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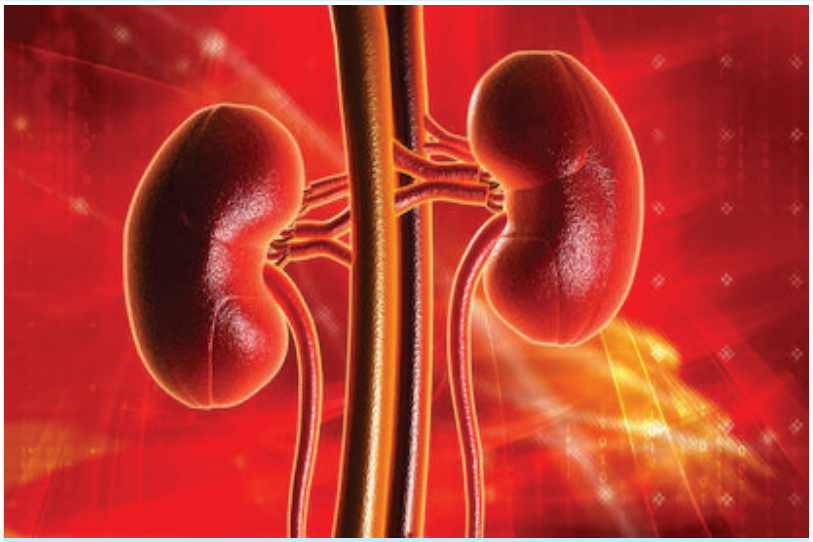

Editorial

"Neonatal Acute Kidney Injury - Do We Need to Pay More Attention?"

Bangladesh Institute of Child Health

Dhaka Shishu (Children) Hospital

DHAKA SHISHU (CHILDREN) HOSPITAL JOURNAL

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Contents

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DS (Child) H J 2018; 34(1) : 1-2

EDITORIAL

Neonatal Acute Kidney Injury - Do We Need to Pay More Attention?

Shireen Afroz

Introduction

Bangladesh has declared the SDG target of reducing neonatal mortality rate to 12 deaths per 1000 live births by 2030.[1]Recently it is observed that neonatal death from acute kidney injury (AKI) are being increasing. Perinatal asphyxia (PNA), sepsis and prematurity are the common etiology of neonatal AKI in Bangladesh.[2]One study from Bangladesh showed prevalence of Neonatal AKI 8 % and common cause being severe perinatal asphyxia.[3]Highest mortality rate is found in infantand neonate from AKI.[3] To attain SDG goal along with national new born health program services, we alsoneed to provide special emphasis on prompt diagnosis of neonatal AKI, immediate referral and proper management.

Worldwide neonatal AKI prevalence and mortality rates

In a recent study incidence of AKI was 605/2022 (29·9%). The rates varied by gestational age groups (i.e., ≥22 to <29 weeks =47·9%; ≥29 to <36 weeks =18·3%; and ≥36 weeks =36·7%). Infants with AKI had higher mortality compared to those without AKI.[4]

Previous research on the definition of AKI has largely excluded neonates. It was unclear whether pediatric AKI definition are applicable to neonates. Moreover high serum creatinine (SCr) during the first postnatal week that reflects maternal creatinine level also creates difficulty in labelling AKI at this period.Kidney Disease Improving Global Outcome has published AKI staging for new born.[5]

Optimizing the definition of neonatal AKI during first postnatal life

The Neonatal Kidney Collaborative (NKC) is an international, multidisciplinary groupcomposed of neonatologists and pediatric nephrologists, dedicated to investigate neonatal AKI.The AWAKEN (Assessment of Worldwide Acute Kidney injury Epidemiology in Neonates) study wasdesigned by NKC to describe the epidemiology of neonatal AKI, validate the definition of neonatal AKI, identify primary risk factors for neonatal AKI, and investigate the contribution of fluid management to AKI events and short-term outcomes.[6]Neonates with serum creatinine (sCr) rise ≥0.3 mg/dl and/or ≥50% sCr rise are more likely to die,

Neonatal acute kidney injury KDIGO classification[5]

Stage	Serum Creatinine	Urine Output
0	No change in sCr or rise <0.3 mg/dl	>1 ml/kg/h
1	sCr rise ≥0.3 mg/dl within 48 hr or sCr rise ≥1.5-1.9 x reference *sCr*[a] within 7 days	>0.5 ml/kg/h and ≤ 1 ml/kg/h
2	sCr rise ≥2-2.9 x reference *sCr*[a]	>0.3 ml/kg/h and ≤0.5 ml/kg/h
3	sCr rise ≥3 x reference *sCr*[a] or sCr rise ≥2.5 mg/dl[b] or receipt of dialysis	≤0.3 ml/kg/h

Difference between proposed neonatal AKI definition and KDIGO include:
[a] Reference *sCr* will be defined as the lowest previous sCr value.
[b] *sCr* value of 2.5 mg/dl represents less than 10 ml/min/1. 73m^2.

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even when controlling for confounders.In a recent published study these thresholds have been tested in newborns and hypothesized that different gestational age (GA) groups require different sCr thresholds. AWAKEN with ≥1sCr on postnatal days 1-2 and ≥1 sCr on postnatal days 3-8 were assessed. The ≥0.3 mg/dL rise outperformed ≥50% sCr rise. Addition of percent rise did not improve mortality predictability. The optimal sCr thresholds to predict AUC and specificity were ≥0.3 and ≥0.6 mg/dL for ≤29 weeks GA, and ≥0.1 and ≥0.3 mg/dL for >29 week GA. The maximum sCr value provides great specificity.Unique sCr rise cutoffs for different GA improves outcome prediction.[7]

Risk factors of neonatal AKI

As detailed in several reviews, risk factors and etiology of neonatal AKI are often multifactorial including condition leading to intravascular volume depletion eg.hypovolemia, sepsis, capillary leak, ischemia, (low cardiac output, vasopressor), nephrotoxic medication and multiple organ dysfunction.Neonates have additional unique conditions predisposing to and causing AKI including prenatal/perinatal events(eg. Maternal medications during pregnancy, prematurity, placental blood loss at birth, and perinatal asphyxia(PNA) with renal ischemia, post natal events (eg. Susceptibility to infections, excessive fluidlossesthrough skin and umbilical catheter associatedrenal vessel thrombosis, urologic anomalies). Premature birth, intrauterine growth retardation and low birth weight, are associated with poor nephron development and are often the consequence of pre-renal cause of AKI.

A study in Bangladesh reported 68% of the neonatal AKI was due to PNA[2]. Renal insufficiency can occur within 24 hours of a hypoxic insult and may lead to irreversible injury in prolonged asphyxia.In critically ill newborn 8-24% are affected with AKI and has a mortality rate of 10-61%.It has been observed that one-third of critically ill children develop AKI which is four fold higher than non-critically ill children.[8]

Prediction of AKI from clinical feature and APGAR score

It is difficult to predict AKI from clinical features, oliguria or APGAR score.[9]Butvery crucial thing is to screen all the babies with PNA for AKI. A single normal value of serum creatininecannot exclude AKI, a serial monitoring is important. Shock should be detected early and treated aggressively, as shock is associated with advanced stages of AKI. Extremely premature infant and those who survive an episode of AKI should be screened for chronic kidney disease (CKD) until early adulthood. Strategies to improve outcomes include thorough careful evaluation of nephrotoxic drugs- may reduce the incidence of AKI and its consequences among this population.

Conclusion

Improving nutritional status early in pregnancy, have the potential to optimize fetal growth and reduce the risk of preterm birth and low birth weight baby, thereby improving kidney health.There are definite criteria and guideline for assessing and diagnosing neonatal AKI. So, we need to improve our diagnostic efficacy and offering dialysis service everywhere for neonate. It is mandatory to keep the survived new born from AKI under regular follow up to prevent long term renal damage.

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DS (Child) H J 2018; 34(1) : 3-4

LEADING ARTICLE

History of Pediatric Anesthesia in Bangladesh

Md. Shahidul Islam

Children are very special people who require special care in order to provide safe anesthesia. The history of pediatric anesthesia is the steps towards maintaining normal limits of neurologic, respiratory, cardiovascular and other body systems. The goal of the specialty of the pediatric anesthesiology is the reduction of perioperative morbidity and mortality and promotion of monitoring, resuscitation and supportive fields through teaching, research, organizational activity throughout the world.[1,2] Before discussing the history of pediatric anesthesia in Bangladesh I want to discuss what was the global condition. Before introduction of ether in 1846, circumcision, amputation, excision of tumors and correction of gross deformity were performed in infants and children without any relief of pain. Struggling could be controlled by use of force. Pain was accepted as an unavoidable part of life. The outcome for both operation and patient was poor. Among advances in medicine during the past 150 years, the introduction of surgical anesthesia must be considered the greatest gift of medical profession to mankind, especially to children.[3]

Pediatric anesthesia has progressed rapidly throughout the years. The first recorded case of pediatric anesthesia was in 1842. Crawford Long a rural physician administered the first documented ether anesthesia in his office to a child of 8 years old African American boy for a toe amputation on July 1842.[4] He did not publish his work for 3 years. William T.G Morton performed the first successful pediatric ether anesthesia for removal of a mandibular tumor on October 16, 1846. It introduced a new era of surgical anesthesia.[5] Children were at greater risk of nausea and vomiting after ether anesthesia. James Young Simpson and John Snow practiced anesthesia with the more potent chloroform. Chloroform had a narrow margin of error with higher incidence of fatal hypotension and cardiac arrest. First recorded cardiac arrest and death by using chloroform was in 1847.[6,7]

Throughout the first decades of 20th century, most physicians treated children as miniature adults. It is believed that the development of modern pediatric anesthesia started in 1930.[8] The rapid growth of pediatric anesthesia was divided into two chronological categories. First were 1930 to 1950 and the second 1950 to present. During the first period the anesthesia techniques and equipment were developed. In the second phase with further techniques, equipment, refinement, modern anesthetics and vital system monitoring were introduced into everyday practice.[9] Ether and chloroform could be given for orthopedic and limb surgery but problems were with cleft lip, palate, abdominal, ENT and chest surgery.[10] Digital tracheal intubation with a soft rubber catheter was done in 1919. Breathing circuits and AYRE T piece with use of muscle relaxant and intubation was performed successfully.[11]

What about in Bangladesh? The history of pediatric anesthesia in Bangladesh was miserable. In early 1970's the only agent was ether and chloroform to anesthetize the pediatric patient. Only ether was continued due to the toxicity of chloroform. During that time pediatric endotracheal tube, laryngoscope, pediatric circuit and IV cannula was not available. IV channel were maintained by butterfly needle. Open ether anesthesia was practiced particularly in the peripheral and district hospital. The death rate was very high due to aspiration and respiratory depression.[12] The condition was horrible for the anesthetists and surgeon. Pediatric surgeon and pediatric anesthetists were not available. Our great teachers after completing their education from abroad came to the country and modern anesthesia was started.

The sacrifice of the pioneers of the anesthesia in our country brought pediatric anesthesia into a modern stage. Prof. A Kader, Prof. SNS Chowdhury, Prof. Afzalunnesa, Prof. KM Iqbal, Prof. Khalilur Rahman, Prof. Rashiduddin Ahmed, Prof. Kaisar Ahmed, Prof. Fakrunnisa and many other respected teachers contributed to the development of pediatric anesthesia

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in Bangladesh. The Dhaka Shishu Hospital is the pioneer of development of pediatric anesthetist and anesthesia. Prof. Jahanara Alauddin after completing her post graduation degree from England devoted herself in Dhaka Shishu Hospital. Her contribution to develop the pediatric anesthesia and training of the pediatric anesthetists is undoubtedly praiseworthy. Contribution from Prof. SNS Chowdhury, Dr. Zaheda Yusuf Zai, Dr. Abdul Jalil Baro Bhuyian, Dr. Nazir, Dr. Masud, Dr. Bashar, Dr. Maksud Isa and so on are also noteworthy. Currently other pediatric hospitals such as - MR Khan Shishu Hospital in Mirpur, Institute of Child and Mother Health in Matuail, Children Hospital in Chittagong are also established and are contributing to the growth of more innovative and successful pediatric anesthesia and surgeries in Bangladesh.

Pediatric anesthesia in the poor countries has not kept pace with the advances made in the developed countries. Access to safe anesthesia and pain relief during surgery could be considered a basic human right in the 21st century. International standard for safe practice of anesthesia adopted by the World Federation of Societies of Anesthesiologists (WFSA) in 1992, are seldom met in developing countries. In a recent survey only 13% of anesthetists are able to provide safe anesthesia for children.[13]

It is impossible to provide truly a complete history of pediatric anesthesia in our country because of lack of authentic documentation. The article is written with the personal experiences faced during 1980's. Now we have advanced a lot, many names and institutions have grown as a specialty. Many advancements and challenges to pediatric anesthesia are there on the horizon, though we are managing new born and critical patients with difficult intubation with modern devices and managing pediatric ICU and acute and chronic pain.[14] Still we are lacking modern instrumental support, proper medical support and skill training, disaster training and patient safety. In the words of Robert Smith, "We have not yet learned how monitor consciousness, and how to measure pain or fear. When we do and succeed, we not only keep children pink and alive, but also keep them smiling. We shall then have achieved something important[15], but we are much closer than we were in 1975 when those words were written.

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DS (Child) H J 2018; 34(1) : 5-10

ORIGINAL ARTICLE

Outcome of Neonatal Acute Kidney Injury in a Special Care Baby Unit (SCABU)

Tahmina Ferdaus[1], Shireen Afroz[2], Md Abid Hossian Mollah[3], Manisha Banerjee[4], Tofazzal Hossain Khan[5]

Abstract

Background: *Acute kidney injury (AKI) is common in neonates admitted in Special Care Baby Unit (SCABU) with high morbidity and mortality.*

Objective: *The present study was intended to see the immediate hospital outcome of neonatal acute kidney injury (AKI) in a Special Care Baby Unit (SCABU).*

Methods: *This observational study was carried out in SCABU, in the Department of Paediatrics, Dhaka Medical College Hospital, from October 2013 to March 2014. A total of 44 neonates (from 3-28 days) with AKI were included in this study. AKI staging was done by using pediatric RIFLE criteria as Risk, Injury, Failure. Patients were managed conservatively and immediate hospital outcome was assessed by SCABU stay, multiorgan failure, resolution of AKI, mortality and dialysis as needed.*

Results: *Demographic profile among the study population the neonate of d"7 days old comprised the main bulk. Majority of the neonates were of average birth weight. The diagnosis was based on estimated creatinine clearance(eCCL) criteria of pRIFLE showed that 40.9% neonates were at risk of AKI, 20.5% have had already injured. Higher proportions of neonates were classified as failure (38.6%).Outcome variables of neonatal AKI predicted by pRIFLE criteria was significantly higher in failure group in respect to SCABU stay (12.1+ 7.9) p value < 0.001, multiorgan failure (41.2 %) p value 0.026 and dialysis needed (88.2 %) p value < 0.001, resolution from AKI (47.1%) p value 0.885, Mortality (41.2%) p value 0.106. Here 43% neonates with AKI were improved with normal renal function and 29% improved with impaired renal function. Increased frequency of death (28%) in this series was due to multiorgan involvement and significantly higher in failure group with adequate dialysis support.*

Conclusion: *From the findings of the study it can be concluded that immediate hospital outcome of neonatal AKI is worst even after adequate dialysis support. Multiorgan involvements, increase length of hospital stay at SCABU, increase need for dialysis, are the important cause of increase mortality and morbidity. So, early detection, prompt referral and immediate supportive therapy could improve the outcome of neonatal AKI.*

Key words: *Neonatal acute kidney injury (AKI), Acute Kidney Failure (AKF),pediatric RIFLE criteria as Risk, Injury, Failure (p RIFLE),Outcome.*

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Introduction

Acute kidney injury (AKI) occurs in as many as 8% of neonates admitted to neonatal intensive care units. Most often, AKI is recognized as urine output < 0.5ml/kg/hour for 8 hours according to pediatric RIFLE criteria although nonoliguric neonatal AKI is being detected with increasing frequency.[1] The mortality of oliguric neonatal kidney failure may be as high as 60% in AKI and even higher in neonates with congenital heart disease or with anomalies of the genitourinary system.[2]

The cause of AKI is multifactorial.[2] The short-term outcome of AKI in neonates is highly dependent on the underlying etiology, the condition of other organs, and the facilities for renal replacement therapy. Mortality is more frequent and morbidity is much worse in neonates with multiorgan failure.[3] A substantial rise in serum creatinine (SCr) and a drop in urine output have been used to determine AKI in neonates. The Acute Dialysis Quality Initiative (ADQI) Group has published a consensus definition and classification system for acute kidney injury (AKI) termed the pRIFLE criteria (risk, injury, failure, loss, and end-stage.[4] The first 3 categories (risk, injury, and failure) of AKI based on whether the amplitude of SCr rise (or decreased in estimated GFR) and/or a drop in urine output[5]. The last two categories (loss and end-stage) defined temporary or permanent loss of kidney function after AKI.[5]

The present study was intended to determine the immediate hospital outcome of neonates with AKI. The findings obtained from the study would help us to institute early and effective intervention in neonates with AKI in order to prevent further progression of the disease and to reduce mortality and morbidity.

Materials and Methods

This observational study was carried out in the SCABU of Dhaka Medical College Hospital, Dhaka, from October 2013 to March 2014. All sick neonates (aged 3-28 days) admitted in SCABU and fulfilled the predefined eligibility criteria of AKI were the study population. A total of 44 neonates with AKI were included in the study as cases. AKI was suspected when urinary output was reduced <0.5 ml/kg/hr according to using pRIFLE criteria. Urine was collected by urine collecting adhesive bag and was recorded as per kilogram of body weight per hour in follow up sheets. From 3rd day of neonates to 28 days of neonates where urinary output was reduced o.5 ml/kg/hr or anuric for 12 hours then 2 ml blood sample was taken and immediately serum creatinine was done. Baseline serum creatinine was considered 0.3 mg/dl. Serum creatinine was noted when raised > 0.3 mg/dl or raised 1.5-2folds from the base line. Estimated creatinine clearance (eCCl) was measure by schwartch formula as follows :

$$eCCL = \frac{k \times Length}{Sr.\ Creatinine}$$

According to acute kidney injury classification (pRIFLE criteria), neonate with impaired renal function were classified as Risk, Injury, Failure group on the basis of eCCL and urine output.Patients with congenital anomalies and parents unwilling to allow their neonates to participate were excluded. Prior permission was taken for this study from the Ethical Committee of Dhaka Medical College Hospital, Dhaka, Bangladesh. Written informed consent was obtained from each parents/attendants. All precautions were taken to protect the anonymity of the participating subjects.

Operational definitions

Acute kidney injury classification: Paediatric RIFLE criteria[6-8]

	Estimated creatinine clearance(eCCL)	Urine output
Risk(stage-1)	eCCl decreased by 25%	<0.5ml/kg/hr for 8 hrs
Injury (stage-2)	eCCl decreased by 50%	<0.5ml/kg/hr for 16 hrs
Failure(stage-3)	eCCl decreased by 75%	<0.3ml/kg/hr 24 hrs or anuria for 12 hrs
Loss(stage-4)	Persistent failure for >4 weeks	
End-stage(stage-5)	Persistent failure > 3 month	

eCCl: Estimated creatinine clearance was measure **(**eCCL) by Schwartch formula as follows:

$$eCCL = \frac{k \times Length}{Sr.\ Creatinine}$$

Where, k (for preterm) = 0.27, k = (for term) = 0.37

Using computer software for SPSS windows version 16, data were processed and analyzed. The test statistics used to analyze the data were descriptive statistics, chi-square (χ^2) or fisher's exact test, probability test (for comparison of data presented on categorical scale), ANOVA statistics (for comparison of continuous data among three categories of AKI) and level of significance was set at 5% and p value <0.05 was considered significant.

Results

A total of 44 neonates (from 3-28 days) with AKI were included in the study. Demographic profile among the study population demonstrated that neonates of ≤7 days old comprised the main bulk. Majority of the neonates were of average birth weight.

Table I
Demographic profile among the study populations (n=44)

Variables	n (%)
Age	
<7 days	28 (64)
8-14 days	11 (25)
15-21 days	03 (7)
>21 days	02 (4)
Sex	
Male	21(48)
Female	23(52)
Male : Female	1: 0.9
Birth weight (gm)	
1000-1500	02(4)
>1500-2500	10(22)
>2500	32(73)
Gestational age	
Term	33(75)
Pre term	11(25)

Table I demonstrated that majority (64%) of the neonates were younger than 7 days age, male to female ratio is 1: 0.9. Most (73%) of them had average birth weight and 75% were term baby.

Table II
Distribution of neonates by their clinical characteristics (n=44) *

Clinical characteristics	No	%
Breathing difficulty	34	77.3
Anemia	33	75.0
Cyanosis	28	63.7
Reluctant to feed	23	52.3
Dehydration	22	50.0
Convulsion	19	43.2
Grunting	25	25.0
Distended abdomen	10	22.7
Fever	9	20.5

* Total will not correspond to 100%, for multiple responses.

