valves in early diastole. The second phase is the atrial contraction wave (A wave) and is a result of atrial contraction at

the end of diastole. Maximum E and A wave velocities are compared as ratios. An E:A ratio <1 indicates diastolic dysfunction (indicating a non-compliant ventricle). Transmitral VTI can be measured to give an estimate of flow across the atrioventricular valves.[16]

The Tei index (or myocardial performance index) has been found to be a valuable quantitative echocardiography index of ventricular function by incorporating both systolic and diastolic performance of the right and left ventricles (Fig.2). It is defined as the sum of isovolumetric contraction and relaxation times divided by the ejection time, which requires measurement of the time interval between the end and onset of mitral or tricuspid inflow (the 'a' interval) and the ejection time of the LV or RV outflow (the 'b' interval).[17]The Tei index is then calculated by the formula (a -b)/b. The Tei index is easy to calculate, reproducible, and independent of heart rate and blood pressure. Normal values in healthy neonates range from 0.25 to 0.38.[18] It is relatively independent of age and also has a low degree of inter and intra observer variability.[19]

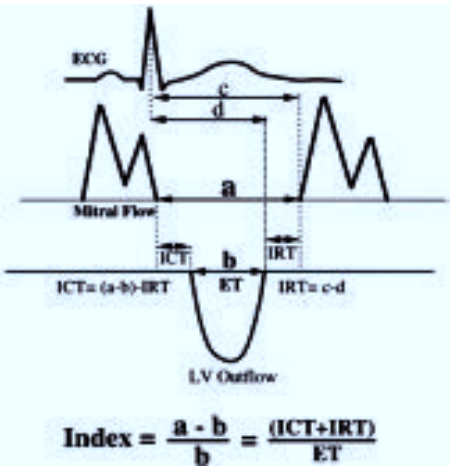


Fig 2 *TEI measurement*

Hemodynamic assessment of a PDA and clinical relevance

Prior to echocardiography, the diagnosis of PDA was reliant on the evolution of clinical signs including: a murmur, increased precordial activity, widened pulse pressure and bounding peripheral pulses. However, the diagnosis of a significant PDA by echo-cardiography precedes the development of clinical signs by a mean of 2 days.[20] There is poor correlation between physical signs and the presence of PDA by echo in the first week of life.[21,22] Bounding pulses and a murmur may be absent in up to 20% of infants with a PDA.[23] Therefore echocardiography remains the gold standard for PDA diagnosis.[20] Measurement of the internal ductal diameter by two-dimensional and colour Doppler imaging allows early prediction of significant PDA in preterm infants. Although a transductal diameter >1.5 mm has a good predictive value of ductal persistence, the measurement is not without limitation.[24] The ductus is a dynamic vessel of variable architecture, with an unpredictable response to treatment. It is not possible to directly quantify the magnitude of transductal flow, but the impact on the pulmonary and systemic circulations is measurable.

Pulmonary overcirculationattributable to excessive transductal flow and the effect of ductal steal on systemic perfusion may also be quantified using echocardiography for a comprehensive evaluation of the significance of the ductal shunt shown in Table-II.[4]

Table II

Surrogate markers of significant PDA[4]

Measurement	Modality & sample gate	Moderate PDA	Large PDA
Ductus arteriosus			
Diameter (mm)	High parasternal ductal view	1.5-3.0	>3.0
Ductal velocity (m/s)	PWD at ductal view(PA)	1.5-2.0	>1.5
PA diastolic flow (m/s)	PWD at left PA	0.3-0.5	>0.5
Pulmonary overcirculation			
LA: Ao ratio	m-Mode: long axix view	1.5-1.7	>1.7
E wave: A wave ratio	Doppler:transmitral view	1.0-1.5	>1.5
IVRT (ms)	PWD between MV & AV	35-45	<35
Systemic hypoperfusion			
Left ventricular output (ml/Kg/min)	PWD at LV outflow tract	200-300	>300
Diastolic descending Ao flow (%)	PWD at beyond PDA	30-50	>50
LVO/SVC ratio	PWD at flow at SVC	<2.4	>2.4
Celiac artery flow: LVO ratio	PWD at celiac artery	0.10-0.15	<0.10

PDA, patent ductusarteriosus; PWD, pulsed-wave Doppler; LA, left atrium; Ao,aorta; IVRT, isovolumic relaxation time; MV, mitral valve; AV, aortic valve; LV, leftventricle; LVO, left ventricular output; SVC, superior vena cava.

Evaluation of severity of pulmonary hypertension

Assessment of right ventricular systolic pressure (RVSP) is possible in the presence of tricuspid regurgitation and calculated using the Bernoulli equation (Fig.-3 & Table-III):

Table III

Grading of pulmonary hypertension

	Systolic (mm Hg)	Diastolic (mm Hg)	Mean (mm Hg)
Grade 1(Mild)	30-50	20-25	>20
Grade 2(moderate)	50-70	26-35	>40
Grade 3(severe)	70-110	36-45	>50
Grade 4(systemic or suprasystemic)	>110	46-55	>60

RVSP = right atrial pressure +(4 x Tricuspid Regurgitation JET Vmax)

Where Vmax = peak velocity

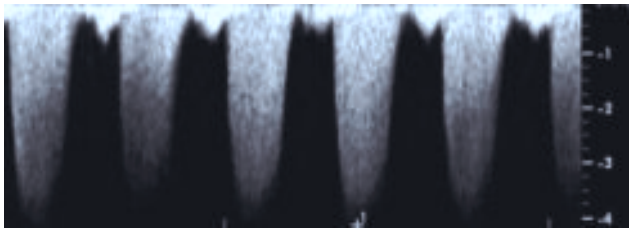


Fig 3 showing Continuous wave Doppler of tricuspid regurgitation. The regurgitant jet is characterized by turbulent flow depicted by a full Doppler envelope (upper panel). The peak velocity of the regurgitant jet was 4.0 m/s, resulting in a pressure gradient of 64 mmHg.

