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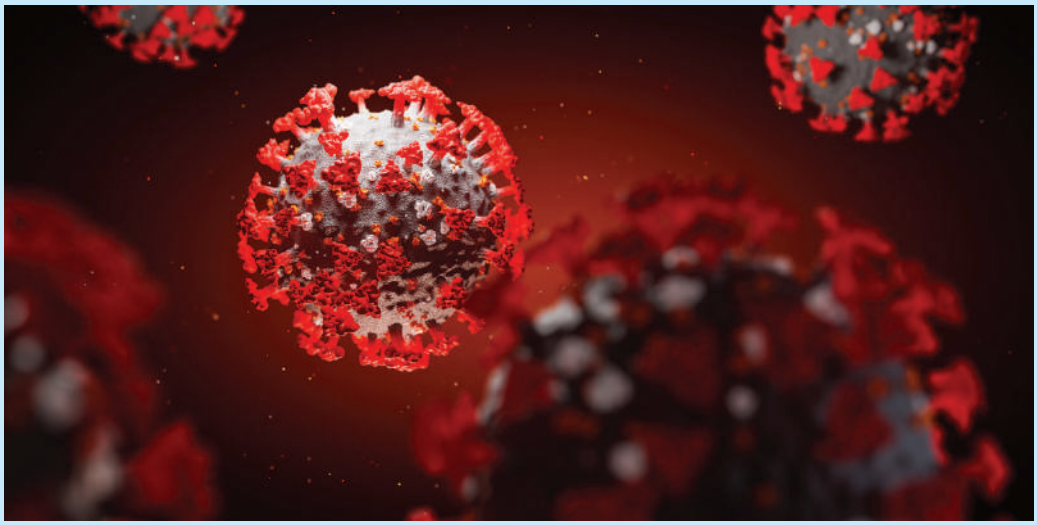

Editorial

"Is COVID-19 Infection A Great Risk for Children?"

Bangladesh Institute of Child Health

Dhaka Shishu (Children) Hospital

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EDITORIAL

Is COVID-19 Infection A Great Risk for Children?

Mohammed Hanif

Coronavirus Disease 2019 (COVID-19) outbreak began in Wuhan, China, and has spread rapidly around the world, making it the biggest public health problem in human history. The WHO declared COVID-19 as a pandemic on the 11th of March 2020. In Bangladesh children are less infected and the mortality rate is low till date. In this situation, children's wellbeing has been jeopardized, they can't go to school, play or visit their mates. The living conditions, family income, schooling are the key determinants for the wellbeing of children which are affected due to this pandemic.[1] The children are getting nervous, some frightened or tired of the unknown pandemic due to the various social distancing laws, wearing masks or washing hands, sometimes infected close relatives or parents.[2] The Centers for Disease Control and Prevention (CDC) of the USA confirmed that children who have developed severe illness from COVID-19 infection have underlying medical conditions. One significant finding is kawasaki like multisystem inflammatory syndrome in children (MIS-C). Children are suffered from recurrent fever and variety of clinical symptoms which may involve multiple organs and elevated proinflammatory markers as MIS-C, and have developed mild or clinically asymptomatic infection few weeks after. In addition, other variety of cutaneous manifestation has been reported like adult.[3]

The greatest mystery is the degree to which children are responsible for the spread of COVID-19 infection. Lee et al[4] studied with 40 children in Geneva University Hospital and confirmed that children can get infected by COVID-19 virus frequently like adult and found responsible for the COVID-19 transmission. However, other researchers have shown different findings, Heald-Sargen et al[5] found that children under the age of five with mild to moderate COVID-19 infection have higher levels of SARS-COV 2 viral RNA in their nasopharynx relative to older children and adults. These children with high viral load are more likely to transmit to others when physical activity in schools is resumed or public health restrictions are withdrawn. In a study of 47 children, Jones et al[6] showed that their nasopharyngeal swab for SARS-COV-2 viral load was similar to those of older age, indicating that children could be as infectious as adults. The SARS-COV 2 virus infected children are so often mildly symptomatic, may have weaker and less frequent cough, releasing infectious fever particles into the surrounding environment. Thus, children require to confine in their home and not allowing them to go to school.

The number of COVID-19 cases among children in the USA increased to 90% in a month and 90 infected children died in a few months after easing restriction and opening schools. This rise in COVID-19 cases is attributed to increased testing and child activity. Between the 9th of July and 6th of August, COVID-19 infection among children has raised 45% and reached 380174 in USA. As of August 6, gross hospitalization and mortality have increased to 0.5-5.3% and 0-0.47%, respectively.[7] Infants are also affected by COVID-19 virus. Several research found that the COVID-19 infection is transmitted from the mother to infant after birth.[8]

In Bangladesh, it is difficult to estimate the infection with COVID-19 in pediatric patients due to low testing, home containment and fear of going with

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their child to the test center. The latest study indicates that about 7-8 % are infected in the pediatric age group with mortality rate of about 0.5-1%.[9] If the preventive measure is not taken, then the future situation for children will be catastrophic.

According to UNICEF, more than 28,000 under five children may die in six months due to the indirect result of the COVID-19 pandemic.[10] Article published on July 13, 2020 in the Financial Express online stated that child labor will rise as a result of the economic situation. According to the Global Immunization news July 2020, immunization has dropped about 22% in May 2020 in Bangladesh.[11]

In this catastrophic scenario, adequate measures require to be taken for the reduction of significant adverse social, developmental and health effects that our children will have to experience before effective treatment or vaccination is produced and administered or faced before we achieve herd immunity. Along with Government/Non-government Organizations, politicians and parents should come forward to fight against this pandemic. Healthcare providers should work with families to keep children up-to-date with all recommended vaccination.

References

1. Sinha I, Bennett D, Taylor-Robinson DC. Children are being sidelined by covid-19. *BMJ* 2020; https://doi.org/10.1136/bmj.m2061
2. Harvard Health, 2020. Coronavirus outbreak and kids - Harvard Health [WWW Document]. Available at https://www.health.harvard.edu/diseases-and-conditions/coronavirus-outbreak-and-kids (accessed 8.22.20).
3. Hageman JR. What Are the Newest Effects of COVID-19 in Children? *Pediatr Ann* 2020;**49**:e242-e243.
4. Lee B, Raszka WV. COVID-19 Transmission and Children: The Child Is Not to Blame. *Pediatrics*. 2020;**146**. https://doi.org/10.1542/peds.2020-004879.
5. Heald-Sargent T, Muller WJ, Zheng X, Rippe J, Patel AB, et al. Age-Related Differences in Nasopharyngeal Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Levels in Patients With Mild to Moderate Coronavirus Disease 2019 (COVID-19). *JAMA Pediatr* 2020;**174**:902-03.
6. Jones TC, Mühlemann B, Veith T, Biele G, Zuchowski M, Hoffmann J, et al. An analysis of SARS-CoV-2 viral load by patient age. *medRxiv* 2020. Available at https://doi.org/10.1101/2020.06.08. 20125484.
7. Mascarenhas L, Maxouris C, LaMotte S. There has been a 90% increase in Covid-19 cases in US children in the last four weeks, report says. CNN. Available at: https://www.cnn.com/2020/08/11/health/covid-19-children-cases-rising-wellness/index.html (accessed 8.22.20).
8. CDC. How COVID-19 (coronavirus) affects babies and children. Mayo Clin. Available at https://www.mayoclinic.org/diseases-conditions/coronavirus/in-depth/coronavirus-in-babies-and-children/art-20484405 (accessed 8.22.20).
9. WHO, 2020b. Coronavirus disease (COVID-2019) Bangladesh situation reports [WWW Document]. Available at https://www.who.int/bangladesh/emergencies/coronavirus-disease-(covid-19)-update/coronavirus-disease-(covid-2019)-bangladesh-situation-reports (accessed 8.22.20).
10. COVID-19: Over 28,000 children could die in 6 months without urgent action. Available at https://unb.com.bd/category/Bangladesh/covid-19-over-28000-children-could-die-in-6-months-without-urgent-action/51543. Accessed on 28.06.2020.
11. Global Immunization news (GIN). Available at https://www.who.int /immunization/GIN_July_ 2020.pdf.

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LEADING ARTICLE

COVID-19 Pandemic and Neonate

Mahfuza Shirin

Introduction

Novel coronavirus (SARS-COV-2) is a new strain of coronavirus causing pneumonia, first was reported in Wuhan, Hubei Province, China, in December 2019.[1] On January 7, 2020 Word Health Organization (WHO) named it as Corona Virus Disease 2019 (COVID-19).[2] COVID-19 emerged as an epidemic in China and spread rapidly to almost all countries over the globe.[3] So, WHO declared COVID 19 as a pandemic on 11 March 2020.[4]

The COVID-19 pandemic has predominantly affected adults of older age groups. The effect of SARS-CoV-2 on children including neonates appears to be trivial. The knowledge on COVID-19 in neonates is only based on a recent experience over the past few months. Moreover, there is limited information regarding impact of corona virus on neonatal care in relation to newborns with confirmed or suspected COVID-19.[5,6] Here, we discuss the basic aspects of the infection, the likely presentation in newborns and the approach of management of neonates with infection or at risk of the infection with SARS-COV-2.

Novel coronavirus infection

The novel coronavirus (SARS-CoV-2), is belong to beta coronavirus family, a single-stranded RNA virus with a helical capsid with radiating spikes (hence the name corona), and the disease is referred to as coronavirus disease 2019 (COVID-19).[7]

The virus is highly infectious and the entire population is generally susceptible. Usually spreads by aerosol and droplet generation by atomization while coughing, sneezing, or even talking and droplet contact spread.[8,9] SARS-CoV-2 RNA has been detected in stool specimens, but fecal-oral transmission has not been clinically described.[10] The incubation period is between 3-7 days on average, with 2 days as the shortest and 14 days longest. [11]

How do neonates get infected?

Postnatal transmission from mothers, other caregivers, visitors, or healthcare personnel who have the infection (or are asymptomatic carriers) through respiratory droplets is the commonest way a baby may get infected.[9]

Early Chinese reports suggested that vertical transmission of SARS-CoV-2 does not occur, as amniotic fluid, vaginal mucus, placenta, umbilical cord, cord blood, and neonatal stool specimens tested negative for the virus.[12,13] Limited reports have raised concern of possible intrapartum or peripartum transmission, but the extent and clinical significance of vertical transmission by these routes is unclear.[14,15]

The role of breast milk in spreading is not yet identified as till date no evidence of presence of SARS-CoV-2 in breast milk of pregnant women with COVID-19 is found.[16]

Clinical presentation

Information on clinical presentation and disease severity among neonates is limited and based on case reports and small case series. The extent to which SARS-CoV-2 infection contributed to the reported signs of infection and complications in neonates is unclear. Neonates presented with symptoms usually milder than other age groups**.** No severe case or death was reported till now.[17-19] The severe disease in adults is a consequence of a cytokine storm,[20] and fortunately, this is less pronounced in children including neonates and that could be a factor behind the milder manifestations in neonates. The Kawasaki like inflammatory syndrome described in older children has not been noted in newborns.

In case of neonates with COVID-19, clinical presentation is nonspecific. Commonly observed

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symptoms are depicted in Table I.[11,21] So suspected neonates should be closely monitored for vitals, respiratory and gastrointestinal symptoms.

Table I
Clinical presentations of neonates with COVID-19

System	Manifestations
Neurological	Temperature instability
	Lethargy
Respiratory	Grunting
	Nasal flaring
	Tachypnea
	Chest retractions
	Central cyanosis/pallor
	Apnea
	Cough
Gastrointestinal	Abdominal distension
	Feeding intolerance
	Diarrhea/watery stools
	Emesis

Diagnosis

Reverse transcription polymerase chain reaction (RT-PCR) in the swab sample taken from deep intranasal and oropharyngeal swabs is currently the only test being used to confirm cases of COVID-19 infection.[21-23]

Laboratory tests including CBC: leukopenia, leukocytosis, and lymphopenia (most common) and mild thrombocytopenia. Various enzymes level is found to be elevated, including creatine kinase, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, and lactate dehydrogenase.[21]

Chest X-ray and computed tomography (CT) and abdominal radiography are not recommended for initial evaluation; should reserve for hospitalized patients or symptomatic patients with specific clinical indications. The likely findings in CXR/Chest CT are ground-glass opacities (GGOs), multiple areas of consolidation, "crazy paving appearance" (GGOs + inter-/intralobular septal thickening), and bronchovascular thickening. Lesions usually have a bilateral, peripheral, and lower lobe distribution. Abdominal radiography may show intestinal ileus.[21]

Case definition[21]

Suspect case: A neonate born to the mother with a history of SARS-CoV-2 infection between 14 days before delivery and 28 days after delivery, or the neonate directly exposed to those infected with SARS-CoV-2 (including parents, family members, caregivers, medical staff, and visitors).

Confirm case: Neonate with positive RT-PCR test for SARS-CoV-2 infection from respiratory tract sample; or virus gene sequencing of the respiratory tract specimen is highly homologous to that of the known SARS-CoV-2 specimen.

When to test the baby[24]

1. Approximately at 24 hours of age if the baby born to a mother with history of SARS-CoV-2 infection. If initial test results are negative, or not available, testing should be repeated at 48 hours of age.
2. As early as possible after admission if the neonates have signs suggestive of COVID-19 or neonates with history of COVID-19 exposure requiring higher levels of care.

Management of neonates born to mothers with COVID-19[24-27]

1. Suspected and confirmed COVID positive mothers should be delivered in separate delivery rooms or operation theaters. Stabilization and resuscitation of the neonates should be done in an adjacent room or the same place at least 6 feet or 2 meters away from the mother with a physical barrier such as a curtain in between. Minimum number of skilled neonatal team members (preferably 2 members) should attend to manage the newborn and wear a full set of PPE including N95 mask. Mother should perform hand hygiene and wear triple layer mask. Delayed cord clamping practices and skin-to-skin care in the delivery room should continue per usual center practice. Mothers with COVID-19 should use a mask while holding their baby. Resuscitation will be carried out as per NRP protocol and in case of any positive pressure ventilation requirement, self-inflating bag with mask should be preferred to T-piece resuscitator.
2. Stable neonates born to COVID-19 positive mothers should be roomed-in with their mothers and be exclusively breastfed. For supporting lactation, nurses trained in essential newborn

care and lactation management should be provided. A healthy asymptomatic willing family member who is not positive for COVID-19, and has not been in direct contact with suspected or confirmed COVID-19 person may be allowed to provide support for mother and neonate. Mother should wash hands frequently including before breastfeeding and wear mask. The mother-baby dyad must be isolated from other suspected and infected cases.

3. Symptomatic/ sick neonates born to a mother with suspected or confirmed COVID19 should be managed in separate isolation facility, as like as sick neonates with COVID-19.
4. Newborn should be monitored regularly for vitals and routine examination by health care personnel with adequate PPE.

Management of sick neonates with COVID-19[25,27-30]

1. Treat suspected, or confirmed cases and symptomatic/sick neonates born to a mother with suspected or confirmed COVID19 in separate room(s) preferably negative pressure room if available. If single rooms are not available, placed them in a common isolation ward for neonates with >6 feet / 2 meters distance should be maintained between the cohorts. It is preferred to use closed incubator for affected neonate. Separate essential instruments including dedicated respiratory support devices.
2. Babies are unlikely to be infectious unless aerosol generating events like crying or sneezing, but healthcare workers should wear full PPE while handling them. Stool may be infective as well, and precautions are essential while handling stools.
3. For infants with suspected/confirmed COVID-19 needing respiratory support, CPAP should be preferred over NIPPV and high flow nasal cannulas (HFNC) and ensure optimal fitting of interface.
4. Intubation should be only for usual indications and should be performed by the most experienced person. Video laryngoscope should be preferred for intubation. For infants on mechanical ventilation, use appropriate size endotracheal tube, in-line suctioning, adequate PPE and small hydrophobic filter at exhalation port.
5. For infants with severe acute respiratory distress syndrome, high-dose surfactant, inhaled nitric oxide, and high-frequency oscillatory ventilation (HFOV) may be effective. In more severe cases, continuous renal replacement therapy and extracorporeal membrane oxygenation (ECMO) may be necessary.
6. Some babies present like acute bronchiolitis and may need a period of respiratory support.
7. As high flow nasal cannula therapy and nasal continuous positive airway pressure (CPAP) are aerosol generating procedures, such babies should be in incubators, with expiratory flow tubing preferably within the incubator.
8. The area providing respiratory support should be a negative air pressure area. Healthcare providers should practice contact and droplet isolation and wear N95 mask while providing care in that area.
9. In babies presenting with gastrointestinal concerns, a period on intravenous (IV) fluids may be needed, but most of these symptoms appear to resolve over 2-3 days.
10. Specific anti-COVID-19 treatment is not recommended in symptomatic neonates. Use of adjunctive therapy such as systemic corticosteroids, intravenous gamma globulin and convalescent plasma is not recommended in symptomatic neonates with suspected or confirmed COVID-19. Symptomatic and supportive therapy are the main principles of management. Antipyretics like paracetamol can be used as normally indicated. If the baby is unwell with respiratory distress, antibiotic cover as per unit policy would be indicated.
11. If mother is not infected and staying with the baby can directly breastfeed her infant if baby is clinically able to suck after taking appropriate precautions (hand and torso washing prior to feeding, clean linens/gown, wearing a mask). A sick baby may receive expressed breastmilk. It can be fed to infant by mother/staff or care giver.
12. Neonatal BCG vaccination can be continued in countries or settings with a high incidence of tuberculosis as per existing practice [61].

Discharge policy[21,24,25,30,31]

Stable neonates born to mothers with suspected or confirmed COVID19 and being roomed-in with their

mothers may be discharged together at the same time. Stable neonates in whom rooming-in is not possible because of the sickness in the mother and are being cared by a trained family member may be discharged from the facility by 24-48 hours of age.

Asymptomatic COVID-19 positive neonates or those with mild to moderate clinical course whose symptoms and need of oxygen abate within 3 days can be discharged from the hospital after 10 days without repeating RT-PCR test. In severe cases, discharge can be done when neonate becomes symptoms free and after 2 consecutive negative tests for COVID-19.

Conclusion

The COVID-19 pandemic has become the most serious public health emergency, we are facing now. Though adults of older age group are the majority, children including newborns are not exempted from this infection, fortunately, disease condition of the neonates is minor. Till date little information about COVID-19 in neonates is unfolded and evidence available is updating day by day. So, emphasis should be to formulate guidelines suitable to handle the neonates on that changed situation.

References

1. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med* 2020;**382**:727-33.
2. WHO. Naming the coronavirus disease (COVID-19) and the virus that causes it [Internet]; [cited 2020 Apr 12]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/ naming-the-coronavirus-disease-(covid-2019)-and-thevirus-that-causes-it.
3. WHO. Coronavirus disease 2019 (COVID-19) Situation Report - 82 [Internet]; [cited 2020 Apr 18]. Available from: https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200411-sitrep-82-covid19.pdf?sfvrsn=74a5d15_2.
4. WHO. Director-General's opening remarks at the media briefing on COVID-19; [Internet]; 11 March 2020 [cited 2020 Apr 18]. Available from: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-oncovid-19.11-march-2020.
5. Ludvigsson JF. Systematic review of COVID-19 in children shows milder cases and a better prognosis than adults. *Acta Paediatr* 2020;**109**:1088-95.
6. Dong Y, Mo X, Hu Y, Qi X, Jiang F, Jiang Z, et al. Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China. *Pediatrics* 2020;**16**:16.
7. Gorbalenya AE, Baker SC, Baric RS, de Groot RJ, Drosten C, Gulyaeva AA, et al. Severe acute respiratory syndrome-related coronavirus – the species and its viruses, a statement of the Coronavirus Study Group. *bioRxiv* 2020. [EpubFebruary 11, 2020].
8. World Health Organization. Coronavirus disease (COVID-2019) situation reports. Available at: https://www.who.int/emergencies/ diseases/novel-coronavirus-2019/situation-reports/. Accessed 15 April 2020.
9. Kutter JS, Spronken MI, Fraaij PL, Fouchier RA, Herfst S. Transmission routes of respiratory viruses among humans. *Curr Opin Virol* 2018;**28**:142-51.
10. Zhang W, Du R-H, Li B, Zhenga XS, Yanga XL, Hua B, et al. Molecular and serological investigation of 2019-nCoV infected patients: Implication of multiple shedding routes. *Emerg Microbes Infect* 2020; **9**:386-89.
11. Chen ZM, Fu JF, Shu Q, Chen YH, Hua CZ, Li FB, et al. Diagnosis and treatment recommendations for pediatric respiratory infection caused by the 2019 novel coronavirus. *World J Pediatr* 2020;**16**:240-46.
12. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: a retrospective review of medical records. *Lancet* 2020;**395**:809-15.
13. Fan C, Lei D, Fang C, Li C, Wang M, Liuet Y, et al. Perinatal transmission of COVID-19 associated SARS-CoV-2: should we worry? *Clin Infect Dis* ciaa226.
14. Dashraath P, Wong JLJ, Lim MXK, Lim LM, Li S, Biswas A, et al. Coronavirus disease 2019 (COVID-19) pandemic and pregnancy. *AJOG* 2020;**222**: 521-31.
15. Kirtsman M, Diambomba Y, Poutanen SM, Malinowski AK, Vlachodimitropoulou E, Parkset ET, al. Probable congenital SARS-CoV-2 infection in a neonate born to a woman with active SARS-CoV-2 infection. *CMAJ* 2020;**192**(24):E647-E650. [published online ahead of print, 2020 May 14].
16. Martins-Filho PR, Santos VS, Santos Jr HP. To breastfeed or not to breastfeed? Lack of evidence on the presence of SARS-CoV-2 in breastmilk of pregnant women with COVID-19. *Rev Panam Salud Publica* 2020;**44**:e59. Doi: 10.26633/RPSP.2020.59.

17. Zhu H, Wang L, Fang C, Peng S, Zhang L, Chang G, et al. Clinical analysis of 10 neonates born to mothers with 2019-nCoV pneumonia. *Transl Pediatr* 2020;**9**:51-60.

18. Chen H, Guo J, Wang C, Luo F, Yu X, Zhang W, et al. Clinical characteristics and intrauterine vertical transmission potential of COVID-19 infection in nine pregnant women: A retrospective review of medical records. *Lancet* 2020;**395**:809-15.

19. Zeng L, Xia S, Yuan W, Yan K, Xiao F, Shao J, et al. Neonatal early-onset infection with SARS-CoV-2 in 33 neonates born to mothers with COVID-19 in Wuhan, China. *JAMA Pediatr*. 2020, http://dx.doi.org/10.1001/jamapediatrics.2020.0878 [Epub ahead of print].

20. Chen L, Liu HG, Liu W, Liu J, Liu K, Shang J, et al. Analysis of clinical features of 29 patients with 2019 novel coronavirus pneumonia. *Chinese J Tuberc Respir Dis* 2020;**43**:E005.

21. Wang L, Shi Y, Xiao T, Fu J, Feng X, Mu D, et al; Working Committee on Perinatal and Neonatal Management for the Prevention and Control of the 2019 Novel Coronavirus Infection. Chinese expert consensus on the perinatal and neonatal management for the prevention and control of the 2019 novel coronavirus infection (First edition). *Ann Transl Med* 2020;**8**:47.

22. Centers for Disease Control and Prevention. Interim guidelines for collecting, handling, and testing clinical specimens from persons under investigation (PUIs) for coronavirus disease 2019 (COVID19). February 14, 2020. https://www.cdc.gov/coronavirus/2019-nCoV/lab/guidelines-clinical-specimens.html (Accessed on April 18, 2020).

23. World Health Organization. Laboratory testing for coronavirus disease (COVID-19) in suspected human cases: interim guidance, 19 March 2020. World Health Organization; 2020

24. Chandrasekharan P, Vento M, Trevisanuto D, Partridge E, Underwood MA, Wiedeman J, et al. Neonatal resuscitation and post resuscitation care of infants born to mothers with suspected or confirmed SARS-CoV-2 infection. *Am J Perinatol* 2020;**37**: 813-24.

25. Chawla D, Chirla D, Dalwai S, et al. Perinatal-neonatal management of COVID-19 infection [published online April 1, 2020]. Indian Pediatr. pii:S097475591600154. PubMed PMID: 32238615. 6. COVID-19

26. Royal College of Obstetricians and Gynaecologists. Coronavirus (COVID19) infection in pregnancy: information for healthcare professionals V4. [Internet]. 2020 April 12 [cited 2020 March 25]. Available from: https://www.rcog.org.uk.

27. Kallem VR, Sharma D. COVID 19 in neonates. *The Journal of Maternal-Fetal & Neonatal Medicine*

28. Paraluppi V, Pintus MC, Fanos V, Marcialis MA. COVID-19 in newborns and in children: the state of the art. *Journal of Pediatric and Neonatal Individualized Medicine* 2020;**9**:e090138. doi: 10.7363/090138.

29. Li F, Feng ZC, Shi Y. Proposal for prevention and control of the 2019 novel coronavirus disease in newborn infants. *Arch Dis Child Fetal Neonatal Ed*. 2020. Doi: 10.1136/archdischild-2020-318996 [Epub March 4, 2020].

30. Neonatal guidelines by Kerala NNF March 2020. http://www.pedijatri.org/wp-content/uploads/2020/03/ Neonatoloski-vodic-iz-Kerale.pdf. Accessed April 20, 2020.

31. Puopolo KM, Hudak ML, Kimberlin DW, Cummings J. Management of infants born to mothers with COVID-19. INITIAL GUIDANCE. American Academy of Pediatrics Committee on Fetus and Newborn, Section on Neonatal Perinatal Medicine, and Committee on Infectious Diseases, April 2, 2020.

DS (Child) H J 2020; 36(1): 8-13

ORIGINAL ARTICLE

Role of Racecadotril in Children with Acute Diarrhea

Azmeri Sultana[1], Parijat Bishwas[2], Shahidul Islam[3], Uzzal Kumar Ghosh[4], Kazi Iman[5], Sharmin Afroze[6], Sheikh Farjana Sonia[7]

Abstract

Background: *Diarrhea is a leading cause of illness and death among children in developing countries. Racecadotril (acetorphan), an enkephalinase inhibitor with antisecretory and anti-diarrheal actions, is an effective and safe treatment for acute diarrhea in adults and children.*

Objectives: *The objective of this study is to evaluate the efficacy and tolerability of racecadotril as a treatment of acute diarrhea in children.*

Methods: *This double-blind, randomized controlled clinical trial was conducted in Dr. MR Khan Children Hospital & Institute of Child Health over 1 year (June 2017-May 2018). The study was approved by the ethical committee of the institute. The efficacy and tolerability of racecadotril (1.5 mg/kg) administered orally 3 times daily) as adjuvant therapy to oral rehydration or intravenous fluid were compared with those of placebo in 40 children aged 3 months to 60 months of children who had acute diarrhea.*

Results: *During the first 72 hours of treatment, patients receiving racecadotril had a significantly lower stool output (grams per hour) than those receiving placebo. The mean (±SE) 72-hours stool output was 54.75± 12.92 g per kilogram in the racecadotril group and 152.50±37.64 g per kilogram in the placebo group (p<0.001). The number of purging is significantly reduced in the racecadotril group than the placebo group (11.95±2.41 Vs 14.85±1.95, p= 0.000) on third day of admission. The duration of hospital stay is significantly lower in the racecadotril group than the placebo group (73.30±23.44 vs. 177.30±25.8. p= 0.000) group. Racecadotril was well tolerated; only 3 patients taking racecadotril had adverse effects like vomiting and 2 patients had hypokalaemia and 3 patients in the placebo group developed vomiting and 1patient developed hypokalaemia which all are mild and transient.*

Conclusion: *In young children with acute watery diarrhea, racecadotril is an effective and safe treatment along with rehydration therapy.*

Keywords: *Acute diarrhea, racecadotril.*

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Introduction

Acute diarrhea in children is a global health problem with an estimated 2 billion episodes each year, mostly in developing countries; make a contribution to 18% of under-five childhood mortality. Diarrheal disease is a leading cause of illness and death in children worldwide.[1-2] Many of the deaths are caused by dehydration resulting from loss of water and electrolytes due to intestinal malabsorption or increased secretion. Replacement of these losses by oral rehydration solution is the mainstay of therapy for children with watery diarrhea.[3] Oral rehydration therapy is well accepted as the most effective treatment for rehydration of children with acute diarrhea and is recommended by the World Health Organization for prevention and management of dehydration.[4] Although the use of oral rehydration therapy has achieved a dramatic reduction in both morbidity and mortality in diarrhea,[3-4] rehydration has little effect on stool volume or frequency. Therefore, the World Health Organization has recommended that drug treatment be added to rehydration therapy, as long as the drug used has proven safety and efficacy in the paediatric population.[4-5]

Racecadotril decreases intestinal hypersecretion but not motility.[6-7] It has proven efficacy and safety use in children and adults with acute watery diarrhea when taken orally.[8-9] A previous study of racecadotril was carried out in children three months to four years old in France.[8]

Racecadotril (acetorphan) is an enkephalinase inhibitor (neprilysin, EC 3.4.24.11), a cell membrane peptidase enzyme located in various tissues, notably the epithelium of the small intestine. It exerts its antidiarrheal effects by preventing the breakdown of endogenous peptides such as enkephalins, neurokinin, and substance P in the gastrointestinal tract.[9-12] Moreover, racecadotril does not increase intestinal transit time,[13] implying that the drug has a selective antisecretory mode of action. In adults, racecadotril has been shown to have better efficacy than placebo in randomized, double-blind clinical trials of patients with acute diarrhea. This efficacy has been combined with a side effects profile similar to that of placebo.[14-16]

The present study was performed to compare the efficacy and tolerability of racecadotril with placebo in hospitalized infants and children (aged 3 months to 5years) and also assess the effect of racecadotril as an adjunct to rehydration therapy in infants and children in Bangladesh

Materials and Methods

This double-blind, randomized controlled clinical trial was conducted in Dr. MR Khan Children Hospital & Institute of Child Health over 1 year (June 2017-May 2018). The study was approved by the ethical committee of the institute. A total of 100 patients were included initially in this study who met the inclusion criteria i.e. children aged 3 months to 60 months of either sex who had watery diarrhea (passed three or more diarrheic stools in the 24 hours before admission to the hospital) and who gave consent. Children with bloody stool, chronic diarrhea, severe dehydration (inability to drink because of drowsiness), or any serious concomitant illness and who didn't give consent were excluded from the study.

Of the 100 patients who enrolled in this study (50 in racecadotril group and 50 in the placebo group), 5 were excluded because their stool weights were not recorded (3 in the racecadotril group and 2 placebo group). Stool weights could not be estimated in 7 other patients receiving racecadotril (4 from 12 to 24 hours and 3 from 24 to 36 hours). These data were therefore recorded as missing. Another 8 patients were discarded from the placebo group due to insufficient data.

The full data set consisted of 40 patients who received racecadotril (Racitril sachet 10 and 30 mg) and 40 who received a placebo, orally every eight hours, in addition to oral or intravenous rehydration solution. Both treatments were administered as saccharose-containing powders of identical appearance and taste, with two spoons water to facilitate swallowing. Treatment with antibiotics, other anti-diarrheal drugs, or any other drugs were not permitted during the study. The efficacy and tolerability of racecadotril (1.5 mg/kg) administered orally 3 times daily) as adjuvant therapy to oral rehydration or intravenous fluid were compared with those of placebo in 40 children. Both groups were comparable in terms of age, duration of diarrhea, the number of stools, hospital stay, and complications.

Diarrhea was considered to have stopped after any patient had passed two consecutive formed stools or had not passed a stool for 12 hours. In addition to oral rehydration solution, the patient was given

milk or soft foods, as appropriate to their age, to provide a daily calorie intake of 100 to 120 kcal per kilogram (excluding the calories from glucose in the rehydration solution), accordance to World Health Organization recommendations that diet was maintained during treatment of diarrhea to prevent malnutrition.[3] Fresh stool collected at admission for a routine microscopic test, stool culture, and presence of rotavirus by ELISA.[12] If stool culture showed any growth of bacteria which need antibiotic then this case was excluded from the study. Serum electrolyte and serum creatinine were measured on day 3 after giving racecadotril and placebo to compare any changes or side effects by racecadotril. We didn't do electrolyte and creatinine at admission as severe dehydration was not enrolled or we enrolled it after correction of severe dehydration by intravenous fluid.

A physical examination was performed each day during the study, and stool weight, intake of oral rehydration solution, and output of vomit were measured every four hours. The primary endpoint was stool output in the first 72 hours because both the fluid loss and the risk of dehydration are maximal during this period. During this period, care was taken to ensure that stools were collected separately from urine. Thereafter, stools were collected in preweighed diapers. Stool output was calculated as the sum of the weights of the watery and loose stools (diarrheic stools) divided by the bodyweight at baseline. The total stool output, duration of diarrhea, and total intake of oral rehydration solution were also measured. These assessments were made at the time of recovery or the end of five. Data were collected in a structured questionnaire form and were analyzed by using SPSS version 20.0.

Results

No significant variation was found in demographic profile between racecadotril and placebo group. Both racecadotril and placebo groups are comparable to the socio-demographic variable (Table I).

The duration of diarrhea at admission in both the racecadotril group and placebo group is almost the same (43.65 ± 17.8 Vs 45.9 ± 13.35, p= 0.65). No significant difference was found (Table II).

