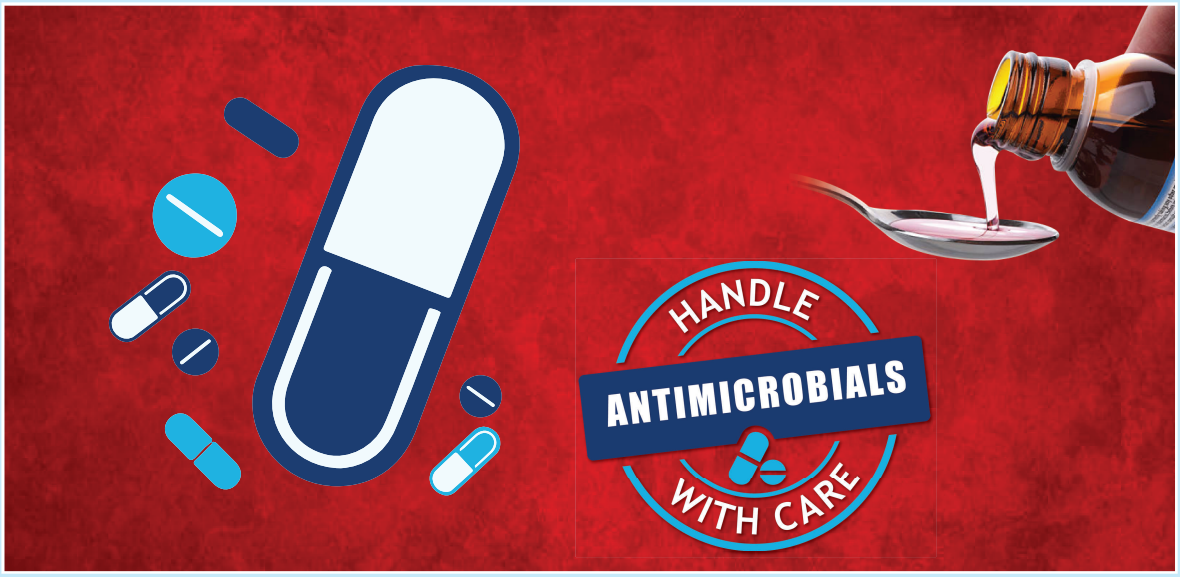
ISSN 1013 - 2295

Dhaka Shishu (Children) Hospital Journal

Vol. 38 | No. 1 | June 2022



Editorial

"Are We Returning to the Pre-antibiotic Era"

Bangladesh Shishu Hospital & Institute

ISSN 1013 – 2295

Contents

Dhaka Shishu (Children) Hospital Journal

Vol. 38 No. 1 June 2022

Dhaka Shishu (Children) Hospital Journal

EDITORIAL BOARD

Published by Editor, Dhaka Shishu (Children) Hospital Journal, Bangladesh Shishu Hospital & Institute
Sher-e-Bangla Nagar, Dhaka 1207. Tel: 55059063, 55059064, 55059051-60
E-mail: info.dshjournal@gmail.com, website: www.bich.gov.bd, www.banglajol.info/index.php/DSHJ
Published in May 2023

DS (Child) HJ 2022;38(1):1-4 DOI: https://doi.org/10.3329/dshj.v38i1.66994

EDITORIAL

Are We Returning to the Pre-antibiotic Era?

ASM Nawshad Uddin Ahmed

Introduction

The early 20th century was a time of ground-breaking scientific progress. One major advance was the development of penicillin and other antibiotics that has prevented thousands, even millions of people from dying of bacterial infections. But the successful use of any therapeutic agent is compromised by the potential development of tolerance or resistance to that compound from the time it is first employed. WHO identifies this as one of the top public health threats around the world. If the world does not move now to preserve the ability to treat infectious diseases that played such a key part in increasing life expectancy and improving human health, the 21st century may see the reversal of that progress.[1]

Antimicrobial resistance (AMR) is a worldwide problem and Bangladesh is a major contributor to this owing to its poor healthcare standards, along with the misuse and overuse of antibiotics. Many doctors in Bangladesh are prescribing antibiotics irrationally without taking consideration of the clinical findings and laboratory investigation reports in most cases. According to public health experts, AMR is on the rise in the country as the authority failed to stop the misuse of antibiotics even after the HC passed the directive in 2019 to stop the sale of antibiotics without prescription. Anyone can still buy antibiotics without prescription while many quacks and medicine shop workers suggest antibiotics to patients without diagnosis. The problem is further exacerbated by self-prescribing of antibiotics by individuals without the guidelines of a qualified clinician.

Luyt et al[2] found that in addition to treatment failure due to AMR, medical malpractice contributed to develop Multidrug-resistant (MDR) strains of bacteria through unnecessary, inappropriate, or suboptimal prescribing, which has been observed in 30% to 60% of the antibiotic therapies given to outpatients as well as to inpatients. As a result of AMR, infections become difficult or impossible to treat, increasing the risk of disease spread, severe illness and death and reversing gains of medical science. Antimicrobial resistance can increase deaths and disability, causing economic costs to rise sharply. Unskilled personnel are less aware of the deleterious effects of inappropriate antibiotic use. Awareness about harmful effect of unnecessary antibiotic use, adherence to treatment protocol and compliance with treatment course of antimicrobials need to be emphasized at different levels.

In addition to human use, antibiotics are commonly used in animal husbandry, beekeeping, fish farming and other forms of aquaculture, ethanol production, horticulture, antifouling paints, food preservation, and domestically. This provides multiple opportunities for the selection and spread of antibiotic-resistant bacteria. Given the current crisis, it is vital that the nonmedical use of antibiotics is critically examined and that any nonessential use halted.[3]

Antibiotic Misuse

Antibiotic misuse, sometimes called antibiotic abuse or antibiotic overuse, has potentially serious effects on health. Misuse of antibiotics include: when antibiotics are prescribed unnecessarily; administration is delayed in critically ill patients; broad-spectrum antibiotics are used too generously, or when narrow-spectrum antibiotics are used incorrectly; the dose of antibiotics is lower or higher than appropriate for the specific patient; the duration of antibiotic treatment is too short or too long; saving unused medicine and take it later for another illness and when antibiotic treatment is not streamlined according to microbiological culture data results.

Misuse of antibiotics drives antibiotic resistance. Studies prove that misuse of antibiotics may cause

Corresponding to: Prof. ASM Nawshad Uddin Ahmed, Department of Paediatric Endocrinology and Metabolic Disorders, Bangladesh Shishu Hospital & Institute, Dhaka. Cell: 01552372200, E-mail: dr_nawshad@yahoo.com

patients to become colonized or infected with antibiotic-resistant bacteria, such as methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *enterococci* (VRE) and highly resistant *Gram-negative bacilli*.[4] Excessive antibiotic use has the potential to result in numerous problems. In case antibiotics like penicillin, not used appropriately or used for a very brief period, there is a possibility of bacteria developing resistance to these drugs. Subsequently, resistant strains become capable of neutralizing the impact of penicillin when they come in contact with them again.

Antibiotic resistance

Antibiotic resistance is defined as the ability of a specific bacterium to survive in the presence of an antibiotic that was originally effective to treat infections caused by the bacterium. Though dozens of 'superbugs' resistant to antibiotics have made headlines over the last quarter century, multidrug-resistant gram-negative bacteria pose the greatest risk.[5]

The effects of antimicrobial resistance are more significant in lower and middle-income countries. Patients here may suffer the most from the increasing prevalence of antimicrobial resistance due to challenges in identifying and diagnosing these infections and lack of second and third-line antibiotics to treat resistant bacteria.[6] It is a contributing factor to the development of antibiotic resistance, including the creation of multidrug-resistant bacteria: relatively harmless bacteria can develop resistance to multiple antibiotics and cause life-threatening infections.[7] Misuse of antibiotics in hospitals is one of the main factors that drive development of antibiotic resistance. Patients in hospitals have a high probability of receiving an antibiotic and 50% of all antibiotic use in hospitals can be inappropriate.[8] Studies prove that misuse of antibiotics may cause patients to become colonised or infected with antibiotic-resistant bacteria, such as MRSA, VRE and highly resistant *Gram-negative bacilli*.[4,9]

Antibiotic resistance in children in Bangladesh

Antibiotic resistance is a public health threat of the utmost importance, especially when it comes to children. According to WHO data, infections caused by multidrug resistant bacteria produce 700,000 deaths across all ages, of which around 200,000 are newborns.[10] Bangladesh is more affected by AMR because of the widespread misuse of antibiotics, non-human antibiotic use, poor quality of drugs, inadequate surveillance and factors associated with individual and national poverty indicators like poor healthcare standards, malnutrition, chronic and repeated infections, unaffordability of more effective and costly drugs. Ahmed et al[11] in a systematic review found a high prevalence of resistance to most antibiotics. Highly pathogenic MDR strains were detected from infected patients in tertiary hospitals of the capital of Bangladesh, which can also contribute to other hospital acquired infections.[12]

Hassan et al[13] in first nationally representative analysis of antibiotic use among under-5 children in Bangladesh, found almost 40% of children received antibiotics for an ARI episode. Resistance to antibiotics is common and often deadly among children with pneumonia in Bangladesh. Chisti et al[14] found that antibiotic resistant Gram-negative bacteremia in young children with pneumonia in Dhaka was associated with a high mortality rate. They found that 40 percent of the gram-negative bacterial infections resisted treatment with first- and second-line antibiotics that are routinely used to treat pneumonia. More alarmingly, children who had antibiotic-resistant bacterial infections were 17 times more likely than others without bacterial infections to die. The pandemic of antibiotic resistance is shortening the lives of young children in Bangladesh, and new approaches to prevent and treat these infections are desperately needed.

Fever in children under five years of age is a common and predominantly self-limiting sign of illness. However, in low- and middle-income countries, antibiotics are frequently used in febrile children, although these children may not benefit from antibiotics. Samir et al[15] performed a multivariable logistical regression to identify the factors associated with antibiotic use in children under five years old with febrile illness in Bangladesh and found 478 (17%) children out of 2784 children aged less than five years with fever received antibiotics. Unqualified sources, including unqualified providers and pharmacies, contributed to 60% of antibiotic prescriptions in children with fever, followed by the private medical sector (29%) and the public sector (23%). The highest use of antibiotics was found in children under six months of age (25%).

Antimicrobial resistance against shigellosis is increasingly alarming. However, evidence-based knowledge gaps regarding the changing trends of shigellosis in Bangladesh exist due to the scarcity of longitudinal data on antimicrobial resistance. Nuzhat et al[16] in their study found that WHO-recommended first-line antibiotic ciprofloxacin resistance gradually reached more than 70% in both the urban and rural site by 2020. In multiple logistic regression after adjusting for age and sex, ciprofloxacin, azithromycin, mecillinam, ceftriaxone, and multidrug resistance (resistance to any two of these four drugs) among under-5 children were found to be increasing significantly ($p<0.01$) in the last 20 years.

Antibiotics are the most common therapies administered in the intensive care unit setting. The rapid emergence and dissemination of antimicrobial resistant microorganisms in intensive care units (ICUs) worldwide constitutes a serious problem now a days. Mamun et al[17] conducted a study in paediatric cardiac intensive care unit (PCICU) of Bangladesh Shishu Hospital & Institute and they found during the study period total 305 patients were admitted and almost all received broad spectrum antibiotics including third generation cephalosporins, carbepenem even piperacillin and colistin before admission in PCICU. Organisms were isolated in 10.82% cases and majority were gram negative (Acinatobactor 42.4%, Klebsiella 21.2%, and Pseudomonas 24.2%). Multi drug resistant Acinatobacter was found in 90.99% cases and 9.09% was pan drug resistant. Klebsiella, Pseudomonas and E. Coli were also found resistant to commonly used antibiotics. Hasan et al[18] conducted another study in cardiac ICU of National Heart Foundation & Research Institute and they found among 680 operated patients during the study period 6% were culture positive. Most common isolated organism was Pseudomonas spp 49.2%, followed by Klebsiella 13.6%, Citrobacter 8.5%, E coli 6.8% and Acinatobacter 6.8%. Pseudomonas was resistant against Penicillin, Ceftriaxone, Macrolid and Colistin in 96.6 - 100% cases. Klebsiella was mostly multidrug resistant including Carbapenems (37.5%) and only Colistin was retaining sensitivity against it. Among the other organisms like E coli, Acinetobacter, Cotrobacter and Enterobacter, Macrolids were mostly resistant and sensitive against 50% cases of Acinetobacter and 66% of Enterobacter. Ciprofloxacin and Carbapenems were 100% resistant against Citrobacter but effective against others. Citrobacter being most notorious organism mostly multidrug resistant and sensitive to only Colistin in 40% and Tigecycline in 80% case. So there is emergence of multidrug resistant organisms in PCICU with very few options to treat.