This measurement will underestimate the severity of the pulmonary hypertension if there is impaired RV contractility. The presence of PDA can also be used to estimate pulmonary pressures if systemic systolic pressures are known. Pulmonary arterial pressure can be estimated in the presence of a PDA with unrestrictive flow. The peak velocity of transductal flow can be applied to the Bernoulli equation to calculate the pressure difference between the systemic and pulmonary circulations. The direction of transductal flow may also be used to evaluate the severity of the pulmonary hypertension. A pure unrestrictive right-to-left shunt is seen with suprasystemic pulmonary hypertension; whereas a bidirectional shunt implies that pulmonary artery pressures approximate systemic pressures. The percentage of right-to-left flow of total transductal flow may also be calculated to further document the severity of the pulmonary hypertension.

Evaluation of right ventricular performance and pulmonary hemodynamics

In some patients the impact of pulmonary hypertension and increased RV afterload may include impaired RV contractility. Although moderate to severe RV systolic dysfunction is obvious by direct visual inspection there is no reliable or early marker of RV failure. Low RV output (<170 ml/min/kg) may also support a diagnosis of impaired RV performance. The complexity of RV anatomy and the fact that it is 'wrapped' around the LV makes quantitative evaluation by m-mode unfeasible. The RV myofiber architecture is composed of superficial circumferential and dominant deep longitudinal layers aligned base to apex that allow for greater longitudinal than radial shortening and minimum twisting and rotational movements.The longitudinal shortening is the dominant deformation of the RV that provides the major contribution to stroke volume during systole. Tricuspid annular plane systolic excursion (TAPSE)can be measured by "2-dimensional echocardiography–guided M-mode recordings from the apical 4-chamber view, with the cursor placed at the free wall of the tricuspid annulus estimates RV function (Fig.- 4 & 5).

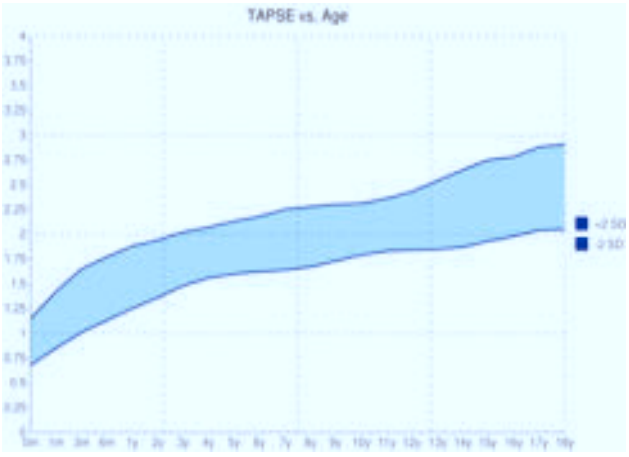


Fig 4 *showed growth curve TAPSE (mean ± 2SD) with age.*

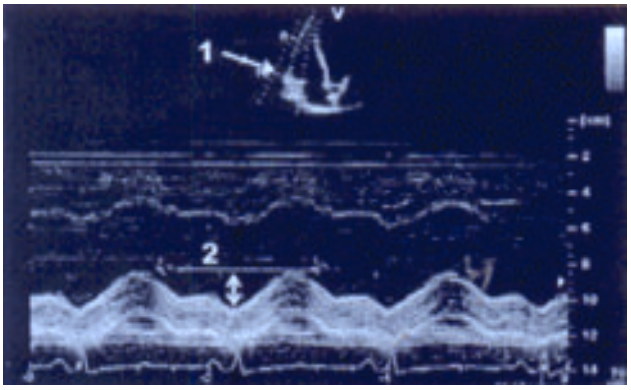


Fig 5 *Tricuspid annular plane systolic excursion (TAPSE).In 4 chamber view a straight line (M mode) is drawn through the lateral tricuspid valve annulus (arrow 1). The level of excursion of the tricuspid valvar plane during systole (TAPSE in mm) corresponds with RV ejection fraction (arrow 2).5 mm=20% RV EF,10mm = 30% RV EF,15 mm =40% RV EF,20mm = 50% RV EF.*

Utility of Functional neonatal echocardiography in the management of neonatal illness

In many parts of the world, neonatologists have developed the necessary skills to perform limited bedside functional echocardiography assessments as a means to enhance the care of critically ill babies.[25]Fecho may provide hemodynamic information that either complements what is clinically suspected or provides novel physiologic insights. The ability to perform timely functional echocardiography is now considered an integral component of the assessment of the critically ill newborn.[26-28]

In Canada, greater use of targeted neonatal echocardiography has only happened in the last few years, and it is just slowly becoming a part of standard neonatal intensive care unit (NICU) care. Harabor et al showed a total of 303 consecutive targeted neonatal echocardiographic studies were performed on 129 neonates. Of the 303 studies, 126 (41.5%) resulted in management changes. They have concluded that targeted neonatal echocardiography is a valuable tool in the NICU and can contribute substantially to hemodynamic management in the first week of life, PDA management in the first 2 weeks of life, and cases of hypotension or shock at any time during the hospital stay.

El-Khuffash et al29 reported a retrospective study of targeted neonatal echocardiographic practice at a large referral outborn NICU in Toronto. Despite differences, the impact of targeted neonatal echocardiography was similar in both studies. Khamkar et al[30] showed Indian experience of Functional echocardiographic studies of a total of 348 performed in 187 neonates (mean 1.86; SD 2.02). The most frequent indication was Patent Ductus Arteriosus (PDA) assessment (n= 174, 50%), followed by haemodynamic instability (n=43, 12.36%). The results of FnECHO modified treatment in 148 cases (42.50%) in the form of addition and/or change in the treatment or avoidance of unnecessary intervention.