Clinical characteristics were breathing difficulty (77.3%) and anemia (75%). The next common characteristics were cyanosis (63.7%), reluctant to feed (52.3%), dehydration (50%) and convulsion (43.2%). Other less common symptoms and signs were grunting, fever and distended abdomen.

Table III
*Causes of AKI in study cases (n=44)**

Perinatal/Neonatal characteristics	No	%
Prerenal		
Perinatal asphyxia stage II or stage III	30	68.2
Meconium aspiration syndrome	23	52.3
Septicaemia with shock	26	59.0
Early onset Neonatal Sepsis (EONS=18)	18	40.9
Late onset Neonatal Sepsis(LONS=8)	8	18.1
Prematurity	11	25.0
Diarrhoea	2	4.5
Vomiting	4	9.1
Renal		
Amino glycosides used during onset of AKI	23	52.3
Post-renal		
Hydro nephrosis with posterior urethral valve	1	2.3
Exostrophy of bladder	4	9.1
Cloacal exostrophy	2	4.5

* Total will not correspond to 100%, for multiple responses

More than two-thirds (68.2%) of the neonates experienced perinatal asphyxia stage-II or perinatal

Table IV
Outcome of different classes of AKI by pRIFLE criteria (n=44)

Outcome variables	pRIFLE			p-value
	Risk (n=19)	Injury (n=10)	Failure (n=15)	
SCABU stay* (days)	4.7 ±0.5	4.8± 0.4	12.1± 7.9	<0.001
Multi organ failure#	1(5.6)	4(44.4)	7(41.2)	0.026
Dialysis needed#	0(0.0)	0(0.0)	15(88.2)	<0.001
Resolution from AKI#	7(38.9)	4(44.4)	8(47.1)	0.885
Mortality#	2(11.1)	3(33.3)	7(41.2)	0.106

*Data were analysed using ANOVA statistics and were presented as mean±SD.
Data were analysed using Chi-square Test (χ^2) and were presented as n (%).

Table V
Immediate hospital outcome of neonates with AKI (n=44)

pRIFLE criteria	Improved with normal renal function	Improved with impaired renal function	Mortality (multi organ involvement, sepsis, perinatal asphyxia)
Risk	07	0	2
Injury	04	06	3
Failure	08	07	7
Total = 44	19(43.18%)	13(29.5%)	12(27.27%)

asphyxia stage-III and 52.3% were exposed to meconium aspiration syndrome during delivery. Prematurity was found in 11(25%) cases. Septicaemia with shock, acute respiratory distress syndrome, history of amino glycosides used in neonates and neonatal jaundice were reported in 59.1% (EONS 40.9% and LONS 18.2%), 20.5%, 52.3% and 13.6% respectively (Table III).

There was no difference between Risk and Injury in terms of duration of SCABU stay. However, failure group had a significantly longer stay compared to Risk and injury group ($p < 0.001$). Multiorgan failure was found to be staggeringly lower in the risk group compared to other two groups ($p = 0.026$). Most of the failure group needed dialysis as compared to the risk and injury group ($p < 0.001$). The resolution from AKI was almost similar among the groups ($p = 0.885$). The mortality was progressively higher from risk to failure groups ($p = 0.106$ but it was not statistically significant.

Overall 27.27 % of the neonates was suffering from acute kidney Injury and there cause of death were multi organ failure, septicemia, perinatal asphyxia, meconium aspiration syndrome and others. Improved with normal renal function (43.18%) and 29.5% improved with impaired renal function.

Discussion

The aims of the present study were to see the immediate outcome of neonates with AKI.The incidence of AKI varies according to the population studied, the level of attention of the hospital center and the country's level of development.[1,2] Presently, the tendency is to perceive AKI as an evo-lutionary spectrum and classify it with scales of severity or stages of AKI like the pRIFLE Scale, which was validated in 2007.[3,4] It has been shown that the incidence of AKI increases when applying the pRIFLE Scale.[5,6,7] Rovetto et al reported the incidence of AKI in the SCABU is 16 times higher than in wards, which shows that the risk of AKI increases as the patient is most critical.[8]

The widespread acceptance of consensus definitions for AKI is reflected in the increased utilization of pRIFLE in the literature. In order to progress further, establishment of a uniform definition for AKI

applicable in a variety of patient populations is necessary.[9-12.]

In compare to other study[13-15] there was no difference in age, sex, birth weight for diagnosis of AKI. Majority of causes are septicemia, hypovolemia, hypotension, multi -organ failure ,intravascular volume depletion, intraventricular hemorrhage, uses of phototherapy due to increased nitric oxide which causes vasodilatation, hypernatremia dehydration, different nephrotoxic drug users.[16-18.]

In the present study the outcome of AKI in neonates predicted by pRIFLE criteria showed significantly higher number of neonates in failure group with respect to SCABU stay. Multiorgan failure was found to be significantly higher in the Failure group. All of the failure group neonates needed dialysis . The mortality was increasingly higher in Failure Groups.

Previous study report also suggested that longest SCABU stay with intervention needed in both failure group.[18-20]

Likewise 15 neonates were diagnosed as acute kidney failure by pRIFLE and all of them needed intermittent peritoneal dialysis. Failure group of pRIFLE criteria had two group improved with normal renal function and improved with impaired renal function .both grops were needed IPD. 08 of neonates in failure group had improved with normal renal function after IPD and also 07 of neonates in failure group had impaired renal function. Impaired renal function group of patients referred to Chronic Kidney Disease follow up clinic.

The pediatric RIFLE (pRIFLE) was found to be better in classifying AKI and reflects the course of AKI in neonates admitted to the intensive care unit (NICU). [21-23]

Conclusion

From the findings of the study it can be concluded that immediate hospital outcome of neonatal AKI is worst even after adequate dialysis support. Multiorgan involvements, increase length of hospital stay at SCABU, increase need for dialysis, are the important cause of increase mortality and morbidity. So, early detection, prompt referral and immediate supportive therapy could improve the outcome of neonatal AKI.

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DS (Child) H J 2018; 34(1) : 11-14

ORIGINAL ARTICLE

Current Antimicrobial Susceptibility Pattern of Salmonella typhi and paratyphi in Children Suffering from Enteric Fever Admitted in a Tertiary Care Hospital

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Abstract

Background: *Enteric fever, specially Typhoid fever is endemic in Bangladesh. Due to lack of clean water, sanitation, and proper awareness it is more common in urban area and slum area of cities. Its diagnosis poses several problems, after diagnosis, it is important to treat with the right antibiotic before any complications can occur.*

Objective: *Aim of the study was to assess the current susceptibility pattern of typhoidal salmonellae to antimicrobial using for treatment of typhoid fever.*

Methods: *A prospective observational study was carried out for blood culture positive Typhoid fever admitted in Dhaka Shishu Hospital, during the period of May 2017 to April 2018. Children from 1year to 15 years with blood culture positive for S.Typhi and S.Para Typhi were included in this study.*

Results: *One hundred ten strain of Salmonella typhi and paratyphi were isolated from June 2017 to July 2018. Out of 110 isolated, 97 (88%) were Salmonella typhi and 13(12%) were paratyphi. Among them sensitivity to Ceftriaxone was 90 %(99) and cefixime 80% (88). Sensitivity to other drugs was Ampicillin or Amoxicillin 54%, Chloramphenicol 48%, Ciprofoxacin 42%, Azithromycin 38%, Co-trimoxazole 20% respectively.*

Conclusion: *In this study antimicrobial sensitivity testing showed that SalmonellaeTyphi as well as para typhi were not 100% sensitive to any drug. Besides this, study showed sensitivity reduce to 60% to 20 to previously used first line drugs and fluoroquinolone groups for treatment of typhoid fever. So judicial use of appropriate antibiotics for treatment of typhoid fever needed.*

Key words: *Typhoid fever, Salmonellae typhi, culture sensitivity.*

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Introduction

Enteric fever includes typhoid fever caused by Salmonella typhi and para typhoid fever by Salmonella paratyphi A B C. Typhoid fever affects roughly 21.6 million people annually, resulting 216,500 death.[1] More than 90%of this morbidity and mortality occurred in Asia.[2]

Enteric fever continues to be a major health problem despite the use of antibiotics and the development of newer antibacterial drugs.[3] If not treated properly, enteric fever carries a mortality rate of 30%, whilst appropriate antimicrobial treatment reduces the mortality rate to as low as 0.5%.[4] In case of enteric fever, it is often necessary to commence treatment before the results of laboratory sensitivity testing.[5] Salmonella typhi has rapidly gained resistance to antibiotics like ampicillin, chloramphenicol and cotrimoxazole and also to previously efficacious drug like ciprofloxacin.[6] The incidence of multidrug resistant (MDR) Salmonella typhi was reported to be as high as 60 per cent.[7]

Due to the variation in the susceptibility patterns of Salmonella typhi, it is important to constantly monitor the susceptibility patterns of Salmonella typhi to commonly prescribed antibiotics and to prevent the emergence of multi drug resistance.

Material and Methods

A prospective study was conducted at Dhaka Shishu Hospital. A total of 110 case of culture positive Salmonella typhi and paratyphi were considered for study. The study period was from May 2017 to April 2018 and data were collected from inpatient department. Inclusion criteria were fever of at least 101° F, minimum duration of 3 days, age were 1 years to 15 years. Blood was collected from patients at the day of enrolment.

Blood culture was done using a BacT/Alert automated system, and positive cultures were characterized using standard bacteriological procedures.[8] Antimicrobial susceptibility profiles were assessed by the disc diffusion method and resistance was determined per Clinical and Laboratory Standards Institute (CLSI) guideline as Needed.[9]

Data were entered and analyzed using SPSS version 23. Data has been summarized using percentage, and table.

Results

The majority of the patients were in the age group 6-15 years (57.77%) as shown in the table I. Out of 110 culture positive case 97(88.18%) were Salmonella typhi and 13(11.82%) were paratyphi. There were 56.36 % (62) male and 43.64% (48) female children.

Table I
Age specific group of enteric fever (n=110)

Age group (Years)	Frequency	Percent
1-5	47	42.23
6-15	63	57.77
Total	110	100

Table II
Laboratory findings in enteric fever (n=110)

		Bacteria isolated		
Parameter		Salmonella typhi	Salmonella paratyphi	Total
Leucocytes/cumm	<4000	19	3	22 (20.1%)
	4000-11000	72	9	81 (73.63%)
	>11000	5	2	7 (6.36%)
Hb (gm/dl) Mean±SD		(9.7±1.78)		
Widal test	1:160-1:320	59 (53.63%)	28 (25.45%)	87 (79.09%)
	>1:320	18 (16.36%)	5 (4.54%)	23 (20.91%)

In this study most of the patients 73.63% (81) had leucocytes count between 4000-11000/cumm, with the median WBC count of 8000/cumm. Leucopenia (WBC<4000/cumm) was 20.1% (22). Widal test 1:160-1:320 was 79.09% (87), >1:320 was 20.91% (23).

Antimicrobial susceptibility pattern of 110 of S. typhi and paratyphi were as sensitivity to ceftriaxone 90% (99), cefixime 80% (88) besides these sensitivity to other antimicrobial were as follows amoxicillin 54% (59), chloramphenicol 48%(52), ciprofloxacin 42% (46), azithromicin 38% (42), cotrimoxazole 32% (35), as shown in Table III.

Table III
Susceptibility pattern of salmonella species (n=110)

Antibiotics	Sensitive n(%)	Intermediate n(%)	Resistant n(%)
Ceftriaxone	99(90)	11(10)	0(0)
Cefixime	88(80)	17(16)	5(4)
Amoxicillin	59(54)	27(24)	24(22)
Chloramphenicol	52(48)	40(36)	18(16)
Ciprofloxacin	46(42)	43(38)	11(10)
Azithromycin	42(38)	46(42)	22(20)
Co-trimoxazole	35(32)	32(29)	43(39)

Discussion

Enteric fever is still a significant public health problem in many developing countries. It is a dread disease because of its long course and associated complications if not detected and treated early. There are reports of changing clinical features in typhoid fever caused by drug resistant S. typhi leading to difficult in clinical diagnosis. [10, 11]

Typhoid fever is endemic in Bangladesh, where there is a high incidence in children.[12]

In this study we found 42.23% of children were less than five years, which is also in agreement with an earlier report of 43.9% prevalence rate in Cebu city, Phillipine[13]. The reason is that children are the most vulnerable group in environments where inadequate water supply and poor environmental hygiene are problems because of their high level of ignorance. They are usually quick to satisfy their thirst irrespective of the water source especially if the water is apparently clean and without color.

In this study73.63% (n=81) had leucocytes count between 4000-11000/cumm, with the median WBC count of 8000/cumm.which was similar finding with the study done in children by Sudharsan et al.[14] that showed WBC count between 5000-10000/cumm in 70.9% cases.

Similarly, in our study leucocyte count below 4000/cumm was seen in 20.1%.which is similar to study done by Joshi et al.[15] where they showed WBC count <4000/cumm in 16% cases. In the present study, among 110 patients, antimicrobial susceptibility to ceftriaxone was 90% sensitive, 10% intermediate and cefixime was 80% sensitive to S. typhi. Whereas amoxicillin, chloramphenicol, ciprofloxacin, azithromycin, co-trimoxazole were sensitive in 54%, 48%, 42%, 38% and 32% respectively. Our study defer with Joshi et al.[15] where they showed S. typhi 100% sensitive to co-trimoxazole, chloramphenical, cefotaxime, ceftriaxone, cefixime and ofloxacin.

At the end of 1980s and 1990s salmonella developed resistance to first line antibiotics, namely amoxicillin, co- trimoxazole and chloramphenicol simultaneously.[16]

Our study showed that ciprofloxacin and azithromycin is sensitive 42% and 38% to S. typhi, this study differ with Misra et al.[17] More than 99% of S. typhi and 86.3% of paratyphi isolated in their study were susceptible to azithromycin. In 2003, the world Health Organization published guidelines that recommended azithromycine, ceftriaxone or cefixime for quinolone-resistant Salmonella typhi and paratyphi A infection.[18] But by the fifteen years S. typhi change its sensitivity to azithromycin and in our study we found only 38% sensitive and 42% intermediately sensitive to azithromycin.

Conclusion

The emergence of MDR strains has reduced the choice of antibiotics in many areas. There are two categories of drug resistance, resistance to antibiotics such as chloramphenical, ampicillin and trimethoprim-sulphamethoxazole and resistance to the fluroquinolone drugs. There are disturbing a recent report of the emergence of fluroquinolone resistant isolates in various parts of Asia & there have been a few reports of resistance to third generation cephalosporin in the same region. In This study antimicrobial sensitivity test showed that Salmonella typhi as well as paratyphi have not 100% sensitivity

to any antibiotics. Ceftriaxone and cefixime is the drug that show 90% and 80% sensitivity respectively.

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ORIGINAL ARTICLE

To Predict Mortality of Critically Ill Neonates Admitted in Intensive Care Unit (ICU) of a Tertiary Care Pediatric Hospital

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Abstract

Background*: Critically ill neonates who need intensive care are vulnerable to various derangement. Early and prompt recognition of these predictor helpful to care and their correction improves survival of these neonates.*

Objective*: To predict mortality of critically ill neonates admitted in ICU.*

Methods*: This observational study was carried out at NICU of Dhaka Shishu (Children) Hospital from January 2015 to July 2015. Total 121 neonates were enrolled according to inclusion criteria and analyzed their valuable biochemical profile specially electrolyte and blood gas status as a part of proper management as well as to predict their outcome.*

Results*: Among critically sick neonates, perinatal asphyxia was common disorder followed by sepsis. Biochemical profile specially electrolyte and acid-base disruption play important role to the outcome of critically sick neonates. Low pH, low potassium and high base-deficit level were found to have significant consequence.*

Conclusion*: Perinatal asphyxia constitute major cause of admission of critically sick neonates. Early detection of electrolyte and acid-base status is helpful to care and overall survival of these neonates. Mortality was the highest among neonatal sepsis followed by perinatal asphyxia. Metabolic acidosis and hypokalaemia were the predict or of outcome of these such neonates.*

Keywords*: Mortality, acid-base, electrolyte status.*

Introduction

Critically ill neonates commonly have acid-base and electrolyte disorder,a valuable predictor to a paediatrician about patient assessment, therapeutic decision and prognosis of the patient.[1] These occur in a variety of conditions and may remain unrecognized leading to morbidity and mortality irrespective of the primary disease, need more vigorous measures to reduce mortality in an emergency situation.

Blood gas measurements permitted the diagnosis of metabolic and respiratory acidosis or alkalosis associated with birth process and postnatal adaptation to air breathing.[1-3] The cardiovascular system undergoes changes after birth, respiratory gas exchange begins instead of 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]

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Blood gas analysis provides p^H, PCO_2 from which [HCO_3^-] and base excess (BE) can be derived.[5-8] Moreover, it is easily understandable and widely used at bed side management.[9] This traditional approaches to analysis of acid-base status adapted from Handerson-Hasselbach equation mathematically links the variables of p^H, PCO_2 and bicarbonate concentration [HCO_3^-].[10] The PCO_2 concentration in a given patient reflects the balance between metabolic production of CO_2 and excretion by ventilation. The normal range of PCO_2 after the first hours of life can be considered 35-45 mmHg, desirable CO_2 values for a specific situation may be either higher or lower.Elevation of PCO_2 concentration 10 mmHg decreases p^H by 0.08 while PCO_2 decrease of 10mm Hg increase p^H by 0.08.[11]

Blood gas measurements specially PaO_2 and SaO_2 provide important information about oxygenation but must be combined with other clinical and laboratory profile to assess a comprehensive picture. PaO_2 values vary considerably throughout the day in sick neonates. Hence O_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 O_2 saturation (SaO_2) not PaO_2 and this is relatively insensitive to detecting hyperoxaemia. Values of PaO_2 and SaO_2 may be lower in premature caused by reduced lung function.[12]

Marked structural and functional difference in children in comparison to adults, 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 blood pressure until late, therefore one cannot rely on hypotension to diagnose shock as in adults.[13] Identify the presence of metabolic acidosis, the categorization ends with a broad differential of anion gap (4-12mEq/L). This includes essential electrolytes eg. Cation (Na^+, K^+) and Anion (Cl^-, HCO_3^-).[14] Hence both acid-base and electrolyte status provide essential information about critically ill neonates and predict their mortality.

Perinatal asphyxia and neonatal sepsis both are common occurrence in neonates,major health problems in Bangladesh like other developing countries and a devastating cause of mortality. The acid-base and electrolyte abnormalities are common in perinatal asphyxia and neonatal sepsis.

Sodium and potassium are the major electrolyte in the body regulate the voltage of action potentials in skeletal muscles, nerves and myocardium. They play important role in maintenance of acid-base and fluid balance in the ECF through osmolality. Maintenance of intracellular osmolality is accomplished through sodium-potassium pump (active transport). Bicarbonate is an important electrolyte acts as a buffer to maintain the normal level of acidity (p^H) in the blood and other fluids in the body.[18]

In perinatal asphyxia and neonatal sepsis, syndrome of inappropriate secretion of antidiuretic hormone (SIADH) is a common problem where severe hyponatremia and hyperkalaemia can occur. Hyperkalaemia results from ischaemic insult reflected cellular changes leading to diminished oxidative phosphorylation and ATP production. This energy failure impairs ion pump function resulting in accumulation of intracellular Na^+ and extracellular K^+.[20] If inappropriate fluid-electrolyte and acid-base are replaced serious morbidity can result.Excessive sodium-bi-carbonate, improper preparation of formula feeds, increased insensible water loss specially in premature babies kept under radiant warmers can cause hypernatremia in neonates.[21]

A high index of suspicion, prompt recognition and through understanding of blood gas and common electrolyte abnormalities are necessary to ensure their total correction as well as reduce mortality of critically ill neonates admitted in ICU.[22]

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 and electrolyte status in critically ill neonates association with primary illness and their impact to predict mortality of these neonates.

Materials and Methods

This observational study was conducted at ICU, Dhaka Shishu (Children) Hospital during the period of January 2015 to July 2015. For each neonate, a detailed history from mother or other care-giver was recorded in a preset questionnaire.

Total 161 neonates admitted during this period among these 40 were excluded from this study due to any congenital anomalies (medical or surgical), 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.

121 neonates were analyzed for electrolyte status, blood gas as well as baseline investigation for proper

management. With all aseptic precaution, blood sample was collected in the disposable syringe.Blood gas analyzer (Gastat-600) based on the principle of potentiometry analyzed p^H, PCO_2respective electrodes. Base excess(BE) and [HCO_3^-] were calculated parameters from p^H and PCO_2were provided by the analyzer. Electrolyte analyzer (Rapid lab-1265) based on the principle of potentiometry analyzed Na^+, K^+, CI^-. Anion gap was calculated from the following formula.[14]$AG=[Na^+ + K^+]- [CI^- + HCO_3^-]$.