Table I
Demographic characteristics of the study population

Variable	Racecadotril Group (n=40)	Placebo Group (n=40)	p value*
Mothers Education			
Uneducated	6	12	
Primary	10	20	
Secondary	16	8	0.46
Graduate	8	0	
Source of water			
Supply water	0	2	
Boiled water	18	22	
Filter water	16	14	
Tube well	6	2	0.41
Family income			
<10,000	4	4	0.60
10,000-25,000	26	22	
>25,000	10	14	
Area of living			
Urban	36	34	0.36
Rural	4	6	

*data were analyzed by independent t-test

Table II
Duration of diarrhea at admission

Variable	Racecadotril Group (n=40)	Placebo Group (n=40)	p value*
Duration of diarrhea in hours at admission Mean ± SD	43.65±17.8	45.9±13.35	0.65

*data were analyzed by independent t-test

There is no significant electrolyte and serum creatinine changes between the racecadotril and the placebo group (Table III).

Table III
S. electrolyte and S. creatinine changes between the two groups

Variable	Racecadotril Group (n=40)	Placebo Group (n=40)	p value*
Serum Na^+ mmol/L (Mean±SD)	138.62±3.63	138.92±4.80	0.825
Serum K^+mmol/L (Mean±SD)	4.08±0.59	4.03 ± 0.51	0.775
Serum Cl^-mmol/L (Mean±SD)	99.77±4.14	101.30±5.06	0.302
Serum creatinine in mg/dl (Mean±SD)	0.23±0.18	0.21±0.06	0.734

*data were analyzed by independent t-test

Table IV
Comparison of stool volume and purging in case and control group

Variable	Racecadotril Group (n=40)	Placebo Group (n=40)	p value*
Stool volume at Day 1 (Mean±SD)	170±40.58	172.5±37.8	0.841
Stool volume at Day 3 (Mean±SD)	54.75± 12.92	152.50±37.64	0.000
Stool volume at discharge (Mean±SD)	34.60±13.39	40.15±5.70	0.096
Number of purging at Day 1 (Mean±SD)	21.40±4.20	19.95±3.22	0.231
Number of purging at Day 3 (Mean±SD	11.95±2.41	14.85±1.95	0.000
Number of purging at Day of discharge (Mean±SD)	4.05±1.35	4.45±0.68	0.236
Duration of hospital stayIn hours (Mean±SD)	73.30±23.44	177.30±25.8	0.000

*data were analyzed by independent t-test

Mean stool volume at day one (D1) in two groups is not significant (170±40.58 Vs 172.5±37.8, p-value 0.84) whereas mean stool volume at day 3 (D3) between the case and placebo group is significant (54.75± 12.92 vs. 152.50±37.64, *p*-value 0.000). The number of purging at day 1 in two groups is not significant but at day 3 number of purging is significantly reduced in the racecadotril group than the placebo group (11.95±2.41 Vs 14.85±1.95, *P*-value 0.000). The number of purging at Day of discharge (Mean±SD) was not significant in two groups (4.05±1.35 Vs 4.45±0.68, p=0.236). The duration of hospital stay is significantly lower in the racecadotril group than the placebo group (73.30±23.44 vs. 177.30±25.8 p= 0.000) (Table IV).

Discussion

Racecadotril when used as an adjunct to oral rehydration therapy, may reduce both the severity and duration of diarrhea and the duration of hospitalization.[17]

Our study showed mean stool volume at day 3 between racecadotril and placebo group is significant (54.75± 12.92 vs. 152.50±37.64; p=0.000) and the number of purging at day 3 (48 hours after starting racecadotril) is significantly reduced in the racecadotril group than the placebo group (11.95±2.41 vs. 14.85±1.95; p=0.000). Jean et al[18] showed during the first 48 hours of treatment, patients receiving racecadotril had a significantly lower stool output (grams per hour) than those receiving placebo. The 95% confidence interval was 43% - 88% for the full data set (n=166; p=0.009) and 33%-75% for the per-protocol population (n=116; p=0.001), which is similar to our study.

Another systematic review and Meta-analysis was conducted for the five most frequently used efficacy parameters showed racecadotril was superior to comparator treatments in outpatients and hospitalized patients with a high degree of consistency as confirmed by meta-analysis. For instance, it reduced time to cure of 106.2 h to 78.2 h (mean reduction 28.0 h; p<0.0001 in 24 studies reporting on this parameter).[19] This meta-analysis supports our findings of the efficacy of racecadotril. In another

recent study in India showed racecadotril had less effect on reducing stool volume and purging in rotaviral diarrhea which is opposite to our findings, it may be due to geographical variation or organism causing diarrhea.[20]

In the present study duration of hospital stay is significantly lower in the racecadotril group than the placebo group (73.30±23.44 vs. 177.30±25.8 p-value 0.000). Our findings support other studies median duration of diarrhea in the racecadotril group was 28 hours and the corresponding values in the placebo group were 72 hours, ($p<0.001$).[17,21,22]

Racecadotril seems to be well tolerated in our study, only 3 patients taking racecadotril had adverse effects like vomiting, and 2 patients had hypokalaemia and 3 patients in the placebo group developed vomiting and 1patient developed hypokalaemia which all are mild and transient.

The incidence of adverse effects did not differ between the racecadotril and the placebo group. And acute diarrhea itself can cause vomiting and hypokalaemia. Moreover, no serious adverse effect was observed in our study. These findings correspond with another study conducted in ICDDR'B Bangladesh.[23]

Conclusion

Racecadotril is an effective, well-tolerated adjunct to oral rehydration therapy in infants and children with acute diarrhea.

References

1. World Gastroenterology Global Guidelines: Acute diarrhea in adults and children: a global perspective. Available at http://www.worldgastroenterology. org/ UserFiles/file/guidelines/acute-diarrhea-english-2012.pdf].
2. Bern C, Martines J, de Zoysa I, Glass RI. The magnitude of the global problem of diarrhoeal disease: a ten-year update. *Bull World Health Organ* 1992;**70**:705-14.
3. World Health Organization, Department of Child and Adolescent Health and Development. The Treatment of Diarrhoea: A manual for physicians and other senior health workers. Geneva: Dept. of Child and Adolescent Health and Development, World Health Organization; 2005.
4. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, et al. Burden and etiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): A prospective, case-control study. *Lancet* 2013;**382**:209-22.
5. World Health Organization. The rational use of drugs in the management of acute diarrhoea in children. Geneva, Switzerland: World Health Organization 1990.
6. Primi MP, Bueno L, Baumer P, Bérard H, Lecomte JM. Racecadotril demonstrates intestinal antisecretory activity *in vivo*. *Aliment Pharmacol Ther* 1999;**13**(Suppl 6):3-7.
7. Hinterleitner TA, Petritsch W, Dimsity G, Bérard H, Lecomte JM, Krejs GJ. Acetorphan prevents cholera-toxin-induced water and electrolyte secretion in the human jejunum. *Eur J Gastroenterol Hepatol* 1997;**9**:887-91.
8. Baumer P, Danquechin-Dorval E, Bertrand J, Vetel JM, Schwartz JC, Lecomte JM. Effects of acetorphan, an enkephalinase inhibitor, on experimental and acute diarrhoea. *Gut* 1992;**33**:753-58.
9. Mar Santos RM. Use of racecadotril as outpatient treatment for acute gastroenteritis: A prospective, randomized, parallel study. *J Pediatr* 2009;**155**: 62-67.
10. Cézard JP, Duhamel JF, Meyer M. Efficacy and tolerance of acetorphan in infant acute diarrhea: a multicentric, double blind study. *Gastroenterology* 1996;**110**:Suppl:A795.
11. Kenny J. Twin brush border metallo-endopeptidases. In: Lentze MJ, Sterat EE, editors. Mammalian brush border membrane proteins. Stuttgart, Germany: Thieme Verlag, 1990. P.75-88.
12. Salazar-Lindo E, Santisteban-Ponce J, Chea-Woo E, Gutierrez M. Racecadotril in the treatment of acute watery diarrhea in children. *New England Medical Journal* 2000;**343**:463-67.
13. Cojocaru B, Bocquet N, Timsit S, Wille C, Boursiquot C, Marcombes F, et al. Effect of racecadotril in the management of acute diarrhea in infants and children. *Arch Pediatrie Organe Off Sociéte Fr Pédiatrie* 2002;**9**:774-79.
14. Marc¸ais-Collado H, Uchida G, Costentin J, Schwartz JC, Lecomte JM. Naloxone reversible antidiarrheal effect of enkephalinase inhibitors. *Eur J Pharmacol* 1987;**144**:125-32.
15. Bergmann JF, Chaussade S, Couturier D, Baumer Ph, Schwartz JC, Lecomte JM. Effects of acetorphan, an antidiarrhoeal enkephalinase inhibitor, on oro-caecal and colonic transit times in healthy volunteers. *Aliment Pharmacol Ther* 1992;**6:**305-13.

16. Bhan MK, Bhatnagar S. Racecadotril: Is there enough evidence to recommend it for treatment of acute diarrhea? *Indian Pediatr* 2004;**41**:1203-04.

17. Eduardo OS, Javier S, Elsa W, Manuel G. Racecadotril in the treatment of acute watery diarrhea in children. *N Engl J Med* 2000;**343**: 463-67.

18. Jean P, France J, Duhamel O, Martin M, Isabelle P. Efficacy and Tolerability of Racecadotril in Acute Diarrhea in Children. *Gastoenterology*. 2001;**120**:799-805.

19. Marion Eberlin, Min Chen, Tobias Mueck, Jan Däbritz. Racecadotril in the treatment of acute diarrhea in children: A systematic, comprehensive review and meta-analysis of randomized controlled trials. *BMC Pediatr* 2018;**18**:124.

20. Gagandeep K, Thuppal SV, R Srinivasan. Racecadotril in the management of rotavirus and non-rotavirus diarrhea in under-five children: Two randomized, double-blind, placebo-controlled trials. *Indian Pediatr* 2016;**53**:595-600.

21. H Hamza, H Ben Khalifa, H Berard. Racecadotril versus placebo in the treatment of acute diarrhoea in adults. *Alimentary Pharmacology & Therapeutics* 2000;**6**:15-19.

22. Mehta S, Khandelwal PD, Jain VK, Sihag M. A comparative study of racecadotril and single dose octreotide as an anti-secretory agent in acute infective diarrhoea. *J Assoc Physicians India* 2012;6**0**:12-15.

23. Alam HN, Ashraf H, Khan WA, Karim MM, G J Fuchs. Efficacy and tolerability of racecadotril in the treatment of cholera in adults: A double blind, randomised, controlled clinical trial. *BMJ journal* 2003;**52**:1419-23.

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ORIGINAL ARTICLE

Hearing Impairment in Children with Congenital Hypothyroidism

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Abstract

Background: *There is increased risk of hearing impairment in children with congenital hypothyroidism (CH). Only a few studies have explored the prevalence of hearing impairment in CH and their results vary widely. There is no data of hearing impairment in Bangladeshi children with CH.*

Objectives: *The aim of this study was to investigate the prevalence of hearing impairment in children with CH, and its relation with age of diagnosis and the dose of thyroxine (T4) they received.*

Methods: *This study was conducted in Paediatric Endocrinology & Metabolic Disorder Department of Dhaka Shishu (Children) Hospital from July 2014 to December 2018. Hearing evaluation of 55 children diagnosed with CH was performed with a battery of tools that included Middle ear analysis, Pure Tone Audiometry (PTA), Behavioral Observation Audiometry (BOA) and Oto Acoustic Emissions (OAE). The choice of assessment tool was based on patient's age.*

Results: *The mean age at diagnosis and at inclusion into the study was 2.0±1.7 years and 3.2±2.3 years respectively. The etiological diagnosis was thyroid agenesis in 40(72.7%), ectopia in 3(5.5%), dyshormonogenesis in 7(12.7%) and hypothyroidism with eutopic gland in 5(9.1%%) patients. Middle ear analysis, PTA, BOA and OAE was done in 35, 28, 32 and 37 patients respectively. Sensorineural hearing loss was detected in 1 out of 55(1.8%) patients while conductive hearing loss was found in 3(5.4%) patients.*

Conclusion: *Hearing loss was present in a small proportion of patients with permanent CH. Further larger studies are required to determine the exact prevalence of hearing impairment in Bangladeshi children with CH.*

Keywords*: Children, congenital hypothyroidism, hearing loss, prevalence.*

Introduction

Thyroid hormone is necessary for normal development of the auditory system[1,2] and the association between thyroid hormone and hearing development has long been recognized in patients with congenital hypothyroidism (CH), endemic cretinism and thyroid hormone resistance.[3,4] Recent genetic studies confirmed the relation between thyroid hormone and hearing system development.[5,6] So, CH, the most common endocrine disorder with an incidence rate of 1/4000-5000 live births also increase the risk of hearing impairment in children.[7]

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Although mental outcome of CH patients is improved if patients are treated early in infancy, during CH screening, but subtle neurological deficits such as fine motor coordination, attention deficient, speech delay, hearing impairment, and hearing problems may develop.[8,9] Many studies, both in animal models and human patients have identified auditory system dysfunction among cases with thyroid disorders.[10] The rate of hearing loss has been reported to be 20-36% in CH patients before Iranian national CH screening program, and reported hearing loss was bilateral and severe.[11] On the other hand, recent reports held after CH screening programs, indicate that mild hearing loss occurs in up to 20% of CH patients.[12,13]

Hearing loss, specially its mild form in children may result in delayed speech and difficulties in comprehension and problems in receptive language, auditory processing and reading, which may persist, especially in those with delayed treatment.[14,15] Therefore, considering the consequences of CH and its related hearing loss and also the fact that CH was more prevalent in our community,[16,17] the aim of this study was to investigate the rate of hearing impairment in CH patients, and its relation with factors such as CH severity and age at starting treatment.

Materials and Methods

Children aged 6 months to 6 years diagnosed as permanent CH and on replacement therapy were recruited from paediatric endocrinology department of Dhaka Shishu (Children) Hospital between July 2014 and December 2018. All patients were underwent audiological evaluation by trained audiologist at specialized centre for hearing (SHAHIK, Dhaka, Bangladesh).

The diagnosis of hypothyroidism was based on low serum free T4 and elevated serum thyroid stimulating hormone (TSH) levels according to reference ranges.[18] Etiological diagnosis was based on the findings of technetium‑99m pertechnetate thyroid scintiscan and thyroid ultrasonography performed routinely at the time of initial evaluation of CH.[19] Perchlorate discharge test was done in selected cases. Those having subclinical hypothyroidism, transient hypothyroidism, history of familial hearing loss, dysmorphism, especially craniofacial anomalies, past history of significant neurological insult (bacterial meningitis, head trauma, mental retardation), otitis media or any other ear disease, significant neonatal problems such as very low birth weight, hyperbilirubinemia, mechanical ventilation, use of ototoxic medications were excluded. Autoimmune thyroid disease was excluded by routinely performing antithyroid peroxidase antibodies in all patients.[20] Children who fulfilled the criteria were enrolled into the study after obtaining written informed consent from the parents/caretakers.

The clinical and biochemical data were recorded into a prestructured proforma. A detailed otorhinolaryngological examination was done to exclude conditions listed in the exclusion criteria. The audiological investigations were done on all the patients by the same audiologist and on same instruments. The choice of hearing assessment tool was based on the patient's age and the ability to cooperate.

After an otoscopic examination to ensure that there was no wax or perforation, Middle ear analysis was performed by inserting the probe of Immittance Meter (MAICO MI 34, MAICO Diagnostics, Berlin, Germany) into the ear canal. A tympanogram was obtained based on the pressure variance at 226 Hz.

Puretone hearing thresholds were estimated in the frequency range of 250 Hz to 8 kHz using Madsen Orbiter 922 Clinical Audiometer Version II (GN Otometrics, Taastrup, Denmark) which was calibrated according to ANSI standards. Air conduction and bone conduction pure tone threshold curves were obtained for each ear separately. High frequency audiometry measuring thresholds at 10, 12, and 16 kHz was performed with the same audiometer. The pure tone average thresholds at 500, 1000, and 2000 Hz were also recorded for each ear. Speech recognition thresholds test was done to determine the faintest level at which a person could hear and repeat words presented at a comfortable intensity (e.g., 30-40 dB above the pure tone audiometry [PTA] of 500, 1000, and 2000 Hz). Speech discrimination score was calculated as the percentage of correctly repeated words after presenting 25 phonetically balanced monosyllables to the test ear at an intensity of 40-50 decibel above the average air conduction threshold for 500, 1000, and 2000 Hz, with the non-test ear masked adequately.

Behavioral responses were recorded to a variety of nonverbal stimuli for children aged <3 years and those not cooperative for PTA. The behavior was analyzed by observing consistent age†appropriate responses.

Transient evoked otoacoustic emissions (TrOAE) and distortion product OAE (DPOAE) were performed on SmartOAE and SmartTrOAE instruments (Intelligent Hearing Systems, Miami, USA), respectively. Individuals with abnormal results on behavioral observation audiometry (BOA) and OAE testing were further considered for brain stem evoked response audiometry.

All data were coded and entered in SPSS for Windows (Version 20.0; IBM Corp., Armonk, NY, USA) for analysis. Descriptive statistics was reported as mean and standard deviation while the qualitative variables were recorded in proportions. Associations were evaluated using Pearson correlation test, Chi square test, and Fisher's exact test. Multiple regression analysis was used to access the relationship of hearing loss to factors such as age at diagnosis and dose of T4. A $p<0.05$ was considered statistically significant.

Results

The study population consisted of 55 children. The mean age at diagnosis was 2.0±1.7 years and their mean age at inclusion into the study was 3.2 ±2.3 years. The interval between diagnosis of CH and the date of enrolment into the study was <1, 1-3 years and >3 years in 15 (27%), 18 (33%) and 22 (40%) patients, respectively (Table I).

Table I
Interval between age at diagnosis and age at inclusion

Age interval	Number of patients (%)
< 1 year	15 (27)
1-3 year	18 (33)
>3 year	22 (40)
Mean age at diagnosis - 2.0±1.7 years	
Mean age at inclusion into the study - 3.2 ±2.3 years	

The etiology of CH based on the results of combined scanning and PDT was thyroid agenesis in 40(72.7%), ectopia in 3(5.5%), DH in 7(12.7%), and hypothyroidism with eutopic gland in 5(9.1%) (Table II).

Table II
Etiological diagnosis of hypothyroidism

Etiology	Number of patients (%)
Thyroid agenesis	40 (72.7)
Ectopia	3 (5.5)
Dyshormonogenesis	7 (12.7)
Eutopic	5 (9.1)
Total	55 (100)

The presenting features included constipation in 22(40%), developmental delay in 11(20%), lethargy in 8(14.5%), prolonged neonatal jaundice in 8(14.5%), growth retardation in 5(9%), and attention deficit in 1(1.8%). Eleven (20%) had nonspecific symptoms. None of the patients complained of hearing loss (Table III).

Table III
Distribution of presenting feature at diagnosis

Presenting feature	Number of patients (%)
Constipation	22(40)
Developmental delay	11(20)
Lethargicness	8(14.5)
Prolonged neonatal jaundice	8(14.5)
Growth retardation	5(9.0)
Attention deficit	1(1.8)
Non-specific symptoms	11(20)
Hearing loss	0(0)

Impedance audiometry was performed in 35 patients. Thirty-two (91.4%) patients had normal type A tympanogram and 3(8.6%) had type B tympanogram suggestive of conductive pathology of the left ears. On the right side, 34(97.2%) patients showed type Atympanogram and 1(2.8%) had type B tympanogram. PTA was done in 28 patients in both the ears and showed normal results. There was no relation between age, age at diagnosis, and dose of T4 and frequencies in both the ears. All the 43 patients who underwent BOA showed normal response in the right ear. In the left ear, response was absent in 1 patient suggestive of mild SNHL. Thirty-seven patients who underwent TrOAE and DPOAE showed normal results (Table IV).

Table IV
Results of audiological investigations

Method	Number of patients performed	Result			
		Normal		Abnormal	
		Left	Right	Left	Right
Impedance audiometry	35	32	34	3	1
Pure tone audiometry	28	28	28	0	0
Behavioral observation audiometry	43	42	43	1	0
Otoacoustic emissions (TrOAE & DPOAE)	37	37	37	0	0

Based on the results of all the hearing assessment tests, SNHL was detected in 1 out of 55 (1.8%) patients while conductive hearing loss was found in 3 (5.4%) (unilateral in 2) patients.

Discussion

All but one of our patients showed normal hearing and the prevalence of hearing impairment was 1.8%, which is close to the lowest (1.2%) reported so far from India.[21] A previous study from Iran estimated a prevalence of 3.2% in CH patients diagnosed by newborn screening and initiated on early treatment.[22] In all other studies, the prevalence of hearing impairment ranged between 20% and 50%.[23-25] However, François et al[26] documented normal hearing in all the 42 children of a cohort of CH. The differences in results can partly be attributed to small sample sizes. The number of patients assessed for hearing impairment ranged between 32 and 75 in the previous studies.[23-26] Other factors that may contribute to differences in prevalence are the methods of hearing assessment, age of hearing examination, or differences in genetic factors in different patient populations.[22] Genetic component in CH is indicated by an increased occurrence in down syndrome,[27] advanced maternal age,[28] and increased occurrence in families.[29] The only patient who was detected to have hearing impairment in our study had DH similar to previous observations.[23] The higher risk of hearing impairment in DH is probably due to the underlying genetic factors.[30]

The effect of treatment or the dose of T4 did not seem to have any relationship with hearing impairment in our patients. Treatment with T4 was shown to improve the minor abnormalities of hearing in a previous study.[31] The improvement was attributed to a better recruitment of neuronal pool of the generators of the auditory brainstem response waves in the brainstem and thalamocortical projections of the auditory pathways which are adversely affected in the hypothyroid state.[31] However, even with early treatment, specific auditory brainstem evoked potential abnormalities were found in 25% of patients in another study.[24] The conductive hearing loss observed in some of our patients is probably because of common occurrence of otitis media in this age group in our set up.[32]

Conclusion

Although a very lower rate of hearing loss found among our studied CH patients, the importance of early treatment of hearing loss in order to prevent speech and language development problems, physicians should look for hearing loss in any patient with CH. Further studies with larger sample size are required to delineate the exact burden of hearing loss in our children with CH.

References

1. Mra Z, Wax MK. Effects of acute thyroxin depletion on hearing in humans. *Laryngoscope* 1999;**109**:343-50.

2. Knipper M, Zinn C, Maier H. Thyroid hormone deficiency before the onset of hearing causes irreversible damage to peripheral and central auditory systems. *J Neurophysiol* 2000;**83**:3101-12.

3. DeLong GR, Stanbury JB, Fierro-Benitez R. Neurological signs in congenital iodine-deficiency disorder (endemic cretinism). *Dev Med Child Neurol* 1985;**27**:317-24.

4. Brucker-Davis F, Skarulis MC, Pikes A. Prevalence and mechanisms of hearing loss in patients with resistance to thyroid hormone. *J Clin Endocrinol Metab* 1996;**81**:2768-72.

5. Knipper M, Richardson G, Mack A. Thyroid hormone-deficient period prior to the onset of hearing is associated with reduced levels of beta-tectorin protein in the tectorial membrane: implication for hearing loss. *J Biol Chem* 2001;**276**:39046-52.

6. Forrest DC, Erway L, Ng L. Thyroid hormone receptor â is essential for development of auditory function. *Nature Genetics* 1996;**13**:354-57.

7. Bradley DJ, Towle HC, Young S. Alpha and beta thyroid hormone receptor (TR) gene expression during auditory neurogenesis: evidence for TR isofrom–specific transcriptional regulation in vivo. *Proc Natl Acad Sci* 1994;**91**:439-43.

8. Bargagna S, Canepa G, Costagli C, et al. Neuropsychological follow-up in early-treated congenital hypothyroidism: A problem-orien-ted approach. *Thyroid* 2000; **10**: 243-49.

9. Vanderscheuren-Lodeweyckx M, Debruyre F, Dooms L. Sensorineural hearing loss in sporadic congenital hypothyroidism. *Arch Des Child* 1983;**58**:419-22.

10. Li M, Rsoyages SC. Detection of extended distribution of beta2-thyroid hormone receptor messenger ribonucleic acid (RNA) in adult rat brain using complementary RNA in situ hybridization histochemistry. *Endocrinology* 1996;**137**:1272-75.

11. Crifo S, Lazzari R, Salabe GB. A retrospective study of audiological function in a group of hypothyroid patients. *Int J Pediatr Otorhino-larygeol.* 1980;**2**: 347-55.

12. Fracois M, Bonfils P, Leger J. Audiological assessment of eleven congenital hypo-thyroidisms before and after treatment. *Acta Otolaryngol* 1993;**113**:39-42.

13. Hebert R, Laurea E, Nanasse M. Auditory brainstem response audiometry in congenitally hypothyroid children under early replacement therapy. *Pediatr Res* 1986;**20**:570-73.

14. Gordon N. Abnormal response to sound and central auditory processing disorder. *Dev Med Child Neurol* 1995;**37**:645-52.

15. Barett KA. Hearing and immittance screening of school age children. In: Katz J, editor. Handbook of Clinical Audiology. 3rd ed. Baltimore: Williams & Wilkins; 1985. P. 621-41.

16. Hashemipour M, Amini M, Iranpour R. Prevalence of congenital hypothyroidism in Isfahan, Iran: results of a survey on 20,000 neonates. *Horm Res* 2004;**62**: 79-83.

17. Karamizadeh Z, Dalili S, Sanei-far H. Does Congenital hypothyroidism have different etiologies in Iran? *Iran J Pediatr* 2011;**21**:188-92.

18. The Association of Clinical Biochemistry. UK Guidelines for the Use of Thyroid Function Tests, British Thyroid Association's; 2006. Available at: http://www.british†thyroid†association.org. [Last accessed on 2015 Sep 15].

19. Dayal D, Sindhuja L, Bhattacharya A, Sodhi KS, Sachdeva N. Agenesis and not ectopia is common in North Indian children with thyroid dysgenesis. *Indian J Endocrinol Metab* 2014;**18**(Suppl 1): S97-S99.

20. Dayal D, Naganur SH, Siakia BK, Singh B. Thyroid dysfunction and autoantibodies in first degree relatives of North Indian children with autoimmune thyroiditis. *Thyroid Res Pract* 2015;**12**:96-99.

21. Dayal D, Hansdak N, Vir D, Gupta A, Jaimanti B. Hearing impairment in children with permanent congenital hypothyroidism: Data from Northwest India. *Thyroid Res Pract* 2016;**13**:67-70.

22. Hashemipour M, Hovsepian S, Hashemi M, Amini M, Kelishadi R, Sadeghi S. Hearing impairment in congenitally hypothyroid patients. *Iran J Pediatr* 2012;**22**:92-96.

23. Crifò S, Lazzari R, Salabè GB, Arnaldi D, Gagliardi M, Maragoni F. A retrospective study of audiological function in a group of congenital hypothyroid patients. *Int J Pediatr Otorhinolaryngol* 1980;**2**: 347- 55.

24. Chou YH, Wang PJ. Auditory brainstem evoked potentials in early treated congenital hypothyroidism. *J Child Neurol* 2002;**17**:510-14.

25. Rovet J, Walker W, Bliss B, Buchanan L, Ehrlich R. Long term sequelae of hearing impairment in congenital hypothyroidism. *J Pediatr* 1996;**128**: 776 -83.

26. François M, Bonfils P, Leger J, Czernichow P, Narcy P. Role of congenital hypothyroidism in hearing loss in children. *J Pediatr.* 1994;**124**:444-46.

27. Dayal D, Jain P, Panigrahi I, Bhattacharya A, Sachdeva N. Thyroid dysfunction in Indian children

with Down syndrome. *Indian Pediatr* 2014;**51** 751- 52.

28. Dayal D, Sindhuja L, Bhattacharya A, Bharti B. Advanced maternal age in Indian children with thyroid dysgenesis. *Clin Pediatr Endocrinol* 2015; **24**:59 -62.
29. Sindhuja L, Dayal D, Sodhi KS, Sachdeva N, Bhattacharya A. Thyroid dysfunction and developmental anomalies in first degree relatives of children with thyroid dysgenesis. *World J Pediatr* 2016;**12**:215-18.
30. Dayal D, Prasad R. Congenital Hypothyroidism: Current Perspectives. *Res Rep Endocr Disord* 2015; **5**:91-102.
31. Anjana Y, Vaney N, Tandon OP, Madhu SV. Functional status of auditory pathways in hypothyroidism: Evoked potential study. *Indian J Physiol Pharmacol* 2006;**50**:341 49.
32. Kalpana R, Chamyal PC. Study of prevalence and aetiology of the hearing loss amongst school going children. *Indian J Otolaryngol Head Neck Surg* 1997;**49**:14.

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ORIGINAL ARTICLE

Clinical Characteristics of Measles in Infancy: A Hospital Based Study

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Abstract

Background: *There is a global resurgence of measles among children in recent years and a number of infants are being affected.*

Objectives: *The aim of the study was to determine the frequency of measles in infancy and to describe their clinical characteristics in a tertiary care children hospital.*

Methods: *A prospective observational study was conducted in Dr. MR Khan Shishu Hospital and Institute of Child Health from March, 2019 to February, 2020. The children who came with signs and symptoms of measles, like fever with maculopapular rash associated with cough, runny nose and conjunctivitis were recorded and frequency of measles in infants among hospitalized measles patients was noted. Infants with measles were enrolled for the study and their clinical characteristics, complications and outcome were determined. Data were analyzed by SPSS version 23.*

Results: *A total of 64 infants were studied. The frequency of measles in infants among hospitalized measles patients was 43%. Forty seven percent infants were between 9 to 10 months. Clinical features were typical and all had fever and maculopapular rash. Pneumonia was the main complication and occurred in 50(78%) cases which was followed by oral ulcer 42(66%), diarrhea 26(41%), febrile seizure 9(14%) and croup 5(8%). Thirty four (53%) infant had normal nutritional status. Only 19.51% infant received first dose of measles vaccine. The mortality rate was 2(3%).*

Conclusion: *A number of children are being affected by measles before completing first year of life and they develop complications which are related to morbidity and mortality. So, control and prevention of measles in infancy should give more importance.*

Keywords: *Measles, infancy, vaccination.*

Introduction

Before the introduction of vaccines, measles virus infected 95%-98% of children by the age 18 years and was responsible for more than 2 million deaths worldwide annually.[1-3] After almost thirty years of effective vaccination program in Bangladesh, measles continues to cause a serious disease in children. It is still responsible for more than 100,000 deaths globally every year.[1] According to World Health Organization (WHO) during the year 2015, globally 367 deaths/ day occurred due to measles in children of below five years.[4] Worldwide measles cases dropped from 850,000 to 132,000 between 2000 and 2016, but cases surged to 360,000 in 2018. In

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2019, about 430,000 measles cases have been reported with 142,000 deaths, mostly children under the age of 5 year.[4,5] So, measles remains an important cause of morbidity and mortality in young children, especially in developing countries.[6] Acute measles infection below one year of age is associated with more complications and increased mortality.[7]

Measles is a highly contagious acute viral illness that includes a characteristic rash.[2] This is transmitted by respiratory secretions during prodormal phase and early stage of rash. The disease starts with fever, cough, coryza and often conjunctivitis. Three to four days later a generalized maculopapular skin rash appears. After exposure up to 90% of susceptible individual develop measles.[8] The disease is self limited but some patients especially younger ones and immunocompromised persons develop complications which may require hospitalization.[8] The most important complications are bronchopneumonia, otitis media, croup, diarrhea and encephalitis.[9,10] Pneumonia is the commonest complication and accounts for 60% of measles related death.[8, 11]

Measles is mainly a childhood disease though it can affect people of any age.[11] This is a vaccine preventable disease. In Bangladesh, first dose of MR (measles, rubella) vaccine is given at 9 months and the second dose at 15 months. It has been assumed that maternal antibody gives protection against measles and other infectious diseases throughout infancy.[12] If vaccination is given earlier natural antibody can hamper humoral antibody response.[13] So, centre for disease control and prevention recommends the first dose of measles vaccine not to be given before one year of age.[14] In recent years it is observed that a number of children below one year of age have been infected with measles, particularly in outbreak settings.[13,15] Recent studies also showed that maternal antibody wanes much sooner, before 6 months.[15] Measles in younger children is associated with severe complications due to their immunecompromised status, a number of deaths occur in this age group.[16,17]

Aim of the study was to determine the frequency of measles occurring in infancy in a tertiary care children hospital and to describe the clinical features, complications, vaccination and nutritional status of children with measles below one year of age.

Materials and Methods

It was a prospective observational study conducted in Dr. MR Khan Shishu Hospital and Institute of Child Health from March, 2019 to February, 2020. The study population was children of 4 months to 12 years admitted in hospital having signs and symptoms of measles. Measles was diagnosed clinically according to case definition criteria by World Health Organization like high fever (>38°C) associated with cough, coryza (runny nose), conjunctivitis (red eye, watering).[18]

After taking informed written consent from parents; history was taken regarding age, sex, socio-economic condition, gestational age, breast feeding and vaccination. Then thorough physical examination was done, their weight and height were recorded and different complications were noted. Investigations like CBC, CRP and CXR were done in all cases.

For data collection structured questionnaire were fulfilled. Data were processed and analyzed by SPSS version 23 and results were given in tabulated form.

Results

A total of 148 children suffering from measles with different complications were admitted during the study period. Among them 64 (43.24%) were below one year of age. Age range was from 4 months to 12 years. So, the frequency of measles in infancy among hospitalized measles children was 43.24%. Among them 30(46.87%) were in age group 9 to 10 months (Table I).

Table I
Age distribution of study population (N=64)

Age group	No of patients	Percentage
<6 months	2	3.13
6 to 8 months	21	32.81
9 to 10 months	30	46.87
11 to 12 months	11	17.19
Total	64	100

Among the study population male were 41 and female were 23. Male to female ratio was 1.8:1. All infants were presented with fever and maculopapular rash. Cough and coryza were the frequent clinical features and were present in 58(90.62%) and 53(82.81%) cases respectively. Conjunctivitis was present in 35(54.68%) and Koplik spot in 23(35.93%) cases (Table II).