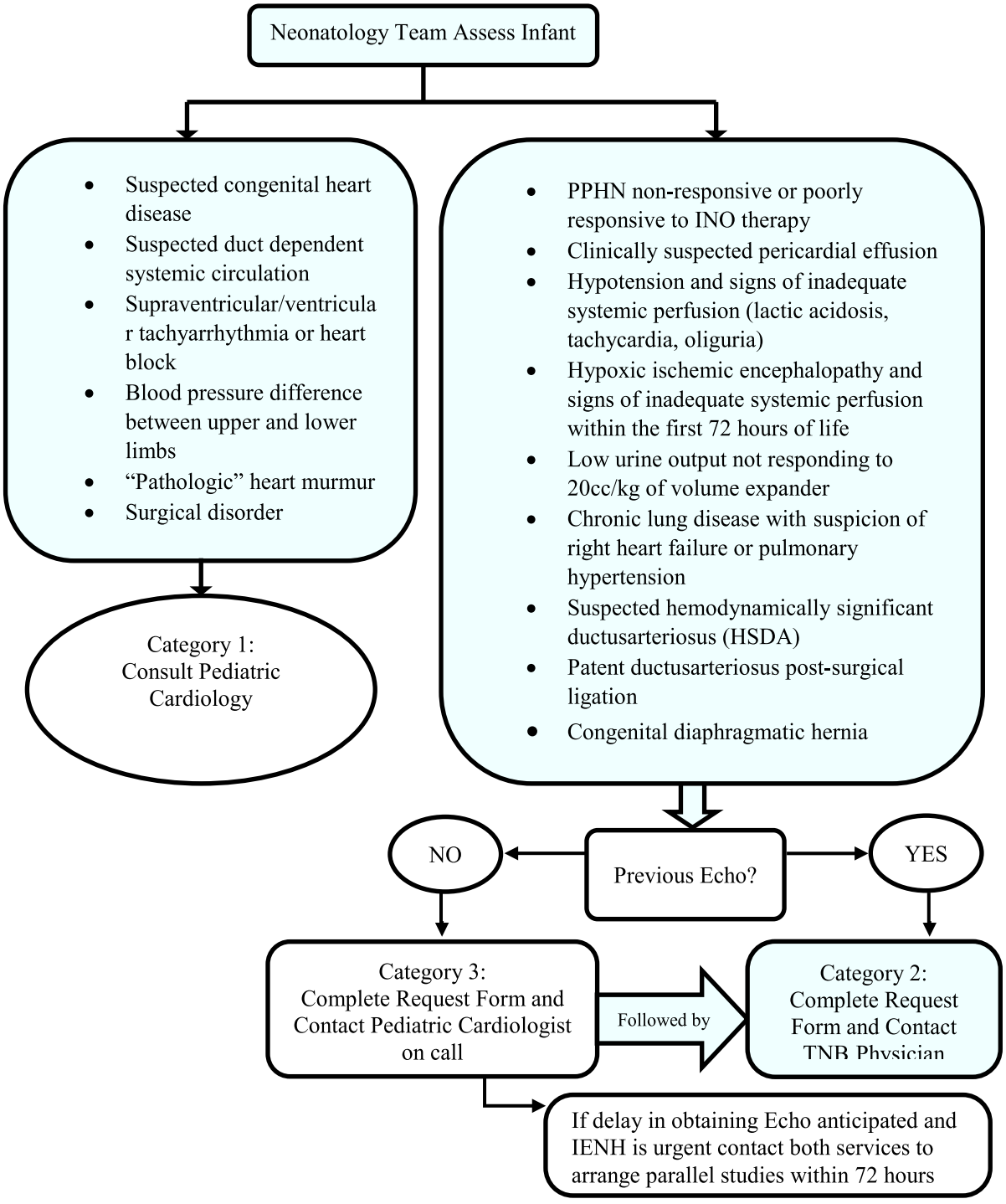
Standards for practice

There is a growing acceptance that neonatologist-performed functional echocardiography is a useful tool in the NICU, with increasing evidence of improved patient outcomes. What is lacking at present is a formalized training and accreditation program necessary for the development of echocardiography skills.31The potential risks of introducing this skill set without formal training include a divergence from clinical assessments and misdiagnosis of congenital heart disease (CHD). This may result in inadvertent withholding of treatments or instituting incorrect therapies. Collaboration with the pediatric cardiology service is essential in developing standards for practice. It is essential that standards are set to ensure that competence is achieved and maintained with ongoing quality assurance. Neonatologists' main concern regarding the use of functional ultrasound by is the potential for misdiagnosis. Although it is important to recognize that CHD can be missed by neonatologists, the presence of a structural cardiac abnormality is almost always detected, even if a full diagnosis is not made.The studies performed by neonatologists serve a different purpose, as alluded to earlier in this review, and should complement those performed by cardiologists. Any abnormality detected or suspected should be confirmed by a trained pediatric cardiologist.

The demand for neonatologist-performed functional ultrasound is rising. There are numerous clinicians around the world who use point-of-care functional echocardiography without formal training. There is an urgent need to develop standardized training and accreditation programs to avoid the potential misuse of this skill. Such formal training programs are lacking. This highlights the need for collaboration with pediatric cardiologists in developing these programs as they possess the necessary skills. Formal training programs should include the use of available DVDs, books alongside didactic lectures. Knowledge of practical skills, ultrasound equipment and

modalities available also form part of the practical skill set. Emphasis should also be put into recognizing limitations and knowing when to call more experienced staff. These should be conducted by experienced neonatologists and interested pediatric cardiologists. Ongoing education and audit should be an integral part of any training program.[32] Once the skill set is acquired; logistic challenges need to be addressed. These include access to equipment, study reporting, archiving and storage. Recently Neonatal Patient Care Teams, HSC & SBH Child Health Standards Committee developed a neonatal clinical practice guideline for targeted neonatal echocardiography.[33]

Clinical Practice Guidelines [34]



Conclusion

Functional neonatal echocardiography proved to be a valuable bedside tool for managing neonatal hemodynamics in different NICU around the world. The expanded role of neonatologist-performed functional echocardiography is gaining momentum. There is mounting evidence that it can provide a more comprehensive assessment of the hemodynamic status of infants, and may influence management. There is an urgent need to encourage collaboration with pediatric cardiologists to establish standards for training and maintenance of competency, to develop guidelines for clinical practice and finally to ensure that the necessary clinical governance is in place to clearly identify the complementary roles of the neonatologist and pediatric cardiologist in this process.