There is an urgent need to address factors that are promoting antibiotic resistance in Bangladesh. Antibiotics can be purchased without a prescription in the country and many people use them to self-treat conditions such as dysentery, cold, cough and fever. Misuse of antibiotics promotes the spread of bacteria that resist the medications. Lab testing for diagnosis of bacterial infections is also inadequate in the country. Lack of access to clean water and adequate sanitation helps spread bacteria that are resistant to antibiotics. Improvements in health care infrastructure and policy changes to rein in the misuse of antibiotics are essential and Bangladesh's health care system also needs better access to more advanced antibiotic therapies for resistant infections.

Conclusion

Antibiotics are one of the most important medical innovations. But its inappropriate use leads to potentially untreatable resistant infections. As there is not enough new antibiotics in the pipeline, it is of utmost importance that the existing ones are used cautiously. Immediate action is needed to stop the world from heading towards a pre-antibiotic era in which all achievements made in prevention and control of communicable diseases will be reversed. There is evidence that controlled and lowered use of antibiotics can abate resistance.

References

1. Antimicrobial resistance: conserving life-saving medicines takes everyone's help: Fact sheet, WHO. [(accessed on 31 March 2023)]. Available form: https://www.who.int/news-room/feature-stories/detail/antimicrobial-resistance-conserving-life-saving-medicines-takes-everyone-s-help.
2. Luyt CE, Bréchot N, Trouillet JL, Chastre J. Antibiotic stewardship in the intensive care unit. *Crit Care* 2014;**18**:480.
3. Meek RW, Vyas H, Piddock LJV. Nonmedical Uses of Antibiotics: Time to Restrict Their Use? *PLoS Biol* 2015;**13**:e1002266.

4. Tacconelli E, De Angelis G, Cataldo MA, Mantengoli E, Spanu T, Pan A, et al. Antibiotic usage and risk of colonization and infection with antibiotic-resistant bacteria: a hospital population-based study. *Antimicrob Agents Chemother* 2009;**53**:4264-69.

5. Kumarasamy KK, Toleman MA, Walsh TR, Bagaria J, Butt F, Balakrishnan R, et al. Emergence of a new antibiotic resistance mechanism. *Lancet Infect Dis* 2010;**10**:597-602.

6. Oluyege JO, Dada AC, Odeyemi AT. Incidence of multiple antibiotic resistant Gram-negative bacteria isolated from surface and underground water sources in southwestern region of Nigeria. *Water Sci Technol* 2009;**59**:1929-36.

7. Harrison JW, Svec TA. The beginning of the end of the antibiotic era? Part II. Proposed solutions to antibiotic abuse. *Quintessence International* 1998; **29**:223-29.

8. Ansari F, Erntell M, Goossens H, Davey P. The European surveillance of antimicrobial consumption (ESAC) point-prevalence survey of antibacterial use in 20 European hospitals in 2006. *Clin Infect Dis* 2009;**49**:1496-504.

9. Safdar N, Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobial-resistant Staphylococcus aureus, enterococcus, gram-negative bacilli, Clostridium difficile, and Candida. *Ann Intern Med* 2002;**136**: 834-44.

10. 4th Global Conference of Women Deliver. WHO Regional Office for Europe; Copenhagen, Denmark: 2016. [(accessed on 19 March 2021)]. Fight Antimicrobial Resistance: Protect Mothers and Newborns. Available from: http://who.int/drugresistance/activities/Women-Deliver-AMR-side-event-Handout-May2016.pdf?ua=1.

11. Ahmed I, Rabbi MB, Sultana S. Antibiotic resistance in Bangladesh: A systematic review. *International Journal of Infectious Diseases* 2019; **80**:54-61.

12. Safain KS, Bhuyan GS, Tasnim S, Hasib SH, Sultana R, Islam MS, et al. Situation of antibiotic resistance in Bangladesh and its association with resistance genes for horizontal transfer. bioRxiv 2020. Available from: https://www.biorxiv.org/content/10.1101/2020.04.06.027391v1.full.

13. Hassan MZ, Monjur MR, Biswas MAAJ, Chowdhury F, Braithwaite J, et al. Antibiotic use for acute respiratory infections among under-5 children in Bangladesh: a population-based survey. *BMJ Global Health* 2021;**6**:e004010.

14. Chisti MJ, Harris JB, Carroll RW, Shahunja KM, Shahid ASMSB, Moschovis PP, et al. Antibiotic-Resistant bacteremia in young children hospitalized with pneumonia in Bangladesh is associated with a high mortality rate. *Open Forum Infect Dis* 2021; **8**:ofab260.

15. Samir N, Hassan MZ, Biswas MAAJ, Chowdhury F, Akhtar Z, Lingam R, et al. Antibiotic Use for Febrile Illness among Under-5 Children in Bangladesh: A Nationally Representative Sample Survey. *Antibiotics* 2021;**10**:1153.

16. Nuzhat S, Das R, Das S, Islam SB, Palit P, Haque MA, et al. Antimicrobial resistance in shigellosis: A surveillance study among urban and rural children over 20 years in Bangladesh. *PLoS ONE* 2022; **17**:e0277574.

17. Mamun MAA, Hussain M, Rima R, Jabbar A, Echo NS. Emergence of antibiotic resistance in Intensive Care Unit. *Dhaka Shishu (Children) Hospital Journal* 2016;**32**:77-83.

18. Hasan MNA, Chowdhury NAH, Shamsuddin AK, Sharifuzzaman M. *Paediatric Heart J of Bangladesh* 2017;**2**:51-56.

DS (Child) HJ 2022;38(1):5-7 DOI: https://doi.org/10.3329/dshj.v38i1.66995

LEADING ARTICLE

Rational Use of Antibiotics

M Nurul Akhtar Hasan[1], Mohammad Abdullah Al Mamun[2]

Introduction

The discovery of Antibiotics is one of the most significant developments in the history of medicine. But the situation is changing over time and very rapidly changing over last few decades due to emergence of antimicrobial resistance (AMR). It is a global public health problem now a days which drew attention to physicians and all related caregivers, medical professional bodies, local and international health organization and even news media.[1,2] AMR has significant adversity including increased morbidity, mortality, increased resource utilization and higher cost of diagnosis and care.[3] Overuse of antibiotic at health facilities, poultry, dairy and other industries are important contributors for this scenario.[4] Unfortunately, newer antibiotics are not coming too frequently, rather the rate of introduction of new antibiotics is gradually decreasing. At the same time when very few antibiotics of existing classes are coming to the market, they are becoming resistant with in very short period of time, either due to over use or due to cross resistance.[5] That's why discovery of new antibiotics or combination of antibiotics with other molecules is not a reasonable solution, because those will not work for a long time and are also very expensive which are increasing the financial burden to the patients and patients' family.[5] So, it's clear that new or combination of antibiotics cannot show us any ray of light, rather preservation of available antibiotic resources by rational use could be the only remaining option.

AMR: How big is the problem?

AMR in microorganisms is a natural phenomenon and the development of resistance is a normal evolutionary process for microorganisms but it is being accelerated by the use or misuse of antibiotics in humans, animals and other industries.[6] The misuse of antibiotics includes inappropriate dose or wrong antibiotics which also include conditions that are not caused by a bacterial infection. In fact, each new antibiotic has been followed by the development of resistance with in very short period of time.[7] As a result, AMR is a serious threat to global public health that currently affects humans, animals and environmental health. It increases morbidity and mortality and is associated with high economic costs due to its health care burden. Infections with multidrug-resistant (MDR) bacteria also have substantial implications on clinical and economic outcomes.[2] It is estimated that that globally AMR leads to 700,000 deaths per year and losses of at least extra healthcare costs of EUR 1.5 billion per year.[8,9]

Causes of antimicrobial resistance

Important cause of AMR is indiscriminate use of antimicrobial agents in both humans and animals, specially at our part of the world, use of antibiotics without a prescription. A national study in Germany in 2011 showed, the prevalence of nosocomial infection has not changed since 1994, but the prevalence of antibiotic use has increased.[10] Up to half of ICU patients receiving empirical antibiotic therapy have no definitively confirmed infection, while de-escalation and shortened treatment duration are insufficiently considered in those with documented sepsis.[5] Irrational and inappropriate use of antibiotics in commercial chicken, aquaculture and animal production industries can also accelerate the antibiotic resistance process in humans and animals. During recent time, non-therapeutic usage of antibiotics in commercial chicken, fish and other livestock industries have raised significant concerns

1. Paediatric Intensivist & Associate Professor, Paediatric Cardiac Intensive Care, Children & Women Cardiac Unit, National Heart Foundation Hospital & RI, Dhaka, Bangladesh.
2. Associate Professor & Intensivist, Department of Paediatric Cardiology, Bangladesh Shishu Hospital & Institute, Sher-e- Bangla Nagar, Dhaka- 1207, Bangladesh.

Correspondence to: Dr. M Nurul Akhtar Hasan, Paediatric Intensivist & Associate Professor, Paediatric Cardiac Intensive Care, Children & Women Cardiac Unit, National Heart Foundation Hospital & RI, Dhaka, Bangladesh. Cell: +8801841249062, E-mail: drhasan.pediicu@gmail.com

about the development of antibiotic resistance.[4,11,12]

Study found that poor knowledge of doctors regarding Antimicrobial Stewardship Program (ASP), non-existence of antibiogram of hospital and lack of rules for the safe use of antibiotics were the main driving factors associated with irrational antibiotic prescription practices and development of Antimicrobial resistance.[1] Physicians' antibiotic prescribing habits, attitudes and behaviors also vary before and after graduation where theoretical antibiotic knowledge is better in the pre-graduation period but doctors forget their theoretical knowledge of antibiotics over time and are unable to follow current developments after graduation. Sustainable education for antibiotic use for physicians after graduation can contribute positively to reduce of antimicrobial resistance rates and to increase awareness about the use of rational antibiotics.[3]

Rational use of antibiotics

Published data notably support the need for better identification of patients at risk of infection including Multi-drug resistant bacterial (MDRB) infection, more accurate diagnostic tools enabling a rule-in/rule-out approach for bacterial sepsis, an individualized reasoning for the selection of single-drug or combination empirical regimen, the use of adequate dosing and administration schemes to ensure the attainment of pharmacokinetics/pharmacodynamics targets, concomitant source control when appropriate, and a systematic reappraisal of initial therapy in an attempt to minimize collateral damage on commensal ecosystems through de-escalation and treatment-shortening whenever conceivable.[5] Although rational use of antibiotics is the mainstay of prevention of AMR, unfortunately even Doctors has misconceptions about the rational use of antibiotics.[1] Available evidences support that, reduction of unnecessary use of antibiotics can have a powerful impact upon antimicrobial resistance. Several biomarkers have been tried to guide the initiation and duration of antibiotic treatments for suspected bacterial infections. CRP-based algorithms and procalcitonin can be used safely to guide antibiotic-related decisions, thereby decreasing unnecessary antibiotic exposure. There are few more promising tools like Neutrophil CD64, serum amyloid A, transcriptomics, metabolomics and proteomics which may come into clinical practice very soon.[13] Antibiotic checklist can also be promising tool to reduce unnecessary use of antibiotics in clinical practice.[14,15]

AMR and rational use of antibiotic: Is there any solution?