Table II
Clinical features of the study population (N=64)

Clinical features	Number	Percentage
Fever	64	100
Maculopapular rash	64	100
Cough	58	90.62
Coryza	53	82.81
Conjunctivitis	35	54.68
Koplik Spot	23	35.93

Pneumonia was the most common complications and developed in 50(78.13%) cases. This was followed by oral ulcer 42(65.62%), diarrhea 26(40.63%), febrile seizure 9(14.06%) and croup 5(7.8%). Oral ulcers were not extensive. Some patients developed both pneumonia and diarrhea (Table III).

Table III
Complications of measles in infants (N=64)

Complications	Number	Percentage
Pneumonia	50	78.13
Oral ulcer	42	65.62
Diarrhea	26	40.63
Febrile seizure	9	14.06
Croup	5	7.81

Regarding nutritional status, 34(53.12%) infant had normal nutrition; whereas 6((9.37%) had severe malnutrition (Fig. 1).

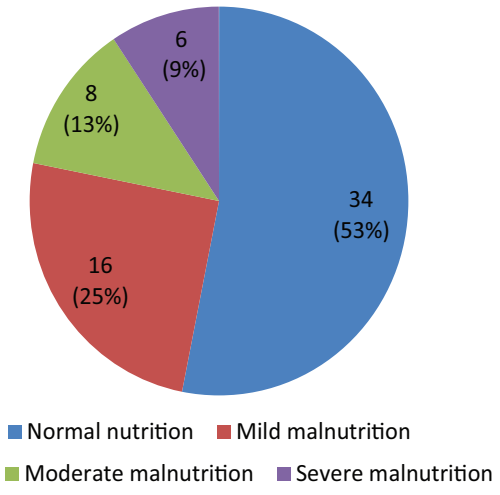

Fig 1 *Nutritional status of the study children*

Among the study children 57(89.06%) born at term, 47(73.44%) were exclusively breast fed upto 6 months. The number of infants from 9 month to 1 year was 41. Among them only 8 (19.51%) received first dose of measles-rubella vaccine and 33(80.48%) did not. Two children died due to pneumonia as complication and they were severely malnourished (Table IV).

Table IV
Clinical characteristics of study children (N=64)

Clinical characteristics	Number	Percentage
Birth History		
Term	57	89.06
Preterm	7	10.94
Breast feeding up to 6 months		
Yes	47	73.44
No	17	26.56
Measles vaccination after 9 month		
N=41 (9 mo to 1 year)		
Yes	8	19.51
No	33	80.49
Outcome		
Recovery	62	96.88
Death	2	3.12

Discussion

Out of total 148 measles cases of 4 months to 12 years, 64(43.24%) were below 1 year of age. These infants were our study cohort. The frequency of measles in infancy among hospitalized measles patient was also 43% in Ahsan et al[19] study and 30% in Khan et al[7] study. Aktaruzzaman et al[20] found 23% of measles cases below 9 month of Bangladeshi hospitalized children.

Male to female ratio in this study was 1.8:1. A male preponderance was observed which was consistent with Ahsan et al[19] (2.5:1) and Khan et al[7] study (1.5:1). In our study lowest age of infant was 4 month, which was 4.5 month in Khan et al[7] and only 27 days in Wu et al[14] study.

The clinical manifestations were typical. Fever and maculopapular rash were present in all cases. Fever was present from beginning and koplik's spot was present in 35.93% cases. Perry et al[1] found koplik's spot in 60-70% cases. Cough was present in 90.62% of our study children and pneumonia was the most common complication (78.13%), followed by oral ulcer (65.62%) and diarrhea (40.63%). In the study done

by Wu et al[14] pneumonia was present in 63% of infants and in Khan et al[7] study pneumonia and diarrhea were present in 56% and 17% cases respectively. Croup was present in 7.8% of our study children which was consistent with Khan et al[7] study (10%). Different study showed otitis media as an important complication of measles but we found only few cases of otitis media.[1, 7]

Most of the infant of our study was term by gestation (89%) and also on exclusive breast feeding up to 6 months (73%). Out of total 64, the number of children from 9 month to 12 month was 41(64%). Among them only 8(19.51%) received first dose of measles-rubella vaccine and rest 33(80.48%) did not. Many of them were suffering from minor illnesses and vaccination was deferred. In some cases parents were not aware of timely vaccination. These could be the reason of poor vaccination status of our study. Ahsan et al[18] showed 82% patient received first dose of measles vaccine and most of the measles children came before they complete the second dose at 15 months. A good number of children 34(53%) had normal nutritional status and 24(38%) had mild to moderate malnutrition. Six (9%) children had severe malnutrition; two of them died.

In this study 23(36%) infant had measles before 8 month of age. In Wu et al[14] study among 220 infants, 80.46% of measles children were below 8 months of age. Other studies also suggested that measles tends to affect those of younger age worldwide particularly in outbreak settings.[17, 21]

In Bangladesh first dose of measles vaccine is given at 9 month with an intention to maternal antibody will not interfere with acquired immunity and to provide immunity to the maximum number of infant. But in recent studies it has been revealed that protection from maternal antibody is short lived.[13] The reason may be that mothers' immunity against measles is due to vaccination rather than natural protection. It is suggested that antibody formed by disease occurrence is longer duration than antibody formed by vaccination.[14] In Leuridian et al[15] study positive measles antibodies in the body was only 7.14% at 8 months of age. It has been reported that, if a mother receives measles vaccine again before pregnancy, the measles antibody levels of the cord blood of her baby will be significantly higher than those of babies whose mother were not revaccinated.[22] So, some country recommends that women at child bearing age should receive revaccination against measles before pregnancy.[14] In endemic areas more than 95% vaccine coverage is required to interrupt transmission of measles.[13] So, routine immunization with maintenance of proper cold chain and timely instituted outbreak immunization response can halt measles progression.

Conclusion

A number of children are being affected by measles before completing first year of life and they develop complications which are related to morbidity and mortality. So, control and prevention of measles in infancy should give more importance.

References

1. Perry RT, Halsey NA. The clinical significance of measles: A review. *Journal of Infectious Disease* 2004;**189**(Suppl I):4-11.
2. McLean HQ, Fiebelorn AP, Temte JL, Wallace G. Prevention of Measles, Rubella, Congenital Rubella Syndrome and Mumps. Summary recommendations of the advisory committee on Immunization Practices (ACIP). 2013;**62**:1-34.
3. Moss WJ. Measles. *Lancet* 2017;**390**:2490-502.
4. WHO. Measles: Key facts.who.int/news-room/fact-sheet/detail/measles.5 December 2019.
5. Kuehn MB. International measles vaccination campaign to reach millions. *JAMA* 2020;**323**:1033.
6. Stebel PM, Cochi SL, Hoekstra E. A World without Measles. *Journal of Infectious Disease* 2011; **204**(Suppl I):1-3.
7. Khan I, Khattak AA, Muhammad A. Complications of measles in hospitalized children. *Khyber Medical University Journal* 2013;**5**:27-30.
8. Kobaidze K, Wallace G. Forgotten but not gone: Update of measles infection for hospitals. *Journal of Hospital Medicine* 2017;**2**:472-76.
9. Leung AKC, Hon KL, Leong KF, Sergi CM. Measles: A disease often forgotten but not gone. *Hong Kong Medical Journal* 2018;**4**:512-20.
10. Gershon A. Measles (rubeola). In: Braunwald E, Fauci AS, Kasper DL, Hauser SL, editors. Harrisons Principles of Internal Medicine. 15th ed. New York, NY: McGrew-Hill; 2001: p. 1143-45.
11. Dardis MR. A review of Measles. *J Sch Nurs* 2012; **28**:9-12.
12. Kumar D, Sabella C. Measles: Back again. *Cleveland Clinic Journal of Medicine* 2016;**83**:340-44.

13. Mellisa J. Infants' Measles protection from mother short lived. AAP News Article. November 21, 2019. aappublications.org/news/2019/11/21/measles/1121

14. L Wu, B Ning, Y Wang. Clinical analysis of 220 infants less than 12 months old with measles. *HKJ Paediatr* 2018;**23**:272-76.

15. Leuridan E, Hutse V, Leven M, Aerts M, Van Damme P. Early weaning of maternal Measles antibodies in case of Measles elimination: Longitudinal study. *BMJ* 2010;**340**:1226-30.

16. Porter A, Goldfarb J. Measles: A dangerous vaccine preventable disease returns. *Cleveland Clinical Journal of Medicine* 2019;**86**:393-98.

17. Antona D, Levy-Bruhl D, Baudon C. Measles elimination efforts and 2008-2011 outbreaks, France. *Emerge Infect Dis* 2013;**19**:357-64.

18. Measles clinical management guideline. December 2019. Reliefweb.int/sites/reliefweb.int/files/ resources/ 20191217.

19. Ahsan RM, Mamun MAA, Alam KHS, Sarker KP, Makbul S, Kabir R, et al. Occurrence of Measles among children admitted in tertiary care hospital. *Bangladesh J of Child Health* 2018;**42**:15-18.

20. Akteruzzaman SM, Cutts FT, Hossain MJ, Wahedi OK, Nahar N. Measles vaccine effectiveness and risk factors for measles in Dhaka, Bangladesh. *Bulletin of the World Health Organization* 2002;**80**:776-82.

21. Huoi C, Casalengo JS, Benet T. A report of the large measles outbreak in Lyon, France, 2010 to 2011. *Euro surveill* 2012;**17**:202-64.

22. Leuridan E, Van Damme P. Passive transmission and persistence of naturally acquired or vaccine-induced maternal antibodies against measles in newborns. *Vaccine* 2007;**25**: 296-304.

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ORIGINAL ARTICLE

Assessment of Iron Status in Hemoglobin E and β Thalassemia Carriers

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Abstract

Background: *About 10-13% people of Bangladesh are carrier of HbE and β-thalassaemia. Many program have been taken by Government and NGOs for supplementation of iron to raise hemoglobin level of children which may not be beneficial or might be harmful to the carriers of this disease.*

Objectives: *of the study was to assess the iron status of Hemoglobin E and β thalassemia carriers thereby to develop iron supplementation strategy for these carriers.*

Methods: *This cross sectional analytic study was on 206 carriers of Hemoglobin E and β thalassemia and 54 healthy controls. Complete blood count with RBC indices, Hemoglobin (Hb) electrophoresis and serum ferritin, serum iron and TIBC were carried out for all subjects following standard protocol. Data were analyzed by Statistical Package for Social Science (SPSS) Version 12.*

Results*: Among 260 subjects 206 were carriers and 54 were control. Number of male was 137 and female was 123 and male to female ratio was 1.1:1. Age of the subjects ranges from 1 year to 59 years with a mean age (±SEM) of 23.07± 0.84 years. Mean age (±SEM) of cases was 22.78 ± 0.971 years and that of control was 24.17 ± 1.63 years. Hematological parameters such as mean (±SEM) Hb concentration, MCV, MCH, and MCHC of carriers were significantly low as compared to the control (p value < 0.01 in all comparison). Mean serum ferritin and iron level in carriers were higher than control however; statistical significance between the values were not found (p value >0.5). Out of 206 carriers 27 (13.1%) cases had IDA and it's frequency was similar among HbE (14.2%) and thalassemia carriers (12.2%) and prevalence of IDA among the carriers were high (37.5 %) in age group 1-5 years which rises to 52.5% in under nourished children.*

Conclusion: *Carriers of HbE and β thalassemia do have relatively higher iron profile as compared to control but not statistically significant. Iron deficiency anemia is not uncommon in carriers especially in children. So there is no contraindication of iron supplementation to the children in general.*

Keywords: *Iron status, hemoglobin E, β thalassemia carriers.*

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Introduction

Thalassemia and hemoglobinopathies are the most common inherited disorder in human and they represent a growing major public health problem in many countries of the world.[1,2] World Health Organization (WHO) estimates that 7% of world populations have hemoglobin disorders and each year 300000-400000 babies are born with severe disease.[1] Among the hemoglobinopathies, HbE is the most common abnormal hemoglobin in South East Asia reaching a carrier state of about 60%.[3,4] It is caused by substitution of glutamic acid by lysine at codon 26 of the â globin chain.[5] It is prevalent in Indian subcontinent including India, Pakistan, Bangladesh and Srilanka.[2,6] In heterozygous state â thalassemia and heterozygous state of HbE and homozygous HbE result in hypochromic microcytosis with minimal anemia.[7-9] The interaction between β thalassemia and HbE results in HbE- β thalassemia having thalassemic phenotype ranging from a condition indistinguisable from ß thalassemi major to a milder form of ß thalassemi intermedia.[10] HbE-â thalassemia is the most serious form of HbE syndromes affecting a million of people worldwide and it is found to be the commonest congenital hemolytic anemia in Bangladesh.[6,11]

In Bangladesh, two separate hospital based study done one in Dhaka Shishu Hospital on 100 samples and another in Pediatric Hematology and Oncology dept of Bangabandhu Sheikh Mujib Medical University on 300 sample showed HbE carrier status of 10-12% and β thalassemia carrier status of 1-2.3%.[12,13] The results indicate that large number of people is carrier of HbE and â thalassemia in our country. These people are having lower concentration of hemoglobin with an otherwise normal physical appearance.[14-16] Sometimes, early laboratory investigation like CBC and blood film shows indistinguishable report from iron deficiency anemia.[17,18] and these patients are regularly being prescribed with Iron supplements for correction of anemia, which might cause iatrogenic iron overload in these carriers. Moreover, many Government and NGO's are running programs for supplementing iron to raise hemoglobin routinely to the children and pregnant mothers which may not help these carriers rather might do harm for them.

One of the major problems of ß thalassemia is iron overload, which causes morbidity and mortality due to dysfunction of organ and tissue because of transfusion, ineffective erythropoiesis and enhanced intestinal absorption. Morbidity from iron overload in non-transfused patients secondary to increased gastrointestinal absorption is also common.[14] So assessment of iron status is necessary for these carriers.

Iron absorption has been studied by different worker with variable result. Bannerman et al[19] found no difference in individual in regard to iron absorption in ß thalassemia trait on the other hand; Crossby et al[20] reported increased iron absorption in individual with heterozygous ß thalassemia. Vichinsky et al[6] also described about increased iron absorption in heterozygous HbE. Variable degree of increased iron absorption is expected in ß thalassemia trait because ineffective erythropoiesis is one of the factors that stimulate iron absorption from gastrointestinal tract.[21] Variable iron statuses in ß thalassemia trait are reported by many workers in different ethnic groups and in different settinngs.[22,23] In our country frequency of coincident of iron deficiency and ß thalassemia trait has been assessed in a small sample however assessment in regard to HbE has not been done.[16] So, this study has been designed to see the iron status of the carriers of HbE and ß thalassemia with a lager sample.

Materials and Methods

This **c**ross sectional analytic study has been carried out in department of Pediatric Hematology and Oncology, Bangabandhu Sheikh Mujib Medical University from May 2009 to June 2010. A total 300 cases were recruited from volunteers who wanted to know their ß thalassemia/Hb E carrier status, siblings, parents and relatives of diagnosed thalassemia syndrome of aged 1 year and more. Patients of known thalassemia syndrome, one who received blood transfusion within three months due to any cause or taking iron containing drugs or suffering from acute or chronic diseases and pregnant women were excluded from the study.

After getting informed written/verbal consent a short history regarding age, sex, family history, blood transfusion, food habit, iron therapy or any acute and chronic illness were taken. A thorough physical survey including measurement of height and weight was also made before primary inclusion. Findings of the history and physical survey were recoded in pretest questionnaire. From each case 4 ml blood

was drawn from ante cubital vein in 5ml syringe. Two ml sample was kept in apendorfs containing 100 µl EDTA (ethylene di amino tetra acetic acid) and 2 ml was kept in plain test tube without anticoagulant from which serum was separated after centrifugation and stored at -80^0 C for serum ferritin, serum iron and TIBC assay. From first sample hematological analysis was done on the day of collection and rest of the sample was then stored at 4^{0}C for Hb electrophoresis. Peripheral blood film was prepared during collection of the sample.

Hematologic analysis was done by Hematology analyzer (XT 800i, Fluorescence Flow cytometry 5 part differential, 40 parameters analyzer, Manufacturer Sysmex Corporation, Country of origin Japan). The reports were checked manually by observing Leishman stained peripheral blood smears.

Hemoglobin electrophoresis was done on each sample to see the variants of hemoglobin within 7 days of collection by Beckman Coulter (made in USA) Paragon^R Hemoglobin (Hb) electrophoresis system KIT (P/N441780) by Hydra Gel (agar gel) electrophoresis in alkaline media following manufacturer's instruction. Serum ferritin was assayed by Abbott A$_X$SYM system analyzer using Microparticle Enzyme Immunoassay (MEIA) technology and serum iron and TIBC were assayed by Dade behring Clinical chemistry analyzer from Biochemistry department of BSMMU, Dhaka.

HbE carrier and disease were considered with concentration of HbA_2+E >17% and <50% and HbA2+E >85% respectively irrespective of RBC indices[24] b thalassemia carrier was considered when HbA_2 level ³3.5% and <6.8%[24,25] irrespective of RBC indices and Hb concentration. Iron deficiency anemia (IDA) was considered when serum ferritin level <12 µg/L.[26]

Data were entered and edited and analyzed by Statistical Package for Social Science (SPSS) Version 12. Mean value with standard deviation of all carriers and control of hemoglobin MCV, MCH, MCHC and RDW; serum ferritin, serum iron, TIBC were calculated. Statistical significance was determined by Student's t test. A p value of <.05 was considered as minimal level of significance.

Results

Among 300 subjects recruited initially, after automated analysis of blood and electrophoresis, 40 cases were excluded and finally 260 cases were analyzed. Out of excluded 40 subjects, 21 had microcytic red cell with normal or low HbA2; 13 subjects had abnormal hemoglobin other than HbE (HbD carrier- 4, HbD disease- 1, Fast moving band-2, Hereditary Persistence of Fetal Hemoglobin (HPFH)- 4) and 5 subjects had microcytic red cell with borderline raised HbA_2 >0.3%.

Table I shows age distribution of subjects in which 18 % was in 1-5 yrs age group, 13 % was in 6-18 years group and 69 % was in the age group of more than 18 years. Age of the subjects ranges from 1 year to 59 years with a mean (±SEM) age of 23.07 ± 0. 84 years. Mean (±SEM) age of cases was 22.78± 0. 971 years and that of control was 24.17 ± 1.63 years. There is no statistical significant difference between the mean ages of the two groups (p value 0.46).

Table I
Age distribution of cases and control (N=260)

Age group (year)	Number	Percentage
1-5	46	17.6
6-18	35	13.4
>18	179	69.0

Table II shows nutritional status of the cases and control. Under nutrition was defined in age group 1-5 years by weight /age of <3rd centile of NCHS mean, in age group 6-18 years by BMI (Body Mass Index) of <5th centile for age and sex and in age group >18 years by BMI <18.5. Overall rate of under nutrition was 20%. In the age group of 1-5 years, frequency of under nutrition was very high (39.1%).

Table II
Nutritional status of the cases and control

Cases and control	Under nourished		Well nourished	
	Number	%	Number	%
All subjects (n=260)	52	20.0	208	80.0
All cases (n=206)	48	23.3	158	76.7
1-5 yrs (n=46)	18	39.1	28	60.9
6-18 years (n=35)	7	20.0	28	80.0
>18 years (n=179)	27	15.0	152	85.0

Among 260 subjects, 137 (52.7%) were male and 123 (47.3%) were female with a male to female ratio of 1:11 (Fig. 1). Most of the cases (41%) came from Dhaka division followed by 27% from Chittagang, 13% from Barishal, 11% from Rajshahi division, 6% from Khulna, and 2% from Sylhet division (Fig. 2).

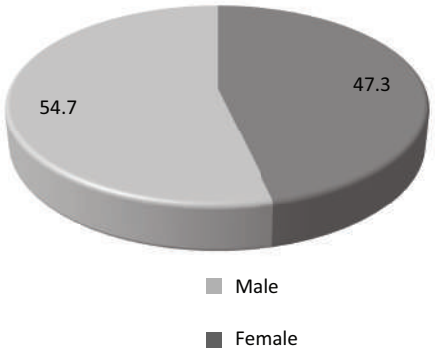

Fig 1 *Sex distribution of the subjects (n=260)*

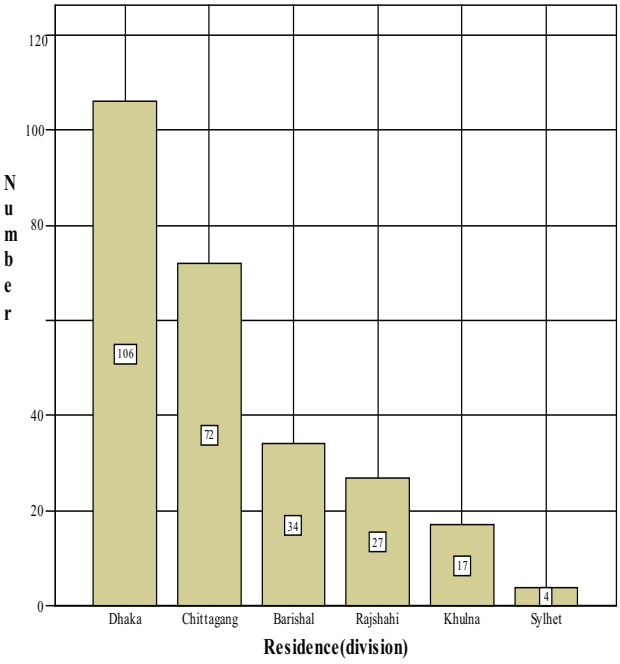

Fig 2 *Demographic distribution of subjects (n=260)*

Among 260 subjects, 206 were carriers of â thalassemia and HbE (HbE also included) and 54 were control. Out of 206 cases 114 cases were â thalassemia carriers of which 14 cases had IDA and 92 cases were HbE carriers and disease of which 13 cases had IDA (Fig. 3).

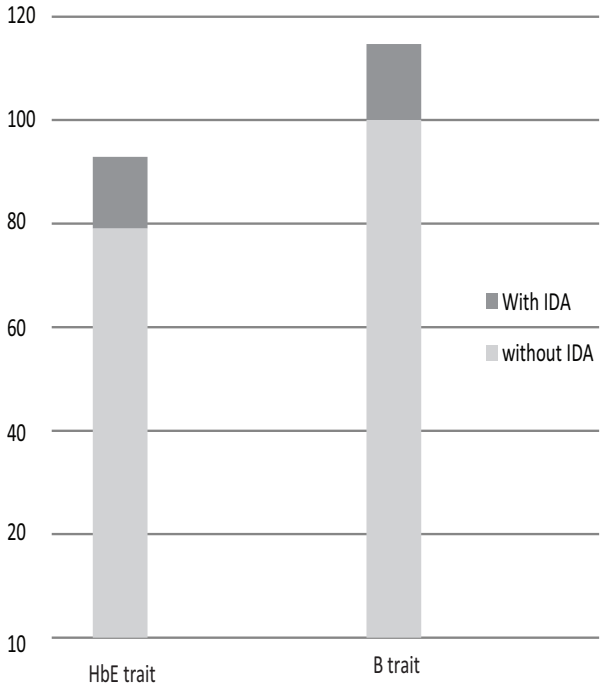

Fig 3 *Category of subjects according to case definition*

Mean (mean± SEM) Hb concentration of control was 12.93±0.23 gm/dl, in HbE carrier it was 10.73±3.49 gm /dl and in ß thalassemia carrier, it was 9.93±0.14 gm/dl. As compared to the control reduction of Hb level was statistically significant in carrier of both ß thalassemia and HbE (p value 0.00). Highest level of mean (mean± SEM) MCV was observed in control (86.6 ± 0.65 fl) and lowest level was found in ß thalassemia carrier (61.81± 0.52fl) and in HbE carrier it was 70.2±0.86 fl. Reduction of MCV observed both in HbE carrier and ß thalassemia carrier as compared to control was highly significant (p value 0.00 & 0.00). Mean value of MCH (mean±SEM) highest in 'Control' (27.13±0.33 pg) and lowest level was observed in ß thalassemia carrier (18.09±0.18 pg), level in Hb E carrier was in intermediate place (21.04±0.30 pg). MCH was also found significantly low both in HbE carrier and ß thalassemia carrier as compared to control (p value 0.001 & 0.00). Mean (mean±SEM) MCHC of HbE carrier was 29.64n±n0.21 gm/dl, 29.18±0.12 gm/dl in â thalassemia carrier, 31.05 ±0.23 gm/dl in control. The values found in carriers were significantly low as compared to the values of control (p <0.01) (Table III).

Table III
Hematological and biochemical parameter of cases and control (N=260)

Parameter	Control	HbE carrier	β thalassemia carrier	t -test(df)	p value
Hb conc	12.93 ±0.23	10.74± 0.21	-	6.8(126.9)	0.00
(mean± SEM)(gm/dl)		-	9.93±0.14	10.88(93.14)	0.00
MCV	86.6±0.65	70.20 ±0.86	-	15.1(143.9)	.000*
(mean± SEM)(fl)		-	61.81±.52	28.0 (68)	.000*
MCH	27.13±0.33	21.04±0.30	-	13.4(27.7)	.001*
(mean± SEM)(pg)		-	18.09 ±0.18	23.59(80)	.000*
MCHC	31.05±0.23	29.64± 0.21	-	4.44(129.8)	0.00
(mean± SEM)		-	29.18± .12	7.1(86.6)	.000
RDW	13.2±.0.12	15.8±.0.29	-	8.0(117.48)	.000
(mean± SEM)		-	17.06±0.20	16.1(164.5)	.000
Serum ferritin	58.45±.6.91	61.41.6.13	-	0.32(124.3)	0.74
(mean± SEM)µg/L		-	67.13±.7.9	82.6(156)	.041
Serum iron	66.36±.2.78	67.49.2.57	-	29(27.7)	0.76
(mean± SEM) µg/dl		-	72.86±.2.89	1.61(149)	0.10
TIBC	373.40±.11.6	354.03±.8.6	-	1.34(143)	0.18
(mean± SEM)µg/dl		-	368±.11.79	.32(166)	0.74

Mean (mean±SEM) serum ferritin value of the cases was 64.58 ±5.15 µg/L (range 0.38- 614.08µg/L), of HbE carrier 61.41±6.13 µg/L, of thalassemia carrier 67.13±7.9 µg/L and of control 58.45±6.91µg/L. Statistical significant difference between the mean values observed in cases and control was not found (p value 0.74 , 0.41). Mean serum iron level in cases was 70.46±1.9 µg/dl (range 15-188 µg/dl) and in control 66.36±2.7 µg/dl (range 171-646 µg/dl) respectively, means TIBC level of cases and control were 361.84±7.6 µg/dl and 373.40±11.7 µg/dl respectively. No statistical significant difference observed for value of serum iron and TIBC among the cases and control (p >0.10 in each comparison) (Fig. 4).

Iron status of the subjects was evaluated further based on serum ferritin (Table IV). Out of 206 carriers 27 (13.1%) had serum ferritin level <12 µg/L and were diagnosed as IDA. So prevalence of IDA among the cases was 13.1%. One hundred seventy six (85.4%) of cases had normal serum ferritin and only 3 (1.5%) carriers showed iron excess but none of cases had serum ferritin >1000 µg/L. Out of 92 HbE carriers 13 (14.1%) had IDA and 14 (12.2%) cases among 114 ß thalassemia carriers. On the other hand only 2 of the 54 (3.7%) controls had low serum ferritin. In the age group 1-5 years, 37.5% cases were IDA on the other hand; only 10% and 6.6% cases with IDA were found in the age group of 6-18 years and more than 18 years respectively.

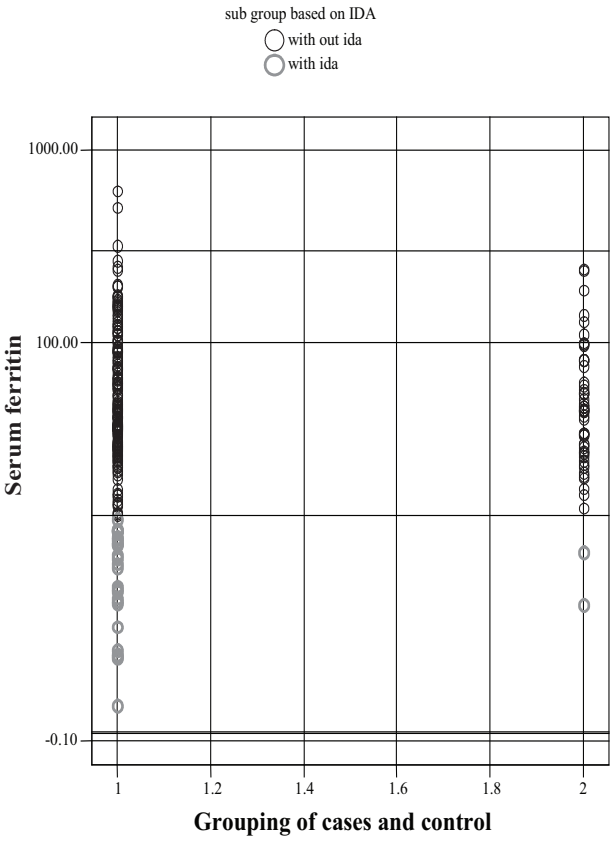

Fig 4 *Serum ferritin level of the study subjects (n=260)*

Table IV
IDA status of carriers in different age groups (N=206)

Age groups	HbE carriers		β thalassemia carriers	
	With IDA	Total numbers	With IDA	Total numbers
1-5 years	8	21	7	19
6-18 years	2	12	1	17
>18 years	3	59	6	78
Total	13	92	14	114

Carriers of HbE and ß thalassemia had significantly low mean Hb concentration, MCV, MCH, MCHC and serum iron and higher level of serum TIBC and RDW (p <0.001 for each comparison) (Table-V).

Table V
Comparison of mean hematological and biochemical parameters of carriers with and without IDA (N=260)

	Cases based on IDA	N	Mean	Std. Error Mean	t	df	p value
Hb concentration of cases	Without IDA	179	10.5417	.1259	5.422	204	.000
	With IDA	27	8.6226	.3663			
MCV of cases	Without IDA	179	66.3442	.5790	3.671	204	.002
	With IDA	27	60.3815	1.663			
MCH of cases	Without IDA	179	19.7975	.1944	5.309	204	.000
	With IDA	27	16.8704	.5972			
MCHC level of cases	With out IDA	179	29.6381	.1152	4.573	30.53	.000
	With IDA	27	27.7481	.3969			
RDW of cases of cases	With out IDA	178	16.138	.1609	-4.665	28.43	.000
	With IDA	26	19.138	.6228			
Serum ferritin level of cases	With out IDA	179	73.4044	5.6458	11.84	182.47	.000
	With IDA	27	6.1111	.64559			
Serum iron level of cases	With out IDA	179	73.4021	2.0785	4.392	37.15	.000
	With IDA	27	50.9900	4.6605			
TIBC of cases	With out IDA	178	348.6047	7.3847	3.753	30.42	.001
	With IDA	27	449.1333	25.745			

Frequency of IDA was 52.9 % in 1-5 years group, 33% in 6-18 years group and 8% in 18 years and more (Table VI).

Table VI
Frequency of IDA in under nourished carriers of different age groups (N=260)

Nutritional status			Sub group based on IDA		Total
			With out IDA	With IDA	
Normal	Age group	1 year - 5 yrs	17	6 (26%)	23
		6-17 yrs	22	1 (4%)	23
		≥18 yrs	105	7 (6.2%)	112
		Total	144	14(8.9%)	158
Under nourished	Age group	1 year -5yrs	8	9 (52.9%)	17
		6-17 yrs	4	2 (33.3%)	6
		≥18 yrs	23	2 (8%)	25
		Total	35	13 (27%)	48

Discussion

Iron status was assessed in carriers of HbE and â thalassemia and the result was compared with that of normal Control. Prevalence of iron deficiency and iron excess were also measured. There were 137 male and 123 were female and male to female ratio was 1.1:1. Ages of the subjects range from 1 year to 59 years with a mean age (±SEM) of 23.06±13.54 years. Mean age of the cases and control was 22.78±13.93 years and was comparable with that of control (24.17 yrs ±12.0) (p 0.46.) Participants were from all corners of the country, with the highest number from Dhaka division possibly due to the location of the study center in the middle of Dhaka division followed by Chittagang, Barishal, Rajshahi, Khulna and Sylhet division respectively.

Hematological parameters (Mean Hb concentration, MCV, MCH, MCHC) of the cases in the present series were lower than those of control and were statistically significant (p <0.001 for each comparison). Mean Hb concentrations of the cases were significantly lower than that of control. This finding was comparable with the findings of other authors.[19,27] Mean MCH was lowest in ß thalassemia trait and also low in HbE trait in the present series. Reduction of MCH found both in HbE and ß thalassemia traits was statistically significant as compared to that of Control (p <0.001 and <0.001). This finding was comparable with other observation.[6,28] Modell et al[29] described that MCH level in ß thalassemi carriers had become low because of defective production of globin chain and it usually had varied from 18-25pg in different thalassemic trait. Mannan et al[13] found lower level of MCH in ß thalassemia and Hb E traits, which was comparable to the finding of the present study. Mean MCV was found lowest in ß thalassemia trait and lower in HbE trait. Reduction of MCV level in both the traits was significant as compared to normal control (p <0.001 and <0.001). Lower levels of MCV reported by Katsanis et al[5], Vichinsky et al[6], Mannan et al[13] were comparable with our finding. Modell et al[29] described that the reduction of MCV in thalassemic red cells is due to reduced MCH that reduces intracellular oncotic pressure and fluid volume. Mean MCHC level observed both in HbE trait and ß thalassemi trait were also significantly low as compared to the level of the control (p <0.05). Other authors made different observation.[28,30] Mean RDW (±SEM) value of the cases (15.84±0.16%) were significantly high as compared to control (13.2±0.12%) and the level was much higher when associated with IDA (16.130.16% vs. 19.13±0.62 %).