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CASE REPORT

Naphrogenic Diabetes Insipidus

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Introduction

Regulation of water intake and excretion helps maintain extracellular fluid tonicity, within a narrow range, which is crucial for proper cell functions. Maintenance of water balance is primarily dependent on an intact thirst mechanism, vasopressin synthesis and renal tubular responsiveness to vasopressin action. Diabetes insipidus (DI) is a heterogeneous clinical syndrome of disturbance in water balance characterized by the passage of large volumes of dilute urine and the presence of an inordinate thirst. In children three pathophysiologic mechanisms give rise to polydypsia and polyuria:Central (vasopressin sensitive, hypothalamic, neurogenic) DI caused by defective vasopressin synthesis and/or secretion. Nephrogenic (vasopressin resistant) DI caused by defective renal tubular response to vasopressin action. Primary polydypsia due to compulsive water drinking (psychogenic) or defective thirst mechanism (dipsogenic). In children, Nephrogenic DI (NDI) is more common than Central DI (CDI) and is most often acquired.X linked NDI accounts for 90% of all the congenital forms of NDI. Nephrogenic diabetes insipidus results from a vasopressin-receptor or AQP_2 water channel defect, with the misfolding of the mutated membrane protein and its retention in the endoplasmic reticulum. The genetic defect is transmitted by an X-linked recessive or autosomal recessive trait. The genetic defect in the $AVPR_2$ is transmitted by an X-linked recessive trait. The AQP_2 gene defect is transmitted by an autosomal recessive trait.The acquired form of nephrogenic diabetes insipidus may result from adverse drug reactions, electrolyte disorders, urinary tract obstruction, or other conditions. Drugs such as lithium, amphotericin, and cisplatin are implicated regularly in this condition. Common electrolytes disorder, such as hypokalemia, hypercalcemia, and hypercalciuria, also can cause acquired nephrogenic diabetes insipidus. Associated systemic diseases include sickle cell disease and trait, amyloidosis, sarcoidosis, Sjögren syndrome, Fanconi syndrome, and renal tubular acidosis, Obstructive uropathy, diffuse renal injury, or any cause of renal failure can precipitate the development of acquired nephrogenic diabetes insipidus. Variance of neoplasms, such as sarcoma, are also associated with this condition. The polyuria associated with these conditions and medications is not as severe as that seen in central diabetes insipidus or nephrogenic diabetes insipidus due to genetic defect.

Case Report

Umayer, a one year eight months old immunized boy, 1st issue of a non-consanguinous parents hailing from Savar, Dhaka, admitted to Dhaka Shishu(Children) Hospital(DSH) with the complaints of excessive thirst, polyuria, and not gaining weight in comparism to other peers for one year and two months. Usually he drinks 3 litres of water per day and he voids nearly same amount. For these complaints he was admitted to DSH 1 year back and was diagnosed as a case of Central Diabetes Insipidus and treated with vesopressin nasal spray and discharged with advice. As the condition of patient

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did not improve again he was admitted to DSH for further evaluation and management. He was delivered at term by LUCS at hospital without any perinatal and postnatal complication. He is developmentally age appropriate. He belongs to a middle class family and is on family diet but his appetite is very poor.

Fig 1 *Umayer at forth day of admission*

On general examination he is active. vitals are within normal limit. His weight is 6.8 kg, supine length is 80 cm, WAZ: -4.7 SD, LAZ: -0.66 SD, WLZ: -5.6 SD, BMI is 10 which falls below 3rd centile . Other systemic examinations revealed no abnormality.

Investigation revealed initial urinary osmolality:70 mosmol/L, Serum osmolality:295 mosmol/L, Urinary specific Gravity:1.010, Serum electrolytes-Na:142.0 mmol/L, k:3.9 mmol/L, Cl:107.2 mmol/L, Urinary electrolytes Na:11.3 mmol/L, K:6.3 mmol/L, Cl:19.4 mmol/L, BUN:4.4 mmol/L, S.creatinine:41.6 µmol/L, RBS:5.3 mmol/L and abdominal ultrasonography revealed nomal finding. After getting all these reports we planned for Water deprivation test, after 8 hours of water deprivation Serum osmolality revealed 298 mosmol/L, and urinary osmolality 110 mosmol/L, then patient was given 2 mcg of Desmopressin intramuscularly after 4 hours of desmopressin serum osmolality revealed 305 mosmol/L and urinary osmolality 150 mosmol/L.

After all history, clinical examination and investigstions, clinical suspicion was strong regarding Nephrogenic Diabetes Insipidus and we planned to treat the patient with Hdrochlorothiazide-2 mg/kg/day 12 hourly and Idomethacin-2 mg/kg/day 12 hourly. With this treatment patient responded dramatically and after 24 hours of initiation of treatment his water intake was 1000 ml and output was 750 ml and his S. osmolality 298 mosmol/L urinary osmolality 350 mosmol/L. Genetic testing was not possible. Finally we conclude the case as Nephrogenic Diabetes Insipidus and the baby was discharged with advice to continue the treatment and follow up after 1 month. In the first follow up visit the baby was playful with normal thirst and normal urination, gained weight (500gm), appetite increases.