Several reports have been published in recent years that outline measures to reduce the consumption of antibiotics. A variety of actions have been proposed and tried locally and globally at different centers including global awareness campaigns, increasing financial resources for infectious diseases in the healthcare sector, the development of new antibiotics and policies aimed at the reduction of antibiotic use, anti-microbial stewardship program, regional local and hospital antibiotic policy, antibiotic check list etc. But considering the situation of increasing AMR and lack of new tool to combat the situation, infection prevention and control would be the primary target, rather than treating infection.[14,15] Reduction of antibiotics use without a prescription will have significant effect in controlling AMR. If necessary, local government must come forward with appropriate legislation and strict implementation.[16] Successful implementation of Antimicrobial Stewardship Program (ASP), development of guidelines for the use of antibiotics, strict legislation regarding use of antibiotics, active participation of healthcare professionals and awareness program among general public about the use of antibiotics could be important initial steps to establish rational use of antibiotics.[1]

Antimicrobial stewardship

Antimicrobial stewardship (AMS), an organizational or system-wide health-care strategy, is designed to promote, improve, monitor and evaluate the rational use of antimicrobials, to preserve their future effectiveness, along with the promotion and protection of public health. It also adopts systematic measures to optimize antimicrobial use, decrease unnecessary antimicrobial exposure and to decrease the emergence and spread of resistance. Implementing ASP in the ICU improves antimicrobial utilization and reduces broad-spectrum antimicrobial use, incidence of infections and colonization with multi-drug resistant bacteria (MDRB), antimicrobial-related adverse events and health care associated costs, all without increase in mortality.[2,5] ASP is a package of quality improvement initiative, requiring (1) an evidence-based, ideally bundled, change package, (2) a clear definition of goals, indicators, and targets, (3) a dynamic measurement and data collection system with

feedback to prescribers, (4) a strategy for building capacity, and (5) a plan to identify and approach areas for improvement and solve quality gaps.[5] Many developed countries, such as, Colombia, the United States (US), Australia, South Africa, and the United Kingdom (UK), have developed and successfully implemented different approaches to halt the spread of AMR.[1]

Conclusion

The use of antibiotics should not be random. It requires reflection and thought and should be based on rules. The correct diagnosis, the patient's condition, the location of the infection, the severity of the microbial cause sensitivities to antibiotics, the pharmacokinetics and pharmacodynamics of antimicrobials, the side effects and cost are the main elements which must be supported in every decision for their use. Local and regional guidelines with periodic revisions and recommendations for treatment of the common infections are necessary to orient rationale and appropriate use of antibiotics at root level and primary caregivers. Sustainable training for rational antibiotic use for physicians can contribute positively to reduce of antimicrobial resistance rates and to be more conscious about the use of rational antibiotics.

References

1. Atif M, Ihsan B, Malik I, Ahmad N, Saleem Z, Sehar A, et al. Antibiotic stewardship program in Pakistan: A multicenter qualitative study exploring medical doctors' knowledge, perception and practices. *BMC infectious diseases* 2021;**21**:374.
2. Majumder MA, Rahman S, Cohall D, Bharatha A, Singh K, Haque M, et al. Antimicrobial stewardship: Fighting antimicrobial resistance and protecting global public health. *Infection and drug resistance* 2020;**13**:4713-38.
3. Kose A, Colak C. Knowledge and awareness of physicians about rational antibiotic use and antimicrobial resistance before and after graduation: a cross-sectional study conducted in Malatya Province in Turkey. *Infection and Drug Resistance* 2021;**14**:2557-68.
4. Chowdhury S, Ghosh S, Aleem MA, Parveen S, Islam MA, Rashid MM, et al. Antibiotic usage and resistance in food animal production: what have we learned from Bangladesh? *Antibiotics* 2021;**10**:1032.
5. Timsit JF, Bassetti M, Cremer O, Daikos G, De Waele J, Kallil A, et al. Rationalizing antimicrobial therapy in the ICU: a narrative review. *Intensive care medicine* 2019;**45**:172-89.
6. Morrison L, Zembower TR. Antimicrobial resistance. *Gastrointestinal Endoscopy Clinics* 2020;**30**:619-35.
7. Christaki E, Marcou M, Tofarides A. Antimicrobial resistance in bacteria: mechanisms, evolution, and persistence. *Journal of molecular evolution* 2020 ;**88**:26-40.
8. O'Neill J. Tackling drug-resistant infections globally: Final report and recommendations, London, 2016. Available from: https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf.
9. ECDC/EMEA, Joint technical report - The bacterial challenge: time to react, Stockholm, 2009. Available from: https://www.ecdc.europa.eu/en.
10. Behnke M, Hansen S, Leistner R, Peña Diaz LA, Gropmann A, Sohr D, et al. Nosocomial infection and antibiotic use - A second national prevalence study in Germany. *Dtsch Arztebl Int* 2013;**110**:627-33.
11. Meena HR, Kumar V. Antimicrobial resistance and rational use of antimicrobials in livestock: developing countries' perspective. Livestock Health and Farming 2019 Nov 27. Intech Open. DOI: 10.5772/intechopen.88458.
12. Di KN, Pham DT, Tee TS, Binh QA, Nguyen TC. Antibiotic usage and resistance in animal production in Vietnam: a review of existing literature. *Tropical animal health and production* 2021;**53**:340
13. Fontela PS, O'Donnell S, Papenburg J. Can biomarkers improve the rational use of antibiotics?. *Current opinion in infectious diseases* 2018;**31**:347-52.
14. Van Daalen FV, Lagerburg A, de Kort J, Rivas ES, Geerlings SE. Implementation of an antibiotic checklist increased appropriate antibiotic use in the hospital on Aruba. *International Journal of Infectious Diseases* 2017;**59**:14-21.
15. Van Daalen FV, Opmeer BC, Prins JM, Geerlings SE, Hulscher ME. The economic evaluation of an antibiotic checklist as antimicrobial stewardship intervention. *Journal of Antimicrobial Chemotherapy* 2017;**72**:3213-21.
16. Grigoryan L, Haaijer-Ruskamp FM, Burgerhof JG, Mechtler R, Deschepper R, Tambic-Andrasevic A, et al. Self-medication with antimicrobial drugs in Europe. *Emerging infectious diseases* 2006;**12**:452-59.

ORIGINAL ARTICLE

Spectrum of Colonoscopy in Children: A Tertiary Centre Experience from Bangladesh

Salahuddin Mahmud[1], Mashud Parvez[2], Madhabi Baidya[3], Rafia Rashid[4], Farhana Tasneem[5], Ahmed Rashidul Hasan[6], Tanzila Farhana[7], Nafis Fatema Asha[8], Jahangir Alam[9], Syed Shafi Ahmed[10]

Abstract

Background: *Pediatric colonoscopy is a safe, sensitive and crucial tool for diagnosing as well as treating children with lower gastrointestinal diseases. In resource-limited countries like Bangladesh, the practice of pediatric colonoscopy remains rudimentary, lacking in trained professionals and appropriate instrumentation.*

Objectives: *The aim of the study was to find out the indications, common colonoscopic findings along with histopathologic evaluation and immediate post procedure complications of colonoscopy in children.*

Methods: *This was a retrospective study; the records of all the patients whose age was less than 18 years and who underwent colonoscopy from January 2017 to December 2021 were studied.*

Results: *Among the total of 196 children (8.23±4.12), the most common indications were lower gastrointestinal bleeding (LGIB) in 107 (54.6%) patients followed by chronic diarrhea in 33 (16.8%), recurrent abdominal pain (RAP) in 16 (8.2%), follow up Inflammatory bowel diseases (IBD) in 14 (7.1%), chronic constipation, weight loss, recurrent oral ulcer, intestinal tuberculosis (TB) and melena. The most common pathologic findings were polyps in 81 (61.4%) children followed by non-specific colitis in 19 (14.4%), IBD in 17(12.9%) and infectious colitis in 09 (6.8%) cases. Minor adverse events occurred in only 2.0% of children.*

Conclusion: *The commonest indication for pediatric colonoscopy was LGIB and the most common findings were colonic polyps. Pediatric colonoscopy is safe and effective diagnostic as well as therapeutic option for lower GI diseases.*

Keywords: *Colonoscopy, lower gastrointestinal bleeding (LGIB), polyp.*

DS (Child) HJ 2022;38(1):8-16
DOI: https://doi.org/10.3329/dshj.v38i1.66996

1. Associate Professor, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh, Shishu Hospital & Institute, Dhaka, Bangladesh.
2. Professor, Department of Pathology, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
3. Assistant Professor, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh, Shishu Hospital & Institute, Dhaka, Bangladesh.
4. Assistant Professor, Department of Paediatric Gastroenterology, Dr. M R Khan Shishu Hospital & Institute of Child Health, Dhaka, Bangladesh.
5. Assistant Professor, Department of Paediatrics, BIHS General Hospital, Diabetic Association of Bangladesh, Dhaka, Bangladesh.
6. Registrar, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
7. Resident Medical Officer, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
8. Registrar (ex.), Department of Paediatrics, Evercare Hospital, Dhaka, Bangladesh.
9. Professor & Head, Department of Paediatric Respiratory Medicine, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
10. Professor and Head, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh, Shishu Hospital & Institute, Dhaka, Bangladesh.

Correspondence to: Dr. Salahuddin Mahmud**,** Associate Professor, Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh. Cell: +8801819292138, E-mail: drsmbablu@gmail.com
Received: 2 January 2022; **Accepted**: 3 April, 2022

Introduction

Flexible colonoscopy in children was introduced slightly later than upper gastrointestinal endoscopy.[1] In the literature, reports of pediatric colonoscopy first appeared in late 1970s.[2] Since then, improvements in fiber optic and video technology, conscious sedation, and physicians' experience have led the establishment of colonoscopy as a procedure for the diagnosis, evaluation, and management of lower gastrointestinal tract disorders in children.[3-7] Due to poor compliance and cooperation in pediatric patients, colonoscopy is technically more challenging than esophagogastro-duodenoscopy.[8]

The safety and effectiveness of diagnostic or therapeutic colonoscopies in adults has been well established in the past two decades. However, its utility for pediatric patients is only recently emerging. Major hurdles for pediatric colonoscopy include the high level of technical challenge, poor compliance with bowel cleansing, and noncooperativeness during the procedure. The slightly higher risk of severe complications when compared with adults might also restrict its use in pediatric patients.[8]

Both diagnostic and therapeutic colonoscopies have had many advances in terms of operator skill and experience and are now being performed by most pediatric gastroenterologists. However, pediatric colonoscopy is far behind that of adults in the field of therapeutic endoscopy especially, such as endoscopic mucosal resection or endoscopic sub mucosal dissection.[1-2] Although the major role of colonoscopy is the screening and diagnosis of colon cancer in adults, there are few children who are diagnosed with colon cancer.[9-12] Recently, the American Society for Gastrointestinal Endoscopy (ASGE) and the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) published modifications of their guidelines for pediatric patients, in which clear indications for colonoscopy in children were recommended.[13-14] Lower gastrointestinal bleeding, chronic diarrhea, and unexplained anemia's are the most common indications for pediatric colonoscopy[15-16], while polyps and colonic inflammation are the most common endoscopic findings. The juvenile polyp is the most common type of colorectal polyp and is generally considered benign.[8] Furthermore the incidence of IBD is increasing worldwide. It has been reported that approximately 20-30% of IBD patients are diagnosed in childhood.[17] Early detection of both polyps and IBD can significantly improve the patients' quality of life and overall health. Therefore, in pediatric patients, colonoscopy is the best tool both for early lesion detection and as an effective therapy to treat lesions and remove polyps.[18]

Currently there are some retrospective reports about the utility of colonoscopy in pediatric patients.[19-22]. However, data regarding the clinical features, endoscopic findings, and the safety and efficacy of pediatric colonoscopy are limited, especially in Bangladesh. In view of this, we conducted a retrospective study among Bangladeshi children with the aim to investigate the demographics and clinical characteristics, find out indications, colonoscopic findings as well as safety and effectiveness by less or no complications in a pediatric patients undergoing colonoscopy.[18]

Materials and Methods

The study was carried out in the department of Pediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh. The medical records of all patients under the age of 18 years who underwent colonoscopy (both inpatient & outpatient department) from January 2017 to December 2021 were reviewed retrospectively. All of the pediatric patients (total 196) on whom colonoscopy was performed during the study period were included in the study. The need for colonoscopy was decided by the pediatric gastroenterologist as well as by the general pediatricians. Informed consent was taken from parents/patients for the procedure after careful explanation of procedure details and potential complications. Patients who did not give consent for colonoscopy and who had low hemoglobin (<8 gm/dl) along with or without thrombocytopenia and coagulopathy were excluded from the study. All pediatric colonoscopy were performed by the faculty members (Figure-1).