Mean serum ferritin and serum iron of the cases were higher than the value observed in control but there was no statistical significant difference between the mean values (p >0.05). On the other hand, mean serum TIBC though lower than the value observed in the control, there was no statistical significance (p >0.05). So the results of the iron profile signify that iron statuses of the carriers were normal. Hussein et al[22] observed that patients with uncomplicated ß thalassemia trait in general have normal iron store. Bannerman et al[19] also stated that iron absorption was normal in ß thalassemia trait. White et al[31] and Mehta et al[23] made different observation that in ß thalassemia trait, ferritin concentrations was higher with lower incidence of iron deficiency anemia. Mehta et al[23] described that ß thalassemia traits had better iron nutrition suggesting these carriers had an advantage of maintaining good iron balance.

In the present series 13.1% of carriers showed iron deficiency anemia in addition to their existing carrier state. Prevalence was higher in the younger age group and gradual decreasing in older age group. In the age group 1-5 years the prevalence of IDA was much higher 37.51%. In the age group 5-18 years 10% of the carriers had IDA but only 6.6% had IDA in the age group of >18 yrs. When under nutrition has been taken in consideration, frequency of IDA was 52.9% among the 1-5 years age group, 33% among 6-18 years group and only 8 % in >18 years age group. Nutritional surveys conducted by Institute of Nutrition and Food Science of Dhaka University reported 65 -80% anemia in children <15 years which is higher than frequency found in our subjects.[32,33] As under nutrition affects mostly children that contributes the development of anemia in carriers also. So, advantage for protection to the development of anemia in the carriers of ß thalassemia and HbE may not be significant. Hinchliffe et al[34] had also similar observation. They had concluded 'clinical iron deficiency occurs with very high frequency in children under 5 years of age with ß thalassemia trait and advantage of iron supply is trivial in this context'. Ehrardt et al[35] also reported a figure of 48.5% prevalence of IDA in young children with ß thalassemia trait.

Only 3 (1.5%) of the carriers in this series had serum ferritin higher than reference value, however their level had not exceeded to the 1000 µg/L and none of them were in the children group and all of them were in well nourished group. Ineffective erythropoiesis with a variable spectrum observed in ß thalassemia trait might explain the possible role in increased iron absorption[22] however possibility of associated other disease of altered iron metabolism that was not evaluated here might be considered in this connection. Little data is available regarding iron status of HbE carriers in home and abroad to compare. However in our series HbE carriers behave like those of ß thalassemia carriers.

Conclusion

Carriers of HbE and â thalassemia do have relatively higher iron profile as compared to control though statistically not significant. A few carriers had high ferritin level than normal reference value but it had not crossed toxic level. Iron deficiency anemia is not uncommon in carriers especially in children and the prevalence is higher in children especially in those associated with under nourishment signifying that protection of iron deficiency by the carriers are not significant. So there is no contra indication of iron supplementation to the children in general.

Acknowledgement

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References

1. Karimaei T, Masoudi Q, Shahrakipour M, Navidian A, Jamazae AA, Bamri AZ. Knowledge, attitude and practice of carrier thalassemia marriage volunteer in prevention of major thalassemia. *Global Journal of Health Science* 2015;**7**:364-70.
2. Weatherall DJ. Inherited hemoglobin disorders: An increasing global health problem. *Bulletin of World Health Organization* 2001;**79**:704-12.
3. Khan WA. Thalassemia in Bangladesh. Seminar on thalassemia situation in Bangladesh (Fight Thalassemia) organized by Dhaka Shishu Hospital Thalassemia Center on May 8, 2002. P1-2.
4. Nuinoon M, Kruachan K, Sengking W, Horpet D, Sungyuan U. Thalassemia and hemoglobin e in southern thai blood donors. *Advances in Hematology*. 2014:1-6.
5. Katsanis E, Luke KH, Hsu E, Yates JR. Hemoglobin E: A common hemoglobinopathy among children of Southeast Asian origin. *CMAJ* 1987; **137**:39-42.
6. Vinchinsky. Hemoglobin E syndrome. *Hematology* 2007;**1**:79.
7. Chernoff, Minnich AIV, Nakorn V, Tuchinda S, Kashemsant C, Krenoff RR. Studies on HbE. Clinical, hematologic and genetic characteristics of HbE syndrome. *J Lab Clin Med* 1988;**47**;455-89.
8. Fucharoen S, Winichagoon P, Pootrakul P PiankijagumA, Wasi P. Variable severity of South Eeast Asian beta thalassemia / HbE disease. *Birth Defects Original Articles series*. 1988;**53**:241-48.
9. Ress DC, Styles L, Vichinsky EP Clegg JB, Weatherall DJ. The Hemoglobin E Syndromes. *Ann NY Acad Sci* 1998;**850**:334-43.
10. Gibbons R, Higgs DR, Olivieri NF, Wood WG. The â and ä â thalassemias in association with structural hemoglobin variants. In: Weatherall DG. Clegg JB, editors. The Thalassemia Syndromes. 4th ed. Oxford, United Kingdom: Blackwell Science; 2001. P. 393-449.
11. Rahman SA, Jamal CY. Congenital hemolytic anemia in Bangladesh: Types and clinical manifestations. *Indian Pediatrics* 2002:**39**:574-77.
12. Haque MS, Alam MA. Thalassemia situation in Dhaka Shishu hospital. Seminar on thalassemia situation in Bangladesh (Fight Thalassemia) organized by Dhaka Shishu Hospital Thalassemia Center on May 8, 2002. P. 3-8.
13. Mannan MA. NESTROFT (Naked Eye Single Tube Red cell Osmotic Fragility Test) as a screening test for the detection of b thalassemia and other hemoglobinopathies - An evaluation against hemoglobin electrophoresis. Submitted to WHO (2006), (unpublished).
14. Gibbons R, Higgs DR, Olivieri NF, Wood WG. Clinical features of the thalassemias. In: Weatherall DJ, Clegg JB, editors. The Thalassemia Syndromes. 4th ed. Oxford: Blackwell Scientific Publications; 2001. P. 287-356.
15. Nesa A, Tayab MA, Sultana T, Khondker L, Rahman QM, Karim MA, et al. RDWI is better discriminant than RDW in differentiation of iron deficiency anemia and beta thalassemia trait. *Bangladesh J Child Health* 2009;100-03.
16. Selimuzzaman M, Belayet M, Mamun MA, Mamun M, Khasru AM, Amin SK, et al. Frequency of coincident iron deficiency and ß thalassemia trait in Bangladeshi children. *DS (Child) H J* 2008;27-32.
17. Hinchliffe RF. Reference values. In: Lilleyman JS, Hann IM, Blanchette VS, editors. Pediatric Hematology. 2nd ed. 1999. Churchil Livingstone, Harcourt Brace and Company: UK; 1999. P-2.

18. British Society of Haematology. The laboratory diagnosis of haemoglobinopathies. *Br J Haematol* 1998;**101**:783-92.

19. Bannerman RM, Callender ST, Hardisty RM, Smith RS. Iron absorption in thalassemia. *Br J Haematol* 1964;**10**:490.

20. Crossby WH, Conard ME. Iron balance in thalassemia minor, problems in Cooley's anemia. *Ann NY Acad Sci* 1964;**119**:616.

21. Vikramsinghe SN, Huges M. Ultrastructural study of erythropoiesis in ß thalassemia trait. *Br J Haematology* 1980;**46**:401.

22. Hussein HF, Hoffbrand AV, Leulicht M, Letsky E. Serum ferritin levels in beta thalassemia trait. *Br Med J Clin Res* 1976;**2**:920.

23. Mehta BC, Pandya BG. Iron status of beta thalassemia. *American J Hematol* 1986;**24**:137-41.

24. Tan GB, Aw TC, Dunstan RA, Lee SH. Evaluation of high performance liquid chromatography for routine estimation of hemoglobin A2 & F. *J Clin Pathol* 1993;**46**:852-56.

25. Shine I, Lal S. A strategy to detect β thalassemia minor. *Lancet* 1977;**1**:692-94.

26. Lanzkowsky P. Iron deficiency anemia. In: Lanzkowsky P, Lipton JM, Fish JD, editors. Manual of Pediatric Hematology and Oncology. 6th ed. Churchill Living stone. 2016. P. 69-83.

27. Sarnaik SA. Thalassemia and related hemoglobinopathies. *Indian J Pediatr* 2005;**72**:319-24.

28. Kwiatkowsky JL. Hemoglobinopathies In: Lanzkowsky P, Lipton JM, Fish JD, editors. Manual of Pediatric Hematology and Oncology. 6th ed. 2016. Churchill Living stone; 2016 P. 166-97.

29. Modell B and Berdoukas V. The clinical Approach to Thalassemia. Grune & Stratton 1984.

30. Maheshwari M, Sadna A, Madhulik K, Menon PSN. Carrier screening and prenatal diagnosis of b thalassemias. *Indian Pediatr* 1999;**6**:1119-25.

31. White JM, Richards R, Jelenski G, Margarete B. Ali M. Iron state in alpha and beta thalassemia trait. *J Clin Pathol* 1986;**39**:256-59.

32. Nutritional survey of rural Bangladesh (1975-76). Institute of Nutrition and Food Science, University of Dhaka.

33. Nutritional survey of rural Bangladesh (1981-82). Institute of Nutrition and Food Science, University of Dhaka.

34. Hinchliffe Rand Lilleyman JS. Frequency of coincident iron deficiency and beta thalassemia in British Asian children. *J Clin Pathology* 1995;**48**:594-95.

35. Ehrhardt P. Iron deficiency in young Bradford's children from different ethnic groups. *BMJ* 1986; **292**:90-93.

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ORIGINAL ARTICLE

Nutritional Status of Under-5 Children in a Slam of Dhaka City and Influence of Immunization and Socio-economic Condition on Malnutrition

Md. Aynal Hoque[1], Hossain Sahid Kamrul Alam[2], Md. Abu Sayeed[3]

Abstract

Background: *In slum area there is a very high prevalence of malnutrition. Many factors can cause malnutrition, most of which relate to immunization, socio economic condition and repeated infections, particularly in underprivileged population.*

Objectives: *To observe the nutritional status and effect of immunization and socio economic condition on malnutrition among under-5 children in a selected slum of Dhaka city.*

Methods: *This cross sectional study was conducted among 384 under-5 children randomly selected from PWD slum in Dhaka city. It was carried out during January-2013 to December-2014. Anthropometric measurements like wasting was determined from weight for height Z-score, stunting was determined from height for age Z-score, underweight was determined from weight for age Z-score and malnutrition also assessed by Mid Upper Arm Circumference (MUAC). Data were analyzed using SPSS version 21.*

Results: *In this study in slum 40.36% were found malnourished according to MUAC, according to weight for height Z-score wasting was present in 29.43% children, according to height for age Z-score stunting was found in 28.39% and according to weight for age Z-score underweight was found in 46.89% children. There is a decreased number of malnutrition cases when family income rise. Out of the 384 study children 68% were completely immunized, 16.9% were incompletely immunized and rest 15.1% were not immunized. Number of MUAC malnutrition, wasting, stunting and underweight cases increases in cases of incomplete immunization and no immunization.*

Conclusions: *Overall, nutritional status of the under-5 child of slum of PWD is not satisfactory. Family income and immunization status plays role in malnutrition. So socioeconomic condition should improve and mass immunization programshould be implemented in urban slum areas.*

Keywords: *Under 5 slum children, nutritional status, anthropometry, Z-score, MUAC.*

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Introduction

Malnutrition is a serious public health problem that has been linked to increase risk of morbidity and mortality.[1] Many factors can cause malnutrition, most of which relate to poor diet or severe and repeated infections, particularly in underprivileged populations. Overpopulation undermines food production, which leads to inadequate food intake, incomplete and no immunization causes to malnutrition. On the other hand, malnutrition itself can have far-reaching impacts on the environment, and can induce a cycle leading to additional health problems and deprivation. A good percentage of the population of Dhaka city is living in the slums.[2] Uncontrollable rapid growth of urban slum population, accompanied by poor nutritional status is a devastating problem. In slum areas of Dhaka city there is a very high prevalence of malnutrition. The prevalence of malnutrition is higher in Dhaka slums than the national average which is 49% for stunting, 17.5% for wasting and 56% for underweight, and indicates exceptionally high levels of malnutrition as judged against World Health Organization criteria.[1] Malnutrition is increasing rapidly among socio-economically deprived sectors of the developing countries where poverty, unemployment, literacy and ignorance are rampant.[3] It was found that more than a third of the world's children are affected by protein energy malnutrition (PEM), and the highest frequency of the indicators are wasting, stunting, and underweight among which 80% of the affected children are from Asia.[4] The nutritional problem in Bangladesh is well known where 69% of children are victim of any form of PEM and 12% children are severely undernourished.[5] PEM is a major cause for childhood mortality and morbidity in underdeveloped countries. Socio-economic condition, maternal age and education status, immunization status, weaning practices, family size, housing etc. were significantly associated with severe PEM.[6] So this study was conducted with a view to determine the nutritional status of under five children of urban slum and effect of immunization and socio economic condition on malnutrition.

Materials and Methods

This cross sectional study was carried out during January 2013 to December 2014 at PWD slum of Dhaka city. A total 384 under-5 children constituted study population. Children living in PWD slum at least 6 months, willing to participate and 2 months to 5 years of age were included. Seriously ill, mentally retarded and unwilling to participate in the study were excluded from the study. Nutritional status like wasting was determined from weight for height Z-score, stunting was determined from height for age Z-score, underweight was determined from weight for age Z-score and malnutrition also assessed by MUAC.

For children 6 months to 2 years of age length was measured by infantometer in lying position and after 2 years up to 5 years height was measured in standing position by stadiometer without footwear, foot together, knees straight and heels, buttocks and shoulder in contact with the vertical wall. The child was held firmly with eyes looking straight up and the body held as straight as possible with the knees pressed straight. The height was measured to the nearest millimeter. Weight was taken by electronic weighing machine. The child was asked to stand on the weighing machine with minimum clothing and without shoes and any weight in hands or touching or catching other things. Weight were recorded to the nearest grams. Age was determined by asking parents and verified from birth certificate/hospital records. MUAC was recorded by measuring tape. The middle of the left arm will be detected by the midpoint of a line between the tip of the acromion process of scapula and olecranon process of ulna. Then at the midpoint the measuring tape was wrapped round gently but firmly avoiding compression of soft tissue keeping the arm in hanging and extended position at the side of the body, then the reading was taken to the nearest 0.1 cm. A questionnaire was ready for data collection. Immunization and socioeconomic condition were taken by asking with the parent. Each questionnaire was minutely checked, verified and corrected on the spot following the interview. After completion of data collection, the data were consolidated, processed and edited to reduce the errors. The data were enter into the computer and analyzed with the help of SPSS (Statistical package for social science) windows programs.

Results

A total 384 under-5 children were studied among them 155(40.4%) were found malnourished according to MUAC. Wasting was present in 113(29.4%)

children, stunting in 109(28.4%) and underweight in 180(46.9%) children (Fig.-1).

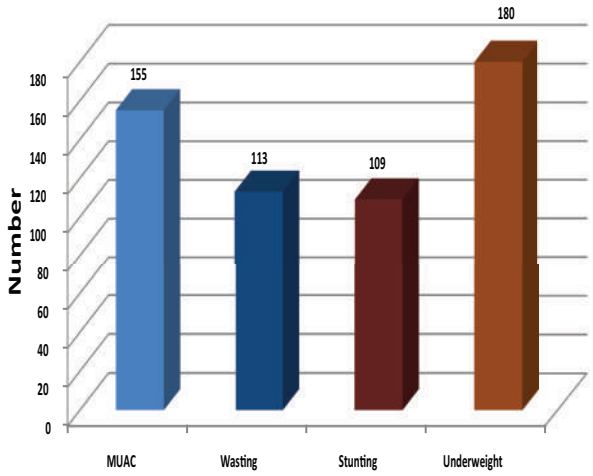

Fig 1 *Pattern of malnutrition*

It was found that, in 160 children, monthly income of the parent were up to 10,000 Tk and malnutrition was present in 73 (55.73%) cases; in 140 children, monthly income of the parent were within 10001-15000 Tk and malnutrition was present in 67(47.86%); in 60 children, monthly income of the parent were within 15001-20000Tk and malnutrition was present in 9(15%); in 53 children income of the parent were more than 20000Tk and malnutrition were found in 8(15%). There is a decreased number of malnutrition cases when family income rise (Table I).

Table I
Distribution of children by family income

Family income	Normal	Malnutrition	%	Total
Up to 10000Tk	58	73	55.7	131.0
10001-15000Tk	73	67	47.8	140.0
15001-20000Tk	51	9	15	60.0
Above 20000Tk	45	8	15	53.0

Out of the 384 study children, 261(68%) were completely immunized, 65(16.9%) were incompletely immunized and rest 58(15.1)% were not immunized (Fig. 2).

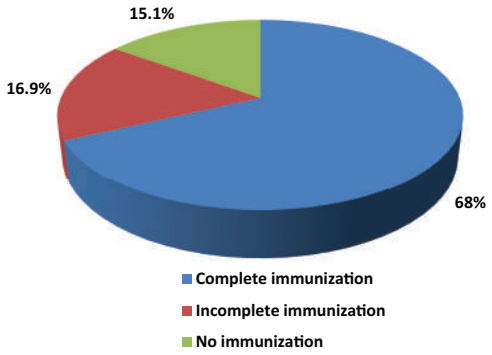

Fig 2 *Distribution of children by immunization status*

Among MUAC malnourished children 35(22.6%) completed immunization, 52(33.6%) incompletely immunized, 68(43.8%) got no immunization;among wasting children 30(26.6%) completed immunization, 36(31.8%) incompletely immunization, 47(41.6%) got no immunization; among stunting children 17(15.6%) completed immunization, 40(36.7%) incompletely immunized, 52(47.7%) got no immunization; among underweight children 48(26.7%) completed immunization, 55(30.5%) incompletely immunized and 77(42.8%) got no immunization. Number of MUAC malnutrition, wasting, stunting and underweight cases increases in cases of incomplete immunization and no immunization (Fig.-3).

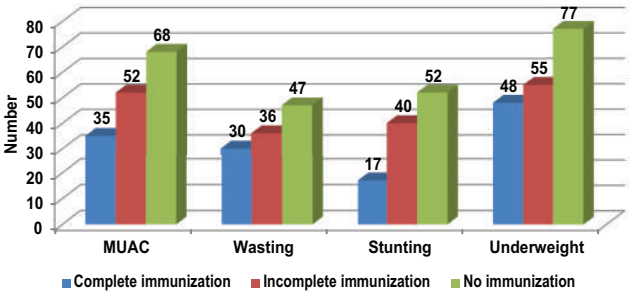

Fig 3 *Distribution of malnourished children by immunization*

Discussion

In this study in an urban slum 40.4% under-5 children were found malnourished according to MUAC, wasting was present in 29.4% children, stunting in 28.4% and underweight in 46.9%. There is a decreased number of malnutrition cases when family

income rise. Out of the 384 study children 68% were completely immunized, 16.9% were incompletely immunized and rest 15.1% were not immunized. Among MUAC malnourished children 22.6% completed immunization, 33.6% incompletely immunized, 43.8%got no immunization; among wasting children26.6% completed immunization, 31.8% incompletely immunized, 41.6% got no immunization; among stunting children 15.6% completed immunization, 36.7% incompletely immunized, 47.7% got no immunization; among underweight children 26.7% completed immunization, 30.5% incompletely immunized and 42.8% got no immunization. Number of MUAC malnutrition, wasting, stunting and underweight cases increases when there is incomplete immunization or no immunization.

Dasgupta et al[7] assessed anthropometric indices on 100 under-5 children with standard anthropometric indices such as weight for age, weight for height, height for age, and mid upper arm circumference and found wasting in 30%, stunting in 28%, underweight in 42% and under nutrition in 48% children. Zaman et al[8] conducted a study on malnutrition on children of 18 months. The prevalence of wasting, stunting and underweight was 24%, 36% and 8% respectively. Popat et al[9] conducted a cross sectional study and found prevalence of wasting, stunting and underweight was 17.2%, 46.1% and 32.4% respectively. Child Nutrition SURVEY-2000 (ages 6-71 months)[10,11] found in their survey that 51% of the children were moderately underweight and 13% severely underweight, 49% moderately stunted and 19% severely stunted and 12% moderately wasted and 1%severely wasted. According to Demographic and Health Survey- 1990-2000 (ages 0-59 months)[12,13] it was found that 48% of the children were moderately underweight and 13% severely underweight, 45% moderately stunted and 18% severely and 10% moderately wasted and 1% severely wasted. According to Z-scores, it was found in the present study that, 29.4% children were wasted, 28.4% stunted and 46.9% underweight which is higher than other studies. Though the prevalence of malnutrition sharply decline in Bangladesh but still the prevalence of malnutrition is higher in Dhaka slums than the national average according to BDHS 2017-18, where the prevalence of stunting is 31%, wasting in 8% and underweight in 22%.[14]

In this study there is a decreased number of malnutrition cases when family income rises and number of MUAC malnutrition, wasting, stunting and underweight cases increases in cases of incomplete immunization and no immunization. Hossain et al[6] conducted a study to find out the Nutritional and Immunization status, weaning practices and socio-economic conditions of under-5 children and found that low household income and absence of BCG vaccination were significantly associated with severe PEM. Ayaya et al[15] conducted a prospective case control study on socio-economic factors predisposing under-5 year old children to severe protein energy malnutrition in Kenya. The social risk factors for PEM were low socioeconomic status and incomplete immunization. Baranwal et al[16] also showed similar result. Chaudhary et al[17] in a community based cross-sectional study conducted in year 2016 to 2017 in slum area of Jaipur city found that malnutrition was associated with low economic status of family.

Conclusion

Overall, nutritional status of the under-5 child of slum of PWD is not satisfactory. Family income and immunization status plays role in malnutrition. So socioeconomic condition should improve and mass immunization programshould be implemented in urban slum areas.

References

1. Rogers S, Rahman A. The epidemiology of good nutritional status among children from a population with a high prevalence of malnutrition. *Public Health Nutrition* 2004;**7**:311-17.
2. Morris LD, Pont A, Lewis SM. Use of a new Hemo Cue system for measuring hemoglobin at low concentrations. *Clinical and Laboratory Haematology* 2001;**23**:91-96.
3. Zondag AM. Nouwen JL, Voorhoeve HW. Immunization and nutritional status of under-five in rural Zambia. *The Central African Journal of Medicine* 1992;**38**:62-66.
4. Atalay YA and Arcasoy M. Oral plasma Zinc tolerance test in patients with protein energy malnutrition. *Archives of Disease in Childhood* 1989;**13**:21-27.
5. Koerper MA, Dallman. Serum iron concentration and transferring saturation in the diagnosis of iron deficiency in children. Normal developmental changes. *The Journal of Pediatrics* 1977;**6**:870-74.

6. Hossain MI, Rahman Y, Kabir I. Nutritional and immunization status, weaning practices and socio-economic conditions of under-five children in three villages of Bangladesh. *Indian Journal of Public Health* 1999;**43**:37-41.

7. Dasgupta A, Sahoo SK, Taraphadar P, Preeti PS, Biswas D, Kumar A, I Sarkar I. Composite index of anthropometric failure and its important correlates: a study among under- 5 children in a slum of West Bengal, India. *International Journal of Medical Science and Public Health* 2015;**4**:414-19.

8. Zaman SU, Seoty NR, Alam M, Haque R, Yasmin N. Household food insufficiency and child nutritional status in urban slum, Dhaka, Bangladesh. *Acta Medica International* 2015;**2**:65-69.

9. Popat CN, Chaudhari AI, Mazumdar VS, Patel SV. A cross sectional study to measure the prevalence of malnutrition and factors associated with malnutrition among under five children of an urban slum of Vadodara city. *Journal of Research in Medical and Dental Science* 2014;**2**:59-64.

10. Bangladesh Demographic and Health Survey 2000, NIPORT, Bangladesh.

11. Nutritional situation and nutrition programs in Bangladesh. Prepared Jointly by NNP, BNNC, IPHN for Global Nutrition Seminar 2005, March 2005; 1.2.

12. Health situation in the South-East Asia: World Health Organization South-East Asia Region. 2004; 9-10.

13. Deolalikar A. Poverty and child malnutrition in Bangladesh. A World Bank Document 2004; 2-20.

14. Bangladesh Demographic and Health Survey 2017-2018. Ministry of Health and Family Welfare Dhaka, Bangladesh, Government of the Peoples of Republic of Bangladesh. Available from https://dhsprogram.com/pubs/pdf/PR104/PR104.pdf.

15. Ayaya SO, Esamai FO, Rotich J, Olwambula AR. Socio-economic factors predisposing under five year old children to sever5e protein energy malnutrition at the Moi Teaching and Referral Hospital, Kenya. *East African Medical Journal* 2004;**81**:415-21.

16. Baranwal K, Gupta VK, Mishra RN, Shiv P, Pandey ON. Factors influencing the nutritional status of under five (1-5 years) children in urban-slum area of varanasi. *Indian Journal of Community Health* 2009;**21&22**:178-95.

17. Chaudhary P, Agrawa M. Malnutrition and associated factors among children below five years of age residing in slum area of Jaipur city, Rajasthan, India. *Asian Journal of Clinical Nutrition* 2019; **11**:1-8.

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ORIGINAL ARTICLE

Mothers' Knowledge about Diaper Rash and Preventive Measures in Bangladesh

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Abstract

Background: *Use of disposable diapers by parents for their children has grown in last few decades. Although, most of the time diaper rash is not life threatening, it is a concern for the parents, and uncomfortable and painful for children*

Objectives: *To measure the knowledge and practice of mothers when diapering and administering perineal care to infants wearing disposable diapers and factors that can influence the frequency of the occurrence of diaper rash in children between 0-12 months in Bangladesh.*

Methods: *This cross-sectional study was conducted during the outpatient visits of mothers and their infants at the Combined Military Hospital located in Cumilla, Bangladesh between 01 February 2015 and 31 July 2015 with their infants. A structured, self-completed, closed-ended questionnaire was provided to 110 mothers who came to visit the Pediatric outdoors.*

Results: *Thirty-seven (33.64%) infants aged one or under were reported to have experienced diaper rash during or prior to enrolment in the study. Study analysis showed that the risk of diaper rash was significantly higher in babies who used only 1-2 diapers/day than for babies who used more than 4 diapers/day (40.0% vs 21.43%). Infants whose mothers had knowledge of the causes and preventions of diaper rash and/or who received information about the importance of the proper cleaning of the diaper area during diaper changes suffered fewer incidents of diaper rash than those whose mothers did not (24% vs 36.48%). The causes of diaper rash were described by 48.65% mothers as heat followed by 27.03% mothers by frequent stool/urine.*

Conclusion: *Frequently changing disposable diapers and cleaning the diaper area thoroughly can reduce cases of diaper rash dramatically in children less than one year old. The knowledge of mothers regarding diaper rash is an important factor in reducing diaper rash in their children.*

Keywords*: Diaper dermatitis, diaper rash, nappy rash, infant, child care.*

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Introduction

The skin is the outermost and the largest organ in the human body and provides many vital functions including protecting internal organs, maintaining water and electrolyte balance by secretion and absorption, thermoregulation, and sensation.[1] In order to maintain these functions, it is important to take care of the skin properly.[2] The skin structure of infants is very distinctive as their skin is exceptionally delicate and can break easily; the improper cleaning of infant skin coupled with an insufficient knowledge around the care of the bottom might compromise the integrity of that delicate area of their skin.[3] It is important that the skin care products that parents use to clean their babies' diaper area are appropriate for their skin as infant skin continues to mature through the first years of life.[4]

Infants are generally not trained to evacuate in the toilet themselves and are not able to communicate with parents when they want to evacuate. Many parents use diapers to prevent soiling and also for convenience. Infrequent changing of diapers and the improper cleaning of the diaper area can result in the presence of urine and stool in the diaper area for extended periods, leading to diaper rash. For the purpose of this paper, the term 'infant' is used for children aged between birth and 12 months of age.[5]

Diaper rash, which is also called nappy rash or diaper dermatitis, can be defined as a number of inflammatory skin conditions that can occur at the diaper area.[6] For the purpose of this study, it will be called diaper rash or diaper dermatitis. Diaper rash is the cause of 20% of dermatology consultations during childhood.[7] Generally, diaper rash is not a life-threatening condition, but it can be severe and painful for babies and a concern for their parents and might need a physician's assessment.[8] Prolonged skin wetness from urine and/or stool can cause or aggravate diaper rash. Fecal protease and lipase enzymes and irritants from urine and stool can cause skin damage, which can result in diaper rash.[9] The rash can appear in any area, such as the genitals, perineum, medial side of thigh, or buttocks.[10] The objective of the study is to determine the knowledge and practices of mothers regarding the use of diapers and diaper rash among their babies.

Materials and Methods

This study was conducted in the outdoor of the Paediatric Unit of the Combined Military Hospital in Cumilla, Bangladesh between 01 February 2015 and 31 July 2015. Participants of this study were mothers who came to the hospital's pediatric outdoor with their children for any reason. The inclusion criteria for the participants were: first time mothers (primi) with babies who were one or less than one year old, mothers who agreed to participate in the study willingly, babies who wore disposable diapers day and night for at least 20 hours per day and babies who were not affected by any congenital diseases. Exclusion criteria included: babies so severely ill that they needed admission to the hospital.

A structured, self-completed, closed-ended questionnaire was provided to mothers to fill out. The questions were written as simply as possible so that the mothers could able to understand. Mothers could only check off one box to answer each question. The questionnaire collected information on eight variables: the gender and age of babies, maternal education level, maternal age, breast-fed vs bottle fed, the number of diaper changes every day, the frequency of cleaning the diaper area during diaper changes, and if the mother received any information regarding diaper rash as part of her antenatal care. A simple statistical analysis was performed to measure the prevalence of diaper dermatitis. Data were recorded using Microsoft Excel Spread Sheets and the SPSS statistical package, version 17.0 for Windows, was used to analysis the statistics. A p-value <0.05 was considered to be statistically significant. Comparison among groups was conducted using the χ^2 test. Results are presented in the article using tables and texts.

Information regarding the material the mother used to clean the diaper area during diaper changes as well as if perineal hygiene was performed and the sources from where they received any information regarding diaper rash (if it was received) were also included in the questionnaire. Mothers were informed of the purpose of the study and were also informed that the study did not have any intervention aspect. They were informed that all the answers would be anonymous and their participation or lack of participation in the study would not affect any treatment options or opportunities for their children. For the purposes of this study, only infants wearing

disposable/one-time use diapers were included. This study showed that babies who used the same diaper for extended periods of time had the highest prevalence of diaper rash and many mothers did not know that the frequent changing of diapers and cleaning the diaper area might reduce the occurrence of diaper rash in their babies.

Results

Thirty-seven (33.64%) infants aged one or under were reported to have experienced diaper rash during or prior to enrolment in the study (Table I).

Out of 110 mothers, 41.82% were at the age of 20-24 years followed by 36.36% participants were between 15-19 years. Diaper rash among the infants of mothers with those age ranges were as 42.50%, 34.78, and 16.67% respectively. Though the highest education (68.18%) of mothers recorded up to class 6-9 followed by class 10 and above, but incidence of highest numbers of diaper rash was found among the infants of lower class educated mother (class 1-5). Maximum (38.46%) infants belonged to the 5-8 months age had higher diaper rash. Univariate analysis showed that diaper rash is significantly associated with the age and education level of the mother as well as the age of baby ($p < 0.05$ for all comparisons), but not with the gender of the baby **(**Table II**)**.

Table I

Distribution of participants (Infants 0-12 months) according to diaper rash (N=110)

Number of babies	Infants had diaper rash		Infants never had diaper rash	
	Number	%	Number	%
110	37	33.64	73	66.34

Table II

Distribution of maternal age, educational level and age and gender of the child

Age of mother in years	Frequency	Percentage (%)	Infants had diaper rash Number (%)	p value
15-19	40	36.36	17(42.50)	<0.05
20-24	46	41.82	16(34.78)	<0.05
25 and above	24	21.82	04(16.67)	
Total	110	100.00	37	
Education of mother in class(grade)	Frequency	Percentage (%)	Infants had diaper rash Number (%)	p value
Class 1- 5	15	13.64	06(40.00)	<0.05
Class 6- 9	75	68.18	26(34.67)	<0.05
Class 10 & above	20	18.18	05(25.00)	
Total	110	100.00	37	
Age of child in months	Frequency	Percentage (%)	Infants had diaper rash Number (%)	p value
0- 4	50	45.45	14(28.00)	<0.05
5-8	39	35.45	15(38.46)	<0.05
9-12	21	19.10	08(38.10)	
Total	110	100.00	37	
Gender of child	Frequency	Percentage (%)	Infants had diaper rash Number (%)	p value
Female	49	44.55	17(34.69)	
Male	61	55.45	20(32.79)	>0.05
Total	110	100.00	37	

Mothers who changed their infant's diapers 1-2 times a day had 40.0% incidents of diaper rash and those whose babies were changed more than 4 times a day experienced diaper rash by only 17.64%. Mothers who breast-fed their infants had only 22.5% diaper rash and 63.3% who did not (Table III).

Assessed if mothers had any knowledge regarding diaper rash and it was reported that only 25 mothers out of 110 mothers had knowledge of diaper rash and 85 mothers did not (Table IV).