Fig 2 *Smiling Umayer after 1 month of treatment*

Discussion

Nephrogenic diabetes insipidus (NDI) is a rare genetic disease caused most commonly by mutations in two different genes. Though the exact prevalence is unknown, Arthus et al. found that the prevalence of NDI in Quebec, Canada to be 8.8 per 1,000,000 males. Interestingly, the Nova Scotia and New Brunswick population exhibited an incidence that was six times higher. In 90% of patients, the affected gene is arginine vasopressin receptor 2 (AVPR 2), whereas the remainder of patients have been shown to have had a defect in the aquaporin 2 (AQP2) gene. Both of these receptors play a crucial role in the concentration of urine by facilitating water reabsorption through the action of anti-diuretic hormone (ADH), also known as vasopressin.The clinical manifestation is similar in both case of

diabetes insipidus, presenting with excessive thirst and excretion of a large amount of dilute urine. Dehydration is common, and incontinence can occur secondary to chronic bladder distension. On investigation, there will be an increased plasma osmolarity and decreased urine osmolarity. As pituitary function is normal, ADH levels are likely to be abnormal or raised. Polyuria will continue as long as the patient is able to drink. If the patient is unable to drink and is still unable to concentrate the urine, then hypernatremia will ensue with its neurologic symptoms.

Our patient is a classical case of nephrogenic diabetes insipidus. He is a 1 year 8 months old male child who presented with polyuria and polydypsia for 1 year and 2 months. He was non responsive to nasal vasopressin and water deprivation test also suggest nephrogenic diabetes insipidus. Renal ultrasound is recommended to evaluate for hydronephrosis, dilatation of the urinary tract, and mega cystitis but we did not find anything wrong in Renal Ultrasonography. Urinary tract dilatation is a well-known but rare complication attributed mainly to the large volume of urine produced. Polyuria usually causes no more than mild to moderate hydronephrosis; however, rare cases of severe urinary tract dilatation have been reported. If a disease causing mutation has been identified in a family, then appropriate genetic testing and counseling should be offered to symptomatic individuals and high risk pregnancies.

General management of NDI involves a low salt, low protein diet with administration of diuretics and non-steroidal anti-inflammatory drugs (NSAIDS). Paradoxically, thiazide diuretics can cause a state of mild volume contraction so that more sodium and water can be reabsorbed in the proximal tubules and less water is delivered to the vasopressin-sensitive site of the principal cell. Prostaglandins may alleviate symptoms by reducing the glomerular filtration rate, increasing proximal tubule or distal tubule sodium reabsorption, and exerting an inhibitory effect on the action of vasopressin. A study that compared the treatment with HCTZ alone, HCTZ/triamterene, HCTZ/amiloride, and HCTZ/acemetacin (NSAID) demonstrated the superiority of the HCTZ/amiloride combination in that it prevented hypokalemia and metabolic alkalosis. In infants, special attention must be paid to minimize polyuria, hypernatremia, and volume depletion. In adults, treatment depends on the clinical symptoms of polyuria since electrolyte abnormalities and volume depletion are generally protected by the intact thirst mechanism. In patients complicated by both diabetes mellitus and insipidus, as in our patient, it may be difficult to discriminate between which entity is truly contributing intractable polyuria. Thus, the first step is to achieve strict glycemic control to avoid the exacerbation of unmitigated glucosuria before employing strategies to treat NDI.

Since the cloning of the V2R gene in 1992, developing the use of chaperones, a rescue mechanism to correct mutations, is possible. Chaperones are pharmacological ligands, which act by binding to and stabilizing specific conformations of their receptors. To this end, Morello and colleagues have successfully used vasopressin analogs capable of acting as chaperones to rescue misfolded mutant V2 receptors to their proper folding and function. A recent human pilot trial also showed that a low-affinity agent for V2R significantly decreased the 24 hour urine volume and water intake. Unfortunately, due to the potential interference with the cytochrome P450 metabolic pathway and hepatic toxicity, this trial was terminated at the phase II level. Despite this, the concept appears to be valid and research using this "chaperone" method continues.

Conclusion

Congenital NDI is a rare genetic disorder in which the majority of the affected are males who are diagnosed during infancy. However, carrier females have variable phenotype causing them to remain undiagnosed early in life. Their quality of life could be affected from distressing symptoms like extreme polyuria and polydypsia, putting them at a risk for dehydration. Strong suspicion should be maintained in the setting of classical symptoms and family history. Genetic testing should be encouraged to confirm the diagnosis.

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CASE REPORT

X - Linked Agammaglobulinemia

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Introduction

Agammaglobulinemia was the first primary immunodeficiency to be described in 1952 by Colonel Ogden Bruton who noted the absence of the "gammaglobulin"fraction on protein electrophoresis in a boy with recurrent bacterial sinopulmonary infections.[1]Subsequently, the gene responsible for X-Linked Agammaglobulinemia(XLA) was identified and named Bruton'styrosine kinase (*BTK*) at Xq21.3. This tyrosine kinase isrequired for maturation of the B-cell lineage. A mutation occurs at the Bruton's tyrosine kinase (Btk) gene that leads to a severe block in B cell development (at the pre-B cell to immature B cell stage) and a reduced immunoglobulin production in the serum. Btk is particularly responsible for mediating B cell development and maturation through a signaling effect on the B cell receptor BCR.

The recurrent bacterial infections typical of XLA begin after 6 months of age when the maternally acquired transplacental antibody levels decrease and the infant is unable to synthesize antibodies normally. Patients typically present in early childhood with recurrent infections, in particular with extracellular, encapsulated bacteria.[2]XLA has an incidence of approximately one in 100,000–200,000 and a prevalenceof one in 10,000.[3]We describe a 2-year-old boy with recurrent infections, pericardial effusion and XLA.

Case report

A 2 years old boy got admitted in Dhaka Shishu (Children) Hospital with cough and low grade intermittent fever for two weeks, generalized edema for the same duration and respiratory distress for the last 5 days prior to admission .

He was the second issue of a non consanguinous parents and was born at term by normal vaginal delivery with birth weight of 2500 grams having uneventful antenatal and perinatal period. He was on exclusive breast feeding up to 6 months of age and he was apparently well till one year of age. Since then he had been admitted several times for respiratory tract infections lasting for 3-5 days requiring perenteral antibiotics. At the age of one and half years he was diagnosed at Dhaka Shishu (Children) Hospital as a case of left sided encysted pleural effusion with residual pleural thickening and needed water seal drainage. Pleural fluid was sent for TB work up which was negative. He was well and asymptomatic for two months. After that period he has been suffering from recurrent lower respiratory tract infections every monthly requiring antibiotics for 5-7 days. He also had two episodes of acute diarrhoea lasting for 7 days requiring hospitalization. Hr has no history of contact with Tuberculus patients. The boy passes adequate urine and his dietary history is appropriate. His only male sib and parents are healthy.