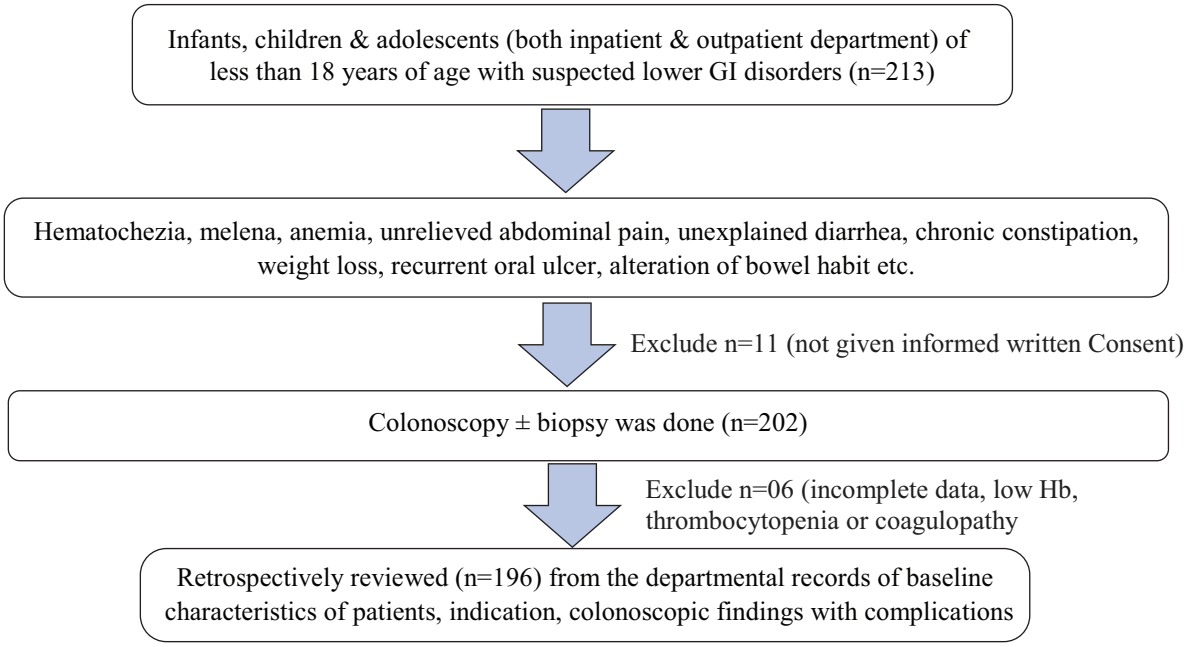


Fig.-1 *Study flow chart of colonoscopy (n=196)*

The patient received either an in-patient or outpatient preparation depending on the patient's age and the cooperation of the family. One to two days prior to the procedure, the patient was advised to begin a clear fluid diet. Children below the age of 6 years were admitted the day before the procedure. On the day before the procedure, patients were made to drink a solution of polyethylene glycol (PEG, 17 g) dissolved in water (250 mL) at a rate of 250 mL every 30 minutes. The stool output was checked in the afternoon, and another PEG solution was administered if the stool output contained solid components. At night, a saline enema was performed if solids particles were still present in the stool. If the patient could not drink the solution, the solution was administered through a nasogastric tube.

The majority of the colonoscopic procedures were done with video endoscopes (OLYMPUS GIF-Q190; Olympus, To-kyo, Japan) for ≥2 years of age. In children less than 2 years or weighing less than 10 kg, colonoscopy was performed with a pediatric video endoscope (OLYMPUS GIF-XP190; Olympus, To-kyo, Japan) with a diameter of 5.8 mm.

Mode of anesthesia was decided by performing faculty member depending upon patient's age, level of cooperation and physicians comfort level. Parenteral Midazolam (0.05–0.1 mg/kg IV, maximum single dose of 4 mg) with or without Ketamine (1 mg/kg I/V) was used as sedatives. Further dosing was considered according to the patient's level of comfort and maximum dose of the medications. In some adolescents, colonoscopy was done without sedation/ anaesthesia but under local xylocaine jelly.

The procedure was performed in the left lateral position. Position change and abdominal pressure were applied according to the procedure progression. In case a colorectal polyp was found, a snare polypectomy was performed and the polyp tissue was sent for histopathological examination.

Colonoscopic findings were documented for each patient and if needed, biopsy materials for histopathology were taken. Patients were kept in observation room to see the immediate post procedure complications. Patient's demographic data including age, sex and length of hospital stay were recorded. For descriptive purpose patients were divided into three age groups. Indications for colonoscopy, findings and post colonoscopic complications were recorded for each patient.

All data on categorical variables were presented as frequencies, percentages and were analyzed with a chi-square test. Data of various indications, colonoscopic findings and complications were entered into the SPSS (statistical package for social science) Version 24.0 statistical program and statistical significance was determined by a p-value less than 0.05.

Results

Over a period of 5 years (2017-2021), a total of 196 children underwent upper GI colonoscopy. Mean age

of patients was 8.6 years with a minimum age of 3 months and a maximum of 18 years. The children aged between 5-10 years had highest frequency of colonoscopy, *i.e.* 40.3% (n=79), followed by older children (>10 years of age), in which frequency of colonoscopy was 35.2% (n=69). The frequency of colonoscopy in youngest children between 0-5 years of age was 24.5% (n=48). Male were 105 (53.6%) and female were 91 (46.4%). The male female ratio was 1.1:1. Out of 196 children, 59 (30.1%) were from outpatient department and 137 (69.9%) from admitted patient. No sedation were required in 38 (19.4%) children especially from >10 year age group. Only midazolam was given in 131 (66.9%) children whereas midazolam plus ketamine were required in only 27 (13.7%) sensitive children. Other than polyps, biopsy obtained from 51 patients and specimen sent for histopathology. Colonoscopic snare polypectomy was done in 81 (41.3%) patients and for others (58.7%), only diagnostic colonoscopy was done (Table I).

Table I
Characteristics of Study population & procedure (n=196)

Variable	No.	Percentage
Age		
<5 years	48	24.5
5-10 years	79	40.3
>10 years	69	35.2
Sex		
Male	105	53.6
Female	91	46.4
Patient status		
Outpatient	59	30.1
Inpatient	137	69.9
Sedation		
No Sedation	38	19.4
Midazolam	131	66.9
Midazolam+Ketamine	27	13.7
Extent of colonoscopy		
Ileum	119	60.8
Cecum 8 (2.9%)	13	6.6
Ascending colon 9 (3.3%)	11	5.6
Transverse colon	33	16.9
Descending colon	11	5.6
Sigmoid colon 27 (9.8%)	09	4.5
Biopsy obtained		
Yes	51	26.0
No	145	74.0
Purpose of colonoscopy		
Diagnostic	115	58.7
Diagnostic+Therapeutic	81	41.3

The most common indications were LGIB in 107 (54.6%) patients. Chronic diarrhea was the next cause (16.8%) of the procedure. In 8.2% patients, colonoscopy was done due to RAP followed by follow up of IBD patients with 7.1%. Other less common indications were chronic constipation (4.1%), weight loss (3.6%), recurrent oral ulcer (2.6%), intestinal TB, melena and others (Figure-2).

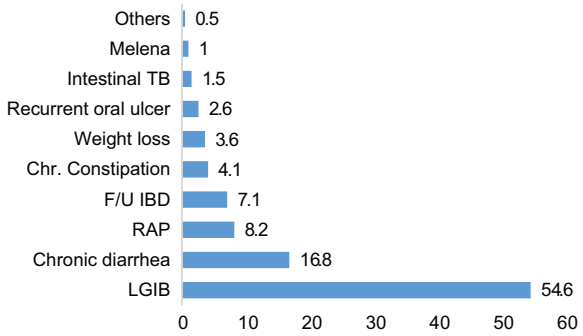


Fig.-2 *Indications of colonoscopy (n=196)*

Colon polyps were the most common colonoscopic finding among 81 (41.4%) children followed by normal cases 64 (32.7%), erythema & linear ulcerations 29 (14.7%) and diffuse nonspecific ulcers 22 (11.2%) cases (Figure-3).

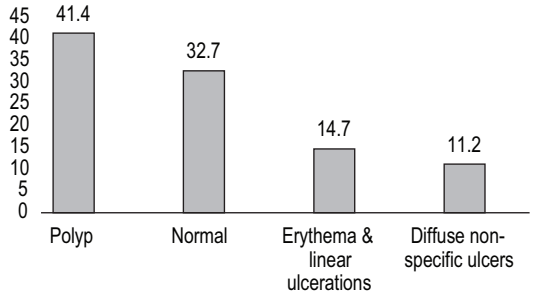


Fig.-3 *Colonoscopic findings of studied children (n=196)*

Pathologic findings after colonoscopy

The most common histopathological finding was juvenile polyps 81 (61.4%) followed by diffuse non-specific colitis in 19 (14.4%) patient, infectious colitis in 09 (6.8%) patient, Ulcerative colitis 7 (5.3%), unclassified IBD in 6 (4.5%), CD in 4 (3.0%), intestinal TB and SRUS of each in 2 (1.5%) cases (Table-II & figure-4).