Surveyed the sources of diaper rash education for the 25 mothers and it showed that 11 (44%) mothers received information from their family members and 10 (40%) mothers received information from physicians or other health-care workers (Table V).

Table III

Distribution of frequency of usage of diapers every day, frequency of cleaning during diaper changes, cleaning material used most of the time during diaper changes and diet of infants (N=110)

Variable	Number of babies	Infants had diaper rash Number (%)	p value
Number of Diapers use/day			
1-2 diapers/day	45	18(40.00)	<0.05
3-4 diapers/day	48	16(33.33)	<0.05
>4 diapers/day	17	03(17.64)	
Total	110	37	
Cleaning frequency during diaper changes			
Every time or most of the time cleaning during diaper change	30	07(23.33)	
Most of the time not cleaning diaper area during diaper change	80	30(37.5)	<0.05
Total	110	37	
Materials used to clean			
Commercial wipes	09	04(44.44)	<0.05
Wet cloth	58	18(31.03)	
Water	40	12(30.00)	
Others/nothing	03	03(100.00)	<0.05
Total	110	37	
Mother breast fed during diaper rash			
Yes	80	18(22.50)	
No	30	19(63.33)	<0.05
Total	110	37	

Table IV

Mothers received information regarding diaper rash and/or care (N=110)

Mother received information regardingdiaper rash /and care	Number of Infants	Infants had diaper rash Number (%)	p value
Yes	25	6(24.00)	
No	85	31(36.47)	<0.05
Total	110	37	

Table V
Sources from where mother received information regarding diaper rash (N=25)

Source	Number	%
Family members	11	44
Friends	04	16
Physician/health care workers	10	40
Others	0	0
Total	25	100

The table shows perceptions of mothers regarding the causes of diaper rash in their children; 18 (48.65%) mentioned heat, 3 (8.11%) not changing diapers for a long time, 10 (27.03%) frequent stool or urine, types of diaper 2 (5.41%), not cleaning diaper area during diaper change 1 (2.7%) and 3 (8.11%) mothers mentioned they did not know the reasons (Table VI).

Table VI
Distribution of aetiology of diaper rash amongst the infants (N=37)

Causes of diaper rash	Number	%
Heat	18	48.65
Wet diaper for a long period	03	08.11
Frequent stool/urine	10	27.03
Types of diaper	02	5.40
Not cleaning during diaper change	01	2.70
Don't know	03	8.11
Total	37	100.00

Discussion

Children one year or less were selected as subject participants for this study, as it was proved that most of the diaper rash was found in children in this age range.[11]

According to this study, more than one third of participated children who suffered at least one incident of diaper rash, were one year old. Philipp et al. conducted a study on diaper rash in the United Kingdom (U.K.) and reported in 1997 that 25 % of the children who participated in the study experienced diaper rash during the first four weeks of their lives.[7]

Diaper rash is a common condition in children, as it is a condition that is seen in infants as frequently as from 7% to 35%.[12] In the present study, the prevalence was found to be 33.64%, which is on the higher side of the average prevalence rate that was mentioned by Weston et al[12]. Gender did not produce significant differences in the number of cases of diaper rash; the finding for female vs male was 34.69% vs 32.79%. It can be mentioned here that in 1983, Harpin et al[13] investigated skin barrier function of infants by assessing transepidermal water loss (TEWL) of infants and they did not find any influence of gender on skin barrier function maturation.

Infants of mothers who had educational level grade (1-5) had the highest prevalence of diaper rash at 40%. This was followed by mothers with educational level grade (6-9), which was 34.67%and the lowest in infants of mothers who had higher level of education at least grade 10 or higher (25%). These numbers prove that the level of education influenced the incidence of occurrence of diaper rash which is also supported by Eke et al[10]. This finding is also consistent with the finding of Philipp et al[17]. But the results of another study which was conducted in 2012 by Li et al[14] in China, is inconsistent with the result of the present study regarding this matter.

It is also noticeable that mothers who were breast-feeding their children had less diaper rash than the children who were formula fed (22.5% vs 63.3% respectively). These statistics support the research that was conducted by Yoshhioka et al[15] in 1983.

The reason was explained as the pH of feces of breast-feeding infants is lower than the pH of feces of formula-fed infants, therefore reducing the potential irritation of infants' skin.[16] It can be mentioned here that the World Health Organization (WHO) recommends mother to breast feed exclusively up to 6 months of age of their babies.[17] Studies also proved that breast feeding can be an effective measure to reduce the occurrence of diaper rash in children.

To understand the practices of mothers during diaper changes, the number of diaper changes in a day were assessed. The results found that the prevalence of diaper dermatitis was lowest (21.43%) when mothers changed their infant's diaper more frequently (more than 4 diapers/day in the present study). Previous

research also found that there was a direct association between diaper rash and the frequency of diaper changes.[10,18] With the present results and those of previous studies, it is established that longer time-exposure of children's skin to urine and/or stool directly effects occurrence of diaper rash. Current research also explored whether or not mothers cleaned the diaper area of their babies every or most times when changing their infants and what they used to clean the diaper area. It was explained to the mothers that "most of the time" meant not cleaning the area a maximum of one time of the total number of times they changed their baby's diaper per day. Results showed that the prevalence of diaper rash in the infants of mothers who performed perineal hygiene most of the time were significantly less than in the babies of the mothers who did not clean the diaper area during diaper changes. The fewest cases of diaper rash were found among the infants who were cleaned by wet clothes or water rather than using commercial wipes.

Efficient knowledge of mothers or caregivers regarding diaper rash can reduce or prevent it.[19] The present study found that 24% of the infants who had diaper rash had mothers who had received knowledge regarding diaper rash, as opposed to the infants of mothers who did not receive that knowledge and who formed 36.48% of the group. When exploring the sources of information, the most two important sources were reported as family members and health-care workers.

Mothers were given an opportunity to share their perceptions about the causes of diaper rash. Only 8.11% of mothers mentioned the infrequent changing of diapers and 2.70% mentioned not cleaning the diaper area during diaper changes, 8.11% did not have any idea why their children had diaper rash. This demonstrates the importance of educating mothers and caregivers regarding diaper rash in order to reduce the frequency of diaper rash in children.

This study also demonstrated that the education of mothers was also an important factor of reducing diaper rash in children, as the children of mothers who studied until at least class 10 suffered a lower percentage of cases of diaper rash compared to mothers who were less educated. Children of mothers who received information regarding diaper rash also suffered significantly less numbers of diaper rash than the children of mothers who did not. From the discussion above it can be recommended that educating mothers and breast-feeding children can be very effective measures to reduce or prevent diaper rash in these children.

One of the two limitations of the study was the small sample size of the study. One of the barriers to achieve higher participants was the inclusion criteria that mothers had to read, writeand speak Bengali. Unfortunately, many young primi mothers could not fulfill these criteria.

Another limitation was not including the financial situation of the mothers as a variable. To buy diapers or cleaning products is an extra burden for many families in developing countries. Research had to exclude this variable, as many mothers could not tell the monthly income of their families or did not want to disclose it. In future studies, these factors should be taken in account.

Conclusion

Diaper rash is a common but preventable condition in infants. The proper knowledge of mothers or caregivers regarding diaper rash, maintaining proper hygiene in the diaper area during diaper changes and frequent changes of diapers can be effective ways to reduce or prevent diaper rash in infants. Health-care workers, including physicians, nurses, and medical assistants, should take responsibility to inform mothers about childcare, including the care of the diaper area, during mothers' visits to health-care institutions.

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References

1. Fluhr JW, Darlenski R, Taieb A, Hachem J, Baudoin C, Msika P, et al. Functional skin adaptation in infancy-almost complete but not fully competent. *Experi-mental Dermatology* 2010;**19**:483-92.
2. Chiou YB, Blume-Peytavi U. Stratum corneum maturation. A review of neonatal skin function. *Skin Pharmacol Physiol* 2004;**17**:57-66.
3. Shee K, Jagtap V. Effect of health teaching on knowledge and practice of postnatal mother admitted in selected hospital regarding using diaper in children to prevent systemic bacterial infection. *International Journal of Health Sciences & Research* 2019;**95**:95-101.

4. Telofski LS, Morello AP, Correa P. The infant skin barrier: Can we preserve, protect and enhance the barrier? *Dermatol Res Pract* 2012;**2012**:1-18.

5. Black's Medical Dictionary. In: Marcovitch H, ed. London: A&C Black Publishers Limited; 2005. p.360.

6. Williams KD, Williams LA. Diaper rash relief: Common sense remedies and treatment for diaper rash. *International Journal of Pharmaceutical Compounding* 2011;**15**:464-70.

7. Philipp R, Hughes A, Golding J. Getting to the bottom of nappy rash. *British Journal of General Practice* 1997:**47**:493-97.

8. Jordan WE, Lawson KD, Berg RW. Daiper dermatitis: Frequency and severity among a general infant population. *Pediatric Dermat* 1986;**3**:198-207.

9. Berg RW. Etiology and pathophysiology of diaper dermatitis. *Advances in Dermatology* 1988;**3**:75-98.

10. Eke GK, Peace IO. Mothers knowledge and home management of nappy rash in Port Harcourt, Nigeria. *The Nigerian Health Journal* 2013;**13**:152-57.

11. Ward DB, Fleischer AB Jr, Feldman SR, Krowchuk DP. Characterization of diaper dermatitis in the United States. *Archives of Pediatrics & Adolescent Medicine* 2000;**154**:943-46.

12. Weston WL, Lane AT, Weston JA. Diaper dermatitis: Current concepts. *Pediatrics* 1980;**66**:532-36.

13. Harpin VA, Rutter N. Barrier properties of the newborn infant's skin. *J Pediatr* 1983;**102**:419-25.

14. Li CH, Zhu ZH, Dai YH. Diaper dermatitis: A survey of risk factors for children aged 1-24 months in China. *Journal of International Medical Research* 2012; **40**:1752-60.

15. Yoshioka H, Iseki K, Fujita K. Development and differences of intestinal flora in the neonatal period in breast-fed and bottle-fed infants. *Pediatrics* 1983;**72**:317-21.

16. Berg RW, Buckingham KW, Stewart RL. Etiologic factors in diaper dermatitis: The role of urine. *Pediatric Dermatology* 1986;**3**:102-06.

17. Saadeh, MR: A new global strategy for infant and young child feeding.*Forum Nutr* 2003; **56**:236-38.

18. Adalat S, Wall D, Goodyear H. Diaper Dermatitis Frequency and Contributory Factors in Hospital Attending Children. *Pediatric Dermatology* 2007;**24**:483-88.

19. Merrill L. Prevention, Treatment and Parent Education for Diaper Dermatitis. *Nursing for Women's Health* 2015;**19**:324-37.

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ORIGINAL ARTICLE

Chronic Diarrhea in Children: Experience at A Tertiary Hospital of Bangladesh

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Abstract

Background: *Chronic diarrhea is insidious onset that persists for 14 days and more, usually of noninfectious origin. Chronic diarrhea in children is not an uncommon problem in our country.*

Objectives*: Objective of this study was to evaluate children with chronic diarrhea by clinical-biochemical profile and outcome.*

Methods: *It was a retrospective observational study done in the department of paediatric gastroenterology and nutrition, BSMMU. The study was done during January 2017 through December 2018. Forty-five patients diagnosed as chronic diarrhea between the ages of 6 months to 18 years were included in this study. We Clinical, laboratory data and outcome of patients were analyzed.*

Results: *Mean age of children was 5.96±2.3 year, 60%(27) were male and 40% (18) were female. Among them under 5 years were 55%(25). All children presented with diarrhea (100%) along with fever (24%), FTT (22%), abdominal pain (20%) and weight loss (20%). About 58% of children had anemia and 14% had hepatomegaly and/or splenomegaly. Raised ESR (40%), leukocytosis (20%), thrombocytosis (16%), raised CRP (13%) and electrolyte imbalance (16%) were observed. Intestinal TB (18%) was the most common etiology of chronic diarrhea. Moreover, chronic constipation with fecal incontinence mimicking diarrhea (11%), IBD (9%), coeliac disease (8%), IBS (7%), HIV enteropathy (4%), primary immunodeficiency disorder (4%) were also found. Improvement of diarrhea was observed in 96% children, 4% patient died due to diarrhea-related complications.*

Conclusion: *Chronic diarrhea in children is not uncommon in Bangladesh and diagnosis of etiologies are challenging. Intestinal tuberculosis found to be an important cause of chronic diarrhea in this study. Although in the majority of the cases, etiology could not be identified, some remote etiologies were found on this study, like chronic constipation with fecal incontinence mimicking diarrhea, IBD, HIV enteropathy, primary immunodeficiency.*

Keywords*: Chronic diarrhea, children, intestinal TB, immunodeficiency disorder.*

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Introduction

Diarrhea is one of the most common causes of morbidity and mortality in children worldwide.[1] In clinical terms, diarrhea refers to either an increased stool frequency or a decreased stool consistency, typically a watery quality. The World Health Organization (WHO) defines a case of diarrhea as the passage of three or more loose or watery stools per day. Diarrhea is also defined as stool volume >10 g/kg per day in infants and toddlers, and >200 g/day in older children. Most acute diarrheal episodes subside by 7 days; few last up to 14 days.[2,3] Persistent diarrhea is an episode of diarrhea, which starts acutely, usually of infectious etiology and lasts for 14 days or more.[4-6] Chronic Diarrhea is one, which has insidious onset that persists for 14 days or more and usually of non-infectious origin.[7] Diarrheal illnesses are estimated to be responsible for approximately 2 to 4 million-childhood death worldwide each year.[3,8] In 2002, the WHO estimated that 13.2% of all childhood deaths were due to diarrheal diseases, 50% of which were from chronic diarrheal illnesses.[4] Persistent diarrhea may lead to fatality in 60% cases due to its difficult treatment and higher cost.[3] Large-scale studies indicated that the prevalence of chronic diarrheal illnesses ranges from 3% to 20%, and the incidence is approximately 3.2 episodes per child per year.[9,10] Chronic diarrhea is also a major problem in our country.[11]

Materials and Methods

It was a retrospective observational study done inthe department of pediatric gastroenterology and nutrition, BSMMU. The study was done from January 2017 to December 2018. Patients diagnosed as chronic diarrhea between the ages of 6 months to 18 years were included in this study. We analyzed clinical, laboratory data and outcome of patients. Patients with incomplete data were excluded from this study. A total of 45 patients were included in this study. We aim to evaluate children with chronic diarrhea by clinical biochemical profile and outcome in hospitalized children. Clinical history, relevant clinical examination findings, investigation reports, diagnosis and treatment history were recorded in a pretested datasheet specially designed for the study.

Results

Mean age of children was 5.96 year. Among them 60% (27) were male, and 40% (18) were female. Under 5-year children were 55% (Table I).

Table I
Demographic characteristics (N=45)

Demographic characteristics	No of patients	Percentage
Sex		
Male	27	60.0
Female	18	40.0
Age		
6mo-1y	7	15.6
>1y-3y	17	37.8
>3y-5y	3	6.7
>5y-10y	3	6.7
>10y	10	22.2

All the patients had diarrhea in common. Besides, 24.4% (11) of them complained about fever. In addition, 20% (9) of them had abdominal pain and complaint of weight loss (Table II).

Table II
Presenting symptoms (N=45)

Presenting complaints	No of patients	Percentage
Diarrhea	45	100.0
Fever	11	24.4
Abdominal pain	9	20.0
Weight loss	9	20.0
Vomiting	8	17.8
Edema	5	11.1
Abdominal distension	5	11.1
Blood mixed stool	1	2.2
Skin lesion	1	2.2

On examination, most of them were anemic (57.8%, n=26). Failure to thrive was also common (22.2%, n=10). Organomegaly (hepatosplenomegaly) observed in a few of the patients along with ascites (Table III).

Table III
Physical findings (N=45)

Physical findings	No of patients	Percentage
Anemia	26	57.8
FTT	10	22.2
Hepatosplenomegaly	4	8.9
Hepatomegaly	2	4.4
Ascites	2	4.4
Rickets	1	2.2

Severe acute malnutrition was not much prevalent in the studied children who were aged under 5 years (29%, 10 out of 35 children) (Fig. 1).

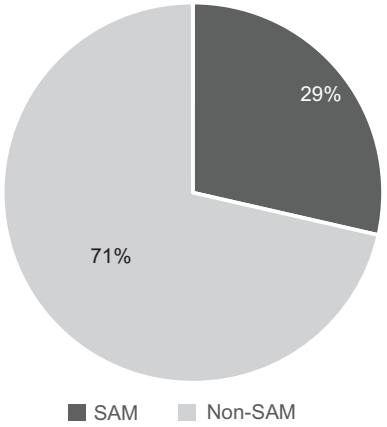

Fig 1 *Distribution of severe acute malnutrition in under 5 children (N=35)*

Laboratory investigations revealed the presence of anemia in 57.8%(26) children. Raised ESR, leukocytosis, and thrombocytosis were found in addition. Electrolyte imbalance was found in 15.6%(7) cases (Table IV).

Table IV
Laboratory findings (N=45)

Laboratory findings	No of patients	Percentage
Anemia	26	57.8
Raised ESR	18	40.0
Leukocytosis	13	28.9
Thrombocytosis	7	15.6
Raised CRP	6	13.3
Electrolyte imbalance (hypokalemia/hyponatremia)	7	15.6
Stool R/M/E (pus cell+/- RBC)	6	13.3
Stool C/S growth	0	0.0

Around 31.1%(14) cases remained undiagnosed in time of discharging from the hospital. Known diagnosis included intestinal tuberculosis, chronic diarrhea, and other forms of abdominal diseases (Table V).

Table V
Diagnosis (N=45)

Diagnosis	No of patients	Percentage
Undiagnosed	14	31.1
Intestinal TB	8	17.8
Chronic constipation with fecal soiling mimicking diarrhea	5	11.1
IBD	4	8.9
Coeliac disease	3	6.7
IBS	3	6.7
HIV enteropathy	2	4.4
P. Immunodeficiency	2	4.4
GSD	1	2.2
Acrodermatitis enteropathica	1	2.2
Cystic fibrosis	1	2.2
Short bowel syndrome	1	2.2

Only 4%(2) children died during hospitalization. Rest of the children's condition improved and been discharged (Fig. 2).

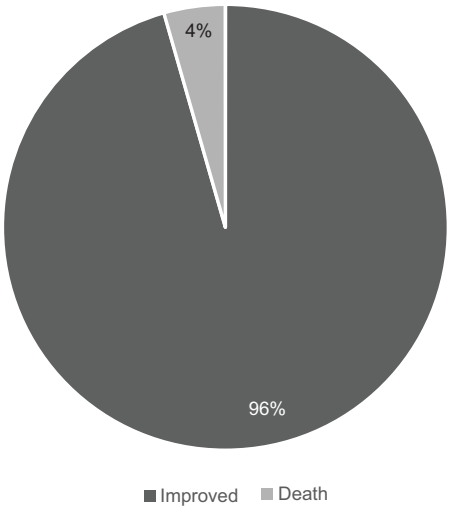

Fig 2 *Outcome of the patients (N=45)*

Table VI
Aetiological comparisons of different studies

Present study	Shenoy et al[14] n=50	Altunaset al[16] n=70	Rastogi et al[17] n=47	Yachha et al[18] n=137	Lee et al[19] n=27
Chronic constipation with fecal soiling mimicking diarrhea-11.1% Primary Immunodeficiency 4.4%	Post infectious-10%	Post-infectious 10% Other infections-4.2%	Tropical enteropathy 47%	Protracted diarrhea 33%	
Intestinal tuberculosis-17.8% IBD-8.9% Coeliac disease-6.7% IBS-6.7%	Parasitic-0 Celiac-12% CMPI -62% TB-2% IBD-2%	Parasitic-19% Celiac-30% CMPI-17%	Parasitic-15% Celiac-7% IBS-11%	Parasitic-9% Celiac -26% CMPI- 6% TB-5%	Parasitic-26% CMPI-29% Sec. lactose intolerance 19%
GSD-2.2% Acrodermatitis enteropathica-2.2% Cystic fibrosis-2.2% Short bowel syndrome-2.2%	Nonspecific 2% Lymphangiectesia-4% Cystic fibrosis- 2% Glucose galactose malabsorption-4%	Cystic fibrosis-10%	NON-SP- 22%	OTHERS-8% Cystic fibrosis Acrodermatitis enteropathica	Lymphangiectesia-7% Glucose galactose malabsorption-7.5%
Unknown-31.1%	Unknown-nil	Unknown-10%	Unknown-nil	Unknown-13%	Unknown-11%

Discussion

Diarrhea is commonest of the diseases that cause morbidity and mortality in children.[1] Over 6 billion children suffer from diarrhea worldwide, and around 1.7 billion of them are from Southeast Asia.[1,6] In Bangladesh, Islam et al[12] in 2018, conducted study in DMCH and ICDDR,B they targeted the under 5 year children, as this group was more vulnerable to diarrhea and found 6.4% were Persistent diarrhea. Chronic diarrhea has a broad etiological pattern and includes a number of heterogeneous conditions with a differentcourse. But there is no study in Bangladesh regarding chronic diarrhea. This study aimed to observe the demography, clinical profile, diagnosis, and outcome of chronic diarrheal illness within a year span in BSMMU.

The mean age of children was found in this study was around 6 years. Mahfuz et al[13] in 2017 found the mean age 4.5 years. Male children (60%) were prevalent than female (40%) with a male-to-female ratio of 1.5:1 and under 5-year children were common (55%). Shenoy B et al[14], 2018 found, 86% of children were <5 years and 14% beyond 5 years of age. The number of more male children than female children reflected the social norms of our country. Male children get more attention and thus taken to hospital.[15]

All the patients had diarrhea, along with fever (24.4%), abdominal pain (20%), and complaint of weight loss (20%). Shenoy et al[14], showed 26% cases had a fever, weight loss, and abdominal pain associated in their study.

On examination, most of them were anemic (57.8%), and failed to thrive (22.2%). Hepatosplenomegaly was observed in a few of the patients (8.9%) along with ascites (4.4%), rickets 2.2%. Shenoy et al[14], found anemia 32%), vitamin D deficiencies 6%, hepatomegaly 10%, splenomegaly 2% and ascites with pedal edema 2%.

Severe acute malnutrition was 28.6% in the studied children who were aged under 5 years. Persistent diarrhea showed a clear relevance with malnutrition,

established by several researchers. Shenoy et al[14] found 12% malnutrition in chronic diarrhea.

Laboratory investigations revealed the presence of anemia (57.8%), raised ESR (40%), leukocytosis (28.9%), and thrombocytosis (15.6%). Electrolyte imbalance was found in a few cases (15.6%). Stool culture in this study revealed no presence of infectious agents. Shenoy et al 2018, found 10% cases were post-infectious.[15]

Around 31.1% (14) cases remained undiagnosed in time of discharging from the hospital. Known diagnosis included intestinal tuberculosis (17.8%), Chronic constipation with fecal soiling mimicking diarrhea (11.1%), IBD (8.9%), Coeliac disease (6.7%), IBS (6.7%), HIV enteropathy (4.4%), primary Immunodeficiency (4.4%),GSD (2.2%), Acrodermatitis enteropathica (2.2%)[14], Cystic fibrosis (2.2%), Short bowel syndrome (2.2%). Shenoy et al 2018 found 62% cow milk protein intolerance (CMPI), 12% celiac disease, 10% post-infectious, 4% glucose-galactose intolerance, 2% non-specific, 2% cystic fibrosis, 2% IBD, TB 2% and 4% lymphangiectasia. Other study found, functional diarrhea (28%), IBD(24%), celiac disease (8%), post enteritis diarrhea (8%), alimentary allergy (14%), infectious diarrhea (8%), congenital diarrhea (1%), no diagnosis (9%).[20,21] In the present study, most of the children were improved (95.6%) and been discharged and 4.4% have died.

This is the first-ever study in Bangladesh regarding chronic diarrhea in children. The etiological pattern of chronic diarrhea in Bangladesh was not known. This study adds valuable information about etiology and demographic variants. Larger sample size and multicenter study are required to find out other causes of chronic diarrhea. Investigation facilities are needed to be made available for proper diagnosis.

Conclusion

Chronic diarrhea in children is not uncommon in Bangladesh and diagnosis of etiologies are challenging. Intestinal tuberculosis found to be an important cause of chronic diarrhea in this study. Although in the majority of the cases, etiology could not be identified, some remote etiologies were found on this study, like chronic constipation with fecal incontinence mimicking diarrhea, IBD, HIV enteropathy, primary immunodeficiency.

References

1. Walker CLF, Rudan I, Liu L, Nair H, Theodoratou E, Bhutta ZA, et al. Global burden of childhood pneumonia and diarrhoea. *Lancet* 2013;**381**:1405-16.
2. Diarrhoeal disease 2019 [cited 2019]. Available from: https://www.who.int/news-room/fact-sheets/detail/diarrhoeal-disease.
3. Das SK, Faruque AS, Chisti MJ, Malek MA, Salam MA, Sack DA. Changing trend of persistent diarrhoea in young children over two decades: Observations from a large diarrhoeal disease hospital in Bangladesh. *Acta Paediatrica* 2012;**101**:e452-e57.
4. Zella GC, Israel EJ. Chronic diarrhea in children. *Pediatrics in Review* 2012;**33**:207-17.
5. Mathai J, Raju B, Bavdekar A, Pediatric Gastroenterology Chapter IAoP. Chronic and persistent diarrhea in infants and young children: Status statement. *Indian Pediatrics* 2011;**48**:37-42.
6. Chen MR, Zhao J, Fu SF, Yu JQ, Zhang X, Zhang QY, et al. Clinical practice of Chinese medicine navel therapy for chronic diarrhea: A literature review. *Journal of Gastroenterology and Hepatology* 2019;**34**:643-99.
7. Schiller LR, Pardi DS, Spiller R, Semrad CE, Surawicz CM, Giannella RA, et al. Gastro 2013 APDW/WCOG Shanghai working party report: Chronic diarrhea: Definition, classification, diagnosis. *Journal of Gastroenterology and Hepatology* 2014;**29**:6-25.
8. Morampudi S, Das N, Gowda A, Patil A. Estimation of lung cancer burden in Australia, the Philippines, and Singapore: an evaluation of disability adjusted life years. *Cancer Biology & Medicine* 2017;**14**: 74-82.
9. Bhutta ZA, Ghishan F, Lindley K, Memon IA, Mittal S, Rhoads JM, et al. Persistent and chronic diarrhea and malabsorption: Working Group report of the second World Congress of Pediatric Gastroenterology, Hepatology, and Nutrition. *Journal of Pediatric Gastroenterology and Nutrition* 2004;**39**:(Suppl 2):S711-S717.
10. Kotloff KL, Nataro JP, Blackwelder WC, Nasrin D, Farag TH, Panchalingam S, et al. Burden and aetiology of diarrhoeal disease in infants and young children in developing countries (the Global Enteric Multicenter Study, GEMS): A prospective, case-control study. *Lancet* 2013;**382**:209-22.
11. Das S, Chandra H, Saha UR. District level estimates and mapping of prevalence of diarrhoea among under-

five children in Bangladesh by combining survey and census data. *PloS one* 2019;**14**:e0211062.

12. Islam SB, Ahmed T, Mahfuz M, Mostafa I, Alam MA, Saqeeb KN, et al. The management of persistent diarrhoea at Dhaka Hospital of the International Centre for Diarrhoeal Disease and Research: a clinical chart review. *Paediatrics and International Child Health* 2018;**38**:87-96.
13. Mahfuz M, Alam MA, Islam SB, Naila NN, Chisti MJ, Alam NH, et al. Treatment outcome of children with persistent Diarrhoea admitted to an Urban Hospital, Dhaka during 2012-2013. *BMC Pediatrics* 2017;**17**:142.
14. Shenoy B, Dodderi SK. The clinical spectrum of chronic diarrhoea in children in a tertiary care hospital in Bangalore, India. *International Journal of Contemporary Pediatrics* 2018;**5**:5.
15. Vlassoff C. Gender differences in determinants and consequences of health and illness. *Journal of Health, Population, and Nutrition* 2007;**25**:47-61.
16. Altuntas B, Gul H, Yarali N, Ertan U. Etiology of chronic diarrhoea. *Indian J Pediatr* 1999;**66**:657-61.
17. Rastogi A, Malhotra V, Uppal B. Etiology of chronic diarrhoea in children. *Trop Gastroenterol* 1998;**19**: 45-49.
18. Yachha SK, Mishra S, Malik AK, Nagi B, Mehta S. Spectrum of malabsorption syndrome in North Indian children. *Indian J Gastroenterol* 1993;**12**: 120-25.
19. Lee WS, Boey CCM. Chronic diarrhoea in infants and young children: Causes, clinical features, and outcome. *J Pediatr Child Health* 1999;**35**:260-63.
20. Guarino A, De Marco G, Italian National Network for Pediatric Intestinal Failure. Natural history of intestinal failure, investigated through a national network-based approach. *J Pediatr Gastroenterol Nutr* 2003;**37**:136-41.
21. Goulet O, Ruemmele F. Causes and management of intestinal failure in children. *Gastroenterology* 2006;**130**(suppl 1):S16-S28.

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ORIGINAL ARTICLE

A 1 year Study on Pattern of Neonatal Admissions and Mortality Related to Neonatal and Maternal Influences in A Tertiary Care Teaching Hospital of Barishal

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Abstract

Background: *Morbid conditions during the neonatal period possess a serious risk to the health and well-being of the baby. The death rate among neonates is very high in Bangladesh and various factors are responsible for this other than neonatal diseases.*

Objectives: *The objective was to compare different aspects of neonatal conditions in a tertiary care teaching hospital and to inspect the effects of neonatal/maternal influences over neonatal morbidity and mortality. Another primary goal was to study if there was any interconnection between neonatal morbid conditions and mortality.*

Methods: *This prospective study was carried out at Special Care Neonatal Unit of Sher-e-Bangla Medical College and Hospital, Barishal from April 2019 to March 2020. A total of 142 mothers were enquired according to our questionnaire. Data about both mothers and neonates were included in the questionnaire. Data were analyzed by using SPSS version 26.*

Results: *A total of 142 mothers and their 150 admitted neonates were included in our cohort. Among 150 neonates, we analyzed 133 and excluded 17. During the hospital stay, 9.8% of 133 neonates died. Mortality and morbidity were dependent on factors like gestational age, birth weight, and twin pregnancy. The causes of admission were PNA with HIE (58.6%), neonatal sepsis (28.6%), neonatal jaundice (9.8%), congenital anomalies (8.3%), RDS (4.5%), IUGR (3.8%), pneumonia (2.3%), and diabetes mellitus (0.8%). Neonates having PNA with HIE showed significant p-value when correlated with the cause of LUCS- oligohydramnios, gestational age, birth weight. Pre-term neonates had substantial cases of RDS (9.8%). Neonatal sepsis was observed more on the initiation of breastfeeding on the first day (39.1%) than later (23%), and oligohydramnios, less fetal movement, prolonged labor were found to be significant causes of it.*

Conclusion: *The study acknowledged LBW, PNA with HIE, sepsis, neonatal jaundice, congenital anomalies, and RDS as the major factors for neonatal admissions, and reasons behind mortality were LBW, prematurity, and twin pregnancy. Awareness among parents and improved infrastructure of the hospital might be helpful to reduce the gravity of the condition in the future.*

Key words: *Neonatal morbidity, mortality, neonatal and maternal influences.*

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Introduction

The first 28 days are considered to be the most vulnerable period in a baby's life.[1] It is called the neonatal period and has been a pivotal factor in child health. Any morbidities during the neonatal period carry grave threat to the health of the baby**.** In 2019, 2.4 million neonates died, which was about 6,700 neonatal deaths per day.[1] About one-third of all neonatal deaths occurred within the first day.[1] One in every 35 babies born in South Asia died within their first month of life, and they were nine times more likely to die in the first month compared to a child from a high-income country.[2] The birth rate in Bangladesh is 18.1 births/ 1000 population.[3] The neonatal mortality rate was 19.06 per 1000 live births in our country.[4] It is estimated that 29.7% is contributed by prematurity in Bangladesh, the direct cause of mortality being sepsis (19.9%), asphyxia and birth trauma (22.9%), congenital anomalies (12.7%), respiratory distress (5.9%).[5] The Sustainable Development Goal 3.2 for child survival cannot be met without a substantial neonatal mortality reduction.[6] Not many studies have been done on the information on the neonatal conditions in our country. This prospective study was done at Sher-E-Bangla Medical College and Hospital (SBMCH), Barishal, to identify the main reasons behind neonatal morbidity and mortality in Bangladesh's context.

Materials and Methods

The prospective study was carried out at the Special Care Neonatal Unit (SCANU) of the Department of Pediatrics, Sher-E-Bangla Medical College and Hospital, Barishal for a period of 1 year (Apr 2019-Mar 2020). This is a tertiary care teaching hospital, where most of the admitted neonates are critically ill. All neonates were admitted on a structured protocol of data entry including particulars of the patient, mode of delivery, the weight of the baby at admission (measured by an electronic machine having Gram as the smallest unit), diagnosis, treatment and discharge criteria. The diagnosis was made based on clinical, radiological and laboratory findings. The inclusion criteria adopted in this study encompassed newborns aging <28 days with their mothers being alive. A questionnaire was prepared including information about both mother and the baby, and consisting of the name of mother and contact details of the parents with telephone numbers. A total of 142 mothers were asked for data related to pre-planned pregnancy, the continuation of oral contraceptive pills (OCP) during early pregnancy unknowingly, para, number of gestations, weeks of gestation, illness during pregnancy (HTN/ DM/APH/Others), number of antenatal care (ANC) visits, TT injection dosage, mode of delivery and causes of LUCS. Birth weight, the need for resuscitation after birth, the day of introduction to breast milk, pre-lacteal food administration, diagnosis, treatment, and hospital outcome of 150 babies were also documented in the relevant sections of the questionnaire. All the data were analyzed with IBM Statistical Package for Social Sciences (SPSS version 26) and Microsoft Excel 2019. Numbers and percentages were compared in groups using Chi-Square. A p-value of <0.05 was considered significant. The risk ratio was also calculated.