On physical examination, the boy was dyspnoeic, febrile (101^0F), edematous, no lymphadenopathy and cyanosis. Oxygen saturation was 92% in room air. Regarding anthropometry, length- 81 cm (LFA 5^{th}

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percentile), weight-9 kg(WFA <5thpercentile). His skin survey revealed BCG mark and another scar mark present on left lateral chest wall. The boy is having tachycardia(150/min) and tachypnoea(70/min) and normal Blood Pressure(90/60 mm of Hg). His air entry was equal in both lung fields and his breath sound was vesicular with bilateral crepitations. The boy had normal JVP, low volume peripheral pulses with normal rhythm, his apex beat is shifted and diffuse in nature, muffled heart sounds without any murmur or gallop. His liver is enlarged(7.5cm), firm and tender and there was no ascites.

Fig 1 *Patient after admission in Cardiac ICU, Dhaka Shishu Hospital*

Our provisional diagnosis was pneumonia with pericardial effusion. Complete blood count showed- Hb 12.1 g/dL, Hct 44%, Platelet- 2,66,000/cmm, WBC- 16,400/cmm (Band 2%, Neutrophil- 75%, Eosinophil-2%, Monocyte- 3%, Lymphocyte- 20%, Absolute lymphocytes count (ALC)- 3280). His serum Albumin- 25g/L, Creatinine- 0.16 mg/dL, LDH- 788 U/L, AST- 30 U/L, ALT-26 U/L. Chest X-Ray showed enlarged cardiac Shadow and difuse infiltration in both lung fields. Echocardiography showed pericardial effusion with decreased ejection fraction (46%). Blood culture revealed *H.influenzae*. Gastric lavage and pericardial fluid analysis were negative for tuberculosis. Pericardiocentesis revealed 110 ml turbid fluid that contains high protein(4.5gm/L) and polymorphonuclear pleocytosis. Ultrasonography of abdomen revealed hepatomegaly.

Fig 2 *CXR showing cardiomegaly and homogenous opacities in both lung fields*

Fig 3 *After pericardiocentesis, about 110 ml of pericardial fluid was drawn*

His clinical condition was not improving after 7 days of broad spectrum antibiotic (Ceftriaxone and Flucloxacillin) therapy, then Meropenem and Vancomycin was added. As there was no improvement primary immunodeficiency was considered and serum immunoglobulins were measured which showed reduced level of IgG (1.34 g/L) and IgA (0.22 g/L). After giving immunoglobulin therapy there was dramatic improvement and after 20 days of treatment he became clinically well and discharged with the diagnosis of Primary Immunodeficiency Disorder (PID) with moderate pericardial effusion with secondary malnutrition. After one month he was further evaluated at CMC (Christian Medical

College), Vellore, India. Tuberculosis and HIV screening were negative. Lymphocyte subset analysis was done and showed severe B cell immunodeficiency (CD19- 0.1 %, 11 cells), (CD3- 90.2 %, 9783 cells), (CD4 – 37.6%, 4078 cells), (CD8- 51.1 %, 5542 cells), (CD56- 3.2%, 347 cells). Final diagnosis was X-Linked agammaglobulinemia with pericardial effusion and secondary malnutrition. He was advised to give prophylactic intravenous immunoglobulin (400mg/kg) once every four weeks. After receiving regular IVIg treatment monthly he is clinically well for the last one year.

Fig 4 *At the age of 3 years after getting regular dose of Immunoglobulin*

Discussion

X-linked Agammaglobulinaemia(XLA) is characterized by absence of mature B cells and the lack of specific antibody production. The classical description of patients with XLA is that they become ill in the first year of life, after maternal immune globulin has been depleted.[4] In our case, the boy started to show symptoms at around one year of age.

Symptoms of XLA may include infections at or near the surfaces of mucous membranes, such as the middle ear, sinuses, and lungs, but may also involve the blood stream, bones, or internal organs. The most common bacteria that cause infection are the pneumococcus, streptococcus, staphylococcus, and Haemophilus influenza. Patients with untreated XLA are prone to develop serious and even fatal infections.[5]The child described here had a history of several episodes of pneumonia, one episode of encysted pleural effusion which needed thoracotomy, two episodes of diarrhea and he presented to us with pericardial effusion and septicemia. His blood culture revealed growth of *H.influenza.*

X-linked Agammaglobulinaemia can be clinically diagnosed by the following clinical criteria: 1. Four or more new ear infections within one year, 2. Two or more sinus infections within one year, 3. Two or more months on antibiotics with little effect, 4. Two or more pneumonia within one year, 5. Failure of an infant to gain weight or grow normally, 6. Recurrent, deep skin or organ abscesses, 7. Persistant thrush in mouth or fungal infection on skin, 8. Need for IV antiobiotics to clear infections, 9. Two or more deep seated infections including septicemia, 10. A family history of PID.

Final diagnosis of XLA is suggested if IgG, IgM, and IgA are markedly reduced or absent. The most characteristic laboratory feature of XLA is the absence of B lymphocytes.[6]This is the most reliable test because it is not influenced by age, previous immunizations, or maternal IgG which passes across the placenta. Testing the gene Btk for mutations is required for molecular confirmation.[5,6]In our case, the child had reduced levels of IgG (1.34 g/L) and IgA (0.22g/L). His Lymphocyte subset analysis was done and showed severe B cell immunodeficiency (CD19- 0.1 %, 11 cells).

The defective gene can not be repaired or replaced, nor can B lymphocytes and plasma cells be induced to appear. The mainstay of therapy for patients with lack of immune globulins is immune globulin replacement Intravenously .[3-5] This therapy must be given at least monthly as the half-life of IgG is about 21 days, and it must be continued for life long. IVIG has been shown to reduce the number of infections in XLA[7] and other primary immune deficiencies in which antibody production is reduced or absent[8]. In our case, after receiving regular IVIg treatment monthly the child is clinically well for the last one year.