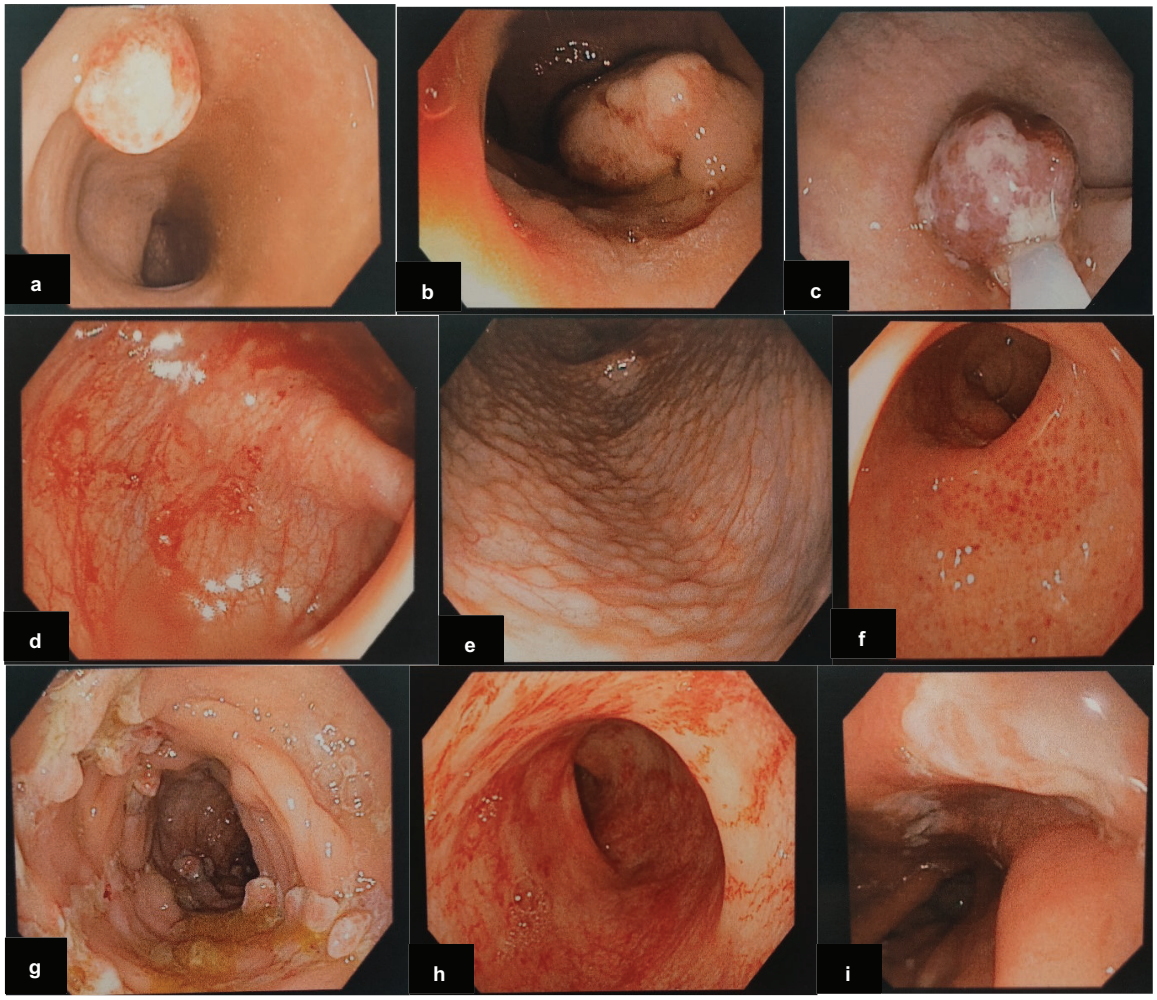


Fig.-4 *Various colonoscopic views:* ***(a)*** *Sessile polyp,* ***(b)*** *Pedunculated polyp,* ***(c)*** *During snare polypectomy,* ***(d)*** *Infectious colitis,* ***(e)*** *Non-specific colitis,* ***(f)*** *Proctitis,* ***(g)*** *Crohn's disease,* ***(h)*** *Ulcerative colitis,* ***(i)*** *SRUS*

Table II
Pathologic findings after colonoscopy (n=132)

Findings	No.	Percentage (%)
Juvenile Polyps	81	61.4
Non-specific colitis	19	14.4
Infectious colitis	09	6.8
Ulcerative colitis	07	5.3
Unclassified IBD	06	4.5
Crohn's disease	04	3.0
SRUS	02	1.5
Intestinal TB	02	1.5
Internal Hemorrhoid	01	0.8
Eosinophilic proctitis	01	0.8
Total	132	100

IBD: Inflammatory bowel disease
SRUS: Solitary rectal ulcer syndrome

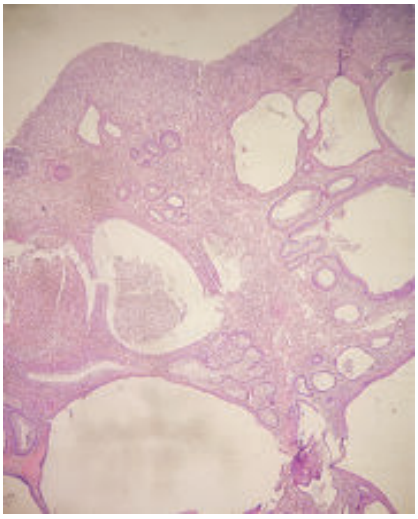


Fig.-5 *H & E stain, low-power image, Juvenile rectal polyp varying sized and cystically dilated glands filled with mucus, devoid of atypical features, and separated by an inflamed and edematous stroma*

Table III
Association of age with polyp (n=81) and other pathological diseases (n=51)#

Age group	Polyp (n=81) (%)	Non-specific colitis (n=19)	Infectious colitis (n=9)	UC (n=7) (%)	Unclassified IBD (n=6) (%)	CD (n=4) (%)	SRUS (n=2) (%)	Intestinal TB (n=2) (%)	Internal Hemorrhoid (n=1) (%)	Eosinophilic proctitis (n=1) (%)	p value
<5 years	39 (48.1)	2(10.5)	2(22.2)	2(28.6)	2(33.4)	1(25)	0(0.0)	0(0.0)	0(0.0)	0(0.0)	<0.001*
5-10 years	36(44.5)	8(42.1)	5(55.6)	4(57.1)	3(50)	2(50)	1(50)	1(50)	0(0.0)	1(100)	
>10 years	06 (7.4)	9(47.4)	2(22.2)	1(14.3)	1(16.6)	1(25)	1(50)	1(50)	1(100)	0(0.0)	

#Other than polyp: Non-specific colitis, Infectious colitis, Ulcerative colitis, Unclassified IBD, Crohn's disease, SRUS, Intestinal TB, Internal hemorrhoids, Eosinophilic proctitis Chi-square test; *Significant

In addition, the study showed that polyps were more common in <5 years age group (48.1%) than other pathology and that was statistically significant (Table-III).

No side effects were observed in 98% of children following colonoscopy procedure. Adverse events were recorded only in 4 (2.0%) cases. Delayed minor bleeding in 3 (1.5%) cases whereas abdominal pain only in 1 (0.5%) case. All of them were minor and did not affect the overall survival and hospital stay (Figure-5).

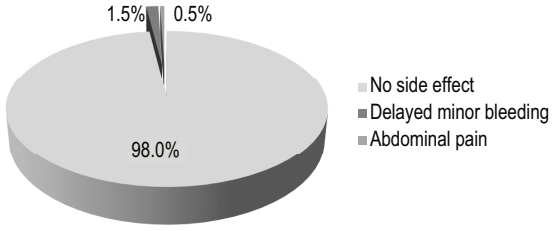


Fig.-6 *Complications of colonoscopy (n=196)*

Discussion

Colonoscopy is routinely performed nowadays, both in infants and children for the evaluation and treatment of lower gastrointestinal diseases, especially under the circumstances when other investigations are not conclusive.[14]

In the present study, older children aged 5-10 years had highest frequency of colonoscopy with 40.3%. Same phenomena were observed in Begum et al[23] (36.7%) from another study of Bangladesh, Sharma et al[24] (43.8%) and Bhadauria et al[25] (63.1%) from India. Less fear and much more lower gastrointestinal diseases in older children probably the possible causes. The Male female ratio was 1.1:1. Different studies from different countries stated different ratio. The ratio was 1.6:1 from Bangladesh[23], 2.1:1 from India[25], 0.8:1 from USA[26] and 0.8:1 from Taiwan[3]. Different geographical distribution as well as variable genetic basis probably the causes.

Colonoscopy is performed less frequently in children than in adults because of difficulties in preparation and sedation, which are usually needed in children. [3] In the present study, due to good bowel preparation prior to colonoscopy, inpatient number (69.9%) was much higher than outpatient (30.1%). No sedation were required in 38 (19.4%) children especially from >10 year age group. Yoshioka et al[14] (18.2%) and Nambu et al[9] (8.0%) from Japan also stated the same phenomena. Appropriate counseling and good co-operation of older children probably the possible etiology. In the present study, mild sedation with intravenous midazolam was given in 66.9% children whereas midazolam plus ketamine were required in only 13.7% sensitive children. Midazolam ± Ketamine were also used in Korea[1] & Japan[9], Midazolam ± Pethidine used in Bangladesh[23] & China[18] and Midazolam ± Propofol used in Taiwan[3]. In different studies[1,3,9,18,23], midazolam was commonly used as a sedative agent during colonoscopy as it is safe, short acting, rapid onset with minimal side effects. Due to unavailability of anesthetic support and inadequate number of experienced pediatric anesthesiologist, conscious sedation is the key for developing countries. Like other developed countries in Japan, general anesthesia (GA) was used in 47% children during colonoscopy.[9]

In the present study, the most common indications were lower gastrointestinal bleeding (LGIB) in 54.6% patients followed by chronic diarrhea (16.8%), recurrent abdominal pain (RAP) (8.2%) and follow up IBD 7.1%. Begum et al[23] (69.8%) from

Bangladesh, Altamimi et al[16] (46.2%) from Jordan, Yoshioka et al.[14] (57.2%) & Nambu et al[9] (75.0%) from Japan, Wu et al[3] (53.5%) from Taiwan, Mantos et al[27] (79.6%) from Philippines and Deep et al.[28] (73.3%) from Egypt were also observed the commonest indication was LGIB.

In the present study, colorectal polyps constituted 81 (41.4%) of all colonoscopy cases. Begum et al[23] (41.3%) & Azim et al[29] (40.4%) from Bangladesh and Deep et al[28] (44.0%) from Egypt also observed the same phenomena. Colorectal polyp was found 26.4% in a study done in Korea which is albeit lower than our findings.[24] In the literature, there are great variations in the prevalence of colorectal polyps in pediatric patients who underwent colonoscopy. It is reported high in India (61.7%-67.7%) and also in Pakistan (75%) compared with western data (4%-17.5%).[3,24,30-32] Almost one third of the children (32.7%) who underwent upper GI endoscopy in our study had normal endoscopic findings. Another study from Bangladesh[23] (36.3%), Korea[1] (36.5%), Japan[14] (29.5%), Jordan[16] (42.0%) and China[18] (29.5%) also observed the same type of findings. In Philipines[27] (9.2%) and Egypt[28] (6.6%), normal findings were much less in relation to other mentioned studies. Patients from different geographical area as well as sampling technique are responsible for these variation. Erythema & linear ulcerations were found during colonoscopy in 29 (14.7%) and diffuse nonspecific ulcers in 22 (11.2%) cases. Begum et al[23] (12% & 10.2%) from Bangladesh and Deeb et al. [28] (25.3% & 24.0%) from Egypt also found consecutively same type of findings.

Next to Juvenile polyp, non-specific colitis was observed in 19 (14.4%) cases. Begum et al[23] (13.5%) from Bangladesh, Deeb et al[28] (20%) from Egypt, Wu et al[3] (22.7%) from Taiwan, Nambu et al[9] (13%) and Yoshioka et al[14] (11.8%) from Japan also found the similar type of results. Non-specific colitis was most common in a study of Philippine[27] (49.5%) which was different from other studies. Poor sampling technique as well as lack of well-trained histopathologist may be the answer. Infectious colitis was found in only 9 (6.8%) cases. Near similar results were observed in Korea[1] (5.0%) cases.

IBD including UC, CD and unclassified IBD are also common etiologies of lower GI bleeding in children. Previous studies have shown that approximately 20% of patients with IBD are diagnosed before the age of 20 years, among whom most are below 15 years of age.[33] In our study, IBD (UC, CD & unclassified IBD) were the 4th most common histological causes of colonoscopy and accounted for 17 (12.9%) of all pathologic patients. Begum et al[23] (6.0%) from Bangladesh and Sharma et al[24] (8.77%) found IBD cases which is close to our study. In our study, UC cases were 07, unclassified were 06 and 04 cases were CD. All the UC cases had pancolitis whereas CD cases had aphthous ulcers and linear ulcers. Non-caseating granuloma was found only one third of cases, probably subcutaneous nature of granuloma could be the cause.

In the present study, intestinal TB and SRUS of each in 2 (1.5%) cases. Begum et al[23] (1.5%) & Azim et al[29] (1.8%) from Bangladesh, Sharma et al[24] (3.5%) from India and Park et al. from Korea (1.0%) also observed a few cases of intestinal TB. All the cases had positive contact with transeverse ulceration. Only one had caseating granuloma. SRUS was found in 2(1.5%) cases. A few study from Bangladesh[23,29] and Jordan[16] also found a few cases of SRUS. In a study from Iran regarding the etiology of lower GI bleed in children, juvenile polyp and solitary rectal ulcer accounted for most of the pathologies that caused rectal bleeding in children and adolescents, respectively.[34] In all our cases of SURS, children had a history of associated constipation and straining during defecation along with mucorrhea.