Results

In this study information about 142 mothers and their 150 neonates admitted to SBMCH were included. Among 150 cases, we excluded 17(11.3%) from our analysis because of lacking one or more data. Therefore, we analyzed the remaining 133 data. Among the study population 12(9.0%) mothers continued taking OCP during the early days of pregnancy unknowingly. Of 133 cases, 57.9% of the pregnancies were pre-planned. The percentages of primigravida (48.9%) and multigravida (51.1%) were almost equal. The incidence of twins was 14(10.5%) (Table I).

The preterm, term, and postdated births amount to 45.9%, 51.9%, and 2.3%, respectively. Among 35 mothers suffering from gestational diseases, 13 were hypertensive, two were diabetic, and 14 had episodes of antepartum hemorrhage (APH). About two-thirds of the mothers were administered TT injections during pregnancy. While 83 mothers went through vaginal delivery, 50 had lower uterine cesarean sections preceded by various conditions such as oligohydramnios (28%), pre-eclampsia (4%), previous history of C/S (28%), twin pregnancy (12%), prolonged labor (4%), PROM (22%), postdated pregnancy (2%), eclampsia (4%), less fetal movement (LFM) (10%) and APH (6%). The percentages of Macrosomia, NBW, LBW, VLBW and ELBW neonates were 0.8%, 36.8%, 45.1%, 15.8% and 1.5%, correspondingly. Among 133 neonates, 71.4% needed immediate resuscitation after birth. There were 46 (34.6%)

Table I
Demographic table

Variables	Attributes	Frequency	Percentage
OCP taken during gestation	Yes	12	9.0
Pre-planned pregnancy	Yes	77	57.9
	No	56	42.1
Para	Primigravida	65	48.9
	Multigravida	68	51.1
Number of gestations	Singletons	119	89.5
	Twins	14	10.5
Gestational age	Preterm (<37 weeks)	61	45.9
	Term (37 - <42 weeks)	69	51.9
	Post-term (≥42 weeks)	3	2.3
Illness during pregnancy	No illness	104	78.2
	Gestational HTN	13	9.8
	Gestational DM	2	1.5
	APH	14	10.5
TT injection dosage	No TT after pregnancy	43	32.3
	TT taken after pregnancy	90	67.7
Mode of delivery	NVD	83	62.4
	LUCS	50	37.6
Cause of LUCS	Oligohydramnios	14	28
	Pre-eclampsia	2	4
	PHO C/S	14	28
	Twin baby	6	12
	Prolonged labor	2	4
	PROM	11	22
	Post dated	1	2
	Eclampsia	2	4
	Less fetal movement	5	10
	APH	3	6
Birth weight	4 kg and more (Macrosomia)	1	0.8
	2.5-3.999 kg (NBW)	49	36.8
	1.5-2.499 kg (LBW)	60	45.1
	1-1.499 kg (VLBW)	21	15.8
	Less than 1.00 kg (ELBW)	2	1.5
Resuscitation after birth	Needed	95	71.4
	Not needed	38	28.6
Introduction to Breastmilk	On 1st day	46	34.6
	After 1st day	87	65.4
Pre-lacteal feed	Given	12	9
	Not given	121	91
ANC visits	Less than 8	114	85.7
	8 and above	19	14.3
Immediate Outcome	Survived	120	90.2
	Expired	13	9.8

newborn babies; who were given breastmilk on their 1st day after birth. Twelve neonates were given prelacteal food. We got 114 (85.7%) cases where mothers did not complete ANC visits (according to new WHO guideline). During the hospital stay, 13 (9.8%) out of 133 neonates died, and 120 (90.2%) survived.

There were various types of neonatal morbid conditions such as PNA with HIE (58.6%), neonatal sepsis (28.6%), neonatal jaundice (9.8%), congenital anomaly (8.3%), RDS (4.5%), IUGR (3.8%), pneumonia (2.3%) and DM (0.8%) within 133 cases (Table II).

Among the mothers with the cause of LUCS-oligohydramnios, 28.6% of their babies developed asphyxia. On the other hand, 61.1% of the neonates

Table II
Demographic table for diseases

Morbidities	Count	Percentage
PNA with HIE	78	58.6
Neonatal Sepsis	38	28.6
Neonatal Jaundice	13	9.8
Congenital Anomaly	11	8.3
RDS	6	4.5
IUGR	5	3.8
Pneumonia	3	2.3
Diabetes Mellitus	1	0.8

Table III
Factors vs morbidities

Factors		Yes	No	Risk ratio	*p value
		PNA with HIE			
Cause of LUCS- Oligohydramnios	Yes	4 (28.6%)	10 (71.4%)	0.47	0.039
	No	22 (61.1%)	14 (38.9%)		
Gestational age	Preterm	26 (42.6%)	35 (57.4%)	—	<0.005
	Term	49 (71.0%)	20 (29.0%)		
	Postdated	3 (100%)	0 (0.0%)		
Birth weight	4.0 kg and more	1 (100%)	0 (0.0%)	—	0.005
	2.5-3.999 kg	37 (75.5%)	12 (24.5%)		
	1.5-2.499 kg	33 (55%)	27 (45%)		
	1-1.499 kg	6 (28.6%)	15 (71.4%)		
	Less than 1 kg	1 (50%)	1 (50%)		
		RDS			
Gestational age	Preterm	6 (9.8%)	55 (90.2%)	—	0.025
	Term	0 (0.0%)	69 (100%)		
	Postdated	0 (0.0%)	3 (100%)		
		Neonatal Sepsis			
Cause of LUCS- Oligohydramnios	Yes	7 (50%)	7 (50%)	2.57	0.031
	No	7 (19.4%)	29 (80.6%)		
Cause of LUCS-Less Fetal Movement	Yes	4 (80%)	1 (20%)	3.6	0.006
	No	10 (22.2%)	35 (77.8%)		
Cause of LUCS- Prolonged Labor	Yes	2 (100%)	0 (0.0%)	4	0.021
	No	12 (25%)	36 (75%)		
Introduction to Breast Milk	On 1st day	18 (39.1%)	28 (60.9%)	1.7	0.05
	After 1st day	20 (23%)	67 (77%)		
		Congenital Anomaly			
Mode of Delivery	NVD	10 (12%)	73 (88%)	—	0.042
	LUCS	1 (2%)	49 (98%)		
Cause of LUCS- Prolonged Labor	Yes	1 (50%)	1 (50%)	—	<0.005
	No	0 (0.0%)	48 (100%)		
Prelacteal Food	Given	3 (25%)	9 (75%)	—	0.027
	Not Given	8 (6.6%)	113 (93.4%)	—	

*χ^2 test

whose mother had a LUCS because of other reasons developed PNA with HIE, and this data was statistically significant (p=0.039 & RR= 0.47). In our study, 42.6% of preterm babies, 71.0% of term babies, and all of the postdated babies developed PNA with HIE, and this data was significant statistically (p<0.005). The correlation between birth weight and PNA with HIE was significant, with a p-value of 0.005. The only macrosomic baby we had in our data suffered from birth asphyxia. Furthermore, 75.5% of the NBW neonates and 55% of the LBW neonates had asphyxia. Among VLBW and ELBW neonates, the percentages of being affected by PNA with HIE were 28.6% and 50%, respectively (Table-III).

Respiratory distress syndrome showed a significant result when linked with gestational age (p=0.025). No term and postdated babies developed RDS, while 9.8% of premature babies suffered from it (Table-III). According to our data, 50%, 80%, and 100% of the neonates developed sepsis whose mothers had LUCS due to oligohydramnios (p=0.031 & RR= 2.57), LFM (p=0.006 & RR=3.6) and prolonged labor (p=0.021 & RR= 4.0), accordingly. Moreover, 39.1% neonates developed sepsis among those who were given breastmilk on their 1st day of birth. On the contrary, 23% of neonates who were given breastmilk after 1st day, developed sepsis. This data was found statistically significant (p=0.05) and the risk ratio was 1.7 (Table III).

In our data, neonates who had any of the congenital deformities were mostly born through NVD (10 out of 11) {p=0.042}. Mothers' LUCS due to prolonged labor had a significance, with 50% being diagnosed with congenital anomalies (p=<0.005). Three of 12 neonates were given pre-lacteal food and had congenital anomalies (p=0.027) (Table III).

A significant result (p=0.013) was seen in the relation between gestational age and mortality. Premature babies were more prone to die (18% out 61 died) than term or postdated babies. According to our data, 42.9% (6) of the twins died, and 5.9% (7) of the singletons deceased (p=<0.005 & RR= 7.29). Moreover, when twin pregnancy was followed by preterm delivery, the result was the same as previous data with similar risk ratio and p-value. The death and survival rate were equal in the case of neonates born through LUCS because of twin pregnancy. This data showed statistical significance (p=<0.005) (Table IV).

With a p-value of <0.005, birth weight showed significance when related to immediate outcome. The relation between weeks of gestation and mortality was disproportionate, which means when the birth

Table IV
Factors vs mortality

Factors		Expired	Survived	Risk ratio	p value*
Gestational age	Preterm	11 (18%)	50 (82%)	—	0.013
	Term	2 (2.9%)	67 (97.1%)		
	Post-term	0 (0%)	3 (100%)		
Twin pregnancy	Yes	6 (42.9%)	8 (57.1%)	7.29	<0.005
	No	7 (5.9%)	112 (94.1%)		
Twin pregnancy with Prematurity	Yes	6 (42.9%)	8 (57.1%)	7.29	<0.005
	No	7 (5.9%)	112 (94.1%)		
Cause of LUCS - Twin pregnancy	Yes	3 (50%)	3 (50%)	—	<0.005
	No	0 (0%)	44 (100%)		
Birth weight	≥4.0 kg (Macrosomia)	0 (0.0%)	1 (100%)	—	<0.005
	2.5-3.999 kg (NBW)	1 (2%)	48 (98%)		
	1.5-2.499 kg (LBW)	4 (6.7%)	56 (93.3%)		
	1-1.499 kg (VLBW)	7 (33.3%)	14 (66.7%)		
	<1kg (ELBW)	1 (50%)	1 (50%)		

*χ^2 test

weight decreased, the death rate increased. Macrosomic (0.0%) and NBW (2%) babies showed fewer death percentages than those with LBW (6.7%) and VLBW (33.3%), among all neonates. The rate of survival and death were equal (one survived and one died) in the case of ELBW neonates (Table IV).

In our data, 14.5% of LBW (other than NBW and Macrosomia) neonates died. In other words, most of the expired neonates were with LBW (12 out of 13). This data was also statistically significant (p=0.019 & RR= 7.23). A total of 53 neonates were premature LBW, and 18.9% of them expired (p=<0.005 & RR= 5.03). Neonates who were twins with LBW showed a higher mortality rate (41.7%). It was also statistically significant with a p-value of <0.005 & a risk ratio of 10.31. Moreover, the death rate, survival rate, and risk ratio were equal to the previous data, when LBW was associated with both prematurity and twin pregnancy (p=<0.005) (Table V).

In total, 66.7% of VLBW neonates survived, while 33.3% died. The relative risk was very high (6.22), and the p-value was <0.005. Those 7 expired VLBW neonates were also premature (p=<0.005 & RR= 6.22). When sepsis was associated with twin pregnancy, we got a significant result (p=<0.005 & RR= 11.91). Two of the twin neonates developed sepsis, and both of them died. Lastly, the death rate of neonates with PNA with HIE (7.7%), neonatal sepsis (13.2%), RDS (0.0%), neonatal jaundice (7.7%), pneumonia (0.0%), IUGR (0.0%), congenital anomaly (9.1%), and diabetes mellitus (0.0%) did not show any significant result when related to mortality, individually (Table V).

Table V
Mortality vs morbidities

Morbidities		Expired	Survived	Risk ratio	p value*
LBW (other than NBW & macrosomia)	yes	12 (14.5%)	71 (85.5%)	7.23	0.019
	no	1 (2%)	49 (98%)		
LBW with prematurity	yes	10 (18.9%)	43 (81.1%)	5.03	<0.005
	no	3 (3.8%)	77 (96.3%)		
LBW with twin	yes	5 (41.7%)	7 (58.3%)	10.31	<0.005
	no	8 (6.6%)	113 (93.4%)		
LBW with prematurity with twin	yes	5 (41.7%)	7 (58.3%)	10.31	<0.005
	no	8 (6.6%)	113 (93.4%)		
VLBW	yes	7 (33.3%)	14 (66.7%)	6.22	<0.005
	no	6 (5.4%)	106 (94.6%)		
VLBW with prematurity	yes	7 (33.3%)	14 (66.7%)	6.22	<0.005
	no	6 (5.4%)	106 (94.6%)		
PNA with HIE	yes	6 (7.7%)	72 (92.3%)	—	0.336
	no	7 (12.7%)	48 (87.3%)		
RDS	yes	0 (0%)	6 (100%)	—	0.409
	no	13 (10.2%)	114 (89.8%)		
Neonatal sepsis	yes	5 (13.2%)	33 (86.8%)	—	0.406
	no	8 (8.4%)	87 (91.6%)		
Neonatal sepsis with twin	yes	2 (100%)	0 (0%)	11.91	<0.005
	no	11 (8.4%)	120 (91.6%)		
Neonatal jaundice	yes	1 (7.7%)	12 (92.3%)	—	0.79
	no	12 (10%)	108 (90%)		
Pneumonia	yes	0 (0.0%)	3 (100%)	—	0.564
	no	13 (10.0%)	117 (90%)		
IUGR	yes	0 (0%)	5 (100%)	—	0.453
	no	13 (10.2%)	115 (89.8%)		
Congenital anomaly	yes	1 (9.1%)	10 (90.9%)	—	0.936
	no	12 (9.8%)	110 (90.2%)		
Diabetes Mellitus	yes	0 (0.0%)	1 (100%)	—	0.741
	no	13 (9.8%)	119 (90.2%)		

*χ test

Discussion

In our study, 42.1% of pregnancies were unplanned, which is about 1.5 times higher than the report from Turkey.[7] The rate of NVD in a study in Karachi was 68%, which is almost similar to our data.[8] Besides, research in Pakistan showed the opposite ratio of NVD and LUCS in comparison with our study.[9] The percentage of neonates introduced to early initiation of breastfeeding (On 1st day) is half in our study compared to the data by Edmond et al.[10] The report from Edmond et al[10] also showed a percentage of newborns having pre-lacteal feed and is higher than the result in our investigation. A report from Iran showed that almost 36% of Afghan women completed at least 8 ANC visits according to the latest WHO guideline and this percentage is 2.5 times higher than the data in our records.[11] Future interventions towards the improvement of neonatal healthcare should focus on the awareness regarding ANC visits among mothers.

The overall death percentage was 9.8% (number of death was 13), which is almost four times less than the study from Haryana et al[12] and a little higher than the report from Sri Lanka.[13]

The incidence of twins (10.5%) in our research is almost similar to a study from Addis Ababa.[14] Twin pregnancy had been a major cause of mortality for neonates, and the risk of death for twins seemed to be 7.29 times greater than the singletons. If twin pregnancy was followed by premature delivery, the risk ratio and death rate had been as same as twin-mortality relation. The mortality rate was very high in LBW twins, and risk decreased 10.31 times when a neonate was not a twin and LBW at the same time. The death rate in this category is 1.5 times higher than a study in Nigeria.[15] All LBW twins were also premature in our data. The death rate (41.7%) among them is nearly 1.5 times higher than a study in Nigeria.[15] All the twins who developed sepsis died in the hospital. Neonates who were born through LUCS because of twin pregnancy showed a high mortality rate (50%).

The percentage of premature births in our research is approximately 1.5 times higher than the studies from Pakistan.[16,9] The rate of term birth (51.9%) is nearly analogous to the report from Addis Ababa [14]. The premature death rate (18%) was six-folds higher than the term death (2.9%) in our study. However, the preterm mortality rate is lower than the study in a secondary health care center in Nigeria.[17]

In a study from Addis Ababa, the percentage of neonates with a birth weight of at least 2.5 kg is almost 1.5 times higher than ours, and the rate of neonates with a birth weight of less than 1 kg is also 1.5 times more compared to our study.[14] The mortality rate increased with the fall in birth weight. Therefore, birth weight plays a pivotal role in neonatal mortality. In a study from Egypt, mortality among LBW neonates was ten times higher than NBW ones[18], but in our report, the death was 7.23 times higher in LBW neonates. The risk of death for premature LBW neonate was five-folds higher. All expired VLBW neonates were premature. The death rate among preterm VLBW babies was very high (33.3%) with about 6 times more risk to die than those who were not both preterm and VLBW. The mortality seems to be affected in the neonates having preterm birth and also under the category of VLBW.

Birth asphyxia was always followed by hypoxic-ischemic encephalopathy in our investigation. PNA with HIE acted as a substantial cause of hospital admission in our data. About 59% of admitted neonates suffered from PNA with HIE, which is almost 3.5 times higher than the study from Uttarakhand.[19] The neonates born through LUCS for reasons other than oligohydramnios had a higher risk of birth asphyxia. Most of the term babies were exposed to birth asphyxia, while the incidence of PNA with HIE was less in preterm births. All of the postdated babies suffered from PNA in our data. More NBW neonates suffered from asphyxia than LBW and VLBW babies. Birth asphyxia was common in all kinds of neonates irrespective of causes of LUCS, gestational age and birth weight. Though the death rate due to PNA with HIE is 2.3 times less than the study from South-East Nigeria, it was very high (7.7%) in our hospital.[20]

Neonatal sepsis comprised high percentages in neonatal morbidity (28.6%) and mortality (13.2%). Turhan et al[21] showed that the incidence of neonatal sepsis was about 11% (351 out of 3219), and mortality due to sepsis was about 7% (24 out of 351), respectively. Their morbidity and mortality rates are much less than ours. Cause of LUCS-Oligohydramnios was one of the main reasons for neonates suffering from sepsis. In our report, 50% of the neonates who were born through LUCS because of oligohydramnios developed sepsis, and

the others had 2.57 times less chance of getting it. Another reason behind sepsis was the cause of LUCS- less fetal movement. Babies who were born through LUCS because of LFM had 3.6 times more chance of developing sepsis than others. All the neonates who were born through LUCS because of prolonged labor had four times more risk of sepsis than the others do. According to our data, those who were given breastmilk on their 1st day of birth had 1.7 times more risk of developing sepsis. Further research and projects in this issue might reveal more about the relation between early breastfeeding and neonatal morbidity/mortality in the context of Bangladesh.

Neonatal jaundice was the third predominant cause of neonatal morbidity and mortality in our study. With about 10% incidence in our data, the similarity is noticed (but four times less mortality rate) with the data from Nigeria.[17] The incidence of congenital anomaly in our study is much higher than the studies from Uttarakhand and Nigeria.[19,17] Most of the babies with congenital defects were born through normal vaginal delivery (10 out of 11). One-fourth of the babies with congenital defects were given pre-lacteal food, as they did not have efficient suction power. The incidence of respiratory distress syndrome (RDS) in neonates of our study was about ten times less than the data showed by Lee et al.[22] According to our analysis, prematurity was the main reason for developing RDS. In our data, all the RDS patients were preterm, while no term and postdated babies suffered from it.

Conclusion

The study acknowledged LBW, PNA with HIE, sepsis, neonatal jaundice, congenital anomalies, and RDS as the major factors for neonatal admissions, and reasons behind mortality were LBW, prematurity, and twin pregnancy. Awareness among parents and improved infrastructure of the hospital might be helpful to reduce the gravity of the condition in the future.

References

1. UNICEF. UNICEF Data: Monitoring the situation of children and women, 2020. [Online]. Available: https://data.unicef.org/topic/child-survival/neonatal-mortality/.
2. UNICEF. Save Newborns, 2015. [Online]. Available: http://www.unicefrosa-progressreport.org/savenewborns.html.
3. Central Intelligence Agency. The world factbook, 2020. [Online]. Available: https://www.cia.gov/library/publications/resources/the-world-factbook/geos/bg.html.
4. UN Inter-agency Group for Child Mortality Estimation. Data, Data and estimates, 2020. [Online]. Available: https://childmortality.org/data.
5. UNICEF. Maternal and newborn health disparities Bangladesh, country profiles, UNICEF Data: Monitoring the situation of children and women, September 2018. [Online]. Available: https://data.unicef.org/resources/maternal-newborn-health-disparities-country-profiles/.
6. World Health Organization. Sustainable development goals (SDGs), 2020. [Online]. Available: https://www.who.int/health-topics/sustainable-development-goals#tab=tab_2.
7. Yanikkerem E, Ay S, Piro N. Planned and unplanned pregnancy: Effects on health practice and depression during pregnancy. *The Journal of Obstetrics and Gynaecology Research* 2013;**39**:180-87.
8. Aijaz N, Huda N, Kausar S. Disease Burden of NICU, at a Tertiary Care Hospital, Karachi. *Journal of the Dow University of Health Sciences Karachi* 2012;**6**:32-35.
9. Hussain S. Neonatal morbidity and mortality pattern in a tertiary care neonatal unit of a teaching hospital. *Annals of Pakistan Institute of Medical Sciences* 2014;**10**:7-11,
10. Edmond KM, Kirkwood BR, Amenga-Ete S, Owusu-Agyei S, Hurt LS. Effect of early infant feeding practices on infection-specific neonatal mortality: An investigation of the causal links with observational data from rural Ghana. *The American Journal of Clinical Nutrition* 2007;**86**:1126-31.
11. Dadras O, Dadras F, Taghizade Z, Seyedalinaghi Z, Ono-Kihara M, Kihara M, et al. Barriers and associated factors for adequate antenatal care among Afghan women in Iran; Findings from a community-based survey. *BMC Pregnancy Childbirth* 2020;**20**: 427.
12. Raikwar P, Parihar D, R awal M, Batra APS, Kaur J, Juneja P, et al. A study of neonatal admission pattern and outcome from rural haryana, *Global Journal for Research Analysis* 2018;**7**:73-75.
13. Narayan R. A study of the pattern of admissions and outcome in a neonatal intensive care unit at high altitude. *Sri Lanka Journal of Child Health* 2012;**41:**79-81.

14. Tekleab AM, Amaru GM, Tefera YA. Reasons for admission and neonatal outcome in the neonatal care unit of a tertiary care hospital in Addis Ababa: A prospective study. *Research and Reports in Neonatology* 2016;**6:**17-23.

15. Onyiriuka A. Incidence of delivery of low birthweight infants in twin gestations. *Nigerian Journal of Clinical Practice* 2010;**13:**365-70.

16. Ali SR, Ahmed S, Loha H. Disease patterns and outcomes of neonatal admissions at a secondary care hospital in Pakistan. *Sultan Qaboos University Medical Journal* 2013;**13**:424-28.

17. Okposio MM, Ighosewe OI. Morbidity and mortality pattern among neonates admitted to the general paediatric ward of a secondary health care centre in the Niger delta region of Nigeria." *Sri Lanka Journal of Child Health* 2016;**45**:84-89

18. Mansour E, Eissa A, Nofal L, Kharboush I, Reda A. Morbidity and mortality of low-birthweight infants in Egypt. *Eastern Mediterranean Health Journal* 2005;**11**: 723-731.

19. Rakholia R, Rawat V, Bano M, Singh G. Neonatal morbidity and mortality of sick newborns admitted in a teaching hospital of Uttarakhand. *CHRISMED Journal of Health and Research* 2014;**1**:228-234.

20. Ekwochi U, Asinobi NI, Osuorah CD, Ndu IK, Ifediora C, Amadi OF, et al. Incidence and predictors of mortality among newborns with perinatal asphyxia: A 4-year prospective study of newborns delivered in health care facilities in Enugu, South-East Nigeria. *Clinical Medicine Insights: Pediatrics: SAGE Journals* 2017;**11**:1-10.

21. Turhan EE, Gürsoy T, Ovalý F. Factors which affect mortality in neonatal sepsis. *Türk Pediatri Ar°ivi 2015;***50**:170-75.

22. Lee J, Seong HS, Kim BJ, Jun JK, Romero R, Yoon BH. Evidence to support that spontaneous preterm labor is adaptive in Nature: Neonatal RDS is more common in "indicated" than in "spontaneous" preterm birth. *Journal of Perinatal Medicine* 2009;**37**:53-58.

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REVIEW ARTICLE

Diagnosis and Management of Patent Ductus Arteriosus in Newborn: An Update

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Abstract

Patent ductus arteriosus is one of the common congenital acyanotic heart disease in neonates, especially in preterm. Patent ductus arteriosus (PDA) is a congenital condition, characterized by a persistent connection between the aorta and the pulmonary artery. Patency of Ductus Arteriosus is essential for fetal survival. Patent ductus arteriosus is one of the most common clinical findings and most frequent source of complications in premature infant. After birth, in term infants, the ductus usually closes within the first day of life, starting with functional closure followed by anatomical closure with vascular remodeling. The persistence of the PDA in preterm infant is inversely related to gestational age and birth weight. The incidence of Patent Ductus Arteriosus is 31% in preterm infant weighing 501 to 1500 gm and gestational age 29 weeks. The treatment options available are conservative medical management, pharmacological therapy or surgical ligation. Conservative medical management involves fluid restriction; watchful waiting and ventilator support.

Key words: *Patent ductus arteriosus, newborn.*

Introduction

The ductus arteriosus is a central vascular shunt connecting the pulmonary artery to the aorta, allowing oxygenated blood from the placenta to bypass the uninflated fetal lungs and enter the systemic circulation. Rapid closure of the ductus arteriosus after birth is essential for vascular transition to the mature, divided pattern of arteriovenous circulation. Failure of ductus arteriosus closure, termed patent ductus arteriosus (PDA), is primarily an affliction of prematurity, with the ductus remaining open at 7 days of age in up to 64% of infants born at 27 to 28 weeks' gestation and 87% of infants born at 24 weeks.[1] Before the use of antenatal corticosteroids, PDA was frequently found in premature infants of all gestational ages and was associated with respiratory distress syndrome. Treatment with indomethacin was standard, and studies evaluated the benefits of early (or even prophylactic) PDA ligation.[2]

With advances in ventilation strategies, use of antenatal corticosteroids and exogenous surfactant, and increased willingness to wait for spontaneous ductus arteriosus closure, today's more mature preterm infants rarely require intervention for a ductus arteriosus.[3]

This article is written with the view to explore the different modalities of investigations and treatment in home and abroad, which would be beneficial for the practicing doctors who deal with neonates.

Risk factors

The incidence of PDA is inversely associated with the degree of prematurity. Other factors associated

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with an increased risk of PDA in the premature infant include respiratory distress syndrome, high volume of intravenous fluids (>170 mL/kg per day) in the first week, sepsis, prolonged rupture of membranes, furosemide, male sex, and other contributors.[4] Evidence also shows that aminoglycoside antibiotics and certain antacids, frequently used in neonates, paradoxically increase the risk of a PDA.[5] Antenatal corticosteroids[6] and maternal hypertension[7] decrease the incidence of PDA.

Diagnosis

The diagnosis is often suspected clinically. Continuous or systolic murmur occur may be present. Murmur may be absent when shunt is large enough that nonturbulent flow fails to generate a detectible murmur. A low diastolic blood pressure (due to runoff into the ductus during diastole, more frequent in the most premature infants). A wide pulse pressure (due to ductus runoff or steal), hypotension (especially in the most premature infants), bounding pulses, increased serum creatinine concentration or oliguria, hepatomegaly, signs of pulmonary edema are often seen, including tachypnea, decreased oxygen saturation, and increasing respiratory support. Chest radiography can show stigmata of pulmonary edema.[7]

Echocardiography is gold starndard for diagnosis. Ductus size alone is inadequate to attribute hemodynamic significance. Although an absolute transductus diameter of more than 1.5 to 1.7 mm by color doppler has been associated with increased propensity for hypoperfusion.[7] A large left-to-right shunt suggests a hemodynamically significant shunt. However, the degree of shunting depends in large part on pulmonary vascular resistance.

Other echocardiographic criteria for determining hemodynamic significance are the presence of reversal of forward flow in the descending aorta during diastole (indicating shunting through the PDA), and left atrial or ventricular dilation, which are the consequence of overcirculation of the pulmonary vascular bed and a chronic hyperdynamic state. Left-to-right shunt across the intra-atrial septum is indicative of a large shunt. The ratio of the left ventricular output to superior vena cava flow is directly proportional to the ductus flow and, when greater than or equal to 4, may indicate hemodynamic significance. A left atrial to aortic root (LA/Ao) ratio is most sensitive when performed after day 1, and is considered abnormal if >1.5.[8]

Biomarkers

B-type natriuretic peptide (NT-proBNP) and mature B-type natriuretic peptide (BNP) may be useful in detecting a hemodynamically significant PDA. BNP is secreted and released by the ventricular myocardium when under stress from either increased volume or pressure.[9]

Biosensors

Bioengineering has also been developed to monitor or detect PDA in preterm infants. Various approaches include interpretation of pulse oximetry information (perfusion index, plethys-mography),[10,11] interpretation of transthoracic electrical signals (impedance, cardiometry, velocimetry, bioreactance),[12] regional oxygenation (near-infrared spectroscopy),[13] alterations in skin microcirculation (side stream dark-field imaging, reflectance spectropho-tometry),[14] resonance Raman spectroscopy.

Outcome

In healthy full-term infants, PDA closes within 48 to 72 hours. In premature infants born weighing more than 1,000 gm, the ductus closes spontaneously in 67% by day 7 and in 94% by discharge.[5] Only 3% of infants weighing more than 1,000 gm may require intervention for a PDA.[1,5]

However, in extremely premature infants weight <1,000 g at birth (extremely low birthweight), 57% to 69% will still have a PDA at 7 to 10 days of age.[5,9] Of those 30% will reopen and may then reclose, or go on to hemodynamically significant and require pharmacologic or surgical closure.

Treatment

Patent ductus arteriosus (PDA) is treated with medicines, catheter-based procedures, and surgery. The goal of treatment is to close the PDA to prevent complications and reverse the effects of increased blood volume. There are prophylactic use of indomethacin to prevent IVH, PDA, and the adverse consequences of PDA in extremely low-birth weight infants.[15]

Pharmacological approach

Pharmacologic treatments are available to induce constriction of a PDA: indomethacin, ibuprofen, and acetaminophen (paracetamol). Indomethacin and

ibuprofen are nonsteroidal anti-inflammatory drugs (NSAIDs), which nonselectively inhibit the cyclooxygenase enzymes, preventing the conversion of arachidonic acid to prostaglandins, which maintain ductuI patency. Since 1976, indomethacin has been used to treat PDA in premature infants. Indomethacin is administered intravenously. Enteral and rectal preparations are also being used. In patients who receive a second course of indomethacin, only half will experience ductus closure. The odds of nonresponse to the second course of indomethacin are increased by 90% if there was nonresponse to the first course. Advancing gestational age appears to predict nonresponse to indomethacin.[16]

Indomethacin and ibuprofen have a similar efficacy (70%) for an initial course of 3 doses. Regardless of the treatment, there is about a 25% rate of reopening, especially in the most premature infants. Because of this high rate of reopening, some advocate a fourth dose of indomethacin, given 24 hours after the third dose.