Conclusion

In any patient who present with recurrent significant bacterial infections that needs hospitalization in early age may need further evaluation for primary immunodeficiency. There remains a need for continued awareness among practitioners so that appropriate testing and treatment can be arranged. Scarcity of investigation facilities especially that for genetic analysis is to be resolved in near future.

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ABSTRACT FROM CURRENT LITERATURE

Diagnostic Accuracy of Indian Scale for Assessment of Autism (ISAA) in Children Aged 2-9 Years

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Indian Pediatrics Volume 52 March 15, 2015:212-216

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Objective: To determine the diagnostic accuracy of Indian Scale for Assessment of Autism (ISAA) in children aged 2-9 year at high risk of autism, and to ascertain the level of agreement with Childhood Autism Rating Scale (CARS).

Design: Diagnostic Accuracy study

Setting: Tertiary-level hospital.

Participants: Children aged between 2 and 9 year and considered to be at a high risk for autism (delayed development, and age-inappropriate cognition, speech, social interaction, behavior or play) were recruited. Those with diagnosed Hearing impairment, Cerebral palsy, Attention deficit hyperactivity disorder or Pervasive developmental disorders (PDD) were excluded.

Methods: Eligible children underwent a comprehensive assessment by an expert. The study group comprising of PDD, Global developmental delay (GDD) or Intellectual disability was administered ISAA by an investigator after one week. Both evaluators were blinded. ISAA results were compared to the Expert's diagnosis and CARS scores.

Results: Out of 102 eligible children, 90 formed the study group (63 males, mean age 4.5y). ISAA had a sensitivity 93.3, specificity of 97.4, positive and negative likelihood ratios 85.7 and 98.7 and positive and negative predictive values of 35.5 and 0.08, respectively. Reliability was good and validity sub-optimal (r low, in 4/6 domains). The optimal threshold point demarcating Autism from 'No autism' according to Receiver Operating Characteristic curve was ISAA score of 70. Level of agreement with CARS measured by Kappa coefficient was low (0.14).

Conclusions: The role of ISAA in 3-9 year old children at high risk for Autism is limited to identifying and certifying Autism at ISAA score of 70. It requires re-examination in 2-3 year olds.

Kawasaki Disease with Autoimmune Hemolytic Anemia

Dhwanee Thakkar, Nita Radhakrishnan, *Pk Pruthi And Anupam Sachdeva

Indian Pediatrics Volume 52, March 15, 2015:245-246

Background: Association of autoimmune haemolytic anaemia has been seldom reported with Kawasaki disease. Case characteristics: A 7-month-old boy, presented with prolonged fever, erythematous rash, severe pallor and hepatosplenomegaly.

Observations: Positive Direct Coombs test and coronary artery aneurysm on echocardiography. He was managed with steroids along with intravenous immunoglobulins and aspirin.

Outcome: Early identification of the condition helped in the management.

Message: Patients of autoimmune hemolytic anemia with unusual features such as prolonged fever, skin rash, and mixed antibody response in Coombs test should be evaluated for underlying Kawasaki disease as a possible etiology.

Nocturnal Enuresis among Nigerian Children and its Association with Sleep, Behavior and School Performance

Ou anyanwu, Rc Ibekwe, Ml Orji

Indian pediatrics volume 52__july 15, 2015:587-589

Objective: To study the association of nocturnal enuresis with sleep, behavior and school performance.
Methods: Hospital-based, cross-sectional descriptive study of 216 children (e"6-year-old) using structured questionnaire and behavioral tools.

Results: Prevalence of enuresis was 37.0%. Nocturnal enuresis was significantly associated with abnormal behaviour (P=0.049) and poor sleep hygiene (P<0.05). School performance was not associated with enuresis.

Conclusion: Children with nocturnal enuresis were at an increased risk of behavioral problems and poor sleep hygiene.

DSH NEWS

Celebration of World Breastfeeding Week, August, 2016 with rally started from Dhaka Shishu(Children) Hospital compound with our honourable Director Professor (Dr.) Manzoor Hussain and Honourable Academic Director Professor (Dr.) MAK Azad Chowdhury

Honourable Chairman of the management board, National Professor Shahla Khatun and Honourable Director of Dhaka Shishu (Children) Hospital, with the Honourable Member of Management Board, are celebrating the successful completion of two years by giving award to the honourable Chairman on 5th November 2016

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 conducts 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 runs its regular academic activities. It has established Basic Science Department since 2006.

Diploma course of paediatric nursing has been 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 Journals.

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.

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Students Qualified from Bangladesh Institute of Child Health

Undergoing Courses of BICH

Institution	Courses
Bangabandhu Sheikh Mujib Medical University	MD (Paediatrics) MD Paediatric Nephrology (sub-speciality) MD Neonatology (sub-speciality) DCH MS (Paediatric Surgery)
Bangladesh College of Physicians and Surgeons (BCPS)	FCPS Part II (Paediatrics) FCPS Neonatology FCPS Paediatric Nephrology FCPS Hematology & Oncology FCPS Paediatric Surgery FCPS Paediatric Neurology & Development FCPS Paediatric Pulmonology
Dhaka University	B.Sc in Health Technology (Lab)
Bangladesh Nursing Council	Diploma in Paediatric

Students Qualified from BICH till- June-2016

Course	Number
DCH	329
MD (Paediatrics)	96
MS (Paediatric)	93
FCPS (Paediatric)	23
MD (Neonatology)	12
MD (Paediatrics Nephrology)	4
Total	**559**

Foreign Student 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 July 2016-December-2016

Name of Courses		Number of Students
DCH	-	11
MD (Paediatrics)	Phase-A	15
MD (Neonatology)	Phase-A	2
MD (Paediatric Nephrology)	Phase-A	2
MS (Paediatric Surgery)	Phase-A	9
FCPS (Paediatric)	Part-II	3
Total		