Each case was thoroughly examined and follow-up regularly. Definite neonatalsepticaemia was diagnosed by positive blood culture and probable septicaemia was diagnosed by a scoring system[23] or positive CRP. Relevant investigations for diagnosis and follow-up included complete blood count, blood culture, serum electrolyte, blood gas analysis, blood grouping, serum bilirubin andchest X-ray.

Normal range of p^H (7.35-7.45), PCO_2(35-45 mmHg), HCO_3 (23-27 mmol/L), Base excess (<10mmol/L) were considered.[11]Hyponatremia and hypernatremia were defined as serum sodium concentration <130mmol/L[24,25]and >150mmol/L[26,27]respectively. Hypokalaemia and hyperkalaemia were defined as serum potassium level <3.5 mmol/L[15,27]and>6 mmol/L[28,29] respectively.

Unpaired t-test was used to test the significance of difference of acid-base and electrolyte status of critically ill neonates and also the significance of difference among survivors and non-survivors.

Results

This study was carried out on the basis of neonates suffering from a wide variety of ailments attending ICU care (Fig 1) over a period of six months.Among 121, 35.53% perinatal asphyxia, 32.23% neonatal sepsis, 16.53% prematurity, 15.70% pneumonia (Fig 1).

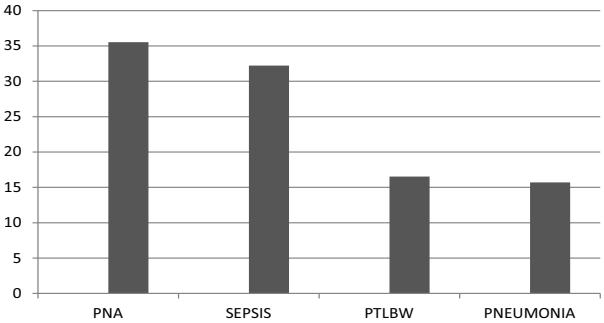

Fig 1 *Disease pattern (%) of Critically sick neonates*

In this study male predominance was found. 84 neonates were male and 37 were female, 2.27:1 (Table I).

On admission blood gas derangement was seen in 78(64.46%) critically sick neonates, 33(42.30%) died (Table II).

Table I
Age and sex distribution of critically sick neonates admitted in NICU

Age distribution (Days)	Sex distribution		Total
	Male (n%)	Female n (%)	n (%)
0 - 2	49(40.50)	24(19.84)	73(60.34)
3 -7	22(18.18)	08(6.61)	30(24.79)
8 - 28	13(10.74)	05(4.13)	18(14.87)
Total	84(69.42)	37(30.58)	121(100.00)

Table II
Disease profile with Acid-Base imbalance (on admission) and percentage of their non-survival (expired)

Primary disease	No. of patient (%)	Acid-Base imbalance (%)	Non-survival among Acid-Base imbalance (%)
Perinatal asphyxia	43(35.54)	27(22.31)	12(44.44)
Neonatal sepsis	39(32.23)	23(19.01)	9(39.13)
Preterm LBW	19(15.70)	15(12.40)	7(46.66)
Others	20(16.53)	13(10.74)	5(38.46)
Total	121(100.00)	78(64.46)	33(42.30)

Table II shows Acid-base status in critically sick neonates. Perinatal asphyxia was common disorder in this group of neonates having acid-base imbalance with the highest mortality.

On admission 91 babies (75.2%) had electrolyte abnormalities 41.32% died (Table III). 23.8% were from hyponatremia, 2.38% from hypernatremia, 14.28% from hypokalaemia, 35.7% were from hyperkalaemia and 23.86% had mixed groups (Table III). Case fatality rate was the highest in those with hypokalaemia (75%) followed by hyponatremia (62.5%), hypernatremia (50%) and lowest with hyperkalaemia (34%). Hypokalaemia was found to have a significantly higher mortality (p=.001) when compared to those with normal electrolyte values and similar underlying disorders (Table III).

K^+ level was found more, Na^+ and initial pH were found less in perinatal asphyxia than sepsis which were statistically significant (Table IV).

Non-survivors had less p^H, less potassium and more base-deficit level than survivors, statistically significant (Table V, Table III).

Overall mortality was the highest among neonatal sepsis (44%) followed by perinatal asphyxia (42%), prematurity (40%), pneumonia (37%) (Fig 2).

Table III

Disease pattern with electrolyte status at admission and mortality statistics (n=121)

Electrolyte status	Survival	Non-survival	Total	Case Fatality (%)	Statistics
Normal electrolyte	22	8	30	26.67	
Perinatal asphyxia	3	2	5	40.00	
Neonatal sepsis	9	4	13	30.76	
Preterm LBW	8	1	9	11.11	
Others	2	1	3	33.33	
Hyponatremia	6	10	16	62.50	p= .032
Perinatal asphyxia	1	6	7	85.71	
Neonatal sepsis	3	2	5	40.00	
Preterm LBW	0	2	2	100.00	
Others	2	0	2	00.00	
Hypernatremia	1	1	2	50	p= 0.744
Perinatal asphyxia	0	1	0	00	
Neonatal sepsis	0	1	1	100	
Others	1	0	1	00	
Hypokalemia	2	6	8	75	p= .001
Perinatal asphyxia	0	1	1	100	
Neonatal sepsis	1	2	3	66.67	
Preterm LBW	0	1	1	100.00	
Others	1	2	3	66.67	
Hyperkalemia	29	15	44	34.09	p= 0.251
Perinatal asphyxia	14	6	20	30.00	
Neonatal sepsis	7	2	9	22.22	
Preterm LBW	4	3	7	42.86	
Others	4	4	8	50.00	
Mixed	11	10	21	47.62	
Perinatal asphyxia	7	3	10	30.00	
Neonatal sepsis	2	6	8	75.00	
Preterm LBW	0	1	1	100.00	
Others	2	0	2	00.00	

Table IV
Acid-Base-Electrolyte parameters in Perinatal Asphyxia and Sepsis (on admission)

	PNA (n=43) Mean±SD	Sepsis (n=39) Mean±SD	p value
pH	7.33± 0.122	7.38± 0.12	**0.042^{s}**
PCO_2(mm of Hg)	32.67± 15.74	29.85± 11.71	0.364^{ns}
HCO_3^- (mmol/L)	16.83±4.91	19.31 ±10.09	0.155^{ns}
BE(mmol/L)	-7.14±5.17	-8.3±17.55	0.681^{ns}
Na^+ (mmol/L)	135.76 ±7.41	140.03 ±9.44	**0.026^{s}**
K^+ (mmol/L)	5.26 ±1.40	4.7 ±1.0	**0.016^{s}**
CI^- (mmol/L)	98.86 ±10.29	102.79 ±15.3	0.176^{ns}
Anion Gap (AG)	25.5±10.25	21.81±14.82	0.193^{ns}

Table IV- Comparative observation of acid-base-electrolyte parameter in major diagnosed critically sick neonates (perinatal asphyxia and neonatal sepsis). Here initial pH and Na^+ were found less, K^+ level was more in PNA than sepsis (statistically significant).

Table V
Pattern of Acid-Base parameters of Critically sick neonates (on admission) among Survivors and Non-Survivors (expired)

	Survivors (n =71) Mean ± SD	Non-Survivors (n =50) Mean ± SD	p value
pH	7.36 ± 0.1	7.3 ± 0.19	**0.011^{s}**
PC02 (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}
BE	-4.3 ± 6.88	-10.74 ±15.89	**0.004^{s}**

p value reached from unpaired t-test

Table V gives a comparative ongoing observation of blood gas status among survivors and non-survivors of critically sick neonates. Non-Survivors had less pH and more BE level than survivors (statistically significant).

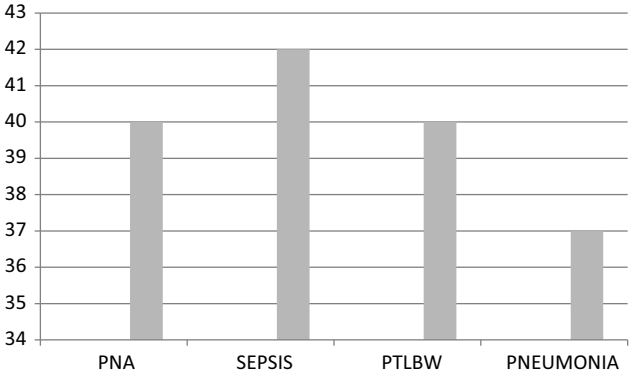

Fig 2 *Disease pattern (%) of non-survivors (expired) among critically sick neonates*

Discussion

This six months prospective study was undertaken in order to document the most common type of diseases with which the sick neonates are admitted in NICU of Dhaka Shishu Hospital and their consequence outcome. The selection was unbiased. The data may therefore be generalized on a population of sick neonates seeking ICU care.

Perinatal asphyxia was common disorder in accordance with the epidemiological pattern observed in this region with the highest mortality followed by sepsis. The patterns of diagnoses in our study are comparable to a similar study done in Lahore, Pakistan.[19]

Among total number of admitted critically sick neonates preponderance of males in this age group consistent with other studies.[20]

In this study critically sick neonates have acid-base abnormalities (64.46%) and **e**lectrolyte imbalance (75%) are discussed as follows to predict their consequence outcome. Acid-base disorders in critically sick neonatal ICU patients predicting survival by the presence of deranged acid-base variables.[26-28]

Metabolic acidosis is one of the most frequent acid-base disorder occurring in non-survivors[29,30] more in perinatal asphyxia[31,32] as this study. An abnormal pH <7.2[33,34] and <7[35] can be used as a predictor factor for unfavorable short term outcome in newborns. In this study lower mean pH in non-survivors was around 7.3.

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 mortality.[36]

Among electrolyte imbalance (75%) in critically sick neonates hyperkalaemia was the commonest (48%). These finding are in contrast to[37,38] who found by hyperkalaemia in 5.4% and 14.4% respectively in ICU admitted neonates.

In 48.7% neonates with hyperkalaemia there was concomitant metabolic acidosis, another important cause. The other possibilities of increased potassium release are tissue destruction, trauma, cephalhaematoma, hypothermia, bleeding, intravascular or extra vascular haemolysis, asphyxia, ischaemia and IVH.[39] Most of these condition were present in our study subjects.

Yuan et al.[17] have found hyperkalemia in 44% of sick neonates which is consistent with the present study.

Hyponatremia was the second most common electrolyte abnormality (13%) noted in this study. In a study conducted in a paediatric ICU, 9.5% of total admissions had hyponatremia.[38]

Hypokalaemia was less common (8.79%), electrolyte abnormality observed in the present study. However, a significantly lower (3.6%)[39] and two higher frequencies (14.8% & 13.9%)[40,37] were observed.

The risk of mortality in our study is significantly higher in patients with hypokalaemia (75%) in comparison to those with normal electrolyte values (26.6%). Higher risk of mortality was also observed in a prospective study of 727 sick children,[40] in contrast lowest mortality with hypokalaemia was reported by Rao et al.[38]

In our study hyponatremia was found to have a significantly higher mortality rate (62.5%) after hypokalaemia which is consistent with other study.[41]

Conclusion

Early detection of blood gas and electrolyte status helpful for overall management and better survival of critically ill neonates. Low p^H, low potassium and more base deficit can predict the mortality in this group of neonates.

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DS (Child) H J 2018; 34(1) : 22-25

ORIGINAL ARTICLE

Efficacy of Preoperative Topical Testosterone Therapy for Micro Phallic Hypospadias: Experience in Dhaka Shishu (Children) Hospital

Md. Ayub Ali[1], Md. Hasanuzzaman[2], Paritosh Kumar Palit[3]

Abstract

Introduction: *Surgical correction of genital defect was formally proposed when the size of the penis is sufficient to permit easy surgical repair. Delaying surgical repair until the phallus is of suitable size or pretreatment with hormones is recommended. In micro phallic hypospadias, temporary stimulation with testosterone either topical or parenteral to enlarge the penile size has been reported.*

Objective: *Aim of this study was to evaluate the efficacy of preoperative topical testosterone therapy in micro phallic hypospadias patients.*

Methods*: This retrospective study was carried out in the division of pediatric surgery, Dhaka Shishu (Children) Hospital. Hospital records of patients with micro phallic hypospadias from July 2015 to December 2017 were analyzed. All patients received testosterone cream 3 times daily for three weeks. Alteration of penile length, glans width and the adverse effects of testosterone therapy were recorded. Data were analyzed by using SPSS version 22.*

Results*: Total 35 patients received topical testosterone therapy during the study period. The mean penile length of penis was changed from 2.71±0.49 cm to 3.46±0.26 cm, which was statistically significant ($p<0.05$). The mean glans width was changed from 1.13±0.18 cm to 1.29±0.13 cm, which was statistically significant ($p<0.05$). Minor adverse effects were noted like pubic hair, genital pigmentation, and dermatitis.*

Conclusion: *Significant penile growth was observed with minor adverse effects after using topical testosterone therapy.*

Key Words: *Hypospadias, testosterone, micro phallus.*

Introduction

The word hypospadias is derived from the Greek words 'hypo', which means below, and 'spadon', which means rent or hole. This condition is characterized by urethral meatus located ectopically proximal to the normal location and on the ventral aspect of the penis. In the severe cases, the urethral meatus opens onto the scrotum and perineum.[1]

Boys with hypospadias are termed micro phallic based on penile length <2 standard deviations (SD) from normal.[2]

Hypospadias is a relatively common malformation. The growth in the penile length takes place for up to 5 years followed by little change until the onset of puberty. According to available data, a small penis in hypospadias is a result of fetal testosterone insufficiency or lack of scrotal fold receptivity during fetal life.[3]

A subgroup of boys with hypospadias, especially proximal cases, has been described as having a "significantly smaller than usual" penis in the context of selecting patients for preoperative androgen therapy. Others characterized boys with hypospadias

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as micro phallic based on penile length <2 standard deviations (SD) from normal (3.5cm), although accurately determining stretched penile length can be difficult in those proximal cases with ventral curvature and abnormal skin attachments from penoscrotal transposition. Glans size potentially is more readily measured, with several studies reporting circumferences in children with hypospadias selected for androgen stimulation.[2]

Micro phallic hypospadias is more common in severe hypospadias, which includes those with urethral opening on the shaft of penis or on the scrotum or perineum. Between1968-1990, the incidence of severe hypospadias has increased from 1.1 to 2.7 per 10,000 live births and by 1993, 5.5 severe cases per 10,000 live births per year.[4]

The lack of hard scientific data, results in the use of empirical judgment when the surgeon confronts with a hypospadiac micro phallic case. Delaying surgical repair until the phallus is of suitable size or pretreatment with hormones and proceeding with early repair is the matter of concern. Surgeons who delay surgery usually do so based on the lack of compelling evidence that endocrine therapy is truly beneficial. It is a matter of concern that prepubertal androgens may be detrimental. In contrast, surgeons who proceed with hormonal treatment and early surgery argue that delaying the operative procedure results in undue and avoidable psychological stress to the infant and parents.[5]

It has been proposed that better surgical conditions are obtained when hormones are used prior to hypospadias surgery, temporarily increasing penile length and glans circumference, favoring better local skin conditions and reducing surgical complications. Different hormones have been proposed: human chorionic gonadotropin (HCG), dihydrotestosterone (DHT) or testosterone. However, there are divergences about the hormone therapy of choice, time of use, appropriate dose, and means of application (topical or parenteral).[6]

If the physician chooses to use testosterone, he/she will face two alternative treatment methods. One can use testosterone propionate cream 2% applied to the penile shaft 3 times daily for 3 weeks or parenteral 2 mg/kg testosterone ethanate intramuscularly.[5]

So, considering the above mentioned facts, present study was undertaken to see the efficacy of topical testosterone therapy in micro phallic hypospadias patients.

Materials and Methods

This retrospective study was carried out in the division of pediatric surgery, Dhaka Shishu (Children) Hospital. Hospital records of patients with micro phallic hypospadias from July 2015 to December 2017 were analyzed. All patients received testosterone cream 3 times daily for three weeks. Alteration of penile length, glans width and the adverse effects of testosterone therapy were recorded. Data were analyzed by using SPSS version 22.

Results

The mean age of participants was 33.51±19.09 months (6 months to 60 months). Middle hypospadias was more common (65.8%) (Table I).

Table I
Types of hypospadias (n=35)

Types of hypospadias	No. (%)
Anterior	6(17.1)
Middle	23(65.8)
Posterior	6(17.1)

Before treatment, the mean length of penis of 35 patients was 2.71±0.49 cm. After 1st follow up, the penile length was increased and the mean was 2.97±0.45 cm. Then, after last follow up, the mean became 3.46±0.26 cm (Table II and Figure 1).

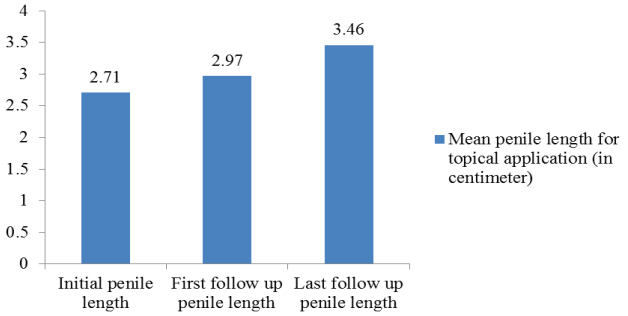

Fig 1 *Alteration of penile length*

Table II
Comparison of penile length before and after topical testosterone therapy

Penile length (In centimeters)	Before topical testosterone therapy (n=35)	After topical testosterone therapy (n=35)	P value*
Mean±SD	2.71±0.50	3.46±0.26	0.0001

*Paired 't' test

The penile length increases significantly in patients after topical testosterone therapy.

Table III
Comparison of glans width before and after topical testosterone therapy

Glans width (cm)	Before topical testosterone therapy (n=35)	After topical testosterone therapy (n=35)	P* value
Mean±SD	1.13±0.18	1.52±0.09	0.0001

* paired 't' test

Before treatment, the mean glans width of 35 patients was 1.13±0.18 cm. After 1st follow up, the glans width was increased and the mean was 1.29±0.13 cm. Then, after last follow up, the mean became 1.52±0.09 cm (Figure 2 & Table III).

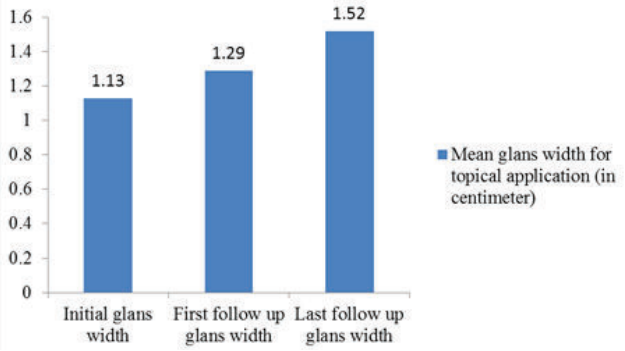

Fig 2 Mean glans width

The glans width also increased significantly ($p<0.05$) after topical testosterone therapy.

Minor adverse effects were noted in table IV.

Table IV
Adverse effects

Adverse effects	n (%)
Pubic hair	13(37.1%)
Genital pigmentation	35(100%)
Dermatitis	10(28.6%)

Discussion

Local or systemic application of testosterone is reported to stimulate penile growth.[2] It is preferable to increase the penile size before surgery for appropriate preoperative surgical condition and to minimize post operative complications. In general consideration, penile size is measured in terms of penile length and glans circumference. Normal penile length is considered >3.5cm (3.1-4.7cm), which is the measurement in newborn.[7]

Netto et al. had done a systematic review on hormone therapy in hypospadias surgery in 2013 and they found that adverse effect varies from study to study. Out of fourteen studies, ten articles reported adverse effects with quite varied results. Of the seven studies that evaluated topical administration, three described genital pigmentation as an adverse effect. Two articles also reported skin irritation at the site of topical application, but in a limited number of patients. The appearance of pubic hair was reported in half the studies, independently of the route of application, but in a limited number of patients. All of these side effects regressed after the end of hormone therapy.[6]

In this study preoperative topical testosterone was used in patients with penile length <3.5 cm and glans width <1.4 cm. Desired penile length was obtained after second follow up. So, their topical testosterone therapy was stopped after second follow up.

Before treatment, the mean length of penis of 35 patients was 2.71±0.50 cm. Then, after 4 weeks, the mean became 3.46±0.26 cm. The penile length increased significantly in patients after topical testosterone therapy as $p<0.05$ (obtained by paired sample t test). So, significant penile growth was noticed after topical testosterone was used. In the study by Chalapathi et al.[3] also, significant penile growth was noticed in topical testosterone therapy.