In the present study, juvenile polyps were huge (61.4%) in relation to other (38.6%) pathology. Polyps were more common in <5 years age group (48.1%) than other pathology and that was statistically significant. Begum et al.[23] & Alam et al.[35] from Bangladesh, Deeb et al.[28] from Egypt and Moravej et al.[36] from Iran also found the similar results.

Perforation is the most serious complication of colonoscopy in children especially in therapeutic colonoscopy. The risk ranges from 0.01% to 0.3%.[37,38] It can be successfully managed with surgical intervention. Bleeding after a diagnostic procedure is very rare in children as in adults. Bleeding after colonoscopy was reported to occur at an incidence of 1.4% in a large-scale study.[29] In the period of 2010-2015, Park et al[1] from Korea found that, two cases of delayed bleeding occurred after colonoscopic polypectomy. In the present study, 3 (1.5%) patients complained of delayed minor bleeding and 1 (0.5%) patient had abdominal pain. Spontaneous hemostasis

developed in all cases. All the adverse events were minor and did not increase morbidity or mortality.

Limitations of the study

This study's primary limitation is that it was a single-center study. Furthermore, its retrospective nature may have resulted in inaccurate findings regarding underreporting of adverse events in OPD patients.

Conclusions

A safe and successful colonoscopy can be achieved in the majority of children with good bowel preparation and adequate sedation. Lower gastrointestinal bleeding & chronic diarrhea was the most typical indication, and polyps, non-specific colitis & IBD's were the most common pathological findings of pediatric colonoscopy. We observed that colonoscopy is beneficial and can be safely used in children of all ages. Children presenting with symptoms or signs of lower gastrointestinal disorders should undergo colonoscopy to obtain a definite diagnosis and prompt treatment.

Acknowledgements

The authors are thankful to all the participants & institute.

References

1. Park JH. Pediatric Colonoscopy: The Changing Patterns and Single Institutional Experience Over a Decade. *Clin Endosc* 2018;**51**:137-41.
2. Victor LF. Colonoscopy. In: Walker WA, Durie PR, Hamilton JR, Walker-Smith JA, Watkins JB, eds. Pediatric gastrointestinal disease: pathophysiology, diagnosis, management. 2nd ed. St. Louis (MO): Mosby; 1996. p. 1533-1541.
3. Wu CT, Chen CA, Yang YJ. Characteristics and Diagnostic Yield of Pediatric Colonoscopy in Taiwan. *Pediatr Neonatol* 2015;**56**:334-38.
4. Squires Jr RH, Colletti RB. Indications for pediatric gastrointestinal endoscopy: a medical position statement of the North American Society of Pediatric Gastroenterology and Nutrition. *J Pediatr Gastroenterol Nutr* 1996;**23**:107e10.
5. Hassall E, Barclay GN, Ament ME. Colonoscopy in childhood. *Pediatrics* 1984; **73**:594e9.
6. Tam YH, Lee KH, Chan KW, Sihoe JD, Cheung ST, Mou JW. Colonoscopy in Hong Kong Chinese children. *World J Gastroenterol* 2010;**16**:1119e22.
7. Kalaoui M, Radhakrishnan S, al Shamali M, Hasan F, al-Nakib B. Findings of colonoscopy in children: Experience from Kuwait. *J Trop Pediatr* 1998;**44**:371e5.
8. Park JH. Role of colonoscopy in the diagnosis and treatment of pediatric lower gastrointestinal disorders. *Korean J Pediatr* 2010;**53**:824-29.
9. Nambu R , Hagiwara S, Kakuta F, Hara T, Shimizu H, Abukawa D et al. Current role of colonoscopy in infants and young children: A multicenter study. *BMC Gastroenterology* 2019; **19**:149.
10. Levin B, Lieberman DA, McFarland B, Andrews KS, Brooks D, Bond J et al. American Cancer Society colorectal Cancer advisory group; US multi-society task force; American College of Radiology Colon Cancer Committee. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US multi-society task force on colorectal Cancer, and the American college of radiology. *Gastroenterology* 2008;**134**:1570-95.
11. Kawada PS, O'Loughlin EV, Stormon MO, Dutt S, Lee CH, Gaskin KJ. Are we overdoing pediatric lower gastrointestinal endoscopy? *J Pediatr Gastroenterol Nutr* 2017;**64**:898-902.
12. Elitsur Y, Teitelbaum JE, Rewalt M, Nowicki M. Clinical and endoscopic data in juvenile polyposis syndrome in preadolescent children: a multicenter experience from the United States. *J Clin Gastroenterol* 2009;**43**:734-36.
13. ASGE Standards of Practice Committee, Lightdale JR, Acosta R, Shergill AK, Chandrasekhara V, Chathadi K, Early D et al. Modifications in endoscopic practice for pediatric patients. *Gastrointest Endosc* 2014;**79**:699-710.
14. Yoshioka S, Takedatsu H, Fukunaga S, Kuwaki K, Yamasaki H, Yamauchi R et al. Study to determine guidelines for pediatric colonoscopy. *World J Gastroenterol* 2017;**23**:5773-79.
15. Gilger MA, Gold BD. Pediatric endoscopy: new information from the PEDS-CORI project. *Curr Gastroenterol Rep* 2005;**7**:234-39.
16. Altamimi E, Odeh Y, A-quraan T, Mohamed E, Rawabdeh N. Diagnostic and therapeutic outcomes of pediatric colonoscopies in Jordanian children. *Journal of Pediatric and Neonatal Individualized Medicine* 2022;**11**:e110211.
17. Lev-Tzion R, Turner D. Is pediatric IBD treatment different than in adults? Minerva *Gastroenterol Dietol* 2012;**58**:137-50.
18. Lei P, Gu F, Hong L, Sun Y, Li M, et al. Pediatric Colonoscopy in South China: A 12-Year Experience in a Tertiary Center. *PLOS ONE* 2014;**9**:e95933.

19. Tam YH, Lee KH, Chan KW, Sihoe JD, Cheung ST, Mou JWC. Colonoscopy in Hong Kong Chinese children. *World J Gastroenterol* 2010;**16**:1119-22.

20. Mudawi HM, El Tahir MA, Suleiman SH, Eltaybe NH, Gamer NM, Abdallha FA et al. Paediatric gastrointestinal endoscopy: experience in a Sudanese university hospital. *East Mediterr Health J* 2009;**15**:1027-31.

21. Wei C, Dayong W, Liqun J, Xiaoman W, Yu W, Xiaohong Q. Colorectal polyps in children: A retrospective study of clinical features and the value of ultrasonography in their diagnosis. *J Pediatr Surg* 2012;**47**:1853-58.

22. Thakkar K, Alsarraj A, Fong E, Holub JL, Gilger MA, Serag BEI. Prevalence of Colorectal Polyps in Pediatric Colonoscopy. *Dig Dis Sci* 2012;**57**:1050-55.

23. Begum F, Nahid KL, Islam F, Majumder W, Rukunuzzaman MD, Karim ASMB. Paediatric Colonoscopy: Experience from Pediatric Gastroenterology and Nutrition Department, BSMMU. *Bangladesh J Child Health* 2021;**45**:25-28.

24. Sharma B, Sharma R, Bodh V, Sharma S, Sood A, Sharma R et al. Chronic lower gastrointestinal bleeding: Etiological profile and role of colonoscopy among children from sub-Himalayan ranges of North India. *J Dig Endosc* 2018;**9**:109-13.

25. Bhadauria N, Dubey SR, Mittal P, Arya AK, Singh RP. Clinicoetiological pattern of lower gastrointestinal bleeding in children (5-18 years age group) at a tertiary care center in central India. *Indian J Child Health* 2016;**3**:290-92.

26. Hochman JA, Figueroa J, Duner E, Lewis JD. Diagnostic Yield Variation with Colonoscopy among Pediatric Endoscopists. *Dig Dis* 2020;**38**:421-30.

27. Mantose JP, Monreal PM, Castro CA. Pediatric colonoscopy in a tertiary center: A 10 year experience. *Gut* 2021;**70(Suppl 2)**:A133-A135.

28. Deeb MM, El-Zayat RS, Heba A. El-Khairb HA. Colonoscopic findings in children with lower gastrointestinal bleeding. *Menoufia Med J* 2016;**29**:247-51.

29. Azim MA, Yousuf M, Shahed MM. Colonoscopic evaluation of per rectal bleeding in children: Our experience. *Chattogram Maa-O-Shishu Hospital Medical College Journal* 2022;**21**:66-69.

30. Poddar U, Thapa BR, Vaiphei K, Singh K. Colonic Polyps: Experience of 236 Indian Children. *Am J Gastroenterol* 1998;**93**:619-22.

31. Boukthir S, Mrad SM, Oubich F, Boussif A, DebbabiA, Barsaoui S. Colorectal polyps in children. A study of 34 patients. *Tunis Med* 2006;**84**:496-99.

32. Clarke G, Robb A, Sugarman I, Macallion WA. Investigating painless rectal bleeding- is there scope for improvement? *J Pediatr Surg* 2005;**40**:1920-22.

33. Yu Bai, Jun Peng, Jun Gao, Duo-Wu Zou, Zhao-Shen Li. Epidemiology of lower gastrointestinal bleeding in China: Single-center series and systematic analysis of Chinese literature with 53951 patients. *J Gastroenterol Hepatol* 2011;**26**:678-82.

34. Zahmatkeshan M, Fallahzadeh E, Najib K, GeramizadehB, Haghighat M, Imanieh MH et al. Etiology of lower gastrointestinal bleeding in children: A single center experience from southern Iran. *Middle East J Dig Dis* 2012;**4**:216-23.

35. Alam S, KMD Islam, Mohammad N, Nooruzzaman M. Per rectal bleeding in children: Experiences in the department of pediatric surgery in BSMMU. *Bangladesh Med Res Counc Bull* 2017;**43**:20-25.

36. Moravej H, Dehghani SM, Nikzadeh H, Male-Kpour A. Lower gastrointestinal bleeding in children: Experiences from referral Centre in southern Iran. *J Compr Ped* 2013;**4**:e8423

37. Thakkar K, El-Serag HB, Mattek N, Gilger M. Complications of pediatric colonoscopy: a five-year multicenter experience. *Clin Gastroenterol Hepatol* 2008;**6**:515-20.

38. Korman LY, Overholt BF, Box T, Winker CK. Perforation during colonoscopy in endoscopic ambulatory surgical centers. *Gastrointest Endosc* 2003;**58**:554-57.

ORIGINAL ARTICLE

Incidence and Outcome of Childhood Acute Leukemia in A Tertiary Care Hospital of Bangladesh Armed Forces

Kamrun Nahar[1], Shormin Ara Ferdousi[2], Ahmed Rashidul Hasan,[3]Afiqul Islam,[4]Azizul Islam[5]

Abstract

Background: *Worldwide cancer is the second leading cause of death in children under 15 years and acute leukemia is the most prevalent cancer among children.*

Objective: *The objective of the study was to analyze the incidence and overall outcome of childhood leukemia patients aged 0-12 years in Combined Military Hospital (CMH), Dhaka.*

Methods: *It was a retrospective cross-sectional study. Children below 12 years of age with confirmed diagnosis of leukemia and received treatment from the paediatric oncology unit of department of paediatrics of CMH, Dhaka were taken for this study. Data has been collected from Hospital based cancer registry records from 2011 to 2021. There present status has been collected from regular OPD or by phone calls.*

Results: *The commonest cancer was found Acute Leukemia (52%), among them Acute Lymphoblastic Leukemia (ALL) 83.15% and Acute Myeloid Leukemia (AML) 16.85%. Morphological (FAB classification) sub-divisions revealed ALL-L2 (31%) was the commonest group for ALL. In case of AML, AML-M3 (APML) was the commonest (27%). Immunophenotyping of cells revealed Pre-B ALL was the commonest. Cytogenetic analysis revealed ETV6-RUNX1 (21%), t(1;19) ((q23,p13) E2A/PBX1 (11%) were two most common genetic abnormalities found in ALL and t(15;17) (q22;q12) M3,M3v PML-RARA was the commonest cytogenetic abnormalities and (8;21) (q22;q22) RUNX1/RUNX1T1 for AML. In case of ALL overall survival was 54% and in case of AML 40%. About 10% of patients reported relapses.*

Conclusion*: Incidence of acute leukemia was the highest among all childhood cancer. At the end of the study, overall survival was 52% of cases, and relapses were seen in 10% of cases.*

Keywords: *Childhood leukemia, cytogenetics, demographic profile, immunophenotyping.*

DS (Child) HJ 2022;38(1):17-26
DOI: https://doi.org/10.3329/dshj.v38i1.66997

1. Classified Specialist in Paediatric Oncology, Department of Paediatrics, Combined Military Hospital, Dhaka.
2. Head of the Department, Pediatric Hemato-Oncology, Gonoshasthaya Samaj Vittik Medical College & Gonoshasthaya Nogor Hospital, Dhaka, Bangladesh.
3. Register, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
4. Professor, Department of Paediatric Hematology and Oncology, Labaid Cancer Hospital & Super Speciality Center, Dhaka, Bangladesh.
5. Consultant Physician General, Bangladesh Armed Forces, Directorate General of Medical Services, Ministry of Defense, Dhaka, Bangladesh.