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Seminar/Symposium & CME/CPD programs held at BICH (July to December, 2016)

Date	Topic	Presenter
31.07.2016	Update of Acute Lymphoblastic Leukemia	Department of Paediatric Haematology & Oncology (MU-8) Dhaka Shishu (Children) Hospital
21.08.2016	Common Skin Disease in Children	MU - VII Dhaka Shishu (Children) Hospital
26.09.2016	Rickets	MU-IX Dhaka Shishu (Children) Hospital
23.10.2016	Meconium Ileus	SU - II Dhaka Shishu (Children) Hospital
27.11.2016	Neonatal Cholestasis	MU – X Dhaka Shishu (Children) Hospital

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INSTRUCTIONS FOR AUTHORS

Dhaka Shishu Hospital Journal is the official organ of BICH which is the academic wing of DSH. It is published twice a year since 1984. The present editorial board has decided that the cover design will be in accordance with the subject of editorial in each issue. The editor welcome articles to be published in the journal as leading article, original article, review article, case report, current issues of child health, short report and junior's page where trainee doctors are encouraged to publish their topic of interest.

Original papers written in *english* will be considered for publication provided these have not been published previously and are not under consideration for publication elsewhere.

Conditions for manuscript submission:

- All manuscripts will be subjected to peer and editorial review.
- Accepted manuscripts become the property of the *Dhaka Shishu Hospital Journal*. Any reproduction in whole or part will require written permission from the editorial board of the journal.
- The author should obtain written permission from appropriate authority if the manuscript contains any table; data or illustration from previously published in other journals. The letter of permission should be submitted with the manuscript.
- If the photographs are not disguised, permission from the patient or parents/ guardians to print should accompany the manuscript. Otherwise identity will be blackened out.
- Rejected manuscripts/electronic copies/ illustrations/photographs will not be returned to the authors.
- Editors are not responsible for courier/postal failure.

Manuscript preparation: The format of the Dhaka Shishu Hospital Journal complies with *"Uniform Requirements for Manuscripts Submitted to Biomedical Journals"* published by the International Committee of Medical Journal Editors in Vancouver, British Columbia in 1979 (the widely accepted ***"Vancouver style"***)' published in the Annals of Internal Medicine 1982; 96: 766-71. All scientific units should be expressed in *System International (SI) units*. Authors are referred to Annals of Internal Medicine 1987; 106: 114-29 for guidance in the use of SI units. All drugs should be mentioned in their generic form.

- Should be typed in english and on one side of A4 (290 x 210cm) size white paper, using *Times New Roman* font size 12, with single space.
- There should be one original and two paper copies and one IBM compatible electronic copy. (CD or Pen drive)
- There should be a margin of 2.5 cm at top and bottom, and 1.2 cm left and right.
- Pages should be numbered in english numerical at the upper right hand, consecutively, beginning with the title page.
- Manuscripts should be submitted in the following order:
  - Title : should not exceed100 characters (Font size 16, bold)
  - Name of authors, e.g. 1. Prof. Saiful Islam FCPS, FRCP, 2. Dr. Nurun Nahar MD, these two author's name will be written like this; S Islam[1], N Nahar[2], etc. (Font size 12) Author's designation and name of place of study will be written after the end of the abstract. (Font size 10).
  - ***Abstract with a specific format with five sections(about 350 words maximum): Background, Objective, Methodology, Results, Conclusion, address of correspondence. All these sections will be Times New Roman, Font size 12 and italic , bold but text will not be bold. No references are allowed in the abstract.***

- Text (Introduction, Materials & Methods, Results, Discussion, Conclusion).
- Acknowledgements
- References

- Photographs:
  - In CD/ Pen drive
  - With appropriate labeling (number in English numerical, title of photographs and title of manuscripts.) It should be placed in appropriate place of the article.
- Illustrations:
  - All illustrations should be cited in the text
  - Illustration should be numbered in English numerical and labeled properly, placed appropriately in relation to text of manuscript.
- Tables:
  - Should be appropriately titled.
  - Numbered with Roman numerical serially in order of text description.
  - Abbreviations if used, should be explained in footnotes.
  - Same table should not be repeated as chart.
- Figures:
  - Should be appropriately titled and title will be placed below the figure.
  - Numbered with English numerical serially in order of text description.
- Placement:
  - All photographs, illustrations, tables and figures should be placed in the text in their appropriate places where their description are given.
- References:
  - *References from journal* should be indicated by superscript numbers consecutively in the text and placed after full stop (e.g. ....has been reported.[1] or as shown by Akbar[2] .....) in the order in which they are first mentioned and should be listed in numerical order on a separate sheet at the end of the article.
  - References cited only in tables or legends or illustrations should be numbered in accordance with a sequence established by the first mention in the text.
  - Titles of journals should be abbreviated according to Index Medicus or given in full.
  - References must include: (i) all authors, surnames and initials (if there are 6 authors or fewer) or if there are more than 6 authors, the first six authors followed by et al; (ii) the full title of the paper; (iii) the abbreviated or full title of the journal in italic; (iv) the year of publication; (v) the volume no will be bold; (vi) the first and last page numbers followed by full stop.*Example*: Khan NZ. A study of mentally handicapped children: aetiology and associated factors. *Bangladesh Journal of Child Health* 1985; **9**(2):102-08.
  - *References from books* must include: (i) authors name, (ii) title of article, (iii) editors name/s, (iv) name of the chapter, (v) place of publication, (vi) name of publisher, (vii) year of publication and page numbers. *Example*:Razvani I. An approach to inborn errors of metabolism. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson Textbook of Paediatrics.Philadelphia:Saunders,2004: p.397-98.
  - *Documents in electronic format* must include: (i) title, (ii) authors name,(iii) year of publication, (iv) web site address, (v) date of access. *Example*: United Nations Programme on HIV/AIDS. Children living in a world with AIDS. Geneva, 1978 (htpp://www.....), accessed on (dd/mm/year).

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