In boys with micro phallic hypospadias, it is difficult to measure stretched penile length especially in proximal cases with ventral curvature and abnormal skin attachment.[3] Glans size is easy to measure in these cases. So, in this study, the maximum glans width was measured before, during and after the therapy. Before treatment, the mean glans width of 35 patients was 1.13±0.18 cm. Then, after 4 weeks, the mean became 1.52±0.09 cm. The glans width increased significantly after 4 weeks of topical testosterone therapy as $p<0.05$ (obtained from paired sample t test). These observations are comparable to

the results of study by Gearhart and Jeffs, who reported that 2mg/kg testosterone enanthate, increased glans width from an average of 1.2 to 1.7 cm in 36 boys.[8]

Testosterone has various adverse effects which may limit its application. Adverse effects such as, development of pubic hair, facial hair, acne, bone growth, genital pigmentation and skin reactions occur topical testosterone therapy. In this study, three adverse effects, appearance of pubic hair, genital pigmentation and dermatitis has been reported. The bone growth was not evaluated due to time constrain.

When considering adverse effects of testosterone therapy, every patient developed genital pigmentation in topical testosterone therapy. This showed strong association of genital pigmentation with topical testosterone. The study by Chalapathi et al also reported that all patients, who were treated with topical testosterone, had pigmentation of genitalia[2]. Topical testosterone is associated with application site skin reactions. It includes mild to moderate erythema, pruritus, blisters or dermatitis.[16] this study revealed that ten patients in topical testosterone therapy developed dermatitis. The study by Chalapathi et al. reported that one patient in topical testosterone group suffered with dermatitis.[3]

Appearance of pubic hair is one of the secondary effects of testosterone. Systemic effect of topical testosterone causes fine pubic hair to appear. In this study, thirteen patients in topical testosterone therapy developed pubic hair. Nerli et al found that fine pubic hair was noted in two children receiving testosterone cream.[9]

A systemic review done by Netto et al. showed greater occurrence of adverse effects associated with topical use of testosterone, such as pigmentation of genitals (69% topical), appearance of pubic hair (35.2% topical) and skin irritation at the site of application (3.8%).[6] The incidence of adverse effects such as genital pigmentation and dermatitis in topical testosterone therapy may relate to unpredictable absorption and uncontrolled application of testosterone by parents.[3] Appearance of pubic hair is common adverse effect in topical testosterone therapy, as it is due to systemic effect of testosterone, which is one of the secondary sexual characteristics in male. These side effects regress after the cessation of testosterone therapy.

Conclusion

Significant penile growth was observed with little or acceptable adverse effects after using topical testosterone therapy.

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ORIGINAL ARTICLE

Oral Atenolol Therapy in the Treatment of Infantile Hemangioma: A Prospective Study

Kh Ahsanul Kabir[1], KMN Ferdous[2], F Hossain[3], MK Islam[4]

Abstract

Background*: Infantile haemangiomas (IH) are the most common tumors ofinfancy with an incidence of >2% of infants in general, and of 10% of Caucasian children, in particular.*

Objective: *The aim of this study was to assess the efficacy and safety of atenolol in the treatment of proliferating IHs.*

Methods*: This prospective study was conducted among 120 patients' up to 30 months of age, clinically diagnosed with IH's in surgical outpatient department (SOPD) of the Dhaka Shishu Hospital from July 2013 to March 2018. Atenolol was started initially 0.5mg/kg. Then doses were titrated according to clinical response (0.5- 3mg/kg/day OD). Parents were instructed to interrupt the administration of the drug if the child had a serious cough with dysponea or gastroenteritis with vomiting or diarrhoea. Patients' were advised to come for follow up visit and in each follow up blood pressure, percentage of regression (of size), color change, complications were recorded. The change in the appearance of IH was evaluated on a visual analogue scale (VAS). Regression in the size and color clearance of IHs were evaluated according to 0%-to-100% scale.*

Results: *Majority of the babies were from 1-10 months age group. Most of the infants were term babies and majority of the infants were girls. Majority of the IHs were located in head and neck regions. Majority of the mothers had multiple gestation pregnancy and few had family history of IH. Excellent, good and fair colour regression was found in 74.17%, 22.50% and 3.33% participants respectively. Excellent, good and fair size regression was found in 57.50%, 38.33% and 4.17% participants respectively. Adverse effects of drug like loose motion (7.50%) and sleep disturbance (3.33%) were found among the participants.*

Conclusion*: Atenolol is effective in the treatment of IHs with few minor side effects.*

Key words: *Infantile hemangioma, atenolol, adverse effect.*

Introduction

Infantile haemangiomas (IH) are the most common tumors ofinfancy with an incidence of >2% of infants in general, and of 10% of Caucasian children, in particular. IH typically presents few a weeks after births, and occur more frequently in girls.[1] Many are benign and do not require treatment, but potential complications include airway obstruction, visual

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compromise, disfigurement, ulceration, congestive heart failure, and death.[2] Previously, corticosteroids were the mainstay of treatment for complicated IHs. However, corticosteroids have undesired side effects, such as temporary growth retardation, an increased risk of infection, and behavioral changes.[3] Recently, propranolol, a nonselective b-blocker, became the preferred treatment for complicated or select types of IHs.[1] Still, its use is not risk-free and many adverse events have been documented, including: hypoglycemia, bronchial obstruction, hypotension, seizures, sleep disturbances, and gastrointestinal symptoms, among others.[4] On the other hand, atenolol, a hydrophilic cardio selective beta-blocker that acts principally on h1 receptors, does not cross the blood-brain barrier and has less h2 effects.[5] The aim of this study was to assess the efficacy and safety of atenolol in the treatment of proliferating IHs.

Materials and Methods

This prospective study was conducted among 120 patients up to 30 months of age, clinically diagnosed with IHs in surgical outpatient department (SOPD) of the Dhaka Shishu Hospital from July 2013 to March 2018. Patients previously treated for Infantile Hemangioma or having hemangioma presenting life threatening condition, cardiovascular disease contraindicating use of propranolol, known hypersensitivity to atenolol were also excluded from the study. Measurement of lesion was taken along long axis and another one perpendicular to this axis in centimeters with flexible soft rubber tape. Photograph was taken with digital camera. These photographs were taken prior to the treatment (baseline) and after the start of treatment at 2-8 weeks and 11-24 weeks. The change in the appearance of IH was evaluated on a visual analogue scale (VAS). The VAS uses a 100-mm scale on which –100 represented a doubling in the size and extent of the IH, 0 represented no change/baseline and +100 represented complete disappearance.[6] Atenolol was started initially 0.5mg/kg. Then doses were titrated according to clinical response (0.5- 3mg/kg/day OD). If no relevant adverse effects were detected after administration and if this was well tolerated, treatment was continued. Parents were instructed to interrupt the administration of the drug if the child had a serious cough with dysponea or gastroenteritis with vomiting or diarrhoea. They were also advised to call the investigator over phone for any adverse effects. Patients were advised to come for follow up visit at 2nd week, 1st month, 2nd month, 4th month, 6th month and 8th month. In each follow up blood pressure, percentage of regression (of size), color change and complications were recorded.

Regression in the size and color clearance of IHs were evaluated according to 0%-to-100% scale. An excellent response denotes 80% to 100% regression or color clearance. A good response denotes 50% to 80%. A fair response denotes 25% to 50% and finally a poor response denotes 25% or less.[7]

Frequency distributions for categorical variables were used to describe the characteristics of the total sample.The findings of the study were presented by frequency, percentage in tables and graphs.

Results

Majority of the babies were from 1-10 months age group. Most of the infants were termed babies and majority of the infants were girls. Majority of the IHs were located in head and neck regions. Majority of the mothers had multiple gestation pregnancy and few had family history of IH (table I). Excellent, good and fair colour regression was found in 74.17%, 22.50% and 3.33% participants respectively (figure 1). Excellent, good and fair size regression was found in 57.50%, 38.33% and 4.17% participants respectively (figure 2). Adverse effects of drug like loose motion (7.50%) and sleep disturbance (3.33%) were found among the participants (table II).

Table I

Base line characteristics of the participants (n=120)

Characteristics	n (%)
Age (in months)	
1-10 months	69(57.50)
11-20 months	38(31.67)
>20 months	13(10.83)
Term baby	110(91.67)
Female	82(68.33)
IH in head and neck region	81(67.5)
Multiple gestation pregnancy	85(70.83)
Family history of IH	5(4.17)

Table II

Adverse effect of drugs (n=120)

Adverse effect	n (%)
Loose motion	9(7.50)
Sleep disturbance	4(3.33)

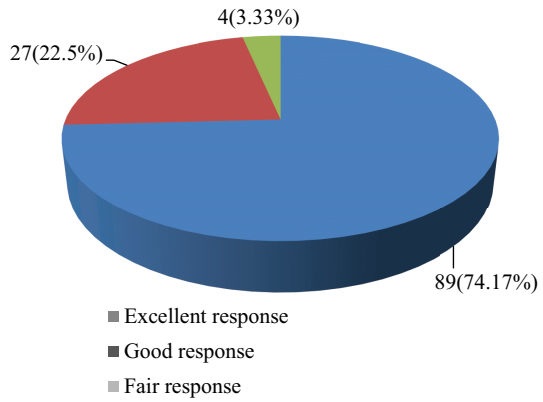

Fig 1 *Regression of color of IH*

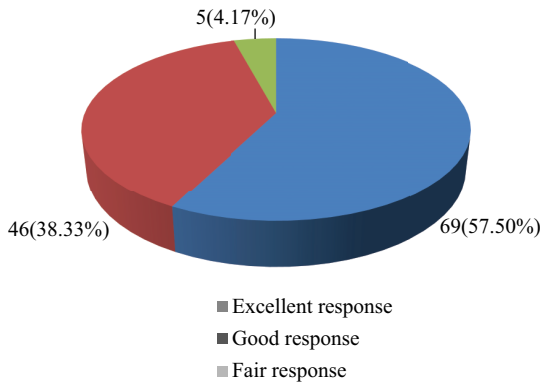

Fig 2 *Regression of size of IH*

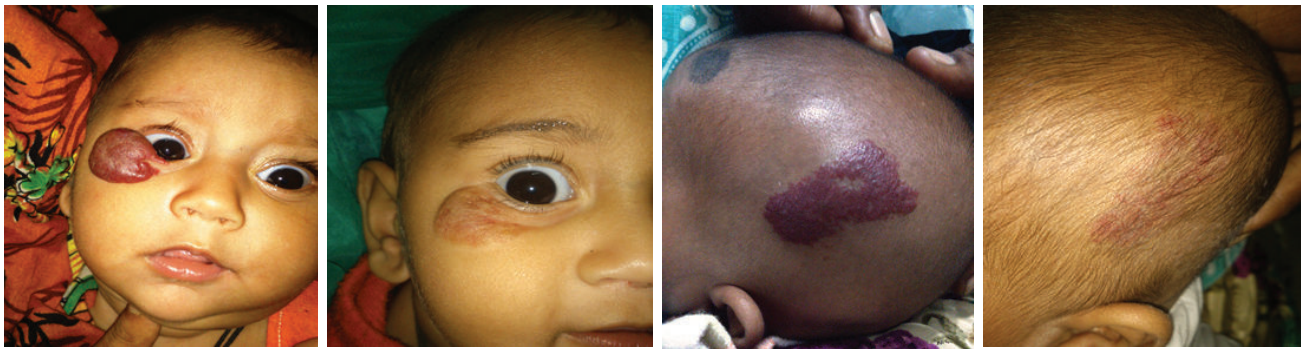

Fig 3 *Pre treatment and 6 months post treatment with atenolol*

Discussion

Infantile hemangiomas (IHs), also known as "hemangiomas of infancy," are common benign tumors of endothelial cells characterized by a unique pattern of rapid proliferation that occurs in the first months of life.

Infertility (IHs) are more common among female infants, however, although older data suggest female to male ratios ranging from 3:1, more recent studies suggest a range of 1.4:1 to 3:1.[2,11] Similar result found in the current study where it was found that majority of the participants were female. The present study also that most of the infants were termed baby and product of multiple gestations. Other study also reported that infants with hemangiomas are more likely to be female, premature, and products of multiple gestations.[12] Hemangioma can be found in all regions of the baby, but they occur most commonly in the head and region (60%), followed by the trunk (25%) and then the extremities (155).[13] Majority of the infants (67,5%) of the current study also had His located in the head and neck regions.

The first noticeable effects on treatment were the changes in color and softening of His, followed by regression of their sizes, Color regression of IH was determined by blind investigator using digital photograph. The photographs were taken prior to be treatment, after the start of treatment at 4 months and at 8 months. Excellent colour regression was found in 74.17% infants, Excellent size regression was found in 57.50% infants. This result was consistent with other studies. 14,15 Abraz, ua-Araya et al. had conducted a prospective comparative study to evaluate the effectiveness of atenolol against propranolol for the treatment of His where they reported that patients treated with atenolol had a complete response of 53.8%.[14] The study of Jiet al.evaluated the efficacy and safety of atenolol in the treatment of proliferating His. They observed an "excellent" treatment response (compete or nearly complete resolution of the IH) in 56.5% of patients at week 24.[15]

Clinical studies that addressed the adverse effects of atenololon children with IH have generated conflicting results. In a study by Abarzua-Araya et al[14] the authors should no significant adverse event in atenolol

treatment during the 6-month follow up. In the present study, any adverse events were recorded by parents between study visits and were documented by investigations at each visit. Among the 120 infants, few developed minor adverse effects like loose motion (7.50%) and sleep disturbance (3.33%). No patients developed any major adverse effects, In the study of de Grannf M, et al[4] mild side effects occurred in 40%)12/30) of patients and severe side effects occurred in 3% (1/30). Other study most common side effects of atenolol in the treatment of IHs were diarrhea, followed by central nervous system effects.[15] These minor side effects occurred in the present study were treatment and ceased after cessation of the drug.

Conclusion

Atenolol is effective in the treatment of IHs with few minor side effects.

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DS (Child) H J 2018; 34(1) : 30-35

ORIGINAL ARTICLE

Guillain-Barré Syndrome: Outcome of Treatment by IVIG vs. Methylprednisolone in Pediatric Intensive Care Unit of a Tertiary Care Hospital

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Abstract

Background: *Guillain-Barré Syndrome (GBS) deserves a serious attention in children. The treatment of GBS consists of supportive and immune-modulator treatments, among which intravenous immunoglobulin (IVIG) is considered as most effective. But IVIG is costly and many patients cannot afford.*

Objective: *To document the outcome of treatment of GBS patients by IVIG and Methylprednisolone.*

Methods: *This is a retrospective study conducted in the Pediatric intensive care unit of Dhaka Shishu Hospital from January 2013 to December 2016. Data was collected from the admission record file in pediatric intensive care unit of Dhaka Shishu Hospital. A total of 36 patients up to the age of 15 years presenting with Guillain-Barré Syndrome were included in the study. Treatment modalities including supportive, Intravenous Immunoglobulins (IVIG) and steroids were selected in patients with GBS depending upon indication and facilities available. Those who were unable to provide IVIG due to financial constrain were treated with Methylprednisolone. Results were analyzed using SPSS (version 16) for Windows.*

Results: *During the study period, a total of 36 patients were diagnosed and treated as GBS in pediatric intensive care unit. Among those, 34 (94.4%) patient were classical GBS. Most patients were in the age range of 3-5 years (21, 58.3%). Total 19 (52.8%) patients were treated with IVIG and rest was treated with steroid (17, 47.2%). 16 (44.4%) patient needed mechanical ventilation and among the patient needed mechanical ventilation 9 (56.3%) got treatment with IVIG and 7 (43.7%) got treatment with Methylprednisolone. After treatment 31 (86.2%) patients were improved and 5 (13.8%) were expired. Among the improved patient 16 (84.2%) were treated with IVIG and 15 (88.2%) were treated with Methylprednisolone.*

Conclusion: *Treatment outcome of GBS patient with Methylprednisolone is comparable with IVIG and can be considered in case of financial constrain.*

Key words: *Guillain-Barré syndrome, IVIG, methylprednisolone, outcome.*

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Introduction

Guillain-Barré syndrome is a post infectious polyneuropathy presumed to be immune mediated and manifests as Acute Flaccid Paralysis involving mainly motor, sometimes also sensory and autonomic nerves. It affects people of all ages including pediatric age group. The paralysis usually follows a nonspecific viral infection such as respiratory tract infection and acute gastroenteritis by one to two weeks. It is the commonest cause of acute flaccid paralysis (AFP) after eradication of poliomyelitis.[1,2] An incidence of 0.5-5/ 100000 children/year has been reported worldwide.[3]

GBS is characterized by muscle weakness and areflexia. Weakness usually begins in the lower extremities, progressively involves the trunk, the upper limbs and finally the bulbar muscles. Bulbar involvement occurs in about half of the cases that results respiratory insufficiency. This interferes with eating and increase the risk of aspiration. Respiratory effort must be monitored to prevent respiratory failure and respiratory arrest. Urinary incontinence or retention is a complication in about 20% of cases.[4,5] The autonomic nervous system is also involved in some cases where cardiovascular monitoring is important. Patients in early stages of this acute disease should be admitted to the hospital for observation because the ascending paralysis can rapidly involve respiratory muscles during the next 24hours& may need mechanical ventilation.[6]

With regard to clinical course and prognosis, classical Guillain-Barré Syndrome has to be differentiated from variants with accompanying central nervous system inflammation and from chronic inflammatory demyelinating polyneuropathy.[7]

AFP includes Guillain-Barré Syndrome, transverse myelitis, viral syndromes, spinal cord compromise (low back trauma, abscesses or tumors), toxins (lead, botulism etc.), metabolic neuropathies (hypokalemia, hypokalemic periodic paralysis, hypophosphatemia, polymyositis and dermatomyositis and tick bite.[8]GBS still remains the leading cause of AFP in developed as well as developing countries.

Diagnosis of GBS is usually clinical. In addition to routine investigations, CSF examination, electrophysiological and nerve conduction studies and plasmapheresis are usually done. CSF shows no pleocytosis and protein is variably normal or mildly elevated.

Rapidly progressive ascending paralysis is treated with intravenous immunoglobulin. Plasmapheresis and/or immunosuppressive drugs are alternatives if IVIG is ineffective. Supportive care such as respiratory support, treatment of secondary bacterial infection is important.

Federal Drug Association (FDA) approved IVIG indications include primary immunodeficiency disease, idiopathic/immune-mediated thrombocytopenic purpura (ITP), human immunodeficiency virus, bone marrow transplanation, Kawasaki disease and chronic lymphocytic leukemia.[9] High-dose immunoglobulin (hdIVIG) given at dose up to 2g/kg total dose has immunomodulatory actions mediated via a number of different effects like autoantibody neutralization and Interleukin 12 production.[10] Therapeutic IVIG is capable of neutralizing neuromuscular blocking antibodies in GBS by dose dependent, antibody mediated mechanism.[11]

Cost of IVIG is a major drawback in case of treating poor patient. Although steroids are not effective but chronic GBS patients are treated with high dose Methylprednisolone. Their effectiveness is less predictable. The dose of intravenous Methylprednisolone is usually considered 30mg/kg/dose for 5 consecutive days.[12]

Prognosis is good with complete recovery in more than 95% patients with GBS but it usually takes weeks to months,[13] 3% mortality due to respiratory & autonomic involvement. It is necessary to have the knowledge regarding practical scenario of critically ill patients of GBS, their treatment in ICU and overall outcome which will ultimately help us to modify the overall management plan in our limited critical care resource.

Materials and Methods

The study was conducted at Pediatric Intensive Care Unit, Dhaka Shishu (Children) Hospital from January 2013 to December 2016. A total of 36patients up to the age of 15 years were admitted and diagnosed as GBS. Detailed history and clinical examination for distribution of weakness, cranial nerve involvement, sensory loss and autonomic dysfunction and involvement of respiratory muscles and bulbar paralysis was recorded. Routine investigations including CBC, ESR, serum electrolytes, and random blood sugar were done in all patients. CSF examination was done in the second week of illness. Nerve

conduction studies and electromyography were not done due to unavailable resources. Treatment modalities including supportive, Intravenous Immunoglobulins (IVIG) and steroids were selected in patients with GBS depending upon indication and facilities available. Indications for IVIG were rapidly progressive disease, paralysis or impending paralysis of respiratory muscles, dysphagia and involvement of autonomic nervous system. Those who were unable to provide IVIG due to financial constrain were treated with Methylprednisolone. Data was collected and results were analyzed using SPSS (version 16) for Windows. A permission to conduct this study was obtained from Dhaka Shishu Hospital authority.

Results

A total of 39 patients were admitted in ICU with the diagnoses of acute flaccid paralysis and out of them 36 were GBS. Among these GBS patients, 34 (94.4%) were classical GBS and 2 (5.6%) was relapsing case. Most patients in this study were in the age range of 3-5 years (21, 58.3%) and other age group was 6-10 years (6, 16.7%), more than 10 years (5, 13.9%),1-2 years (4, 11.1%), and no patient were below 1 year age (Table I). In our study,numberof male patients was 20 (55.6%) and female was 16 (44.4%).