Correspondence to: Dr. Kamrun Nahar, Classified Specialist Paediatric Oncology, Combined Military Hospital, Dhaka. Cell: 01711220833, E-mail: drka_nahar2006@yahoo.com
Received: 2 January 2022; **Accepted**: 12 April, 2022

Introduction

Cancer is cruel and spares no age. A cancer diagnosis is upsetting at any age, but especially so when the patient is a child. Even countries like the United States estimated that for the year 2021 they would have about 10,500 newly diagnosed cases of childhood cancer and about 1,190 children are expected to die from the disease.[1,2] This incidence varies worldwide between 50 and 200 per million children[3], and ranked the leading cause of death.[1] The most common types of cancer seen in children are leukemia, followed by brain and other central nervous system (CNS) tumors, lymphomas, neuroblastoma, kidney tumors, and malignant bone tumors.[1] Childhood cancers are neglected in developing countries, even though approximately 84% of the cancer cases under 15 years old occur in low-income and middle-income countries (LMICs).[4] In Bangladesh, the incidence of paediatric cancer is alarming and most of these patients die without a correct diagnosis and adequate medical treatment.[5] It is now one of the major causes of mortality and morbidity among non-communicable diseases in Bangladesh.[6] The overall incidence of childhood cancer in Bangladesh is largely unknown, due to population-based cancer registries are still unavailable.[7,8] It is estimated around 13,000 new cases per year,[9] but fewer than 500 children receive hospital based treatment annually.[10] World child cancer estimated that every year around 9,000 to 12,000 children get cancer in Bangladesh, but only one-third receive a proper diagnosis.[11] The proportion of childhood cancers is expected to be high because of the young population structure, at present about 30% (47.4 million) of the population is under 15 years of age.[10]

Leukemia is the most common type, accounting for about 25-30% of total cancer in children less than 15 years of age.[12] It accounts for 27% of childhood cancers in the United States,[13] 30% in France[14] and Ireland,[15] 33% in Germany,[16] 35% in Shanghai, China[17], and 76% in Chennai, India.[18] Acute leukemia (cancer of blood cells) represents a clonal expansion and arrest at a specific stage of normal myeloid or lymphoid hematopoiesis. They constitute 97% of all childhood leukemia. It consists of two main types - acute lymphoblastic leukemia (ALL), accounting for 75%, and acute myeloid leukemia (AML) is about 20%. It can occur at all ages, from birth to adulthood, but the peak incidence is between 2 and 6 years of age. Improvements in treatment have led to remarkable gains in survival, estimated at 79% at 5 years.[12] The outcome is poorer for acute myeloid leukemia (AML) than for acute lymphoblastic leukemia (ALL), with a 5-year survival rate of 41%. Risk factors of childhood leukemia are barely known, highly probable of the interaction of environmental and genetic factors.[19]

In Bangladesh, the overall cancer burden including adolescent and childhood cancer is largely unknown due to the nonexistence of population-based cancer registries.[6-8] The objective of the study was to analyze the incidence and overall outcome of childhood leukemia patients aged 0-12 years in Combined Military Hospital (CMH), Dhaka, Bangladesh.

Materials and Methods

This retrospective cross-sectional study was conducted in the Paediatric Oncology Unit of the Department of Paediatric in Combined Military Hospital (CMH), Dhaka, Bangladesh. We here enrolled all the diagnosed cases of childhood leukemia below 12 years of age from 2011 to 2021 from our hospital-based cancer registry and analyzed them. The data were collected after obtaining informed consent from parents. The data were then put on computer software MS office Excel datasheet and analyzed using computer software (Microsoft Excel 2019 & SPSS version 25). It is to be mentioned that, paediatric dataset included data from the paediatric cancer registries collecting data in children below 15 years but here in our study we collected data for children who have completed 12 years because our department is designated for the 0 to 12 years age group. Here inclusion criteria were a) all newly diagnosed acute leukemia patients b) age completed 12 years And exclusion criteria were a) age above 12 years and b) patient having a relapse.

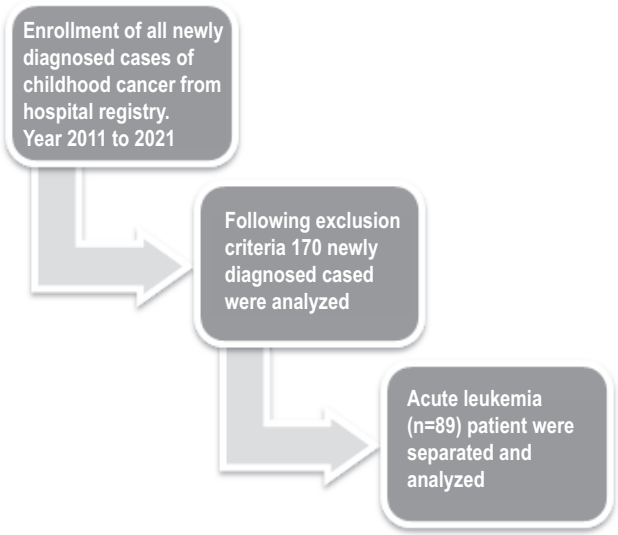


Fig.-1 *Scheme review of data analysis*

Results

During this study period of 11 years, a total of 170 newly diagnosed childhood cancer patients came to the Pediatric Oncology unit. Among these enrolled patients, haemopoietic cancer 102 (60%) and solid tumor 68 (40%) [Fig.-2]. Disease distribution analysis showed most common cancer was childhood leukemia 52.4%, and lymphoma was 7.65%. Other common cancers were CNS tumors, Neuroblastoma, Liver tumors, Renal tumors, etc. The present analysis provides a gist of the incidence of our main childhood cancer, leukemia.

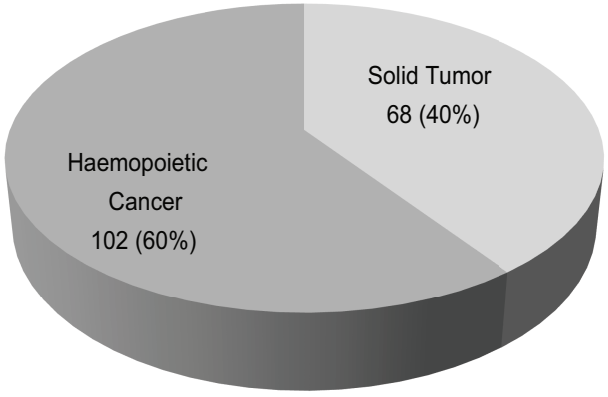


Fig.-2 *Distribution of Childhood Cancer (N=170)*

Distribution of childhood cancer showed that haemopoietic cancer was found in102(60%), and solid tumor in 68(40%) cases (Fig.-2).

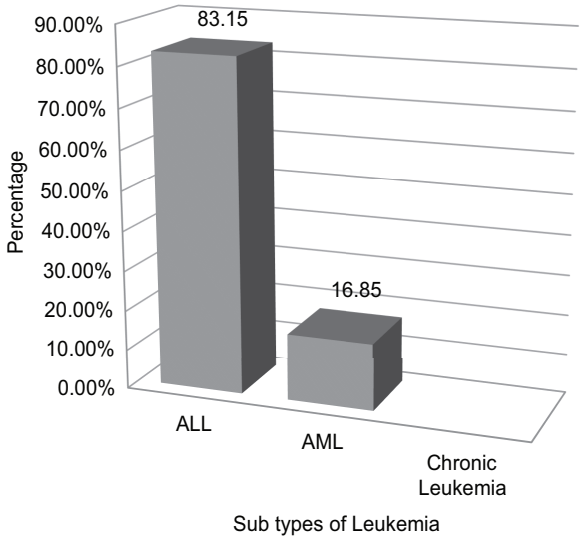


Fig.-3 *Distribution of Childhood Leukemia (n=89)*

Among all leukemia patients, ALL were 83.15%, AML 16.85%, and no patient was diagnosed with chronic leukemia (Fig.-3).

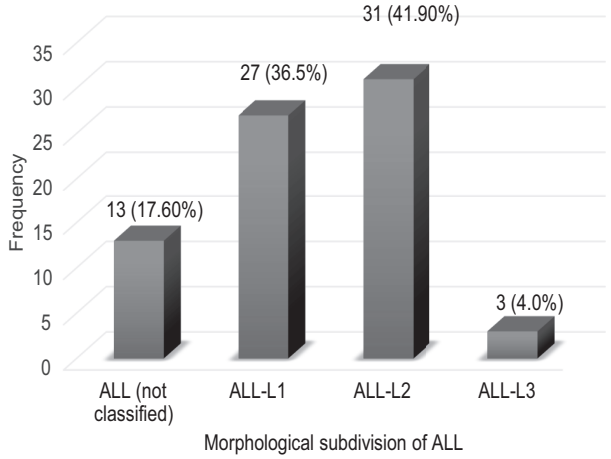


Fig.-4 *Distribution of ALL (n=74) based on French-American-British (FAB) morphological classification*

In Fig.-4 further sub-division of the 74 ALL patients were done according to their morphological findings based on French-American-British (FAB) classification. Here, L1 was 36.5%, L2 was 41.9% (most common) and L3 was 4%. Rest 17.6% were not classified.

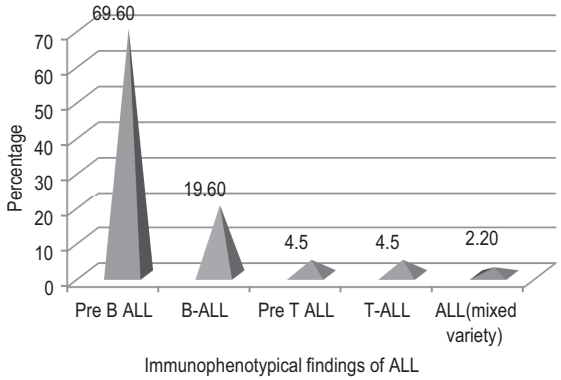


Fig.-5 *Distribution of Immunophenotyping (IPT) analysis of ALL (n=46)*

Immunophenotyping (IPT) findings of ALL (n=46) showed that Pre-B-ALL was the most common presentation (69.60%) (Fig.-5).

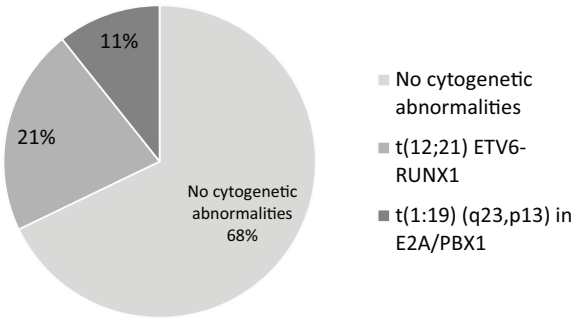


Fig.-6 *Cytogenetic Abnormalities in ALL (n=28)*

Cytogenetic analysis reported in 28 ALL patients showed majority of the patient (68%) had no genetic abnormalities. Most common abnormalities found ETV6-RUNX1 fusion genet(12;21) (p13q22). t(12;21), [TEL-AML], were positive in 21%patients. Abnormalities of t(1:19) (q23, p13) in E2A/PBX1 gene were present in 11% of patients of ALL having B-Cell (Fig.-6).