Acetaminophen decrease prostaglandin synthesis by interrupting prostaglandin synthesis at the peroxidase site of prostaglandin H2 synthetase (cyclooxygenase). Acetaminophen for treatment of PDA is associated with less elevation in serum creatinine concentration and oliguria compared to ibuprofen or indomethacin, and less elevation in bilirubin compared to ibuprofen.[17] Acetaminophen has been used for rescue therapy after failed response to indomethacin in extremely premature infants, resulting in 46% of infants having a smaller or closed ductus.[18] When used as primary treatment, the efficacy ranges from 70% to 81%.[19] Efficacy appears to be affected by both gestational age and postnatal age, with improved efficacy noted when treatment was started within the first week.[20]

The range of reported treatment regimens for acetaminophen, from 7.5 mg to 10 or 15 mg/kg every 6 hours for 3 to 7 days. Acetaminophen can be given orally, at the same dosage and interval, with similar reported efficacy as the intravenous route.[21]

A hemodynamically significant PDA can reduce forward blood flow to the superior mesenteric artery during diastole, and indomethacin acutely decreases gut blood flow. On the other hand, fasting is associated with intestinal mucosal atrophy which could increase the risk for NEC. So patients must have their oral feed during oral administration of indomethacin or ibuprofen.[22]

Ligation

Candidates for surgical ligation hemodynamically significant PDA that results in cardiac dysfunction, renal failure, or respiratory failure. Ligation is typically performed with an open thoracic approach, and either using a metal clip or tying off the vessel. Intravascular approaches with placement of an occluding coil are available for patients weighing more than 5 kg.[23] Adverse effects ligation are: vocal cord paralysis, postoperative hypotension, diaphragm paralysis,[24] bronchopulmonary dysplasia, and worse neurodevelopment. Early PDA ligation is an independent risk factor for BPD and worse neurodevelopment compared with ligation at a later age.[25]

Diagnosis and treatment option followed in some international institute:

In National University Hospital (NUH) Singapore

In their institute when they suspect PDA in a premature baby by clinical examination. An echocardiography of the heart (ultrasound scanning) done at the bedside can confirm the diagnosis. Treatment options include fluid restriction, medical treatment with drugs such as indomethacin and occasionally, surgical ligation (where the PDA is ligated in a surgical operation). In the majority of instances medical management is effective in closing a PDA. In the rare occasion of failure with medical therapy, surgical ligation is done by the cardiothoracic surgeons under general anesthesia. They have a support group (early starter club) for parents of premature babies that comprises doctors, nurses, medical social workers as well as parents of previous premature babies managed in NICU. In their VLBW cohort (2015-2019), 78 out of 268 (29%) VLBW babies had a symptomatic PDA. 73% of 78 VLBW babies with symptomatic PDA were successfully treated with medication and the remaining 27% underwent surgical ligation. There were no deaths in babies who had ligation.[26]

In All India Institute of Medical Sciences (AIIMS)

Patent ductus arteriosus (PDA) is a major morbidity in preterm infants, especially in extremely premature infants less than 28 weeks in NICU in AIIMS. The clinical signs and symptoms of PDA in preterm

infants are nonspecific and insensitive for making an early diagnosis of significant ductal shunting. Functional echocardiography is emerging as a new valuable bedside tool for earlydiagnosis of hemodynamically significant ductus, even though there are no universally accepted criteria for grading the hemodynamic significance. Echocardiography has also been used for early targeted treatment of ductus arteriosus, though the long term benefits of such strategy are debatable. The biomarkers like BNP and N- terminal pro. BNP are currently under research as diagnostic marker of PDA. The primary mode of treatment for PDA is pharmacological closure using cyclo-oxygenase inhibitors with closure rate of 70-80%. Oral ibuprofen is emerging as a better alternative especially in Indian scenario where parenteral preparations of indomethacin are unavailable and side effects are comparatively lesser. Though pharmacological closure of PDA is an established treatment modality, there is still lack of evidence for long term benefits of such therapy as well as there is some evidence for the possible adverse effects like increased ROP and BPD rates, especially if treated prophylactically. Hence, it is prudent to reserve treatment of PDA to infants with clinically significant ductus on the basis of gestation, birthweight, serial echocardiography and clinical status to individualize the decision to treat.[27]

PDA with PPHN

Persistant pulmonary hypertension (PPHN) is common association with PDA. Echocardiography remains the gold standard diagnosis of PPHN. Right-to-left or bidirectional shunting of blood at the foramen ovale and/or the ductus arteriosus is classically seen, as well as high pulmonary arterial/right ventricular systolic pressure estimated by Doppler velocity measurement of tricuspid regurgitation jet. The direction of the shunt at atrial and ductual level also provides clues to management. Left-to-right shunting at the foramen ovale and ductus arteriosus with marked hypoxemia suggests predominant intrapulmonary shunting, and interventions should focus on optimizing lung recruitment (increasing PEEP/mean airway pressure or intratracheal surfactant). The presence of right-to-left shunting at foramen ovale and/or ductus arteriosus is suggestive of extrapulmonary shunting and which may respond to pulmonary vasodilator therapy. Similarly, right-to-left shunting at the ductal level and left-to-right shunting at the atrial level suggest PPHN with left ventricular dysfunction with pulmonary venous hypertension as seen in CDH, asphyxia or sepsis. Ductal dependent systemic circulation syndromes may be associated with a similar shunt pattern. Adequate resuscitation, careful and intensive monitoring, careful fluid and electrolytes management,minimal handling prevent PPHH. Mechanical ventilation, surfactant therapy, pressor agent like dopamine is use to treat this condition. There are some other modalities of treatment like- inhaled nitric oxide, Milrinone (a type 3 phosphodiesterase inhitor), Sildenafil, Prostacyclin, inhaled/nebulized PGI_2, Bosentan, Paralyzing agent like-pancuronium, Magnesium sulphate. Extracorporial membrane oxiganation is indicated for term and near term infants with PPHN who fail to respond to conventional therapy.[28]

Treatment of PDA in full term baby

PDA accounts for 10% of all congenital heart diseases in full term infants. The PDA in a full term infant is structurally different, so the sensitivity of the ductus to the relaxing effect of prostaglandin $E_2$is lost shortly after birth. That's why it does not respond appropriately to the various stimuli for closure. Indomethacin is usually ineffective. The infant should monitored carefully, and surgical ligation should be considered at the earliest signs of significant congestion. Even without signs of failure, the PDA should be ligated before 1 year of age to prevent endocarditis and pulmonary hypertension.[29]

Conclusion

PDA is a common condition among premature infants born at less than 28 weeks' gestation. Recent advances include the addition of acetaminophen (paracetamol) to the arsenal of available treatments. Improvements are still needed regarding standardized echocardiographic criteria, optimal timing of treatment (when indicated), dosing regimens for acetaminophen, and development of endovascular occlusive devices for the smallest preterm infants.

References

1. Clyman RI, Couto J, Murphy GM. Patent ductus arteriosus: are current neonatal treatment options better or worse than no treatment at all? S*emin Perinatol* 2012; **36**:123-29.

2. Mosalli R, Alfaleh K. Prophylactic surgical ligation of patent ductus arteriosus for prevention of mortality and morbidity in extremely low birth weight infants. *Cochrane Database Syst Rev* 2008; (1):CD006181.

3. Nemerofsky SL, Parravicini E, Bateman D, Kleinman C, Polin RA, Lorenz JM. The ductus arteriosus rarely requires treatment in infants >1000 grams. *Am J Perinatol* 2008;**25**:661-66.

4. Gillam-Krakauer M, Cotton RB, Reese J. Patent ductus arteriosus. In: Feld LG, Mahan JD, Lorenz JM, Seigel WM, editors. Succinct Pediatrics: Evaluation and Management for Newborn, Genetic, Neurologic, and Developmental-Behavioral Disorders. Elk Grove Village, IL: American Academy of Pediatrics; 2017. p.137-50.

5. Vucovich MM, Cotton RB, Shelton EL, Goettel JA, Ehinger NJ, Poole SD, et al. Aminoglycoside-mediated relaxation of the ductus arteriosus in sepsis-associated PDA. *Am J Physiol Heart Circ Physiol* 2014;**307**:H732-H740. Doi 10.1152/ajpheart. 00838.2013.

6. Chorne N, Jegatheesan P, Lin E, Shi R, Clyman RI. Risk factors for persistent ductus arteriosus patency during indomethacin treatment. *J Pediatr* 2007; **151**:629-63.

7. Alverson DC, Eldridge MW, Johnson JD, Burstein R, Papile L, Dillon T, et al. Effect of patent ductus arteriosus on left ventricular output in premature infants. *J Pediatr* 1983;**102**:754-57.

8. Iyer P, Evans N. Re-evaluation of the left atrial to aortic root ratio as a marker of patent ductus arteriosus. *Arch Dis Child Fetal Neonatal Ed* 1994;**70**:F112-F11.

9. Weisz DE, McNamara PJ, El-Khuffash A. Cardiac biomarkers and haemodynamically significant patent ductus arteriosus in preterm infants. *Early Hum Dev* 2017;**105**:41-47.

10. Khositseth A, Muangyod N, Nuntnarumit P. Perfusion index as a diagnostic tool for patent ductus arteriosus in preterm infants. *Neonatology* 2013;**104:** 250-54.

11. Vidal M, Ferragu F, Durand S, Baleine J, Batista-Novais AR, Cambonie G. Perfusion index and its dynamic changes in preterm neonates with patent ductus arteriosus. *Acta Paediatr* 2013;**102**:373-78.

12. Weisz DE, Jain A, Ting J, McNamara PJ, El-Khuffash A. Non-invasive cardiac output monitoring in preterm infants undergoing patent ductus arteriosus ligation: A comparison with echocardiography. *Neonatology* 2014;**106**:330-36.

13. Underwood MA, Milstein JM, Sherman MP. Near-infrared spectroscopy as a screening tool for patent ductus arteriosus in extremely low birth weight infants. *Neonatology* 2007;**91**:134-39.

14. Hiedl S, Schwepcke A, Weber F, Genzel-Boroviczeny O. Microcirculation in preterm infants: profound effects of patent ductus arteriosus. *J Pediatr* 2010;**156**:191-96.

15. Reese J, Shelton EL, Slaughter JC, McNamara PJ. Prophylactic indomethacin revisited. *J Pediatr* 2017;**186:**11-14.e1. Doi:10.1016/j.jpeds.2017.03.036.

16. Louis D, Wong C, Ye XY, McNamara PJ, Jain A. Factors associated with non-response to second course indomethacin for PDA treatment in preterm neonates. *J Matern Fetal Neonatal Med* 2018; **31**:1407-14.

17. El-Mashad AE, El-Mahdy H, El Amrousy D, Elgendy M. Comparative study of the efficacy and safety of paracetamol, ibuprofen, and indomethacin in closure of patent ductus arteriosus in preterm neonates. *Eur J Pediatr* 2017;**176**:233-40.

18. Weisz DE, Martins FF, Nield LE, El-Khuffash A, Jain A, McNamara PJ. Acetaminophen to avoid surgical ligation in extremely low gestational age neonates with persistent hemodynamically significant patent ductus arteriosus. *J Perinatol* 2016;**36**:649-53.

19. Le J, Gales MA, Gales BJ. Acetaminophen for patent ductus arteriosus. *Ann Pharmacother* 2015;**49**: 241-46.

20. Terrin G, Conte F, Scipione A. Efficacy of paracetamol for the treatment of patent ductus arteriosus in preterm neonates. *Ital J Pediatr* 2014;**40**:21.

21. Kessel I, Waisman D, Lavie-Nevo K, Golzman M, Lorber A, Rotschild A. Paracetamol effectiveness, safety and blood level monitoring during patent ductus arteriosus closure: A case series. *J Matern Fetal Neonatal Med* 2014;**27**:1719-21.

22. Clyman R, Wickremasinghe A, Jhaveri N, Hassinger DC, Azzridge JT, Sanocka U, et al. Ductus Arteriosus Feed or Fast with Indomethacin or Ibuprofen (DAFFII) Investigators. Enteral feeding during indomethacin and ibuprofen treatment of a patent ductus arteriosus. *J Pediatr* 2013;**163**:406-11.

23. Backes CH, Rivera BK, Bridge JA, Armstrong AK, Berman DP, Fick T, et al. Percutaneous patent ductus arteriosus (PDA) closure during infancy: A meta-analysis. *Pediatrics* 2017;**139**: e20162927. Doi: 10.1542/peds.2016-2917.

24. Hsu KH, Chiang MC, Lien R, et al. Diaphragmatic paralysis among very low birth weight infants following ligation for patent ductus arteriosus. *Eur J Pediatr* 2012;**171**:1639-16.

25. Weisz DE, Mirea L, Rosenberg E, Jang M, Ly L, Church PT, et al. Association of patent ductus arteriosus ligation with death or neurodevelopmental impairment among extremely preterm infants. *JAMA Pediatr* 2017;**171**:443-49.

26. Patent Ducts Arteriosus (Children). Available at : https://www.nuh.com.sg/Health-Information/Diseases-Conditions/Pages/Patent-Ductus-Arteriosus-(Children).aspx

27. Sasi A, Deorari AK. Patent ductus arteriosus in preterm infants. *Indian Pediatrics* 2011;**48**:301-09.

28. Gomella TL, Cunningham MD, Eyal FG, Zenk KE. Persistant pulmonary hypertension of the newborn. In: Gomella TL, Cunningham MD, Eyal FG, Zenk KE, editors. Lange Clinical Manual of Neonatology. New York: McGraw-Hill Medical Publishers 2013: P815-22.

29. Gomella TL, Cunningham MD, Eyal FG, Zenk KE. Patent ductus arteriosus In: Gomella TL, Cunningham MD, Eyal FG, Zenk KE, editors. Lange Clinical Manual of Neonatology. 7th ed. New York: McGraw-Hill Medical Publishers, 2013:P800-804.

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CASE REPORT

Solitary Rectal Ulcer Syndrome in a Teenage Girl: A Case Report

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Introduction

Solitary rectal ulcer syndrome (SRUS) is rare and uncommon disorder of rectosigmoid region which is mostly reported in adults and is very rare in children. This disorder is diagnosed by clinical findings, colonoscopy findings and histopathological changes.[1] The cause of this syndrome is still not known and is usually caused by chronic constipation, which can be associated with excessive straining during defecation, rectal manipulation, trauma and ischemia. The condition was first described by Cruveilhier in 1830 and detailed clinical and histopathological features were reported by Madigan and Morson in 1969.[2] It occurs most commonly in the 3rd decade in men and in the 4th in women, with only a few reported paediatric cases.[3,4] The annual incidence rate of SRUS is 0.001%.[5] SRUS usually presents with rectal bleeding, constipation, mucous discharge, prolonged straining, tenesmus, and lower abdominal pain.[6] The term "SRUS" is a misnomer, and is sometimes referred to as "the three-lie disease,"as the lesion is not always solitary (it may be multiple), is not ulcerative (it may be polypoidal /nodular or affecting the erythematous mucosa only) and is not restricted to the rectum (it may also involve the sigmoid colon).[7] Histological examination is the gold standard for the diagnosis of SRUS.

Case report

A fifteen years old girl was admitted in the department of Paediatric Gastroenterology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka, Bangladesh in middle of July, 2019 with the complaints of per rectal whitish discharge for twenty days. She also complained of per rectal bleeding and abdominal pain for same duration. The girl had history of constipation and weight loss with this illness. She was quite alright two years back. Then she developed occasional per-rectal bleeding. At the same time she suffered from intermittent lower abdominal pain. For this illness she was admitted previously in several institutions but no significant improvement occurred. Previously she was undergone colonoscopy for two times which showed nonspecific histopathological results. As Bangladesh is a tuberculosis prone country, so she was treated with anti-tubercular drug for six months. Though she had no contact with tubercular patient previuosly. Initially some improvement occurred with anti-tubercular drug but not totally subsided. Few days later she had again full blown symptoms along with mucorrhoea. She was admitted in BSMMU for second time colonoscopy. She was diagnosed as inflammatory bowel disease at that time and treated accordingly. She was transfused with two unit of blood as her hemoglobin (7.6 gm/dl) dropped down at that time. She was on tab. mesalamine and tab. steroid for one month with mild improvement. But gradually she developed further deterioration of her health. Per rectal bleeding, passage of mucous, abdominal pain became more pronounced along with gradual weight loss. In the recent admission, she was again evaluated with third time colonoscopy. Routine laboratory test results

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including blood cell counts, coagulation, hepatic function, C-reactive protein levels, and the erythrocyte sedimentation rate were normal. A stool examination for bacteria and parasites was negative, Macroscopically the whole colon including terminal ileum (Fig. 2,3) was normal but rectal ulcerations, erythema and sloughing exudates (Fig. 1) were found (5 cm from the anal verge) which was easily bled after light touching. Several biopsies were obtained from both the lesion and the ileal mucosa. Ileal biopsy was normal. A histopathological examination of rectal biopsy revealed chronic inflammatotry cell infiltration in the lamina propria and surface erosion. The crypts were diamond shaped. The muscularis mucosa was thick and thin bands of smooth muscle fibers were present in between the crypts. We took proper history of constipation and habit of straining during defecation. So, on the basis of clinical suspicion, colonoscopy and histology finding, we made a rare diagnosis of this illness as 'Solitary Rectal Ulcer Syndrome'. We managed the girl with sucralfate enema. As sucralfate enema is not available in our country, we prepared it locally by adding two tablet of sucralfate in 10 ml distilled water. Then introduced this solution per rectally twice a day for 14 days. Management of constipation with polyethelene glycol and lactulose went on side by side. All the symptoms (per rectal bleeding, passage of mucus, abdominal pain) subsided in just two weeks with this treatment. Now the girl's condition is much improved. She is on polyethelene glycol and lactulose for last two months. She was advised to take high fiber diets and also advised not to strain during defecation. She was routinely followed-up and assessed for further bleeding. As further bleeding did not occur repeat colonoscopy was postponed.

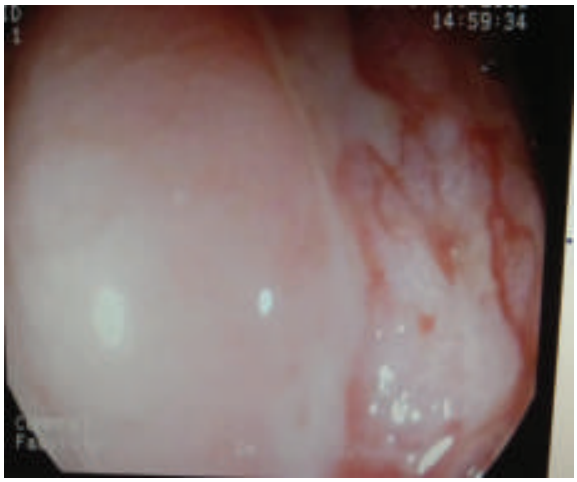

Fig 1 *Rectal ulcerations, erythema*

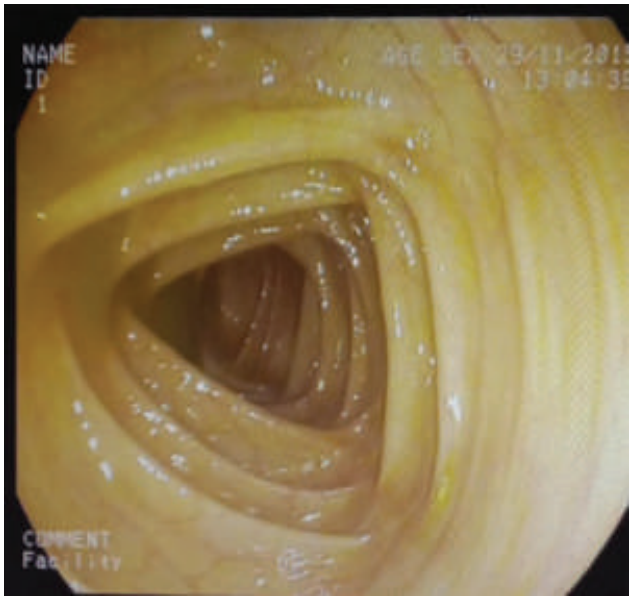

Fig 2 *Normal colon*

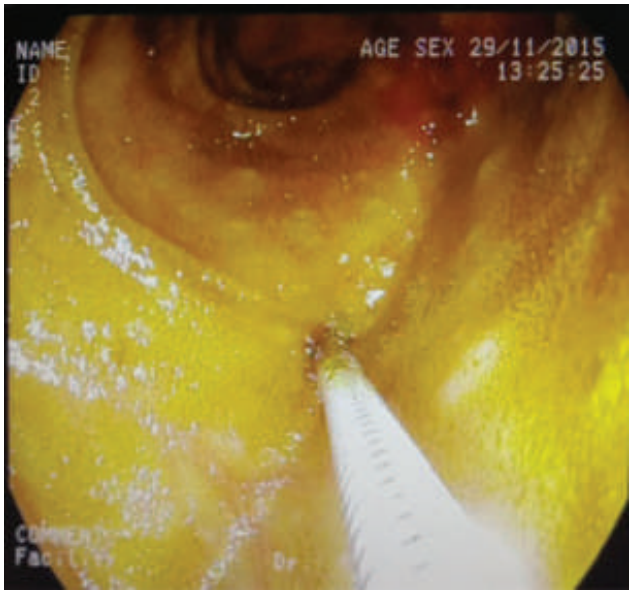

Fig 3 *Normal terminal ileum*

Discussion

SRUS is a rare benign condition of children where individuals experience difficult defecation. It is characterized by rectal bleeding, constipation, passage of mucus, mucosal prolapse, feeling of incomplete evacuation, rectal pain (tenesmus) or intermittent lower abdominal pain. The patient in the current case experienced abdominal pain, passage of mucus and rectal bleeding. The etiology of SRUS may be associated with certain lifestyles such as enema use or insertion of suppositories, self

digitation, staying in the toilet for a long time having the habit of straining during defecation, use a stream of water, or cleaning the inside part of rectal as far as possible. The patient of the current report had the habit of straining during defecation. Her diet was lack of fruits and vegetables which is rich in dietary fibers and had constipation for last few years, which is a risk factor for SRUS. Ischemic injury of rectal mucosa is recognized as the main mechanism of SRUS. The reasons for ischemic injury of rectal mucosa include paradoxical contraction of the pelvic floor, external anal sphincter, and abdominal pressure. The youngest reported patient with SRUS was a 1.5-year-old child but the majority of cases are children older than 8 years.[8] The average time from the onset of symptoms to diagnosis is 5 years, ranging from 1.2 to 5.5 years.[8] The average time from the onset of symptoms to diagnosis is 3.2 years, ranging from 1.2 to 5 years in children, which is shorter than in adult patients (5 years; range, 3 months to 30 years).[9] It was 2 years in our patient. It has been reported that 75% to 80% of children with SRUS is male.[9] Our patient is a teenage girl.

Anemia is not typically present in SRUS.[10,11] A lengthy period of misdiagnosis may cause anemia due to prolonged bleeding, but blood transfusion in SRUS is rare.[12] Our case had anemia, received two unit of blood transfusion. The gold standard of diagnosis of SRUS is the histopathological findings. The histology of solitary rectal ulcer has a distinct feature including thickening of the mucosal layer with disrupting crypts structure, infiltration of the lamina propria with fibroblasts, muscle and collagen fibers that lead to hypertrophied and disrupted muscularis mucosa which look like fibromuscular obliteration.[8] Our patient's histology report revealed chronic inflammatotry cell infiltration in the lamina propria and surface erosion. The crypts were diamond shaped. The muscularis mucosa was thick and thin bands of smooth muscle fibers were present in between the crypts. This finding was consistant with SRUS. Macroscopically, SRUS typically appears as shallow ulcerating lesions on a hyperemic surrounding mucosa, most often located on the anterior wall of the rectum at 5 to 10 cm from the anal verge, ranging from 0.5 to 4 cm in diameter but usually are 1 to 1.5 cm in diameter.[13] The polypoid variant is very rare among the cases reported in children.[14] Our case had shallow ulceration (4 cm in diameter) in rectal wall (5 cm from anal verge). Repeat endoscopies were not routinely carried out unless patients had persistent symptoms.[7] We did not perform colonoscopy during follow up as symptoms were resolved in our patient. Though SRUS is benign, the patient's morbidity is significant. As symptoms persist over a periods of time requires multiple admissions.[15] Our patient had multiple admissions in different institutions for this illness.[16-18]

At the time of diagnosis, patients should be counseled about taking high-fiber diet and bulk laxatives. They also need to be trained for avoidance of straining and anal digitation. The toilet habits (time spent in the toilet) should be adjusted. Dietary and behavioral changes, especially in patients with mild to moderate symptoms, can be dramatically effective in the absence of mucosal prolapse, which can help in the improvement and prevention of disease progression.[19]

The current treatment protocol is the use of enemas containing sucralfate, salicylate, corticoste-roid, sulphasalazine, mesalazine, and topical fibrin sealant.[3] Surgery is indicated in cases not responding to conservative treatment.[7] In the study by Dehghani et al[9] conservative treatments, behavioral and dietary changes were recommended as the initial treatment. In that study, 58.3% of the patients (7 out of 12 patients) had the complete recovery of symptoms after treatment with sucralfate enema and recommend this as a suitable treatment for children. One of their patients responded to Salicylate enema, 1 to corticosteroid enema, 2 to corticosteroid injection and 1 of the patients were finally treated with rectopexy.[9] Our patient responded well with bulk laxative and modified sucralfate enema. Though duration of treatment is not properly mentioned in any literature, we gave sucralfate enema for 14 days.

Conclusion

Solitary rectal ulcer syndrome (SRUS) is a rare benign and reversible condition in children. Few reported cases have undergone detailed investigations, treatments have been extremely varied and outcome poorly reported. The clinical features of SRUS is easily confused with other common diseases such as inflammatory bowel disease, infectious proctocolitis. So paediatric gastroenterologists and pathologists should have a high index of suspicion about SRUS and be alert about the patient if he/she has gastrointestinal

hemorrhages specially when other diagnosis is not matched. It is noteworthy that conservative management, patient education, fiber consumption, and bulk laxatives are the first strategies at initial stage. Surgical management is preserved for late stages.

References

1. Zhu QC, Shen RR, Qin HL, Wang Y. Solitary rectal ulcer syndrome: Clinical features, pathophysiology, diagnosis and treatment strategies. *World J Gastroenterol* 2014; **20**:738-44.
2. Chiang JM, Changchien CR,Chen JR. Solitary rectal ulcer syndrome: An endoscopic and histological presentation and literature review. *Int J Colorectal Dis* 2006;**21**:348-56.
3. Dehghani SM, Malekpour A, Haghighat M: Solitary rectal ulcer syndrome in children: Literature review. *World J Gastroenterol* 2012;**18**:6541-45.
4. Perito ER, Mileti E, Dalal DH, Cho SJ, Ferrell LD, McCracken M, Heyman MB: Solitary rectal ulcer syndrome in children and adolescents. *J Pediatr Gastroenterol Nutr* 2012;**54**:266-70.
5. Dehghani SM, Bahmanyar M, Geramizadeh B, Alizadeh A, Haghighat M. Solitary rectal ulcer syndrome: Is it really a rare condition in children? *World J Clin Pediatr* 2016;**5**:343-48
6. Suresh N, Ganesh R, Sathiyasekaran M. Solitary rectal ulcer syndrome: A case series. *Indian Pediatr* 2010;**47**:1059-61.
7. Urgancý N, Kalyoncu D, Eken KG. Solitary rectal ulcer syndrome in children: A report of six cases. *Gut Liver* 2013;**7**:752-55.
8. Abreu M, Alves RA, Pinto J, Campos M, Aroso S: Solitary rectal ulcer syndrome: A paediatric case report. *GE Port J Gastroenterol* 2017;**24**:142-46.
9. Dehghani SM, Haghighat M, Imanieh MH, Geramizadeh B. Solitary rectal ulcer syndrome in children: Prospective study of cases from southern Iran. *Eur J Gastroenterol Hepatol* 2008;**20**:93-95.
10. Martin de Carpi J, Vilar P, Varea V. Solitary rectal ulcer syndrome in childhood: A rare, benign, and misdiagnosed cause of rectal bleeding. Report of three cases. Dis Colon Rectum 2007; 50:534-39.
11. Pi RR, Mathai AM, Magar DG, Tantry BV. Solitary rectal ulcer syndrome in childhood. *Trop Gastroentaerol* 2008;**29**:177-178
12. Ertem D, Acar Y, Karaa EK, Pehlivanoglu E. A rare and often unrecognized cause of hematochezia and tenesmus in childhood: Solitary rectal ulcer syndrome. *Pediatrics* 2002;**110**:e79. Doi:10.1542/peds.110.6.e79.
13. Tjandra JJ, Fazio VW, Church JM, Lavery IC, Oakley JR, Milsom JW. Clinical conundrum of solitary rectal ulcer. *Dis Colon Rectum* 1992;**35**:227-34.
14. Saadah OI, Al-Hubayshi MS, Ghanem AT. Solitary rectal ulcer syndrome presenting as polypoid mass lesions in a young girl. *World J Gastrointest Oncol* 2010;**2**:332-34
15. Chong VH, Jalihal A. Solitary rectal ulcer syndrome: Characteristics, outcomes and predictive profiles for persistent bleeding per rectum. *Singapore Med J* 2006;**47**:1063-68.
16. Keshtgar AS. Solitary rectal ulcer syndrome in children. *Eur J Gastroenterol Hepatol* 2008;**20**:89-92.
17. Ertem D, Acar Y, Karaa EK, Pehlivanoglu E. A rare and often unrecognized cause of hematochezia and tenesmus in childhood: Solitaryrectal ulcer syndrome. *Pediatrics* 2002;**110**:e79.
18. Ruan M, Zhang Y, Feng Z, Qu B, Han M, et al. Solitary rectal ulcer syndrome in a young patient: A case report. *Iran Red Crescent Med J* 2017;**19**:e15106. doi:10.5812/ircmj.15106.
19. Sharara AI, Azar C, Amr SS, et al. Solitary rectal ulcer syndrome: Endoscopic spectrum and review of the literature. *Gastrointest Endosc* 2005;**62**:755-62.

DS (Child) H J 2020; 36(1): 70-74

CASE REPORT

Constrictive Pericarditis Leading to Cardiac Cirrhosis: A Rare Cause of Chronic Liver Disease

Nahid-e-Subha[1], Sharmin Akter[2], Aysha Sabiha[3], Md. Shariful Hasan[4], Farhana Bayes[5], Wahiduzzaman Mazumder[6]

Introduction

The relation between diseased heart and liver may manifests as acute liver injury, chronic congestive hepatopathy, even cardiac cirrhosis. Congestive hepatopathy caused from impaired blood return to the right ventricle with increased filling pressure.[1] Chronic liver disease (CLD) is the most frequent presentation of hepatobiliary disease.[2,3] Neonatal cholestasis and metabolic liver disorders are the leading causes of paediatric CLD, whereas autoimmune hepatitis, chronic hepatitis B, C infections, NAFLD, congenital hepatic fibrosis, BUDD chiary disease is least common.[4] Very rare cause, like long term right heart failure may also be a cause of underlying disease for CLD. Our case will present such a short report or cardio-hepatic relations.

Case report

A 11 years old boy of nonconsanguinous parents immunized as per EPI schedule, admitted at BSMMU at Paediatric Gastroenterology and Nutrition department with the complaints of gradual abdominal distention since 6 years of age, more marked for last 2 weeks and legs swelling, respiratory distress for last 2 months associated with exertional dyspnea, orthopnea and nonproductive cough. He also developed jaundice for last 1 month. Patient gave the history of osteomyelitis at 4 years of his age, operation needed two times four months apart for osteomyelitis followed by pericardiocentasis also needed along with injectable antibiotics for 6 weeks. Then he developed anasarca and was treated with oral diuretic (furosemide) off and on. Developmentally he is age appropriated. He has no family history of liver disease, no previous history of jaundice, fever, bleeding manifestations or contact with tubercular patient.

On general physical examination he was cooperative, dyspnoeic, afebrile, moderately pale, mildly icteric, engorged neck veins present, pulse-116 beats/min, low volume, BP-100/60 mm of Hg, BCG scar present. His right arm was deformed with a scar mark. Stigmata of CLD (thenarar-hypothenar wasting, leukonychia) and pedal oedema present. Bed side urine for albumin was nil. He was severely undernourished, severely stunted, mildly wasted. On

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systemic examination, abdomen was hugely distended, flanks were symmetrically full, seen, nontender hepatomegaly (10 cm from the right costal margin, firm with smooth surface.) No splenomegaly, ascites was present. Respiratory system revealed dyspnea, respiratory rate - 44 breaths /min, Spo_2 was 96% in room air. There was Intercostal and subcostal in drawing. No mediastinal shifting. Vocal fremitus was decreased, percussion note dull, breath sound and vocal resonance diminished at both lowest part of chest. Cardiovascular system revealed, location of apex beat on 5th intercostal space at midclavicular line, no palpable heart sound, S_1 S_2 was audible, muffled, no gallop rhythm, no murmur was detected. Neurological system showed no abnormalities.

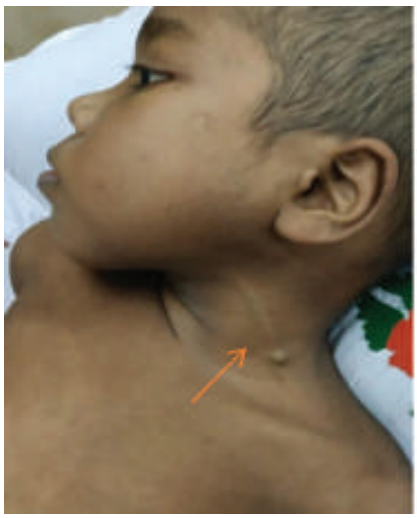

Fig 1 *Engorged neck vein*

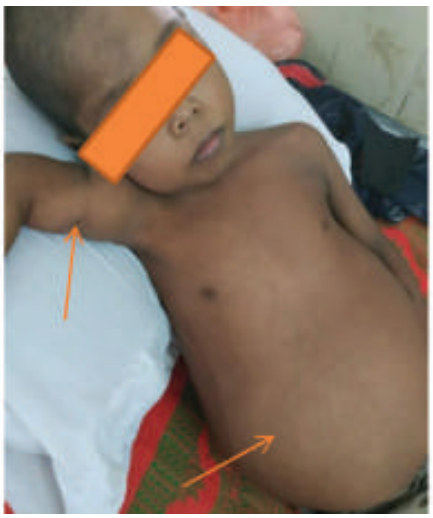

Fig 2 *Deformed right arm with scar mark, huge ascitis*

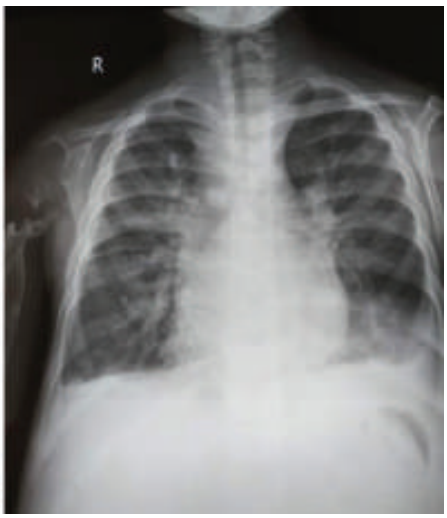

Fig 3 *Bilateral mild pleural effusion, normal heart shape*

Table I
Investigation reports

Investigations	Results	References
Hb% (g/dL)	11	11.5-16
ESR (mm in 1st hour)	15	0- 10
WBC total (/cu mm)	5500	4500-11000
N %	80	40-80
L %	14	20-40
M %	06	2-10
Platelets (/cu mm)	420000	150000-450000
Serum-		
ALT (U/L)	21	35-50
AST (U/L)	76	10-40
Albumin (g/dL)	1.9	3.5-5.0
Alkaline phosphatase (U/L)	150	Upto 300
Ceruloplasmin (mg/dL)	23	20-60
LDH (U/L)	295	208-378
Creatinine (mg/dL)	0.43	0.68
c- GT (U/L)	110	<55
PT (sec)	12	12-16
INR	1	<1.4
Mantoux test (mm)	0	Up to 10

CXR showed bilateral mild pleural effusion with plethoric lung field.