Table I
Age group distribution of the GBS patients admitted in ICU (n=36)

Age group (Years)	Number	Percentage
1-2	4	11.1
3-5	21	58.3
6-10	6	16.7
>10	5	13.9

Main reason of ICUadmission was respiratory muscle and bulbar paralysis (33, 91.7%), and other causes were autonomic involvement, aspiration pneumonia and for close monitoring. In 29 (80.6%) patients the antecedent event was respiratory tract infection and gastrointestinal infection was in 3 (8.3%) cases. In 4 (11.1%) cases there was no significant preceding illness. Regarding clinical assessment areflexia and paraesthesia was present in all cases, autonomic dysfunction in 20 (55.6%) and cranial nerve involvement was in 2 (5.6%) cases (Table II).

Table II
Major clinical findings of the enrolled cases (n=36)

Clinical findings	Number	Percentage
Areflexia	36	100
Autonomic dysfunction	20	55.6
Cranial nerve palsy	02	5.6
Paraesthesia	36	100

Cerebrospinal fluid study was done in 29 (80.6%) patients and albumin-cytological dissociation was found in 25 (86.2%) cases. The criteria for albumin-cytological dissociation were CSF protein more than 80mg/dl and cells less than 10/cmm.

Out of 36 patients, 19 (52.8%) were treated with IVIG and rest (17, 47.2%) were treated with intravenous steroid, as they could not afford IVIG. Mechanical ventilation in course of treatment was needed in 16 cases out of total 36(44.4%). Respiratory muscle paralysis (13, 81.3%) was the commonest indication of mechanical ventilation and cardiac arrest (3, 18.7%) was another cause.

Out of 16 patients who needed mechanical ventilation 9 (56.3%) were treated with IVIG and among them 6 (66.7%) were improved and 3 (33.3%) expired. Seven (43.7%) patients who needed mechanical ventilation were treated with Methylprednisolone and among them 5 (71.4%) were improved and 2 (28.6%) expired (Table III). Mean duration of ICU stay of patients treated with IVIG was 12.3±4.1 days in comparison to 14.8±6.0 days for Methylprednisolone group. Though the duration of ICU stay was shorter in IVIG group, it is not statistically significant (p=0.15).

Out of 36 patients, 31 (86.2%) patients were improved and transferred to ward and there average duration of ICU stay was 16.8 days. On the other hand, 5 (13.8%) patients expired during treatment in ICU and there average duration of ICU stay was 5.6 days, which indicates either rapid progression of the disease or delayed transfer to PICU. Total 16 (84.2%) patients were improved those who were treated with IVIG and 3 (15.8%) were expired and 15 (88.2%) were improved those who were treated with Methylprednisolone and 2 (11.8%) expired (Table IV).

Table III
Hospital outcome of the GBS patients admitted in ICU (n=36)

IVIG group (n=19, 52.8%)		Methylprednisolone group(n=17, 47.2%)		p-value
Improved	Expired	Improved	Expired	
16 (84.2%)	3 (15.8%)	15 (88.2%)	2 (11.8%)	0.89 (not significant)

Table IV
Outcome of cases those received mechanical ventilation (n=16)

IVIG group(n=9, 56.3%)		Methylprednisolone group(n=7, 43.7%)		p-value
Improved	Expired	Improved	Expired	
6 (66.7%)	3 (33.3%)	5 (71.4%)	2 (28.6%)	0.73 (not significant)

During treatment in PICU 12 (33.3%) patients developed aspiration pneumonia, cardiac arrest 3 (8.3%) and autonomic involvement was 20 (55.5%) (Figure I). There was no steroid related complication.

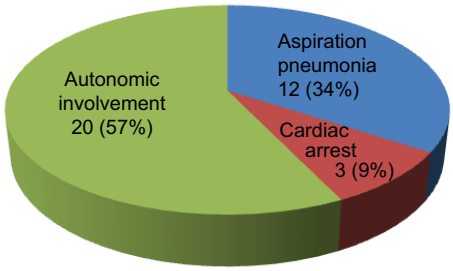

Fig 1 *Complications during treatment (n=35)*

Discussion

Acute flaccid paralysis in children is defined as acute onset of flaccid paralysis in one or more limbs or of bulbar paralysis in any child less than 15 years of age.[1] GBS is the commonest cause of AFP worldwide. Other causes include transverse myelitis, botulism, Tic bite paralysis and traumatic neuritis. In our study the commonest cause of AFP was also GBS followed by transverse myelitis. In a study from Australia common causes of AFP were GBS (47%) and transverse myelitis (19%) followed by acute disseminated encephalomyelitis, traumatic neuritis, tic bite paralysis and infantile botulism.[1] A study from Hongkong showed GBS 42%, followed by transverse myelitis 15% as the common causes of AFP in children.[2] Two different studies in Pakistan also describes GBS as the leading cause of AFP.[14,15]

Among the children with GBS 25 (69.4%) were under 5 years of age. It could be due to high incidence of infections in young children which is consistent with other studies from Hong Kong and Central America.[2,16] Male to female ratio in our study was 1.2:1 which also correlates with a study from Malaysia where this ratio was 1.3:1.[17]

Involvement of respiratory muscles was present in 27 (75%) patients. It is higher comparedto a study from Pakistan where this figure was 55.9%.[18] Cranial nerve involvement was found in 3.6% children which have been found to be 45% and 50% in other studies in pediatric patients.[19,20] Autonomic dysfunctions were noticed as 55.6% which is comparable with a study in children where it was 51%.[19]

CSF albuminocytological dissociation was present in 25 among 29 cases where CSF study was done(86.2%) in our study while in another study it was found in 97.5% of patients.[20] We performed CSF examination in second week of illness and our criteria for dissociation was protein >80 mg/dl and cells <10/cmm.

In our patients with GBS mortality was 13.8%. All these patients belong to mechanically ventilated group with or without other treatment modalities. Total 16 (44.4%) patient needed mechanical ventilation during treatment in ICU, which was 15% to 20% in other studies.[21,22]

It shows that the patients who have severe disease at onset and required mechanical ventilation had poor prognosis. The high mortality in this group also be related to complications like infection, aspiration, autonomic dysfunction and cardiac arrest.

Data on the course of recovery in our patients are better than in the literature. Briscoe et al reported a mean time of recovery after reaching the maximum

disability of the disease of 28 days, where in our study it was 13.5 days (5-28 days).[23]

In our study 52.8% patient received IVIG and 47.2% patient was treated with steroid. Patients treated with IVIG improved earlier than those with steroid, though not statistically significant, which is comparable with the study of Gureset al.[24] In children, three cases with rapid improvement during administration of intravenous immunoglobulin within four to seven days have been observed which is comparable with other studies.[24-28]

We have the impression that the benefit of intravenous immunoglobulinsis is better in children for GBS. Although in our study corticosteroids were also shown to be of value, their effectiveness seems to be inferior to immunoglobulins. But can be of lifesaving when IVIG is not available.

Conclusion

Treatment outcome of GBS patient with Methylprednisolone is comparable with IVIG and can be considered in case of financial constrain.

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ORIGINAL ARTICLE

Pattern and Outcome of Respiratory Disease in Dhaka Shishu Hospital: A One Year Analysis

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Abstract

Background: *Respiratory diseases are one of the major causes of childhood morbidity and mortality in Bangladesh. It is also a leading cause of hospital admission. The aim of this study is to analyze the pattern of respiratory disease admissions in a tertiary care hospital in a developing country.*

Methods: *We carried out a retrospective study on patients that presented with respiratory condition from January 2016 to December 2016.The medical records of patients admitted in the department of pediatric respiratory medicine unit (Pulmonology) over one-year period were reviewed. Information obtained included demography, diagnosis, mean duration of hospital stay and outcome of illness.*

Results: *Total 21 types of respiratory illness were categorized. The male to female patients ratio was 1.3:1. Among the patients 76.4% were less than five years old, 21.07% were between 5 and 9.9 years old, while 2.45% were 10 years and above. Pneumonia (54.41%) was the most common cases seen, followed by bronchiolitis (21.07%), PTB (2.94%), acute asthma (2.45%), pleural effusion (1.96%) and disseminated TB (1.96%). The median duration of admission was 12.9 days. Majority (93.6%) of admitted cases were discharged with advise, death was recorded in 2 (0.98%) children.Deaths occurred in children less than 5 years old, one with Bronchiolitis Obliterans Organizing Pneumonia and another with Tuberculosis.*

Conclusion: *Pneumonia, bronchiolitis and TB were the leading respiratory diseases among children admitted in Dhaka Shishu Hospital.*

Key Words: *Tuberculosis, pneumonia, bronchiolitis.*

Introduction

Respiratory tract infections are the leading cause of childhood hospital admissions.[1,2] But in the developing world, respiratory tract infections along with malaria and diarrheal diseases constitute the major causes of childhood morbidity and mortality particularly in the under-five age group.[3] Globally 7·6 million deaths occurred in children younger than 5 years in 2010. In these children, pneumonia (14·1%; 1·071 million), diarrhoea (9·9%; 0·751 million) and malaria (7·4%; 0·564 million) claimed the most lives.[4] Between 2000 and 2010, the global burden of deaths in children younger than 5 years decreased by 2 million, of which pneumonia, measles, and diarrhoea contributed the most to the overall.[4] Apart from the pneumonia, children may suffer a variety of respiratory illnesses ranging from common cold, nasopharyngitis, laryngitis, sinusitis, bronchiolitis, tonsillopharyngitis, asthma, tuberculosis to foreign body aspiration. Some of these cases may require hospital admission based

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on its severity.[5] Epidemiological studies have shown different estimates of the burden of respiratory diseases in different countries[6] but data on the pattern of pediatric respiratory illnesses admitted in the hospital is minimum and therefore, this study was done to ascertain the pattern and outcome of respiratory diseases in children presenting to the pediatric respiratory medicine unit of a tertiary level of hospital, Bangladesh.

Materials and Methods

This retrospective descriptive study was conducted in children between 0 month to 15 years of age admitted with respiratory illnesses in the department of pediatric respiratory medicine, Dhaka Shishu Hospital from January 2016 to December 2016 after taking permission from Dhaka Shishu Hospital ethical committee. All children between this age limit with acute respiratory illnesses were included in the study. We retrospectively analyzed the cases, admitted and treated in our department during the study period. Patients were admitted directly or referred from other units, clinics or hospitals. Data obtained from the registrar of pediatric pulmonology unit. Children who had coexisting morbidities like congenital heart disease, immunodeficiency and syndromic patients were excluded from the study. Data extracted from the records included total number of admissions and deaths, age, gender, mean duration of hospital stay, provisional diagnosis. Final diagnosis was based on the final assessment by the managing unit. It was based on the presenting clinical features and the results of laboratory tests. The obtained data were analyzed by using SPSS version 13.0 for Windows (SPSS Inc, Chicago, IL, USA).

Results

Total 204 patients with respiratory illness were admitted under pulmonology unit during January 2016 to December 2016. The prevalence of respiratory illness was highest in the age group 6-12 months. Respiratory illness was more often for boys than for girls (Figure 1). Maximum age of patients was 13 years and minimum age was one day. Their age distribution showed that 76.4% were less than five years old, 21.07% were between 5 and 9.9 years old, while 2.45% were 10 years and above (Table I). There were 21 categories of respiratory diseases among those admitted patients. The two common respiratory illnesses admitted during the period were pneumonia (54.41%) and bronchiolitis (21.07%) (Table II). Repeated admissions were noted among 18.3% of the children. Majority (93.6%) of admitted cases were discharged with advise.Death was recorded in 2 (0.98%) children. Deaths occurred in children less than 5 years old (Table IV).

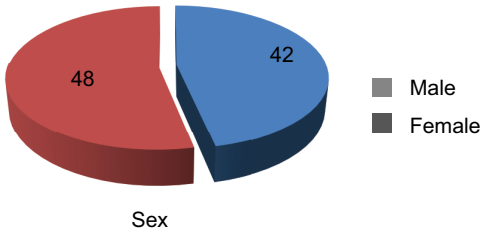

Fig 1 *Sex distribution among study patients(n=204)*

Table I
Distribution of study population according to Age and Sex (n=204)

Age Group	Number	Percentage
0-2 months	42	20.5
2-6 months	47	23.03
>6-12 months	67	32.8
>1-5 years	30	14.7
>5-10 years	13	6.3
>10 years	05	2.4

Table II
Frequency of respiratory illness by categories (n=204)

Diagnosis	Frequency	Percentage
Pneumonia	111	54.41
Bronchiolitis	43	21.08
Bronchial asthma	5	2.45
Pulmonary TB	6	2.94
Pleural Effusion	4	1.96
Disseminated TB	4	1.96
Pneumothorax	4	1.96
Pyopneumothorax	4	1.96
Collapse consolidation	4	1.96
Cystic Fibrosis	3	1.47
Bronchiolitis Obliterans	3	1.47
CCAM	2	0.98
Laryngomalacia	2	0.98
Cough and cold	2	0.98
Lung Abscess	1	0.49
Congenital Lobar emphysema	1	0.49
Atelectasis	1	0.49
Congenital Lung agenesis	1	0.49
Bronchiectasis	1	0.49
Croup	1	0.49
Kerosene poisoning	1	0.49

CCAM: Congenital Cystic Adenomatoid Malformation

Table III
Average duration of hospital stay (n=204)

Diagnosis	Duration (days)		
	Mean (SD)	Lower Limit	Upper Limit
Pneumonia	8.2(1.8)	2 days	25 days
Bronchiolitis	4.6(2.7)	3 days	7 days
Pleural Effusion	15.7(3.9)	12 days	29 days
Bronchial asthma	5.1(2.2)	3 days	10 days
Pulmonary TB	17.8(2.3)	12 days	31 days
Disseminated TB	19.7(3.6)	18 days	28 days
Pneumothorax	16.3(4.2)	12 days	23 days
Pyopneumothorax	15.5(2.8)	12 days	20 days
Collapse consolidation	21.6(4.2)	19 days	24 days
Cystic Fibrosis	20.1(3.7)	21 days	23 days
Bronchiolitis Obliterans	23.3(4.3)	21	24
CCAM	17.1(3.2)	18	24
Laryngomalacia	5.2(4.6)	3	18
Cough and cold	2.9(1.6)	2	3
Lung Abscess		15	15
Congenital Lobar emphysema		24	24
Atelectasis		7	7
Congenital Lung agenesis		15	15
Bronchiectasis		27	17
Croup		5	5
Kerosene poisoning		7	7

CCAM: Congenital Cystic Adenomatoid Malformation

Table IV
Disease outcome according to respiratory illness (n=204)

Outcome	Number (Percentage)
Discharge with advise (DA)	191 (93.6)
Discharge on request (DOR)	6 (2.9)
Referred	4 (1.9)
Death	2 (0.98)
DORB	1 (0.49)

Discussion

Respiratory diseases cause significant morbidity and mortality particularly in children less than five years old. In this study we found most of the respiratory illness occurred under five years. Various studies showed communicable diseases of the respiratory system cause significant morbidity and mortality particularly in children less than five years old. Chang et al[7] in Australia had a median age of 1.8 years which is similar to ours. Hospital-based case series studies in Nigeria; Port Harcourt et al[8], Benin et al[9] showed similar findings. The under-five age group is vulnerable to respiratory illness due to immature immune systems as well as less compliant lungs which increase their susceptibility to infections and other airway diseases resulting in increased morbidity and hospital admissions.[10] The frequency of respiratory disease decreases with age. We found respiratory illness was more often for boys than for girls. Uijen et al[11] in Netherlands and Ugwu et al[12] in Niger-Delta region of Nigeria both noted preponderance of males.

Pneumonia is a major childhood respiratory disease particularly in the developing parts of the world. In this study Pneumonia was the commonest respiratory condition followed by Bronchiolitis and Tuberculosis. They account for 78.4% of respiratory admissions. Similarly, in other studies, pneumonia, bronchiolitis, rhino sinusitis made up 96.8% of all respiratory illnesses and they found pneumonia as the most common of all the respiratory diseases.[8, 13-15] Desalu et al[16] found the most important causes of respiratory disease hospitalization with tuberculosis and pneumonia occupying the first and third most frequent indications for hospitalization. On the other hand, Kerevold et al[17] showed the upper airways diseases had the increased a preponderance in Norway. Some other studies showed chronic non-infective respiratory diseases predominate.[8,18]

Hospital stay in this study was longer for tuberculosis patients compared with other disease. Alamoudi et al[18] in Saudi Arabia reported similar findings; a majority of asthma and pneumonia patients were hospitalized for less than a week, while tuberculosis, and bronchiectasis accounted for most of the patients that spent more than two weeks following admission. Desalu et al[16] found the similar result. Length of hospital stay is an outcome that can be used to compare quality of care. It is also a key variable in economic evaluations of health care facilities. These data may provide information for the management of children hospitalized with ARI, which comprises about one third of pediatric admissions in Bangladesh.

In this study 93.6% patients were discharged with advise after completion of treatment. Four (1.9%) patients were referred for surgical management (Two patients for decortication, one patient for lobectomy, one patient for pleurodesis) to National institute of chest disease hospital. In this study 2 (0.98%) deaths were attributed, one with Bronchiolitis Obliterans Organizing Pneumonia and another with Tuberculosis. Mortality rate is a reflection of disease severity in any center. Different investigators have reported varying mortality rates for tuberculosis. In this study one death was attributed to Disseminated TB. In Ethiopia by Tessema et al[19], Busari et al[20] in Ido-Ekiti South-West, Nigeria, Salako et al[21] in Sagamu, South-West, Nigeria. They found a much higher mortality rate. In their study 23.2% of the hospitalized patient had unfavorable outcome. There are limitations of this study. This was a retrospective study. We found some incomplete records which affected our ability to quantify some variables.

Conclusion

We must pay attention to respiratory illness in children to reduce the morbidity in the population. This study has highlighted pneumonia, bronchiolitis and tuberculosis as major cause of respiratory diseases in our hospital.

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REVIEW ARTICLE

Importance of Bleeding Disorder in the Management of Dental Patients

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Abstract

Dental practitioners must be aware of the importance of bleeding disorders in the management of dental patients. Initial recognition of such bleeding disorders, knowledge of their possible systemic causes and clear idea in the management of the cases for dental treatment or when to refer those cases to secondary care, plays a crucial and important role in reducing potential complications and negative side effects. The purpose of this article is to review common bleeding disorders, complications and their management that dentists might find in their daily dental practice.

Key Words: *Bleeding disorders, complications, dental health care.*

Introduction

Dental practitioners must be aware of the impact of bleeding disorders on the management of their patients. Proper dental and medical evaluation of patients is therefore necessary before treatment, especially if an invasive dental procedure is planned. Patient evaluation and history should begin with standard medical questionnaires. Patients should be queried about any previous unusual bleeding episode after surgery or injury.

The patient should be asked for any history of significant and prolonged bleeding after dental extraction or bleeding from gingivae. A history of nasal or oral bleeding should be noted. Many bleeding disorders, such as hemophilia and von Willebrand disease, run in families; therefore, a family history of bleeding disorders should be carefully elicited.

A complete drug history is important. If a patient is taking anticoagulant drugs, it will be important to consult his or her physician before any major surgical procedure. In addi tion, a number of medications may interfere with hemostasis and prolonged bleeding. Drugs of abuse, such as alcohol or heroin, may also cause excess bleeding[2] by causing liver damage resulting in altered production of coagulation factors. Patients with liver disease may have jaundice, spider nevi, ascites and other signs of impaired hepatic function. A cardiac patient can show tachycardia or hypertension, which may make hemostasis more difficult to achieve. When a bleeding disorder is suspected, laboratory investigations, including blood counts and clotting studies, should be carried out.

Preoperative laboratory test

Preoperative laboratory tests of the hemostatic system [1-2] are:

- bleeding time to determine platelet function (normal range: 2-7 minutes)
- activated partial thromboplastin time to evaluate the intrinsic coagulation pathway (normal range: 25 ± 10 seconds)
- Prothrombin time (normal range 12-15 seconds) with international normalized ratio (normal range: 1.0) to measure the function of extrinsic coagulation pathway.
- platelet count to quantify platelet function (normal range: 150,000–450,000/¼L).

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Table I
Laboratory-based investigations

Name of test	Evaluate	Normal values	Prolonged in
Bleeding time	To assess the platelet and normal blood vessel functions	2-9 minutes, Depend on the Method used	Platelet disorders,vessel-wall disorders,fibrinogen disorders and Von Willebrand's disease
Activated partial thromboplastin time (APTT)	The intrinsic pathway of blood coagulation(which includes Factor II , V, X	25± 10 second	Heparin treatment, liver diseases,hemophilia, DIC,massive transfusion and in some auto-imune treatments, such as in lupus anticoagulant
Prothrombin time (PT)	The extrinsic pathway (Factors II,V,VII,X and fibrinogen)	12- 15 seconds	Warfarintreatment,liver disease,vitamink deficiency, DIC

Types of Bleeding Disorders

Bleeding disorders can be classified as coagulation factor deficiencies, platelet disorders, vascular disorders, or fibrinolytic defects (Table I).[3,4]

Among the congenital coagulation defects, hemophilia A, hemophilia B (Christmas disease) and von Willebrand's disease are the most common. Hemophilia A is due to a deficiency of clotting factor VIII or antihemophilic factor. It is an inherited X-linked recessive trait found in males. Symptoms may include delayed bleeding, ecchymosis, deep hematomas, epistaxis, spontaneous gingival bleeding and hemarthrosis. A factor VIII level of 6% to 30% of normal factor activity (mild hemophilia) is associated with bleeding during surgery or trauma; 1% to 5% with bleeding after mild injury; and <1% (severe hemophilia) with spontaneous bleeding [3].

Management

Management of hemophilia A among patients undergoing dental surgery consists of [2] increasing factor VIII levels, replacing factor VIII and inhibiting fibrinolysis (Table II).

Options for factor VIII replacement are factor VIII concentrates, fresh frozen plasma and cryoprecipitate.

Antifibrinolytic therapy can be used postoperatively to protect the formed blood clot. Epsilon-aminocaproic acid and tranexamic acid are the common agents used. Tranexamic acid in an oral rinse helps prevent postoperative bleeding from surgical wounds.

Table II
Common bleeding disorders

Coagulation factor deficiencies	Congenital Hemophilia A and B von Willebrand's disease **Acquired** Liver disease Vitamin K deficiency, warfarin use Disseminated intravascular coagulation
Platelet disorders	Quantitative disorder (thrombocytopenia) Immune-mediated Idiopathic Drug-induced Collagen vascular disease Non-immune-mediated Disseminated intravascular coagulation Leukemia **Qualitative disorder** Congenital von Willebrand disease Acquired Drug-induced Liver disease Alcoholism
Vascular disorders	Scurvy Purpura
Fibrinolytic defects	Streptokinase therapy

Table III
Presurgery treatment for Hemophilia A[4]

Condition	Treatment and dose	Potential complication
Mild bleeding	Dose:15 U/ kg factor VIII every 8-12 hours for 1-2 days Target: 30% of normal level	Hemarthosis, oropharyngeal or dental bleeding, epistaxis, hematuria
Major bleeding	Dose: 50 U/kg factor VIII every 8-12 hours for 7-14 days Target:80-100% of normal level	Same potential complications as for mild bleeding,as well as central nervous system hemorrhage, gastrointestinal bleeding

Table IV
Systemic diseases causing coagulopathies[1]

Disease	Common causes	Resulting coagulation defect
Renal failure and uremia	Diabetes mellitus Glomerulonephritis Hypertension	Inhibition of adhesion and primary aggregation of platelets from glycoprotein IIb-IIIa deficit
Hepatic failure	Alcohol abuse Hepatitis B and C Cancer(e.g.) Hepatocellular carcinoma	Obstructive jaundice: deficiency of vitamin k-dependent factors II,VII,IX and X Loss of liver tissue and all clotting factors except VIII and von Wllebrand factor
Bone marrow failure	Renal failure and uremia	Reduced number of functioning platelets Anemia from bone marrow suppression

Postoperative use of epsilon aminocaproic acid can considerably reduce the level of factor required to control bleeding when used in conjunction with presurgical infusion of factor required to control bleeding when used in conjunction with presurgical infusion of factor VIII concentrate.[5]

Hemophilia B is the result of factor IX deficiency. It is managed by replacement therapy with highly purified, virally inactivated factor IX concentrates. Prothrombin complex concentrates can also be used for factor IX replacement von Willebrand disease is the most common hereditary coagulation disorder with an incidence of 1 in 10,000. It is not sex linked. It is classified as Type I to Type III and may vary in severity. For mild conditions, use of DDAVP may be sufficient, but severe disease warrants factor VIII replacement.

Other than congenital diseases, coagulation defects may be acquired and from a variety of sources (Table IV). In liver diseases, the synthesis of clotting factors may be reduced due to parenchymal damage or obstruction.[8] These patients may have a variety of bleeding disorders depending on the extent of their liver disease. Management options for hemostatic defects in liver disease[5] include vitamin K and fresh frozen plasma infusion (immediate but temporary effect) for prolonged prothrombin time and partial thromboplastin time; cryoprecipitate for replacement of factor VIII deficiency; and replacement therapy for disseminated intravascular coagulation. Patients suffering from viral hepatitis are a potential source of cross infection, and necessary precautions should be taken during procedures. Drug doses frequently need to be modified in these patients due to impaired liver function. The patient's physician should be consulted before making any changes in the drug regimen.

Table V
Principal agents for systemic management of patients with bleeding disorders[3]

Agent	Description	Common indications
Platelets	1 unit=50mL; may raise count by 6,000	Platelet count <10,000 in nonbleeding individuals <50,000 in presurgical level >50,000 in actively bleeding individuals
Fresh frozen plasma	1 unit = 150-250 mL 1 hour to thaw Contains factors II, VII, IX, X, XI, XII, XIII, and heat-labile V and VII	Undiagnosed bleeding disorder with active bleeding Severe liver disease When transfusing >10 units of blood
Cryoprecipitate	1 unit = 10-15 mL	Hemophilia A, von Willebrand's disease, Fibrinogen deficiency
Factor VIII concentrate	1 unit raise factor VIII level 2% Heat-treated contains von Willebrand's factor	Hemophilia A, with active bleeding or presurgery; some case of von Willebrand's disease
Factor IX concentrate	1 unit raises factor IX level 1-1.5% Containts factors II, VII, IX, and X	Hemophilia B, with bleeding or presurgery
Tranexamic acid	Antifibrinolytic: 4.8% mouth rinse Systemic: 25 mg/kg every 8 hours	Adjunct to support clot formation for any bleeding disorder

Coagulopathies can be drug induced. Warfarin, low-molecular-weight heparin and dicumarol (coumadin) are the most commonly used anticoagulant drugs. Treatment must be modified in accordance with the medications that the patient is taking and their impact on coagulation. Platelet disorders can be hereditary or acquired and may be due to decreased platelet production, excess consumption or altered function. The most common clinical features are bleeding from superficial lesions and cuts, spontaneous gingival bleeding, petechiae, ecchymosis and epistaxis. The minimum blood platelet level before dental surgical procedures is approximately 50,000/μL; extensive surgery may require > 100,000μL. Replacement therapy may be required if the count is below this level. Usually, platelet transfusion is carried out 30 minutes before surgery. In patients with platelet levels below 100,000μ/L prolonged oozing may occur, but local measures are usually sufficient to control the bleeding. In cases of idiopathic thrombocytopenic purpura, an acquired platelet disorder, oral systemic steroids may be prescribed 7-10 days before surgery to increase the platelet count to safe levels.[9]

Vascular defects are rare and usually associated with mild bleeding confined to skin or mucosa.[10] Scurvy, hereditary hemorrhagic telangiectasia and other vascular defects are usually treated with laser ablation, embolization or coagulation. Recognizing vascular lesions during examination, aspiration or advanced imaging may lead to modification of treatment planning.

Table VI
Local hemostatic agents

Brand name	Generic name or description
Gelfoam (Pfizer, Markham)	Absorbant gelatin sponge material
Surgicel (Ethicon, Markham)	Oxidized cellulose
Tissel (Baxter, Mississauga)	Fibrin sealant
Thrombostat (Pfizer)	Topical thrombin
Cyklokapron (Pfizer)	Tranexamic acid
Amicar (with, Markham)	Epsilone-aminocaproic acid

Oral Findings

Platelet deficiencies can cause ecchymosis in oral mucosa and promote spontaneous gingival bleeding. These disorders may be present alone or in conjunction with gingival hyperplasia in cases of leukemia.Hemosiderin and other blood degradation products can cause brown deposits on the surface of teeth due to chronic bleeding.

People with Hemophilia may have multiple bleeding events over their lifetime. The frequency of bleeding depends on the severity of hemophilia. Hemarthrosis of the temporomandibular joint is uncommon.[3]

The incidence of dental caries and periodontal diseases is higher in patients with bleeding disorders, which may be because of lack of effective oral hygiene and professional dental care due to fear of oral bleeding.

Dental Management

The management of patients with bleeding disorders depends on the severity of the condition and the invasivness of the planned dental procedure. If the procedure has limited invasiveness and the patient has a mild bleeding disorder, only slight or no modification will be required. In patients with severe bleeding disorders, the goal is to minimize the challenge to the patient by restoring the hemostatic system to acceptable levels and maintaining hemostasis by local and adjunctive methods. The patient's physician should be consulted before invasive treatment is undertaken. In patients with drug-induced coagulopathies, drugs may be stopped or the doses modified. For irreversible coagulopathies, replacement of missing factors may be necessary (Table IV).

Pain Control

In patients with coagulopathies, nerve-block anesthetic injections are contraindicated unless there is no better alternative and prophylaxis is provided, as the anesthetic solution is deposited in a highly vascularized area, which carries a risk of hematoma formation.[10,11] The commonly used blocks require minimum clotting factor levels of 20% to 30%.

Extravasation of blood in the oropharyngeal area by an inferior alveolar block or in the pterygoid plexus can produce gross swelling, pain, dysphasia, respiratory obstruction and risk of death from asphyxia.[12,14] Anesthetic infiltration and intraligamentary anesthesia are potential alternatives to nerve block in many cases. An anesthetic with a vasoconstrictor should be used when possible. Alternative techniques, including sedation with diazepam or nitrous oxide–oxygen analgesia, can be employed to reduce or eliminate the need for anesthesia. Patients undergoing extensive treatment requiring factor replacement may be treated under general anesthesia in a hospital operating room.

Oral Surgery

Surgical procedures carry the highest risk of bleeding, and safety precautions are needed. For coagulopathies, transfusion of appropriate factors to 50% to 100% of normal levels is recommended when a single bolus infusion is used in an outpatient setting. In patients with hemophilia, additional postoperative factor maintenance may be required after extensive surgeries. This can be done with factor infusion, cryoprecipitate or fresh frozen plasma depending on the patient's condition. The patient's hematologist should be consulted before planning, and patients with severe disease should be treated in specialty centres.

Local hemostatic agents (Table V) and techniques such as pressure, surgical packs, sutures and surgical stents may be used individually or in combination and may assist in the local delivery of hemostatic agents, such as topical thrombin and vasoconstrictors. However, caution is needed with the use of vasoconstrictors be cause of the risk of rebound vasodilatation, which may increase late bleeding risk. The use of absorbable hemostatic materials may favour clot formation and stability. However, these materials also carry a risk of infection and may delay healing; they should therefore be avoided in immunosuppressed patients.

Topical thrombin is an effective agent when applied directly on bleeding wound as it converts fibrinogen to fibrin and allows rapid hemostasis in a wound.Topical fibrin glue can reduce the amount of factor replacement needed when used alonged with antifibrinolytic agents.[15-18]

The patient's physician should be consulted before any decision is made to modify the patient's drug regimen, and the potential risk-benefit ratio should be determined. For patients taking warfarin, their international normalized ratio (INR) should be measured before a surgical procedure. The normal therapeutic range is 2.0-3.0. According to current recommendations, most oral surgical procedures can

be performed without altering the warfarin dose if the INR is less than 3.0.[19] If INR values are greater than 3.0, physician referral is suggested. It is important to consider the risk of reducing the level of anticoagultion in patients on warfarin due to the risk of a thromboembolic event.[20] Patients taking heparin are often those who are on hemodialysis due to end-stage renal disease. Heparin has a short half-life (about 5 hours) and patients can often be treated safely on the days between dialysis.

Periodontal Procedures

Periodontal health is of critical importance in patients with bleeding disorders[3] as inflamed and hyperemic gingival tissues are at increased risk of bleeding Periodontitis may cause tooth mobility and warrant extraction, which may be a complicated procedure in these patients. Patients with coagulopathies may neglect their oral health due to fear of bleeding during tooth brushing and flossing, which leads to increased gingivitis, periodontitis and caries.

Periodontal probing, subgingival scaling and polishing can be done normally without the risk of significant bleeding. Factor replacement is seldom needed for subgingival scaling and root planing if these procedures are done carefully. Ultrasonic instrumentation may result in less tissue trauma. For severely inflamed tissues, initial treatment with chlorhexidine mouth washes and gross debridement are recommended to reduce tissue inflammation before deep scaling.[21] Factor replacement may be required before extensive periodontal surgery and use of nerve blocks.

Restorative and Endodontic Procedures

General restorative procedures do not pose a significant risk of bleeding. Care should be taken to avoid injuring the gingiva while placing rubber dam clamps, matrices and wedges.

Endodontic therapy is preferred over extraction whenever possible in these patients. Endodontic therapy does not usually pose any significant risk of bleeding and can be performed routinely. Endodontic surgical procedures may require factor replacement therapy.

Prosthodontic and orthodontic Procedures

These procedures do not usually involve risk of bleeding. Trauma should be minimized by careful post-insertion adjustments. Oral tissue should be handled carefully during the various clinical stages prosthesis and orthodontic therapy

Choice of Medications

Many medications prescribed in dental practice, especially ASA, may interfere with hemostasis. In addition, many drugs interact with anticoagulants, increasing their potency and the risk of bleeding. When used for prolonged periods, ASA and nonsteroidal anti-inflammatory drugs (NSAIDS) can increase the effect of warfarin. Penicillins, erythromycin, metronidazole, tetracyclines and miconazole also have potentiating effects on warfarin. Care should be taken when prescribing these drugs to patients with bleeding tendencies or those receiving anticoagulant therapy, and it may be desirable to consult the patient's physician before planning the dose regimen.

Conclusion

For proper dental treatment specially when an invasive surgical procedure to be planned in bleeding disorder patients adequate knowledge for management the patients is very important. Knowledge about causes of bleeding disorder, management procedure, when and where to refer the cases for secondary care plays an important role in reducing potential complications and negative side effects.

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REVIEW ARTICLE

Oxygen Therapy in Children - An Update

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Abstract

In 1774, Joseph Priestley of England discovered the colorless, odorless, tasteless gas that Antoine Lavoisier named oxygen.Oxygen is a lifesaving drug has safe dose ranges, adverse physiologic effects, and toxic manifestations that are associated with higher doses and prolonged use. So, the administration of oxygen should be done with as much care and attention as any other drugs. Oxygen is transported in the blood in two ways: dissolved in the serum and in combination with hemoglobin.Children with any of the following signs are likely to have hypoxemia: central cyanosis, nasal flaring, inability to drink or feed due to respiratory distress, grunting with every breath and depressed mental state, severe lower chest wall indrawing, tachypnea or head nodding. The sources of oxygen and its delivery depend on the facility and the availability of resources. Most commonly use devices for oxygen delivery are nasal cannula, nasal prongs, simple face mask. An FiO_2 of >0.5 is considered toxic. After only a few hours of breathing 100% O_2, mucociliary function is depressed and clearance of mucous is impaired followed by nonproductive cough, substernal pain and nasal stuffiness may develop. More prolonged exposure to high O_2 tention may lead to changes in the lung that mimic adult respiratory distress syndrome. In premature neonates, lower SpO2 may be targeted to reduce the toxic effects of oxygen therapy, such as retinopathy of prematurity or bronchopulmonary dysplasia.

Introduction

Oxygen is the most frequently used "drug" in the management of sick children.[1] Oxygen is a drug, like most drugs, has safe dose ranges, adverse physiologic effects, and toxic manifestations that are associated with higher doses and prolonged use. So, the administration of oxygen should be done with as much care and attention as any other drugs.[2] Oxygen therapy is the process of increasing the concentration of oxygen in inspired air to treat hypoxia.[3] The goal of oxygen therapy is to give just enough oxygen to return the arterial oxygen saturation to the appropriate amount for the patient. The usual target is 90% in the infant, child and adult. Oxygen should be administered to saturate the hemoglobin 92% or better and this will safely achieve a PaO_2 of about 60-70 mm Hg.

History of oxygen as a drug

In 1774, Joseph Priestley of England discovered the colorless, odorless, tasteless gas that Antoine Lavoisiernamed oxygen.[2] It is not flammable but does support combustion. Oxygen is a highly reactive, non-metallicchemical element of atomic number 8 that readily forms compounds, particularly oxides, with most elements. Oxygen normally exists in the atmosphere as a diatomic gas, O_2, and makes up 0.209 the earth's atmosphere by volume and 0.232 by weight.[4] In 1907, Budin recommended oxygen "supplied through a funnel, the large opening of which is placed beside the infant's face" for the treatment of

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cyanotic episodes in newborns. Nearly 150 years afterits discovery, Finnish pediatrician Arvo Ylppo¨ recommended the intragastric administration of this gas to infants.[4] It was not until 1934 that Dr Julius Hess, Chief of Pediatrics at the Michael Reese Hospital in Chicago, createdthe first inhaled oxygen delivery device for infants and young children.[5] His "oxygen box," which consisted of a metal hood with a small window, was the first oxygen chamber used within an incubator.[5] The device was criticized both for making it difficult to view the infant and for its inability to provide high oxygen concentrations, but it paved the way for the development of oxygen administration devices in pediatrics. By the 1940s, a commercially available incubator capable of providing and facilitating oxygen therapy for the treatment of cyanosis, apnea, andperiodic breathing in newborns was the standard of care.[3,6] Further development and use of these delivery devices has resulted in significant health-care benefits, including a reductionin mortality. Today the administration of oxygen by inhalation continues to play an essential role in the survival of infants and children.[4,7] Before the 1960s and 1970s, oxygen administration was guided by the clinical observation of skin color, as well as the breathing frequency, regularity, and work of breathing. It was not until the 1960s and 1970s that technology (micro sampling of blood gases, transcutaneous oxygen monitoring, and later pulse oximetry) became available formore precise monitoring of the physiologic effect.[8]

Oxygen transport in the blood

Oxygen is transported in the blood in two ways: dissolved in the serum and in combination with hemoglobin. The oxygen dissolved in the serum is measured as the PaO_2 that constitutes only 2% to 3% of the total O_2 transported in the body. There is 0.0031 ml of O_2 dissolved in each 100 ml blood for each 1 mm Hg partial pressure of O_2. Thus, at a PaO_2 of 100 mm Hg, only 0.3 ml O_2 would be carried per 100 ml of plasma. Most O_2 in the body (97% to 98%) is transported to the cells in combination with hemoglobin and is measured as the percentage of O_2 saturation SpO_2. The percentage of saturation of blood is that portion of the total hemoglobin saturated with O_2. It is a relationship between the amount of O_2 that is carried and the amount that can be carried. Each gram of hemoglobin can transport 1.34 ml of O_2 per 100 ml of blood.[9]

Assessment of Inadequate Oxygen Delivery

To identify a patient's, need for oxygen, several physical signs and laboratory values can be assessed. Hypoxemia is often diagnosed by a lower than normal PaO_2, most often considered <80 mm Hg. A routinely sited indication for providing oxygen is when $PaO_2$is <60 mm Hg in children, yet PaO_2 alone is inadequate to determine oxygen delivery. Oxygen delivery is determined by the concentration ofhemoglobin in the blood; its oxygen saturation; the rate of blood circulation; and, last, the efficiency with which oxygenis unloaded from the hemoglobin to the tissues. Oxygen delivery is often expressed in the following equation:

$$DO_2 = CO\ [(Hb \times SaO_2 \times 1.34) + (PaO_2 \times 0.0031)]$$

where DO_2 is the rate of oxygen delivery, Hb is the hemoglobin concentration, and SaO_2 is the percentage of saturatedhemoglobin with oxygen.[16] The 1.34 represents theoxygen carrying capacity of the hemoglobin. The PaO_2 is the PO_2 in the arterial blood. The 0.003 is the solubility coefficient for oxygen in blood. CO is cardiac output. Therefore, you can see within this equation that PaO_2 is based on a relatively insignificant amount dissolved within the blood. In a patient who is anemic or hypovolemic, hasan abnormal hemoglobin with increased affinity for oxygen, or has a low CO, his/her oxygen delivery may be inadequate even in the presence of a normal PaO_2. Inadequate oxygen delivery in this case is often referred to ashypoxia.[9,10]

Table I

Signs and symptoms of hypoxemia

System	Mild to moderate	Severe
Central nervous system	Confusion, agitation, combativeness	Lethargy, obtunded mental status
Cardiac	Tachycardia, ectopy, hypertension	Bradycardia, hypotension
Respiratory	Dyspnea, tachypnea, shallow respirations, labored breathing	Increasing dyspnea and tachypnea, possible bradypnea or agonal respirations
Skin	Cool, clammy	Cyanosis
Arterial blood gas	PaO_2: 60-80 mm Hg	PaO_2 : <60 mm Hg

Since a PaO_2 of 60 and 80 corresponds with a noninvasive SpO_2 value of approximately 90 and 95%, respectively, in the patient with a normal pH, PCO_2, temperature, and diphosphoglycerate. Oximetry is often used to help identify hypoxemia, has its limitations and is known to be inaccurate in carbon monoxide poisoning. The patient condition needs to be considered during the assessment of adequate oxygen delivery. Underlying pathophysiologic mechanisms of hypoxemiaare: pulmonary disease, hypoventilation, uneven matchingof ventilation to perfusion, diffusion defects, intrapulmonary shunts or "right to left" cardiac shunts, or reduced oxygen-carrying capacity due to anemia or abnormal blood hemoglobin. Physical signs, such as cyanosis, confusion, tachycardia, retractions, nasal flaring, and expiratory grunting (infants) can be indications of an oxygen need.[11] Hypoxiais more serious and is defined as a deficit of oxygen at the cellular level. It is commonly caused by hypoxemia or hypoxia due to inadequate oxygen delivery due to high metabolic demand, such as sepsis, or abnormal cardiac function like heart failure or localized decreases in perfusion, such asstroke.[12] It is often a proper assumption that if left untreated, severe hypoxia can lead to serious and permanent brain injury and death.[7,8,13-15] It must be emphasized that hypoxia is determined not by PaO_2 or SpO_2/SaO_2 alone but also by hemoglobin, oxygen extraction, and metabolic demand of the body as described previously.