USG of whole abdomen showed moderate hepatomegaly with coarse parenchyma, dilated hepatic vein, huge ascites, no splenomegaly.

Doppler USG of IVC, hepatic vein and portal vein showed features of congestion in IVC and hepatic vein, no evidence of portal hypertension, coarse hepatic parenchyma, huge ascites and bilateral pleural effusion.

Echocardiography showed increased echogenicity and thickness of pericardium dilated right and left atrium, ventricular wall thickness-normal, moderate mitral and mild

tricuspid regurgitations, normal pulmonary atrial pressure, and tissue. Doppler E velocity mildly increased dilated inferior venacava and non-collapsing, diastolic flow reversal during expiration in hepatic vein, suggestive constrictive pericarditis.

Table II
Reports of S. electrolyte, viral markers and ascitic fluid analyusis

Investigations	Results	References
S.Electrolyte		
Na (mmol/L)	127	135-145
K (mmol/L)	4.7	3.5-5.1
CL (mmol/L)	99	95-107
Viral markers		
HBsAg	Negative	
Anti-HCV IgG	Negative	
Ascetic fluid analysis:		
Appearance	Clear	Clear
Biochemical		
protein (gm/dl)	0.7	0.3-4
glucose(mmol/L)	8.2	7-10
Cytological		
WBC (/cumm)	20	<500
N (%)	10	<250
L (%)	90	
malignant cell	00	
Serum ascetic fluid albumin gradient (SAAG) (gm/dl)	1.2	
ADA (U/L)	12.1	1-28

Fibroscan of liver; Median stiffness was 37.4 Kpa, IQR/MED-10%, which correlate with stage-4 fibrosis, that is cirrhosis. Our final diagnosis was cardiac cirrhosis.

Child was kept in bed rest with propped up position and saturation was maintained by oxygen inhalation, salt was restricted in diet with adequate protein supplementation.

Nebulization was given with salbutamol solution and normal saline to relieve bronchoconstriction and breathlessness; 20% Human albumin 1gm/kg along with IV furosemide was given to increase intra vascular compartment volume, to minimize hypoalbuminia and also to reduce the respiratory distress.

According to the cardiac consultation combination of spironolactone and furosemide along with digoxin was given for the treatment of heart failure. Proper cardiac monitoring was done during the hospital stay. During his discharge further follow up plan for both cardiovascular system and also for hepatobiliary system was given. After his discharge from the hospital, he continued to take proton pump inhibitor for the prevention of stress ulcer and lactulose for constipation and also for the prevention of hepatic encephalopathy as per advice.

Discussion

Any type of hepatic fibrosis occurring in cardiac patient is known as cardiac cirrhosis.[5] It is a very uncommon cause of CLD and it's difficult to distinguish from other causes of liver cirrhosis. The most important mechanisms responsible for the development of congestive hepatopathy are hepatic congestion, decreased hepatic blood flow and hypoxemia[6] followed by atrophy, necrosis of hepatocytes, thrombi resulting due to cholestasis.[7]

This case report is one of such scenario of chronic liver injury, leading to fibrosis due to long term congestive heart failure. Causes of cardiac cirrhosis are valvular heart disease, cardiomyopathy, pericardial disease, ischemic heart disease, primary lung disease.[8] Our patient had constrictive pericarditis, bacterial origin, secondary to osteomyelitis. Though in the developing countries tuberculosis is the most common etiology for constrictive pericarditis,[9,10] to support our diagnosis, our patient had negative Monteux test and had no contact history to tubercular patient, Gene Xpart of ascetic fluid was negative. But he had history of osteomyelitis cured by surgery and followed by pericarditis which improved by pricardiocentesis and injectable antibiotics. Subsequently he developed chronic congestive heart failure for 7 years and treated at different hospitals by oral frusemide only Later he developed congestive hepatopathy, menifestrated as jaundice, dyspnea, engorged neck vein, huge hepatomegaly, ascites and pedal oedema, normal S. ALT, alkaline phosphatase levels, raised AST, LDH, bilirubin and low albumin. In congestive hepatopathy, liver function tests do not show the specific pattern as in patient with hypoxic hepatopathy.[11] Cholestatic enzymes together with low albumin and high bilirubin are the strongest risk factor for poor outcome, in case of chronic heart failure.[12] Our patient has high bilirubin and low albumin level. Chest X-ray was suggestive of constrictive pericarditis as there is plueral effusion without significant bilateral enlargement of left and right ventricle. Though calcification may be found in 20%-40% cases of constrictive pericarditis but

more common in tubercular pericarditis.[13] He had also high SAAG (1.1 g/dL) that is transudative.[14] He had no contact history of tubercular patient, Mantoux test, X-Ray chest and ascitic fluid analysis all were negative for tuberculosis. Doppler study shows feature of congestion in IVC and hepatic vein and coarse hepatic parenchyma due to fibrotic changes. Fibro scan by transient elastrography is also now widely recognized as a reliable method to asses liver fibrosis.[15] Though, liver stiffness, shown by transient elastography is not a reliable marker for identifying fibrotic stage of congestive hepatopathy, but it may become a useful non-invasive tool for screening cardiac patients and those who are at risk of cardiac cirrhosis, as increased venous pressure is a risk factor for cardiac cirrhosis[16]. As our patient was suffering from chronic congestive heart failure and ascites, transabdominal liver biopsy is at risk and transjaugular liver biopsy is not practiced at our setting for the evaluation of cirrhosis. So, fibro scan was done and result was suggesting liver cirrhosis. A patient with constrictive pericarditis, develops chronic right heart failure due to markedly elevated ventricular filling pressure, causes passive congestion of hepatic vein, leading to relative ischemia, hepatic necrosis and fibrosis.[17]

Conclusion

Thought constrictive pericarditis and cardiac cirrhosis both are very uncommon, our interest was to highlight the cardiac cause should be evaluated in a dysphonic child, where the causes of CLD were not certain.

References

1. Fouad YM, Yehia R. Hepato-cardiac disorders. *World J Hepatol* 2014;27;6:**41**-54.
2. Yachha SK. Current spectrum of hepatobiliary in Northern India. *Indian Pediatr* 1997;**34**:885-90.
3. Shah I, Bhathnagar S. Clinical profile of chronic hepatobiliary disorder in children: Experience from tertiary referral center in Western India. *Trop Gastroenterol* 2010;**31**:108-10.
4. Abou-taleb A, Ahmed RH A, EI-Herrawy A. Pediatric CLD; A clico- Pathological study from a tertiary care center. *Int J Pediatr* 2019;**7**:9305-15.
5. Blumgart HL, Katzin H. Cardiac cirrhosis of the liver, a clinical and pathological study. *Trans Am Clin Climatol Assoc* 1938;**54**;82-86.
6. Moller S, Hendrickson JH. Cardiovascular complications of cirrhosis. *Gut* 2008;**57**:268-78.
7. Dai DF, Swanson PE, Krieger EV, Liou IW, Carithers RL, Yeh MM. Congestive hepatic Fibrosis score: A novel histological assessment of clinical severity. *Mod Pathol* 2014;**27**:1552-58.
8. Kubo SH, Walter BA, John DH, Liver function abnormalities in chronic heart failure. Influence of systemic hemodynamic. *Arch Intern Med* 1987; **147**:12227-30.
9. Chen RF, Lai CP. Clinical characteristics and treatment of constrictive pericarditis in Taiwan. *Cinc J* 2005;**69**:458-60.
10. Linc Y, Zhou M, Xiao J, Wang B, Wang Z. Treating constrictive pericarditis in a Chinese single-center study: A five - year experience. *Ann Thorac Surg* 2012;**94**:1235-40.
11. Mollaer S, Bernardi Interactions of the heart and the liver. *Eur Heart J* 2013;**34**:2804-11.
12. Chokshi AL, Cheema FH, Schaefle KJ, Jiang J, Collado E, Shahzad K, et al. Hepatic dysfunction and survival after orthopic heart transplantation; application of the MELD scoring system for outcome prediction. *J Heart lungs Treatment* 2012;**32**:591-600.
14. Runyon BA. Cardiac arcites: A Ccharacterization. *J Clin Gastroenterol* 1988;**10**;410-12.
15. Castera L, Foucher J, Bernard PH, Carvalno F, Allaix D, Merrouche W, et al. Pitfalls of liver stiffness measurement: a 5-years prospective study of 13,369 Examinations. *Hepatology* 2010;**51**;828-35.
16. Colli A, Pozzoni P, Berzuini A, Gerosa A, Canovi C, Motteni EE, et al. Decompensated chronic heart failure; Increased liver stiffness measured by means of transient elastrography. *Radiology* 2010:**257**: 872-78.
17. Kyriakakis C, Herbst P, Doubell A. Constrictive pericarditis-prevalence, causes and clinical presentation. *European Society of Cardiology* 2017; **15**:22-28.

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CASE REPORT

A Male Neonate with Congenital Adrenal Hyperplasia: A Case Report

Ruma Parvin, Nobo Krishna Ghosh, Sharmin Mahbuba, Farhana Jaya Chudhury, Sultana Amena Ferdoucy

Introduction

Congenital adrenal hyperplasia (CAH) is an autosomal recessive disorder related to deficiency of enzyme needed to the biosynthesis of cortisol and aldosterone. More than 90% of cases of CAH are due to deficiency of 21-hydroxylase resulting inincreased levels of progesterone and 17-hydroxyprogesterone which is converted into androstenedione and then to testosterone.[1] The net effect is prenatal virilization of girls and rapid somatic growth with early epiphyseal fusion in both sexes known as simple virilization form. Most of patients are unable to synthesize sufficient aldosterone to maintain sodium balance and are termed salt-losing forms. This predisposes them to episodically develop potentially life-threatening hyponatremic dehydration. Besides this 8-9% of cases, there may be a nonclassic mild late onset forms of CAH due to deficiency of 11-â hydroxylase.[2] Female newborns with CAH can be diagnosed early due to genital ambiguity but male with CAH are usually asymptomatic at birth and are usually diagnosed after life threatening adrenal crisis or they die unsuspected.[3] We reported a male neonate with CAH salt-losing form. The case is reported to orient clinicians so that they may be able to manage the problem timely.

Case report

A 11 days old male infant, 3rd issue of a consanguineous parent from Brahmanbaria district was admitted in the SCANU of Dr. MR Khan Shishu Hospital & ICH with lethargy, less feeding, and weight loss. Mother, 25 years old, was under regular antenatal check up and her pregnancy was uneventful. The baby was delivered by caesarian section at term, without any adverse perinatal events. Weight of the baby was 3200 gram which falls on 50th percentile on growth chart. Breastfeeding was started within 1 hour of delivery and he was on exclusive breastfeeding. He was ok for the initial one week, then he became weak, unable to suck breast properly and losing weight gradually. Mother also noticed his body was becoming black. Mother gave history of 2 sib death. First baby was female, apparently normal, died at 9 months of age with unknown etiology. 2nd baby, male died at 12th days of life with severe sepsis at hospital. There was no history of similar disorders in the families either of parents. He was treated with injectable antibiotics in a local hospital for 2 days with the diagnosis of sepsis but his condition didn't improve and admitted in our hospital.

On admission, the infant was dehydrated, hypotonic and tachypnoeic. Respiratory rate was 66 breaths per minute. His genitalia was examined and was noted normal male genitalia but scrotal hyper pigmentation present. His reflex activity was moderate. Other examination findings were normal. His weight was 2800 gram and calculated weight loss was 12.5%.

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Fig 1 *Photograph of congenital adrenal hyperplasia patient on day-1*

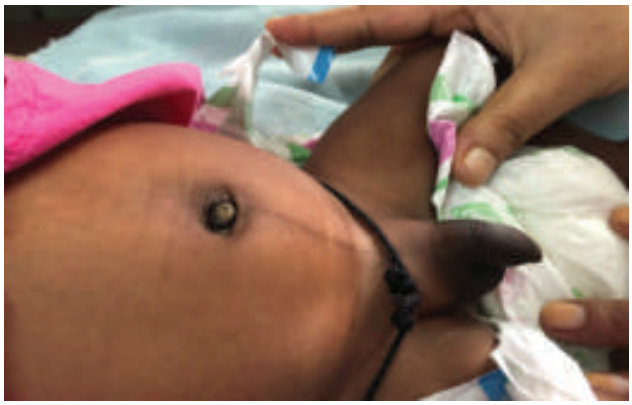

Fig 2 *Hyperpigmentation of genitalia*

Supportive measures were taken. Septic screening was normal. Blood sugar was normal on several occasions. Serum electrolytes showed hyponatremia (Serum sodium - 125mmol/L), hyperkalemia (Serum potassium - 7.9 mmol/L, hypochloremia (Serum chloride - 84 mmol/L), renal profile was normal (Serum creatinine - 0.75 mg/dl and urea - 50mg/dl). Sodium correction was done by fluid therapy (increase sodium = 12meq/l/24 hours) and hyperkalemia was treated with injection calcium gluconate, nebulization with salbutamol and insulin glucose infusion but his serum sodium and potassium was not corrected. So our provisional diagnosis was CAH. An ultrasound of abdomen with special attention to adrenal gland was normal. Serum 17-hydroxyprogesterone (17-OHP) was >50ng/ml - highly suggestive of CAH. Seruma aldosterone was normal (141.70pg/ml) but Serum cortisol level was low (99.07nmol/L) and plasma Renin is high (46.09pg/ml). Serum testosterone (0.46nmol/L) and ACTH (54.12pg/ml) was high. Urinary sodium concentration is high (67meq/l). So the diagnosis of CAH (classic, salt-losing variety) was made. Then he was started on replacement therapy (hydrocortisone 100 mg/m^2/day, fludrocortisone 150 µg/day). Within 5 days of therapy there was significant improvement both in clinically and biochemically. On discharge his weight was 3.7 kg. The steroids were gradually tapered over the next one week and he was discharged on maintenance doses of oral steroids (hydrocortisone 20 mg/m^2/day and fludrocortisones 100 µg/day and sodium chloride 1mmol/kg twice daily). Parents were counseled about the disease and an instruction to his parents was given to double the dose of his oral hydrocortisone if the baby has intercurrent illness (e.g. fever, cough, vomiting and diarrhea). They were also given an emergency card that he can be assessed and managed immediately by the pediatric team whenever he presents to the hospital.

The baby came at 45 days of her age for follow up visit. His growth and development was normal. His weight was 5.3 kg and he is very alert and active. His Serum electrolyte was within normal range.

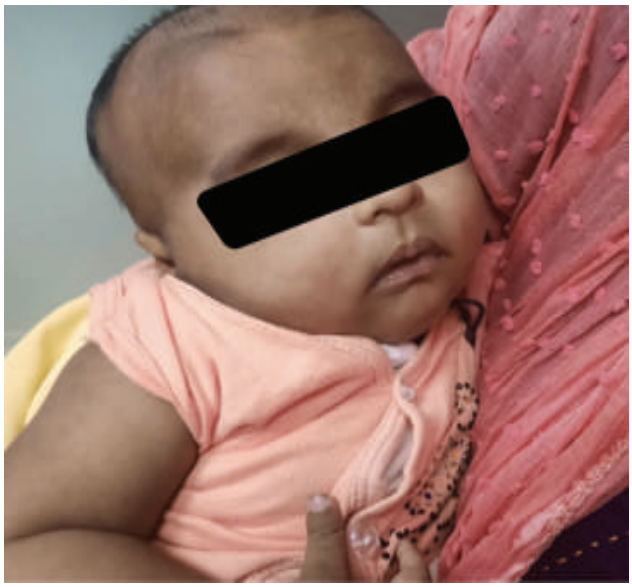

Fig 3 *Photograph of the congenital adrenal hyperplasia patient at 45 days of age*

Discussion

In CAH, the body is missing an enzyme that stimulates the adrenal gland to release cortisol and aldosterone. More than 90% of cases of CAH are caused by 21-hydroxylase deficiency due to mutations in CYP21A2 gene.[4] The salt-losing crisis is the most important variant of CAH. These patients cannot

synthesize sufficient aldosterone to maintain sodium balance and may develop potentially fatal 'salt-wasting' crisis if not treated. Urinary sodium concentrations may exceed 50 meq/l. The infant can't maintain blood volume; hyponatremic dehydration begins to develop by the end of first week of life. Potassium and acid secretion are impaired leading to hyperkalemia and metabolic acidosis gradually. The early symptom is poor weight gain, but most infants with severe CAH develop vomiting, severe dehydration, and shock by the 2nd or 3rd week of life.[5] Females with classic 21-hydroxylase deficiency are exposed to excess androgens prenatally and are born with virilized external genitalia.[6] If routine screening test of CAH was not done, the male infant may remain undiagnosed as males have no genital ambiguity to alert physician and presented with life threatening salt loosing crisis.[3,7] Infants of the salt-wast-ing type were typically characterized by skin pigmentation, likely related to abnormal hor-mone levels.[8] If CAH is not diagnosed and treated early,neonates are susceptible to sudden death in the first few weeksof life.[9] In this case, salt loosing crisis were reported and he presented with less feeding, unable to suck and dehydration and genital pigmentation. The infant was attended earlier.

It is important to consider this disorder in all cases of otherwise unexplained electrolyte abnormalities during the first few weeks of life.[7] In this case, remarkable electrolyte abnormality was found. Diagnosis of 21-OHD is confirmed by steroid analysis in newborn screening or later on. Standard medical treatment consists of oral glucocorticoid and mineralocorticoid administration in order to suppress adrenal androgens and to compensate for adrenal steroid deficiencies.[10] In the index case, the high concentration of 17-hydroxyprogesterone(17-OHP) is suggestive of CAH. While on replacement therapy, the child should be closely followed up for growth, development, biochemical and radiological parameters to monitor the effect to titrate the dose of the replaced steroids.[11] The newborn responded well with recommended medical treatment and the baby gained weight during discharge. During follow up, the baby was found to be growing appropriately.

Conclusion

The salt-loosing variant of congenital adrenal hyperplasia (CAH) is a rare disorder and is a medical emergency. A male infant with CAH is usually remaining undetected at birth and the mortality rate for boys with CAH is thus higher than that of girls. So routine neonatal screening is essential for diagnosis of CAH in male infant if there is a history of parental consanguinity or presence of other affected siblings. Prompt treatment is essential to save the life of neonate. Counseling of parents with follow up is crucial part of management of CAH.

References

1. Qureshi S, Roohi M, Khaliq M. Congenital adrenal hyperplasia. *Professional Med J* 2008;**15**:403-06.
2. Das JC, Khanom M, Islam R. Congenital adrenal hyperplasia: A case report. *JCMCTA* 2013;**24**:44-47.
3. Nordenstrom A, Ahmed S, Jones J. Female preponderance in congenital adrenal hyperplasia due to deficiency in England: implications for neonatal screening. *Horm Res* 2005;**63**:22-28.
4. White PC, Speiser PW. Congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Endocr Rev* 2000;21:245-91.
5. Trakakis E, Loghis C, Kassanos D. Congenital Adrenal Hyperplasia because of 21-Hydroxylase deficiency. A genetic disorder of interest to obstetricians and gynecologists. *Obstet Gynecol Surv* 2009;**64**:177-89.
6. Fleming L, Knafl K, Van Riper M. How the child's gender matters for families having a child with congenital adrenal hyperplasia. *J Fam Nurs* 2017;**23**:516-33.
7. Bhakri BK, Biswas K. Congenital Adrenal Hyperplasia: Presentation in a male infant. *Journal of Clinical and Diagnostic Research* 2010;**4:**2910-12.
8. Bonfig W. Growth and development in children with classic congenital adrenal hyperplasia. *Curr Opin Endocrinol Diabetes Obes* 2017;**24**:39-42.
9. Ishii T, Anzo M, Adachi M. Guidelines for diagnosis and treatment of 21 hydroxylase deficiency (2014 revision). *Clin Pediatr Endocrinol* 2015;**24**:77-105.
10. Riepe FG, Sippell WG. Recent advances in diagnosis, treatment, and outcome of congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Reviews in Endocrine and Metabolic Disorders* 2008;**8**: 349-63.
11. Livak K, Foster PJ, Thalange N. Short term growth in children with congenital adrenal hyplasia. *Horm Res* 2009;**71**:142-47.

ABSTRACTS FROM CURRENT LITERATURE

Severe Coronavirus Disease-2019 in Children and Young Adults in the Washington, DC, Severe Coronavirus Disease-2019 in Children and Young Adults in the Washington, DC, Metropolitan

Region Roberta L. DeBiasi, Xiaoyan Song, Meghan Delaney, Michael Bell, Karen Smith, Jay Pershad, Emily Ansusinha, Andrea Hahn, Rana Hamdy, Nada Harik, Benjamin Hanisch, Barbara Jantausch, Adeline Koay, Robin Steinhorn, Kurt Newman, David Wessel

J Pediatr. 2020;223:199-203.

Despite worldwide spread of severe acute respiratory syndrome coronavirus-2, few publications have reported the potential for severe disease in the pediatric population. We report 177 infected children and young adults, including 44 hospitalized and 9 critically ill patients, with a comparison of patient characteristics between infected hospitalized and nonhospitalized cohorts, as well as critically ill and noncritically ill cohorts. Children 15 years of age were over-represented among hospitalized patients (p=.07). Adolescents and young adults were over-represented among the critically ill cohort (p=.02).

Epidemiological characteristics of 2143 pediatric patients with 2019 coronavirus disease in China

Yuanyuan Dong, Xi Mo, Yabin Hu, Xin Qi, Fang Jiang, Zhongyi Jiang, Shilu Tong

Pediatrics. 2020; doi: 10.1542/peds.2020-0702

Objectives: To identify the epidemiological characteristics and transmission patterns of pediatric patients with COVID-19 in China.

Methods: Nationwide case series of 2143 pediatric patients with COVID-19 reported to the Chinese Center for Disease Control and Prevention from January 16 to February 8, 2020 were included. The epidemic curves were constructed by key dates of disease onset and case diagnosis. Onset-to-diagnosis curves were constructed by fitting a log-normal distribution to data on both onset and diagnosis dates.

Results: There were 731 (34.1%) laboratory-confirmed cases and 1412 (65.9%) suspected cases. The median age of all patients was 7 years (interquartile range: 2-13), and 1213 cases (56.6%) were boys. Over 90% of all patients were asymptomatic, mild, or moderate cases. The median time from illness onset to diagnoses was 2 days (range: 0 to 42 days). There was a rapid increase of disease at the early stage of the epidemic and then there was a gradual and steady decrease. Disease rapidly spread from Hubei Province to surrounding provinces over time. More children were infected in Hubei province than any other province.

Conclusions: Children at all ages appeared susceptible to COVID-19, and there was no significant gender difference. Although clinical manifestations of children's COVID-19 cases were generally less severe than those of adults' patients, young children, particularly infants, were vulnerable to infection. The distribution of children's COVID-19 cases varied with time and space, and most of the cases concentrated in Hubei province and surrounding areas. Furthermore, this study provides strong evidence for human-to-human transmission.

The role of children in transmission of SARS-CoV-2: A rapid review

Xue Li, Wei Xu, Marshall Dozier, Yazhou He, Amir Kirolos, Evropi Theodoratou

J Glob Health. 2020 Jun; 10(1): 011101.

Background: Understanding the role of children in the transmission of SARS-CoV-2 is urgently required given its policy implications in relation to the reopening of schools and intergenerational contacts.

Methods: We conducted a rapid review of studies that investigated the role of children in the transmission of SARS-CoV-2. We synthesized evidence for four categories: 1) studies reporting documented cases of SARS-CoV-2 transmission by infected children; 2) studies presenting indirect

evidence on the potential of SARS-CoV-2 transmission by (both symptomatic and asymptomatic) children; 3) studies reporting cluster outbreaks of COVID-19 in schools; 4) studies estimating the proportions of children infected by SARS-CoV-2, and reported results narratively.

Results: A total of 16 unique studies were included for narrative synthesis. There is limited evidence detailing transmission of SARS-CoV-2 from infected children. We found two studies that reported a 3-month-old whose parents developed symptomatic COVID-19 seven days after caring for the infant and two children who may have contracted COVID-19 from the initial cases at a school in New South Wales. In addition, we identified six studies presenting indirect evidence on the potential for SARS-CoV-2 transmission by children, three of which found prolonged virus shedding in stools. There is little data on the transmission of SARS-CoV-2 in schools. We identified only two studies reporting outbreaks of COVID-19 in school settings and one case report of a child attending classes but not infecting any other pupils or staff. Lastly, we identified six studies estimating the proportion of children infected; data from population-based studies in Iceland, Italy, South Korea, Netherlands, California and a hospital-based study in the UK suggest children may be less likely to be infected.

Conclusions: Preliminary results from population-based and school-based studies suggest that children may be less frequently infected or infect others, however current evidence is limited. Prolonged faecal shedding observed in studies highlights the potentially increased risk of faeco-oral transmission in children. Further seroprevalence studies (powered adequately for the paediatric population) are urgently required to establish whether children are in fact less likely to be infected compared to adults.

COVID-19 in Children: A Narrative Review

Alireza Razavi, Lotfollah Davoodi, Layla Shojaei, Hamed Jafarpour

Open Access Macedonian Journal of Medical Sciences. 2020 May 20; 8(T1):23-31.

Background: In December 2019, coronavirus (CoV) disease 2019 (COVID-19) was detected in Wuhan, China, which is known as severe acute respiratory syndrome CoV 2 (Severe acute respiratory syndrome [SARS]-CoV-2).

Aim: This study attempted a narrative review of the researches about COVID-19 in children.

Methods: We searched all articles between 2000 and April 2020 in PubMed, Scopus, and ScienceDirect related to COVID-19 in children, using the following terms: "COVID-19," "coronavirus," "SARS-CoV-2" in combination with "pediatrics," or "children."

Results: The most common method of transmitting the disease to children was through close contact with family members through respiratory droplets. Coinfection is common in pediatric with COVID-19 infection. One of the most important transmission routes is oral feces. The severity of the disease was mild or asymptomatic in most children. The most common clinical symptoms were fever and cough, and gastrointestinal symptoms were more common in children than in adults. Infants and preschoolers had more severe clinical symptoms than older children. The most common radiographic findings from the lungs were bilateral ground-glass opacity. Increased procalcitonin and lactate dehydrogenase should be considered in children. The use of intravenous immunoglobulin, lopinavir/ritonavir, and oseltamivir, along with oxygen therapy, had the greatest effect on improving children's conditions.

Conclusion: The most important way to prevent this disease in children is to follow the health tips of family members. Although the number of children with the disease is low, children are vulnerable to infection. Antiviral medications along with the use of muscle relaxants and oxygen therapy have a great impact on children's condition.

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 Paediatric & MS Paediatric Surgery Residency Cource, MD Paediatrics and MS Paediatric surgery Non Residency Cource, B.Sc in Health technology and Diploma in Paediatric Nursing. It also conducts different sub-specialty courses e.g. FCPS Neonatology, FCPS Paediatric Haemato-oncology, FCPS Paediatric Nephrology, FCPS Paediatric Neurology and Development, Paediatric Pulmonology, Paediatric Cardiology, MD Neonatology and MD Paediatric Nephrology. It conducts 3 months certificate course in Paediatrics and 15 days Intensive course for MCPS. It organizes defferent programme on paediatrics. Apart from this, the Institute also runs its regular academic activities. It has established Basic Science Department since 2006.

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.

DS (Child) H J 2020; 36(1): 81

Postgraduate Courses/Training in Paediatrics in BICH

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 Medicine and Surgery).
3. Recognized centre for course and training in different subspeciality: Neonatology, Paediatric Nephrology, Paediatric Haematology and Onchology, Paediatric Pulmonology, Paediatric Neuroscience and Paeditric Cardiology.
3. MD Residency Program in General Paediatrics, Neonatology, Paediatric Nephrology and MS Paediatric Surgery Phase A Course: In the month of March a every year. MD Paediatrics and Paediatric Surgery Non Residency Course: Part II and Part III in the month of January and July.
4. DCH course : Once in a year in the month of July every year.
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 (1st August - 31st October).
6. Training programme on Essential Newborn Care for doctors and nurses, KMC (Kangaroo Mother Care) traing, ETAT (Emmergency Triage, Assessment and Treatment) training, IMCI (Integrated management of childhood illness) etc.

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Students Qualified from Bangladesh Institute of Child Health

Undergoing Courses of BICH

Affiliated with	Courses
Bangabandhu Sheikh Mujib Medical University (BSMMU)	MD (General Paediatrics) MD Paediatric Nephrology MD Neonatology DCH MS (Paediatrics Surgery)
Bangladesh College of Physicians and Surgeons (BCPS)	FCPS Part II (Paediatrics) FCPS Neonatology FCPS Paediatric Nephrology FCPS Haematology & Oncology FCPS Paediatric Surgery FCPS Paediatric Neurology & Development FCPS Paediatric Pulmonology FCPS Paediatric Cardiology
Dhaka University	B. Sc in Health technology (Lab)
Bangladesh Nursing Council	Diploma in Paediatric Nursing

Student qualified from BICH till June 2020

Course	Number
DCH	370
MD Paediatrics	116
MS Paediatrics	109
FCPS Paediatrics	28
MD Neonatology	13
MD Pediatrics Nephrology	05
Total	641

Foreign student qualified from BICH till June 2020

Course of origin	Course	Number
Nepal	DCH	23
	MS (Paediatric Surgery)	02
	MD (Paediatrics)	01
India	MD (Paediatrics)	01
Iran	DCH	01
Iraq	DCH	01
Somalia	DCH	01
Sudan	DCH	01
Total		31

Present Students (June 2020)

Name of Courses	Number of Students
MD (General Paediatrics) Phase - A	14
MD (Neonatology) Phase - A	1
MD (Paediatric Nephrology) Phase - A	2
MS (Paediatric Surgery) Phase - A	10
FCPS (Paediatric) Part - II	2
MD (Paediatrics) Part - III	4
FCPS (Paediatric Cardiology)	1
FCPS (Paediatric Nephrology)	1
MS (Paediatrics Surgery) Part - III	4
DCH	22
MD (General Paediatrics) Phase - B	22
MD (Neonatology) Phase - B	3
MD (Nephrology) Phase - B	4
MS (Paediatric Surgery) Phase - B	11
Total	101

INSTRUCTIONS FOR AUTHORS

Dhaka Shishu (Children) Hospital Journal is the official organ of Bangladesh Institute of Child Health (BICH) which is the academic wing of Dhaka Shishu (Children) Hospital. It is a peer reviewed, open access journal published twice a year since 1984. This journal is recognized by Bangladesh Medical and Dental Council (BMDC) which is the highest body for the recognition of medical journals in Bangladesh. All parts of the journal are indexed/tracked/covered by DOI/CrossRef and BanglaJOL. The present Editorial board has decided that the cover design will be in accordance with the subjects of editorial in each issue. The editor welcomes articles to be published to the journal as leading article, original article, review article, case report, current issues of child health, short report and junior's page where trainee doctors are encouraged to publish their topic of interest.

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

Conditions for manuscript submission:

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

Manuscript preparation:

The format of the Dhaka Shishu Hospital Journal complies with *"Uniform requirements for Manuscripts Submitted to Biomedical Journals"* published by the International Committee of Medical Journal Editors in Vancouver.

Manuscripts should be submitted in the following order.

- 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.
- Manuscript should be typed in English and on one side of A4 (220) x 210 cm) 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.
- Title should not exceed 100 characters (Font size 16, bold).
- Name of authors, e.g. 1. Prof. Saiful Islam, 2. Dr. Nurun Nahar, these two author's name will be written like this; Saiful Islam1, Nurun Nahar2, 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 structured format with five sections (about 250 words maximum): Background, Objective, Methods, Results and Conclusion. All these sections will be in Times New Roman, Font size 12, italic and bold. Text will not be bold and after the text there will be Key words (not more than 10). No references are allowed in the abstract.

For review article abstract will be non structured and in case report no need to give abstract.

- Text will also comprises with five sections (Introduction, Materials and Methods, Results, Discussion and Conclusion).
- **Photographs:** With appropriate labeling (number in English numerical, title of photographs will be placed below the photographs). It should be placed in appropriate place of the article.
- **Illustration:** 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.
- **Acknowledgements**:

References:

- References from journal should be indicated by superscript numbers consecutively in the text and placed after full stop [i.e. ….. has been reported from Dhaka Shishu (Children) Hospital.[1] or as shown by Akbar et al[2] in his study.] in the order in which they are mentioned and should be listed in numerical order on a separate sheet at the end of the article.
- References cited in tables or legends or illustrations should be numbered in accordance with in 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 in sentence case; (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 retarded children: aetiology and associated factors. *Bangladesh Journal of Child Health* 1983; **9**:102-08.
- *References from books include:* (i) authors name, (ii) title of article, (iii) In: editor name/s. (iv) name of the chapter, (v) place of publication, (vi) name of book, (vii) year of publication and page numbers. *Example:* Bazvani I. An approach to inborn errors of metabolism. In: Behrman RE, Kliegman RM, Jenson HB, editors. Nelson textbook of Paediatrics. Philadelphia: Saunders, 2004: p.397-98.
- *Documents in electronic formal must include:* i) title, (ii) authors name, (iii) year of publication (iv) web site address, (v) date of access. Example: United Nations programme on HIV/AIDS Children living in a world with AIDS. Geneva, 1978 (htpp:// www…….) accessed on (dd/mm/year).

Manuscripts Submission: The manuscripts should be submitted to the editor with a **covering letter,** mentioning that the work has not been published or submitted for publication anywhere else with **signature of all authors**.