Where there is no pulse oximetry, clinical signs may be used to guide use of oxygen. Children with any of the following signs are likely to have hypoxemia:

- Central cyanosis
- Nasal flaring
- Inability to drink or feed (when this is due to respiratory distress)
- Grunting with every breath
- Depressed mental state (i.e., drowsy, lethargic)

In some situations, and depending on their overall clinical condition, children with the following less specific respiratory signs may also have hypoxemia:

- Severe lower chest wall indrawing,
- Respiratory rate of >70/min, or,
- Head nodding (i.e., a nodding movement of the head, synchronous with the respiration and indicating severe respiratory distress).[9]

Indications

The need for supplemental oxygen should be determined through evaluation of the patient's arterial blood gas and clinical assessment findings. In general, indications for oxygen therapy include the following:

- Correction of hypoxemia, thereby decreasing the work of breathing and the myocardial workload it imposes, and promotion of adequate oxygen delivery to the tissues. The correction of hypoxemia, in and itself, will not ensure the sufficient delivery of oxygenated blood to the tissues. A competent cardiovascular system is also necessary for carrying the adequately oxygenated blood to the tissues.
- Improvement of oxygenation in patients with decreased O_2 carrying capacity (i.e., those with anemia, sickle cell anemia).
- Promotion of the reabsorption of air in body cavities (e.g., pneumo-cephalus, small pneumothorax).[10]

Contraindications

Although there are very few contraindications to oxygentherapy, in congenital heart disease patients who have ductal-dependent lesions oxygen therapy may cause over circulation within the pulmonary system as a potent pulmonary vasodilator. In premature neonates, lower SpO2 may be targeted to reduce the toxic effects of oxygen therapy, such as retinopathy of prematurity or bronchopulmonary dysplasia.[16]

Complications associated with oxygen use

Administering supplemental oxygen, once hemoglobin is fully saturated (99% to 100%), places the patient at risk of having toxic effects of this drug.[17] The detrimental effects of oxygen therapy were first recognized in the late 19th century by Paul Bert, usinghyperbaric oxygen systems. It has been known for years that breathing an FiO_2 of 1.0 for as little as 3 h can start tocause chest pain, with longer periods leading to signs similar to broncho-pneumonia. Exposure to high concentrations of oxygen first damages the capillary endothelium, followed by interstitial edema (0-12 h), worsening complianceand vital capacity (12–30 h), followed by thickeningof the alveolar-capillary membrane (30-72 h).[18] If theprocess continues, type I alveolar cells are destroyed, andtype II cells proliferate. An exudative phase follows, resultingin a low ventilation/perfusion ratio, physiologic shunting, and worsening hypoxemia.[18]

Generally, an FiO_2 of >0.5 is considered toxic. The first sign of oxygen toxicity is due to the irritant effect of oxygen and reflect an acute tracheobronchitis. After only a few hours of breathing 100% O_2, mucociliary function is depressed and clearance of mucous is impaired followed by nonproductive cough, substernal pain and nasal stuffiness may develop. More prolonged exposure to high O_2 tention may lead to changes in the lung that mimic adult respiratory distress syndrome. Disruption of the endothelial lining of the pulmonary microcirculation results in leakage of proteinaceous fluid. An exudate consisting of edema, hemorrhage, and white blood cells forms in the lung. The damage to the lung may progress to cell death. The function of the pulmonary macrophage is also depressed, rendering the patient more susceptible to infection. The tissue injury in the lung caused by hyperoxia is generally agreed to be due to the production of biochemically reactive, oxygen derived free radicals that overwhelm the body's antioxidant defense.[9,19] FiO2>0.50 presents a significant risk of absorption atelectasis. Breathing high levels of oxygen quickly depletes body nitrogen levels. As blood nitrogen, a relatively insoluble gas decrease, the total pressure of venous gases rapidly decreases. Under these conditions, gases that exist at atmospheric pressure within the alveoli rapidly diffuse into the venous blood, and collapse occurs. The risk of absorption atelectasis may be greatest in children breathing at low tidalvolumes.[20] Oxygen-induced hypoventilation may occur because of suppression of the hypoxic respiratory drive. Normally, CO_2 is the primary stimulant driving the respiratory system. However, in patients with chronic hypercapnia ($PaCO_2$ >45mmHg), the CNS response to an elevated CO_2 level becomes blunted and hypoxemia becomes the major ventilatory stimulus. Administration of oxygen-enriched gas to these individuals may result in hypoventilation, hypercapnia, and possibly apnea.[21]

Sources and delivery of oxygen

The sources of oxygen and its delivery depend on the facility and the availability of resources. The most common sources of oxygen are cylinders, concentrators and pipelines or central piped oxygen. Many devices for administering supplemental oxygen are available. These devices are classified into two general categories; low-flow and high-flow systems. Whether a system is low or high flow does not determine its capability of delivering low versus high concentrations of oxygen. When choosing the appropriate technique for delivering supplemental oxygen, one must consider the device's advantages, the FiO_2 limits of the device and its appropriateness for a particular patient.[9,10]

The methods used to deliver oxygen should be safe, simple, effective, inexpensive. There are different delivery methods. The noninvasive methods are face mask, head box, incubator or tent or holding tubing close to infant's face and semi-invasive methods are insertion of prongs or catheters into the upper airway. Semi-invasive delivery methods require a low oxygen flow and are cheaper than non-invasive methods, which require high oxygen flow. Nasal and nasopharyngeal catheters have a beneficial effect on lung function, as they produce a positive end expiratory pressure (PEEP) of up to 5 cm of H_2O to improve oxygenation. PEEP production may also be effective in the management of apnea associated with prematurity or bronchiolitis. The recommended methods for neonates, infants and children are nasal prongs, nasal catheters and nasopharyngeal catheters.[22]

Table II

Oxygen delivery systems

Low-flow Systems	High-flow Systems
Nasal cannula	Venturi mask
Nasal prongs	Large-volume aerosol system
Simple face mask	• High-humidity face mask
Partial rebreathing mask	• High-humidity face tent
Nonrebreathing mask	• High-humidity tracheostomy mask/collar
	• High-humidity T piece or blow-by

Nasal Prongs

Nasal prongs are the preferred oxygen delivery method in most circumstances for an optimal balance between safety, efficacy and efficiency. Prongs are a device that ends in two short tapered tubes (about 1cm in length)designed to lie just within the nostrils. They are also called nasal cannula. Standard flow rates through nasal prongs are 0.5-1L/min for neonates, 1-2 L/min for infants, 1-4 L/min preschool children and 6 L/min in school children. Humidification is not required with standard flow rates, as the natural nasal mechanisms heat and humidify the inspired oxygen. There is slight risk of obstruction by mucus if a high flow with no humidification is used, but there is no risk of gastric distention. The fraction of inspired oxygen (FiO_2) depends on the oxygen flow rate, the relation between prong and nasal diameters and the patients body weight, which partly determines the volume delivered per minute. PEEP production with nasal prongs is unpredictable. In infants up to 10 kg, oxygen flows of 0.5 L/min, 1 L/min and 2 L/min result in FiO_2 values of about 35%, 45% and 55% respectively.

Nasal Catheter

A nasal catheter is a thin, flexible tube that is passed into the nose and ends with its tip in the nasal cavity. Nasal catheters are usually well tolerated, and they are unlikely to be dislodged. In neonates and infants, 8 (F) size catheters should be used and passed for a distance from the side of the nostril to the inner margin of the eyebrow (about 2.5 cm). The tip usually reaches the posterior part of the nasal cavity and should not be visible below the uvula. Nasal catheters are usually well tolerated, and they are unlikely to be dislodged. The oxygen does not have to be humidified because the tip of the catheter lies in the nasal cavity. The maximum flow rate should be set at 0.5-1 L/min for neonates and 1-2 L/min for infants and children. A nasogastric tube should be in place at the same time, in the same nostril so as not to be obstruct both nostrils. Higher flow rates without effective humidification may cause drying of the nasal mucosa with associated bleeding and airway obstruction.Actual FiO_2 values or PEEP achieved with nasal catheters have not been established.

Nasopharyngeal Catheters

Oxygen delivery through a nasopharyngeal catheter is the most economical of all the methods. Better oxygenation is achieved with a lower oxygen flow than the nasal prongs, because of the relatively high FiO_2 in the trachea and significant PEEP production of about 2.8 cm of H_2O with 1L/min. These catheters are inserted through the nose to a depth 1 cm less than the distance from the side of the nose to the front of the ear (tragus) and passed into the pharynx just below the level of the uvula (about 7 cm in infants). In neonates and infants, (8F) catheters should be used. The maximum flow rate should be set at 0.5 L/min for neonates and 1L/min for infants. Higher flow rates without effective humidification may cause drying of the nasal mucosa, with associated bleeding and airway obstruction. Nasopharyngeal catheters can be displaced downwards into the esophagus and caused gagging, vomiting and gastric distention, a nasogastric tube should also always be in place, in the same nostril to permit rapid decompression of the stomach. Their use should therefore be limited to situations in which nasal prongs are unavailable, staff are familiar with the insertion technique and with supervision, the oxygen supply is limited and in the case of children in whom cyanosis or oxygen desaturation is not relieved by oxygen given via nasal prongs or a nasal catheter. The catheter should be removed and cleaned at least twice a day.[23]

Simple face mask

The simple face mask has vent holes on the sides for the entrainment of room air and the release of exhaled gases. It has no valve or reservoir bag. It should be securely placed over the patient's mouth, nose and chin, then press the flexible metal pieces over the bridge of the nose to create a seal for prevention of gas loss. Finally adjust the strap around the patient's head. The placing of mask over the patient's face increases the size of the oxygen reservoir beyond the limit of anatomic reservoir; therefore, a higher FiO_2 can be delivered up to 0.60. The oxygen flow must be run at a sufficient rate, usually 5L/min or greater, to prevent collection, and thus rebreathing of exhaled gases high in carbon dioxide.[24]

Head boxes, incubators and tents

Non-invasive methods of oxygen administration have some advantages like oxygen piped into the head box, incubator or tent, the actual FiO_2 can be determined precisely with an oxygen analyzer placed near the infant's mouth. There is no increased risk of airway obstruction by mucus or of gastric distention, and

humidification is not necessary.[25] The disadvantage of these methods is however carbon dioxide toxicity if the flow of oxygen is inadequate, setting the oxygen flow too low or from kinking or disconnection of the oxygen tubing. When a head box is used with an inappropriately tight seal around the infant's neck, carbon dioxide can be retained. A gas flow of 2-3 L/Kg per minute is necessary to avoid rebreathing of carbon dioxide in a head box. Head boxes, face masks, incubators and tents all require high oxygen flows to achieve adequate concentrations of oxygen and avoid carbon dioxide accumulation, and they are therefore expensive and wasteful. Head boxes and face masks also interfere with feeding. Therefore, these methods are not recommended for oxygen administration, especially in settings where oxygen supplies are inadequate.[26]

Mechanical Ventilation

Mechanical ventilation is often used to deliver oxygen therapy and treat moderate to severe hypoxemia. Current clinical teaching emphasizes the avoidance of hypoxemia during mechanical ventilation. Continuous Positive Airway Pressure (CPAP) is a form of noninvasive ventilation delivers PEEP with a variable amount of oxygen to the airway of a spontaneously breathing patient to maintain lung volume during expiration. CPAP decreases atelectasis, respiratory fatigue and improves oxygenation. It is indicated for infants with severe respiratory distress, hypoxemia or apnea despite receiving oxygen.[9,10]

Table III

Estimated FiO_2 with low-flow oxygen delivery devices

100% O_2, Flow rate (L/min)	FiO_2
Nasal canula	
1	0.24
2	0.28
3	0.32
4	0.36
5	0.40
6	0.44
Simple oxygen mask	
5-6	0.40
6-7	0.50
7-8	0.60

Monitoring of oxygen therapy

After introduction of oxygen therapy, a planned desired physiologic outcome and the adequacy of the patient's response to therapy should be monitored. Assessment frequency should be based on the severity of hypoxemia (e.g., level of FiO_2 required), overall severity of illness, or variability of oxygen delivery device. Oxygen administration by any method must be supervised by trained personnel to detect and manage complications appropriately. A nurse should check every 3 hours that the prongs or catheter are in the correct position and not blocked with mucus, that all connections are secure, that the oxygen flow rate is correct, that the airways are not obstructed by mucus and that there is no gastric distension. Prongs or catheters should be removed and cleaned at least twice a day.[27] Most use a noninvasive monitoring strategy like pulse oximetry or arterial blood gases for the acid/base balance (indicator of hypoxia leading to a metabolic acidosis) or a PaO_2 to assist with their clinical assessment. Venous or capillary blood gases are not used to evaluate oxygenation. Pulse oximetry, the most appropriate way to monitor children to determine whether they need oxygen and to determine how long children should receive oxygen. Children receiving oxygen should be monitored clinically at least twice a day by pulse oximetry. For children in a stable condition, and with SpO_2 >90%, oxygen should be interrupted once a day for 10-15 minutes and carefully examined for changes in clinical signs and SpO_2 to assess whether supplemental O_2 is still required.[28] Where oxygen supplies are ample, children should receive supplemental oxygen until their SpO_2 on room air is ≥90%. If the SpO_2 is ≥90% after a trial on room air, they should remain off oxygen, and the SpO_2 should be rechecked after 1hr, as late desaturation can sometimes occur.[29]

Conclusions

Oxygen therapy is important, universally accepted as a life-saving therapy and has saved many lives. Oxygen administration should be considered in the same way as other drugs and titrated to ameasured end point to avoid excessive or inadequate dosing. Withholding oxygen can have detrimental effects; however, continuing to provide oxygen therapy when it is no longer indicated can prolong hospitalization and increase the cost of care. One must ensure that oxygen content and cardiacoutput are adequate when assessing the effectiveness of oxygen therapy. Device selection is vitally important in pediatrics because not

only is the size of our patients avariable, but what they will wear is an additional consideration.

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DS (Child) H J 2018; 34(1) : 55-58

CASE REPORT

Jejunal Duplication Cyst - a Rare Cause of Massive Gastrointestinal Bleeding: A Case Report

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Introduction

Alimentery tract duplication is a relatively rare congenital anomaly. It can be symptomatic or are discovered incidentally. W.E Ladd first introduced the term duplication in 1934. Most duplications are benign, but the presence of ectopic gastric mucosa and the potential for malignant degeneration remain a concern.[1]

Congenital duplication cyst can occur anywhere in the gastrointestinal(GI) tract, although it most commonly occurs in the ileum, oesophagus and colon.[1] Approximately 75% of duplications have been reported to be located within the abdominal cavity, whereas the remaining is intrathroacic (20%) or thoracoabdominal (5%). Ileal lesion are the more common (53%) followed by mediastinal (18%), colonic (13%), gastric (7%), duodenal (6%), rectal (4%), oesophageal (2%), cervical (1%) lesion. They may present as solid or cystic tumours, intussusception, perforation or gastrointestinal bleeding.[2] Most intestinal duplication lie on the mesenteric side of the intestine and share a common mascular wall and blood supply with the native bowel.[3] Appropriate surgical management is required, for this the attending surgeon should be familiar with the pathology and clinical characteristics of these rare cysts.[3] Due to the rarity of this condition the vast majority of literature on enteric duplication cysts is in the form of case reports. Very few case series have been published previously.

Case report

A 12 months old boy, presented with complaint of melena 1-2 times/day, 2-3 days interval for last 2 months (figure 1). He had no history of fever, vomiting, abdominal pain, abdominal distension or cow's milk allergy, ingestion of offending drugs/ toy/button. He received PRBC transfusion 5 times during the course of illness. On examination baby was sick looking, severely pale, vital: normal, well thriving and abdomen was nontender, no organomegaly, bowel sound present. Other systemic examination reveal normal.

Laboratory parameters showed severe anemia (Hb% 6.8 gm/dL), normal platelate count, on PBF- normocrocytic anemia, feature of colitis on stool routine examination (RBC: 6-8/HPF, pus cell: 5-6 /HPF), positive occult blood test, ultrasonography of whole abdomen was suggestive of duplication cyst or Meckel's diverticular cyst at right iliac region. Meckel's scan showed heterotopic gastric mucosa in gut wall in hypogastrium. Esophagogas-trodudenoscopy was normal. Barium meal & follow through showed a large globular compressive effect that compressing distal bowel loops with gross narrowing of rectosigmoid region. Barium enema was normal (Table-I).

After correction of anaemia, laparotomy was done. A duplication cyst was seen 10 cm from duedenojejunal junction, measuring about (10x8) cm arising from

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Table I
Laboratory Investigations

CBC	Hemoglobin Total count of WBC Platelate	6.8 gm/dL 9000/mm3 380000/mm3
PBF	Normocytic anemia ,otherwise normal.	
Stool routine examination	RBC Pus cell	6-8/HPF 5-6/HPF
Occult blood test	Positive	
USG of whole abdomen	Suggestive of duplication cyst or Mickel diverticular cyst intestinal atresia fluid filled dilation area measuring 7.6cm x 5.9cm seen at right iliac region	
Mickel's scan	Heterotopic gastric mucosa in gut wall in hypogastrium	
Esophagogastrodudenoscopy	Normal	
Digital Barium meal of stomach, duodenum & follow through	A large globuler compressive effect is seen in lower part of abdomen little towards left, compressing distal bowel loops with gross narrowing of rectosigmoid region. Possibility of cystic mass in lower part of abdomen is to be considered	
Barium enema	No organic lesion in large gut	
Histopathology	Two mucosal layers sharing a sumucosal within muscular layer .Gastric mucosal lining is seen. No malignancy found.	

upper part of jejunum. Excision of duplication cyst and adjacent gut with end to end anastomosis was done. Postoperative period was uneventful. He was discharged on the 10th postoperative day. The resected intestinal loop was sent for histopathological examination (figure 3).

Fig 1 *(a) Patient (b) Melena*

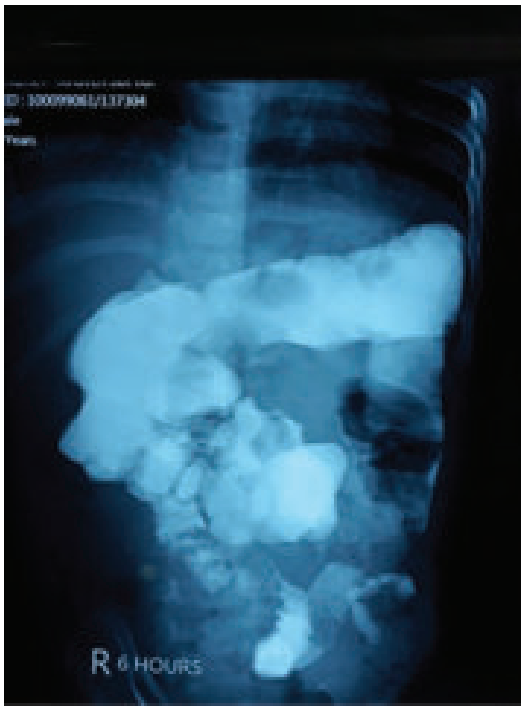

Fig 2 *Barium follow through*

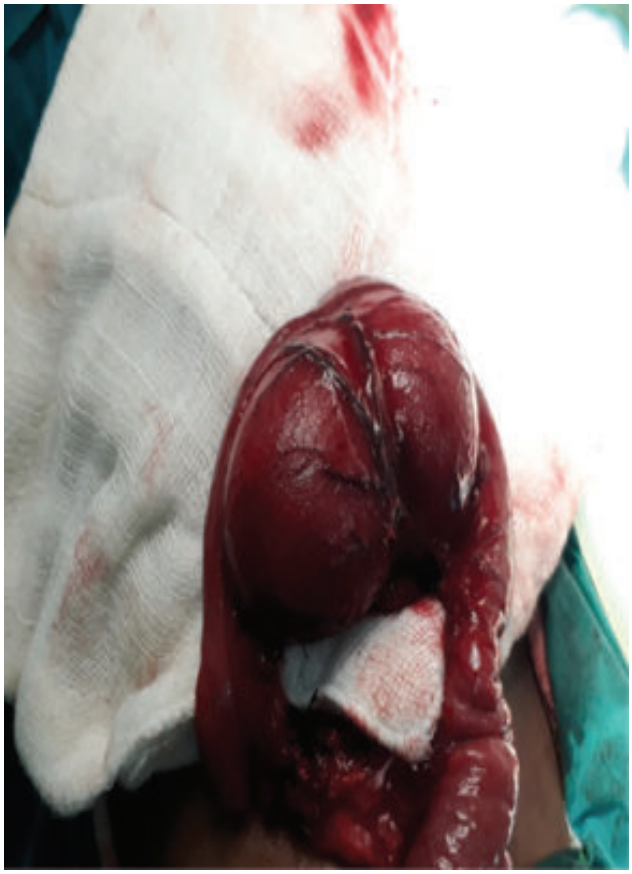

Fig 3 *Resected duplication cyst*

Discussion

Jejunal and ileal duplications are the most common alimentary tract duplication and are usually found on the mesenteric border of the intestine.[5] Duplication parts usually share a common muscularis and common blood supply with the adjacent gut. There are two types of duplications- cystic and tubular. Tubular type of duplication usually communicates with the lumen of the adjacent normal intestine either caudally, distally or at several points in between. When there is no communication they fill with secreted mucus and cause pain and usually presents with a mass in the abdomen. When a tubular type of duplication communicates with the normal bowel at its cephalic end, the lumen greatly distends with intestinal secretions causing obstruction or even perforation. On the other hand in a caudal type of communication the duplicated part empties readily. Cystic or secular type of duplications usually have no communication with the lumen of adjacent bowel. Gastric type of mucosa usually lines part or the whole of the length of the tubular duplication. Secretion of acid peptic juice from the ectopic gastric mucosa can cause peptic ulcer, bleeding and even perforation with peritonitis.[6-8] Ectopic pancreatic tissue can also be found in the wall of some of these duplications.[9] The sign-symptoms of duplication depends on its type and location. Symptoms usually begin from early childhood.[9] Our patient presented at 12 months of age.

Mass in the abdomen, pain from distension of cyst and intestinal obstruction due to compression of adjacent intestine may be the presenting complaints. Segmental intestinal vascular obstruction can lead to gangrene of adjacent normal bowel. Bleeding from ulceration either within the duplication itself or in the adjacent normal intestine occurs in approximately 20% of parents.[10, 11] Our case presented with painless gastrointestinal bleeding in the form of melena. He was moderately pale with history of 5 unit blood transfusion, which signified massive blood loss.

The causes of intestinal duplication cyst have not yet been established. Several theories have been put forward to explain different types of duplications. Of these persistence of fetal gut diverticula, defects in re-canalization of the solid stage of primitive gut, partial twining and the split notochord theories are popular.[12,13] Bentley et al suggested that a split notochord that resulted from abnormal adhesions presenting between the ectoderm and endoderm was the primary defect, and that a herniation of the Yolk sac between the two halves of vertebra resulted in the subsequent duplication of the gut. However, the split-notochord theory cannot explain formation of the intra-abdominal duplications that are not associated with spinal deformity.[1]

The clinical diagnosis of duplication may be difficult before surgery. Abdominal ultrasonography and in difficult cases CT scan can detect duplication. Enteric duplication cyst has an echogenic inner lining due to mucosal layer and a surrounding hypoechoic rim due to muscular layer and when identified together preoperatively, combinations of these two layers are highly suggestive of enteric duplication cysts.[14] The presence of these two layers helps to exclude other cystic mass such as mesenteric or omental cyst, choledochal cyst, ovarian cyst, and pancreatic pseudocyst.[15] In our patient ultrasonography of whole abdomen was suggestive of duplication cyst or Meckel's diverticular cyst.

Technetium scan demonstrates ectopic gastric mucosa in duplication and is helpful in cases of unexplained gastrointestinal bleeding. In our case Meckel's scan showed heterotopic gastric mucosa in gut wall in hypogastrium.

The management of symptomatic duplication is surgical. Laparotomy was done in our case and a duplication cyst was found arising from upper part of jejunum. Excision of duplication cyst and end to end anastomosis was done.

Infants with subclinical intestinal duplication discovered incidentally on scan are commonly offered surgery to prevent the future risk of complication by obstruction or perforation.

Conclusion

Though duplication cyst is a rare cause of gastrointestinal bleeding, jejunal duplication cyst may present with massive gastrointestinal bleeding should be kept in mind during managing of such a case of massive gastrointestinal bleeding.

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DS (Child) H J 2018; 34(1) : 59-62

CASE REPORT

Cutis Laxa Syndrome: A Rare Genetic Disorder of Elastolysis

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Introduction

Cutis laxa is a heterogeneous group of disorders with variable phenotypes and inheritance pattern[1]. Incidence is 1 in every 2 million babies, it may be acquired or inherited forms. Include autosomal dominant CL (ADCL); autosomal recessive CL(ARCL) I, IIA, IIB, Urban-Rifkin-Davis Syndrome (URDS); Macrocephaly-alopecia-CL-Scoliosis (MACS) syndrome, arterial tortuosity Syndrome (ATS) or X-Linked CL(XLCL).[2] ARCL has most commonly reported particularly II, Cutis laxa (elastolysis) affect person of all races. Male and female affect equally.

Autosomal recessive has earlier presentation, Autosomal dominant form has a later onset, acquired cutis laxa may develop at any age, but often be appeared in adult hood.

The cutis laxa is diagnosed by physician on the basis of clinical feature. Inherited form ADCL may present from birth to early adult hood with predominantly skin findings.[3-5] Patients have loose inelastic redundant skin that typically worsen with age, characteristic facial features include an aged appearance, long philtrum, large fore head, large ear lobes and broad nose.[6]

Systemic manifestation can have from mild to severe cardiac and pulmonary complication, such as bronchiectasis and emphysema, aortic aneurysm, severe congestive lung disease and pulmonary artery disease.[7] Approximately 30% of patient with ADCL have denovo mutations with no family history.

ARCL Type-I: Clinical findings, manifestations of ARCL-I began at birth with abnormal faces , redundant fold around the face and neck and aged appearance.[8-10] Compared with ADCL, ARCL-I is more often associated with emphysema and diaphragmatic defect, arterial tortuosity and aneurysms[9,11,12] joint laxity and muscular hypotonia. Patient die from pulmonary or cardiac complications in early child hood.[9,11,12] Joint laxity and muscular hypotonia is also observed. Mental and motor development usually normal.[8,13,14] Some case of ARCL-I results from FBLN5 or FBLN4 mutation.

ARCL Type IIA: Include more frequent motor nervous system abnormalities, cardiaovascular abnorma-lities, patent anterior fontanel and female predominance. Microcephaly, hypotonia, seizures, myopia neurodegeneration and Dandy-Walker malformation are also associated with this varity.[15,16]

ARCL Type IIB : Features of ARCL-llB Overlap those of geroderma osteodysplasticum, ARCL-llA/wrinkled skin syndrome and De Barsy syndrome(DBS). [17-19]

ARCL Type III (DBS): DBS is also known as ARCL-lll progeroid syndrome of De Barsy, or CL-corneal clouding- mental retardation syndrome.[20]

Acquired CL: Acquired CL (ACL) is a rare disorder with insidious onset that most often occurs in adulthood and may be associated with various conditions and drugs.[21,22]

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Case summary

Samia, 16 months old female child second issue of consanguineous parents admitted to Dhaka Shishu (Children) Hospital, with characteristics facial features including age appearance with sagging jaws, a hooked nose with everted nostrils, a short columella, along with upper lips and everted lower eyelids and downwards slanting palpebral fissures, a broad flat nose and large ears (Fig 1). Her birth and development were normal and past history was negative except for an episode of pneumonia at the age of 4 months and was treated on an inpatient basis at another hospital. The family history was negative for any individuals with a similar appearance or any unusual deaths during infancy or childhood.

We have done skin biopsy (Fig 2) which revealed epidermis is thin and mild hyperkeratosis. The dermis revealed a decrease in the number, fragmentation, and disorderly arrangement of connective tissue fibers especially elastic fibers. Few lymphocytes infiltrations are noted in the upper dermis.

We have done chest X-ray and Echocardiogram to evaluate complications, but the reports revealed normal findings.

Cutis Laxa Syndrome

Fig 1 *Cutis Laxa syndrome, samia 16 month, note redundancy of skin folds sagging jaws, a hooked nose with everted nostrils, a short columella, along upper lips and everted lower eyelids and downwards slanting palpebral fissures, a broad flat nose and large ears.*

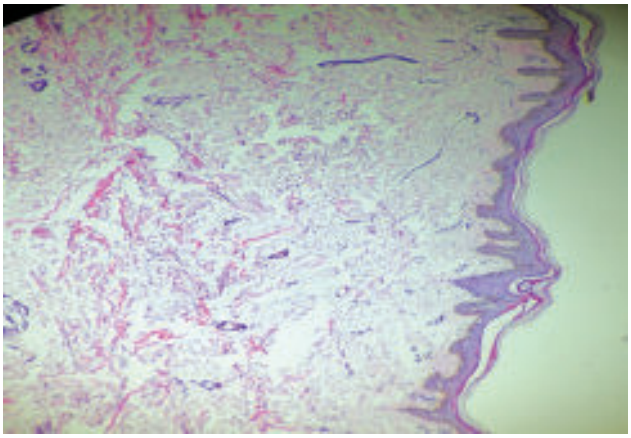

Fig 2 *Histopathology slide picture of skin biopsy*

Discussion

Cutis laxa (CL), or elastolysis, is a rare, inherited or acquired connective-tissue disorder in which the skin becomes inelastic and hangs loosely in folds. Patients develop a prematurely aged appearance.

The clinical presentation and the mode of inheritance show considerable heterogeneity. Autosomal dominant, autosomal recessive, and X-linked recessive patterns have been need in inherited forms. A serine to proline amino acid substitution in the fibulin5 (*FBLNS*) gene has been associated with problems in normal elastogenesis, resulting in a dominant form of cutis laxa (elastolysis) in humans.

Autosomal recessive cutis laxa is a genetically heterogeneous condition. A combined disorder of N- and O-linked glycosylation has been described in children with congenital cutis laxa in association with severe central nervous system involvement, brain migration defects, seizure, and hearing loss.

The X-linked form is currently classified in the group of copper transport disease. The precise cause is unknown, but it may be due to abnormal elastin metabolism resulting in markedly reduced dermal elastin content. Autosomal dominant congenital cutis laxa (ADCL) is genetically heterogeneous and shows clinical variability. Mutation in the elastin gene (ELN) have been described.

In both the inherited type and the acquired type, the internal organs are frequently involved. Cutis laxa (elastolysis) may be preceded by an inflammatory rash, such as urticaria, or it may develop spontaneously.

Cutislaxa (elestolysis) affects person of all races and affects men and women equally. The autosomal dominant form has a later onset than the autosomal recessive form. Acquired cutis laxa (elestolysis) may develop at any age, but it often begins in adulthood.

Treatment and prognosis of cutis laxa vary depending on the specific type of the disorder and the individual case Treatment generally involves ongoing care and monitoring by a variety of specialists, such as a cardiologist, dermatologist, internits, geneticist and pulmonologist. People with the form of cutis laxa only affects the skin may be able to live a normal lifespan. Complications, such as ruptured aortic aneurysm and corpulmonale can be fatal.

Treatment for Cutis laxacont: Sometimes plastic surgery can often improve the appearance of the skin, although the improvement may only temporary.[23,24]

The lifespan of some patients with cutis laxa (elestolysis) may be significantly decreased, Patients with the autosomal dominant form have a normal life expectancy.

Conclusion

Most of the case of cutis laxa are genetic origin and few are acquired, so treatment are supportive and multidisciplinary approaches. Recent studies have greatly contributed to our understanding, classification, and treatment of CL and related syndrome. As this is rear disease so all case should have to recorded and monitor nationally and internationally and more study and lifelong follow-up needed.

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DS (Child) H J 2018; 34(1) : 63-64

ABSTRACT FROM CURRENT LITERATURE

Pediatric Asthma and Food Allergy

Haoquan Zhou & Chuanlin Dai & Jiahua Pan

Indian J Pediatr. 2017 Aug; 84(8):585-590.

Objective: To quantitatively summarize the evidence from observational studies on the relation between pediatric asthma and food allergy.

Methods: A literature search was conducted in Medline and EMBASE (August 2016). Two independent reviewers appraised the studies and extracted the estimates of interest. Methodological quality of the included studies was assessed using National Heart Lung and Blood Institute (NHLBI) Quality Assessment Tools. Data were pooled using random effects meta-analysis.

Results: A total of 32 relevant studies were identified but only 8 studies met the inclusion criteria. Using random-effect model, food allergy showed strong association with asthma in children (OR = 2.87 [95% CI: 2.05–4.00]; P < 0.0001).

Conclusions: This study suggested that food allergy is associated with an increased risk of asthma in children.

Keywords: Pediatric; Asthma; Food allergy

Psychosocial Needs of Patient's Relatives and Health Care Providers in a Pediatric Critical Care Unit.

Kandasamy S, Vijayakumar N, Natarajan RK, Sangaralingam T, Krishnamoorthi N.

Indian J Pediatr. 2017 Aug;84(8):601-606.

Objective: To describe the needs of relatives of children admitted to an Intensive Care Unit and compare their needs with the perspectives of doctors, nurses and administrators.

Methods: This is a descriptive comparative study done at a tertiary care PICU from South India. A modified Critical Care Family Needs Inventory (CCFNI) (internal consistency reliability =0.93) was used to assess the needs of 35 family members, 30 nurses, 30 doctors and 30 administrators. Four needs pertaining to developing countries were included. Their responses were ranked by means and analysed by multivariate analysis of variance.

Results: The responses were significantly different between the groups for 13 needs (28%) and two domain items of proximity and support. Needs of relatives correlated with doctors more strongly than with nurses (r_s = 0.80 vs. 0.68; p < 0.001). No significant difference was found between the perceived needs of family members and hospital staff for assurance, information and comfort. Both doctors and administrators underestimated the proximity needs but overestimated the support needs of relatives.

Conclusions: The CCFNI with minor modifications can be used in developing countries for assessing the needs of families of children in ICU. Making sure that the relative feels assured about the care given to the child and timely information regarding the child's condition, are the two most important domains from the perspective of family members and hospital staff. Meeting these needs might help family members to cope better and be more supportive to their critically ill child.

Keywords: CCFNI; Critically ill children; Family needs

The association of sleep and late-night cell phone use among adolescents

Babak Amra, Ali Shahsavari, Ramin Shayan-Moghadam, Omid Mirheli, Bita Moradi-Khaniabadi, Mehdi Bazukar, Ashkan Yadollahi-Farsani, e Roya Kelishadi

J Pediatr (Rio J). 2017;93(6):560-567

Objective: This study aims to assess the relationship of late-night cell phone use with sleep duration and quality in a sample of Iranian adolescents.

Methods: The study population consisted of 2400 adolescents, aged 12-18 years, living in Isfahan, Iran. Age, body mass index, sleep duration, cell phone use

after 9 p.m., and physical activity were documented. For sleep assessment, the Pittsburgh Sleep Quality Index question-naire was used.

Results: The participation rate was 90.4% (n = 2257 adolescents). The mean (SD) age of partici-pants was 15.44 (1.55) years; 1270 participants reported to use cell phone after 9 p.m. Overall, 56.1% of girls and 38.9% of boys reported poor quality sleep, respectively. Wake-up time was 8:17 a.m. (2.33), among late-night cell phone users and 8:03 a.m. (2.11) among non-users. Most (52%) late-night cell phone users had poor sleep quality. Sedentary participants had higher sleep latency than their peers. Adjusted binary and multinomial logistic regression models showed that late-night cell users were 1.39 times more likely to have a poor sleep quality than non-users (p-value < 0.001).

Conclusion: Late-night cell phone use by adolescents was associated with poorer sleep quality. Participants who were physically active had better sleep quality and quantity. As part of healthy lifestyle recommendations, avoidance of late-night cell phone use should be encouraged in adolescents.

Point-of-care C reactive protein to identify serious infection in acutely ill children presenting to hospital: prospective cohort study

Jan Y Verbakel, Marieke B Lemiengre, Tine De Burghgraeve, An De Sutter, Bert Aertgeerts, Dominique M A Bullens, Bethany Shinkins, Ann Van den Bruel, Frank Buntinx

Arch Dis Child 2017;0:1-7. doi:10.1136/archdischild-2016-312384

Objective: Acute infection is the most common presentation of children to hospital. A minority of these infections are serious, but early recognition and adequate management are essential. We aimed to develop improved tools to assess children attending ambulatory hospital care, integrating clinical features with point-of-care C reactive protein (CRP).

Design: Prospective observational diagnostic study.

Setting and patients: 5517 acutely ill children (1 month–16 years) presenting to 106 paediatricians at six outpatient clinics and six emergency departments in Belgium.

Index test: Point-of-care CRP alongside vital signs and objective symptoms measurements.

Main outcome: Hospital admission for >24 hours with a serious infection <5 days after presentation.

Results: An algorithm was developed consisting of clinical features and CRP. This achieved 97.1% (95% CI 94.3% to 98.7%) sensitivity and 99.6% (95% CI 99.2% to 99.8%) negative predictive value, excluding serious infections in 36.4% of children. It stratifies patients into three groups based on CRP level: high-risk group with CRP >75 mg/L (26.8% risk of infection), intermediate-risk group with CRP 20-75 mg/L and at least one of seven clinical features (8.1%), and lower risk group with CRP <20 mg/L with at least one of the 11 features (3.8%). Children in intermediate-risk or low-risk groups with normal clinical assessment have 0.6% and 0.4% risk of serious infections, respectively.

Conclusions: Conducting a CRP test may first enable children to be stratified into three risk groups, guiding assessment of clinical features that could be performed by junior doctors or nurses. In one-third of acutely ill children, the algorithm could exclude serious infection. Prospective validation of the algorithm is needed.

DSH NEWS

Chairperson of Management Board of Dhaka Shishu Hospital, National Professor Shahla Khatun inaugurate 'Shishu Kanan & celebration of Bangla Nobo Borsho -1425' on 16 April 2018

Rally on the occasion of World Asthma Day - 2018 held on 3 May 2018 organized by Pediatric Pulmonology unit of Dhaka Shishu Hospital

BICH NEWS

BICH is the academic wing of Dhaka Shishu Hospital. It was established in 30th January, 1983. It is affiliated with Dhaka University, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bangladesh College of Physicians and Surgeons (BCPS). It has been conducting different courses e.g. DCH, FCPS, MD Paediatrics, MS Paediatric surgery & B.Sc in Health technology. It also 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.

Postgraduate courses/training in paediatrics and child health

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

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DS (Child) H J 2018; 34(1) : 68

Students Qualified from Bangladesh Institute of Child Health

Undergoing Courses of BICH

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

Student Qualified from BICH till June 2018

Course	Number
DCH	358
MD (Pediatrics)	113
MS (Pediatrics)	103
FCPS (Pediatrics)	28
MD (Neonatology)	13
MD (Pediatrics Nephrology)	5
Total	**620**

Foreign Student Qualified from BICH till January 2013

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

Present Students (January 2018 - June 2018)

Name of Courses	Number of Students
MD (Pediatrics) Phase - A	14
MD (Neonatology) Phase - A	03
MD (Nephrology) Phase - A	02
MS (Pediatric Surgery) Phase - A	10
FCPS (Pediatrics) Part - II	02
MD (Pediatrics) Part - III	07
MS (Pediatric Surgery)	02
MD (Pediatrics) Part - II	04
DCH (Old)	10
DCH (New)	10
Total	64

DS (Child) H J 2018; 34(1) : 69

Seminar/Symposium & CME/CPD programs held at BICH (January - June 2018)

Sl. No.	Topic	Unit	Date
1	Precocious Puberty	MU - IX	21.01.2018
2	Chronic Diarrhoea in Children	MU - X	24.02.2018
3	Mixed connective tissue disorder (MCTD) - An update	MU - XI	18.03.2018
4	Malrotation of the Gut	SU - II	22.04.2018
5	Infective endocarditis in childen : An update	MU - I	13.05.2018
6	Management of nephrotic syndrome: An update	MU - II	24.06.2018
7	Posterior urethral valve: A spectrum of Disease		27.06.2018

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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.
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- 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.
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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 exceed 100 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:
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  - 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.
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