Next we evaluated 15 patients who were diagnosed with AML, accounting for 16.85% of our acute Leukemia cases.

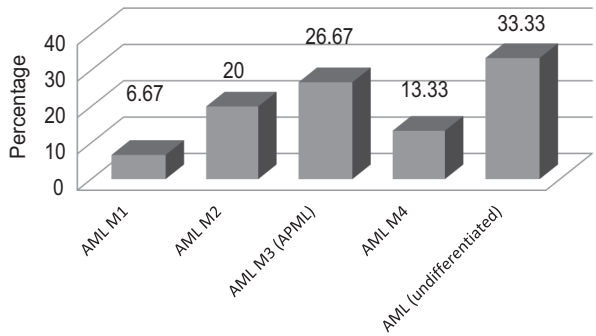


Fig.-7 *Distribution of AML based on FAB classification*

Distribution of AML patients according to FAB classification showed M1 (6.67%), M2 (20%), M3 (26.67%), M4 (13.33%), and 33.33% patients were not categorized in any group. IPT was done in 53% of cases; of them, APML alone was 50% & other myeloid groups of cells were represented in rest 50% of patients (Fig.-7).

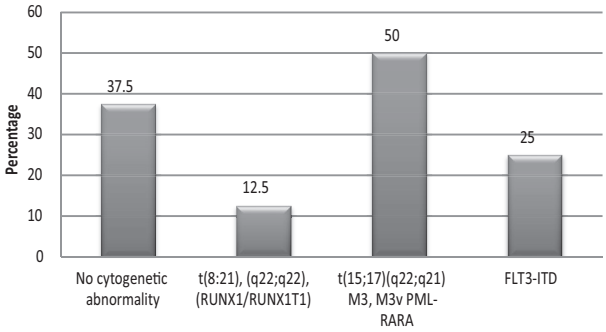


Fig.-8 *Cytogenetic analyses of AML (n=8)*

Cytogenetic analyses of AML showed, 37.5% had no abnormalities. About 50% had t(15;17)(q22;q12) PML-RARA gene fusion, FLT3-ITD mutation or point mutations in 25% and 12.5% had t(8:21), (q22;q22), (RUNX1/RUNX1T1) was positive (Fig.-8).

Table I
Gender and age distribution of Acute Leukemia with histological subtypes (N=89)

Age & Gender	Acute leukemia (n=89)		ALL (n=74)		AML (n=15)	
	Number	Percentage	Number	Percentage	Number	Percentage
Gender						
Male	49	55	43	58	6	40
Female	40	45	31	42	9	60
M: F	1.23:1		1.4:1		0.66:1	
Age Group						
0-4 years	44	49.44	40	54.05	4	26.67
5-9 years	35	39.32	25	33.78	10	66.67
>10 years	10	11.24	9	12.16	1	6.67

Table-I showed demographic characteristics of all studied cases. Gender distribution analysis revealed in case of ALL, males were predominance (58%) and in case of AML, females were predominance (60%). In general their age distribution revealed '0-4 years age group' was most common group. Median age was 5.7 years. But in separate analyses ALL found more in '0-4 years age group' (54%) whereas in case of AML, most common group was '5-9 years age group' accounting 66.7%.

Table II
Distribution of Infantile Leukemia

Leukemia	Number	Percentage
Infantile AML	1	1.12
Infantile ALL	4	4.50
Acute Leukemia more than 1 year of age	84	94.38

Here in Table-II, infantile acute leukemia (Leukemia diagnosed below 1 year of age) were found in 5.6% of all leukemia cases. Of them, 4.5% of patients were suffering from ALL and 1.12% patients had AML.

Table III
Distribution of Acute leukemia with Down syndrome (DS)

Disease	Number	Percentage
AML with DS	1	1.12
ALL with DS	1	1.12
Acute leukemia not associated with DS	87	97.76

Table III showed among all acute leukemia patients 2 had Down syndrome. Of them ALL 1.12%, and AML 1.12%.

Table-IV revealed among the 89 patients with acute leukemia, 91% of patients started receiving treatment. About 4.5% of patients refused to do it. Other 4.5% of patients presented with advanced disease and had an early death. On the day of last follow-up (10th Jan 2022), about 51.7% of patients are alive and 41.55%of patients has been expired. About 10% of patients reported relapse and 6.75% were lost to follow-up. In case of ALL, 90% of patients started treatment, but 5% of patients refused treatment, and 5% of patients experienced an early death. Overall survival of ALL 54%. Among AML 100% of patients started treatment, but only 40% of patients survived. Overall mortality is 39% in ALL, and 53.3% in AML.

Table IV
Treatment status of Childhood Acute Leukemia

Treatment status	Acute Leukemia (n=89)		ALL (n=74)		AML (n=15)	
	Frequency	Percentage	Frequency	Percentage	Frequency	Percentage
Rx received	81	91.0	66	89.19	15	100
Refused treatment	4	4.5	4	5.4	0	0
Early death	4	4.5	4	5.4	0	0
Alive	46	51.70	40	54	6	40
Relapse	9	10.11	8	10.81	1	6.66
Expired	37	41.55	29	39.2	8	53.33
Lost to follow up	6	6.75	5	6.8	1	6.66

Discussion

Every year new cases of childhood cancer exceed 2 million globally and the majority of them (>80%) belong to the developing world.[20,21]In developing countries every year childhood cancer happens to be increased by 30%.[22] The situation of our country's children with cancer is similar to other developing countries.[23] Still now no national population-based childhood cancer registry is available for us.[24,25] According to World Child Cancer Report 2005, Bangladesh has some 1.3 to 1.5 million childhood cancer patients.[23,26] Available scenario in nearby countries like Pakistan incidence is 100 per million and in India, it is 64 per million in <15 years of age.[27,28] In India, cancer is the 8th most common cause of death among children between 5 and 14 years of age, covering 2.9%.[29] In 2010, the national pediatric cancer death rate was 39 for children aged 0 to 14 years.[30]

Over the last 11 years, 170 newly diagnosed childhood cancer patients admitted to CMH Dhaka. Ferdousi et al[31] reported, that per month around 5000-5500 visits happen in child OPD of CMH Dhaka. Per year average of 17 malignant cases came to the paediatric oncology unit. The overall incidence rate is about 3.6 per ten thousand per year, among them ALL 8 patients per year (1.7 per ten thousand per year), CNS tumors 1.4 patients per year (0.29 per ten thousand per year) and other solid tumors were 6.6 patients/year (1.4 per ten thousand per year).[31] Over time, childhood and adolescent cancer incidence has increased mostly due to improved referring knowledge. GLOBOCAN 2018 reported worldwide leukemia (32.5%) appears to be the most common cancer in children aged 0-14 years. The highest incidence was recorded in Asia (62.6%).[32] The next common cancer was CNS tumor and Lymphoma. Over one-year (2012) BSMMU found 68% Acute leukemia cases (ALL 58%, AML 10%).[26] In this study in the pediatric oncology unit we observed, the incidence of Acute leukemia was 89 (52.4%) patients. Of them, ALL were 83.15% and AML 16.85% and no patient was diagnosed with chronic leukemia. This result is similar to the findings of Ferdousi et al[31] Jabeen et al[33] reported childhood cancer was 4.4% of total cancers cases in the National Institute of Cancer Research & Hospital (NICRH), among them most common was lymphoma (24.2%), and leukemia (14.3%). Khasru et al[23] also found similar results. The distribution is similar to other developed countries. It made up about a third of paediatric cancers in Australia,[34] 27% of paediatric cancers in the United States,[13] 30% in France[14] and, in Ireland,[15] 33% in Germany,[16] 35% in Shanghai, China[17] and Chennai, India.[18] Studies have shown that in Eastern Mediterranean countries, prevalence of leukemia is around 30-50% of all childhood cancers.[35-38] Gender distributions revealed males in predominance (55%) and females 45% with a ratio of 1.23:1. These results are quite similar to the results from BSMMU[26] and NICRH.[33] We also found, in case of ALL, males were in predominance (58%), and in case of AML, females were predominance (60%). But Hossain et al[39] reported AML was male predominance. Age distribution analysis showed, in case of acute leukemia, 0-4 years age group was 49.44%, 5-9 years age group was 39.32%, and >10 years age group was 11.24%. Median age was at 4.6 years. The commonest group for ALL was 0-4 years covering 54%. Then 5-9 years was 34% and >10 years was 12%. In case of AML, most common group was 5-9 years accounting for 66.7%, next 0-4 years was 26.7%, and >10 years was 6.7%.

Hossain et al[24] report stated the mean age of leukemia in South Asian countries (Bangladesh, India, and Pakistan) was higher (6-7 years) than those of Western countries (between 0 to 4 years). In their study they found, Leukemia was mostly diagnosed in children aged 5-9 years (41%), ALL was common in 5-9 years group whereas AML was found more commonly in children aged 10-14 years (45%). Jabeen et al[33] reported majority of childhood leukemia belonged to 10-14 years (37.7%), followed by 5-9 years (31.4%) and 0-4 years (30.9%). American cancer society reported ALL is most common in early childhood, peaking between 2 and 5 years of age. AML tends to be more spread out across the childhood years, but it's slightly more common during the first 2 years of life and the teenage years.[40] In our study, the incidence of children below 1 year of age having acute leukemia (Infantile leukemia) was 5.6%, of them 4.5% ALL and 1.1% AML. Infants account for approximately 2-5% of all children with ALL.[12]

French American British classification (FAB) classifications of ALL & AML were made based on morphological findings of the leukemic cell. ALL were divided into 3 types; L1, L2 &L3. In our study, L2 was the most common variety (41.90%), L1-36.5%, and L3- 4%. Rest 17.6% of patients were not morphologically classified. Madhumathi et al[41]

reported B-ALL between 72.9%-91%. Pakistani studies also found similar results; B-ALL in 78.5-87%[42,43] and T-ALL 13-23%.[44,45]About 2.2% of patients had a mixed variety of ALL. Cytogenetic analyses were done in 28 ALL patients and found majority of patients (68%) had no genetic abnormalities. This aberration is known to predict a favorable prognosis with high remission rates and long median survival.[46,47] Most common ETV6-RUNX1 fusion gene t(12;21) (p13q22) [TEL-AML], were positive in 21%patients. About 11% patients presented with t(1:19) (q23,p13) in E2A/PBX1 gene. ETV6-RUNX1 fusion gene t(12;21) (p13q22) previously referred to as TEL-AML1 considered the most common translocation in childhood ALL, with a prevalence of 20-25%.[48] It is seen in B-ALL &associated with an excellent prognosis.[12] FAB classified AML based on morphology and in our study, we found M1-6.67%, M2-20%, M3-26.67%, M4-13.33%, and rest 33.33% patients were not categorized into any group. Immunophenotyping was done in 8 patients, who had a high number of CD33, CD15, CD64, and other myeloid groups of cell surface markers. Of them, APML was 50%. Cytogenetic analyses were done in 8 AML patients and 37.5% had no abnormalities. The t(15;17)(q22;q21) fuses RARA gene on chromosome 17q21 to PML gene on chromosome 15q22.[49] This mutation is present in 25-40% of children with APML which is similar to our study result,[50] we found it in 50% cases. FLT3-ITD mutation or point mutations were also identified in 25% of all cases. The reciprocal translocation t(8;21)(q22;q22) between 8 & 21 chromosomes results in AML1/ETO (RUNX1/CBFA2T1) fusion gene is considered to have the highest incidence in childhood AML (12%), mostly AML-M2.[51-53] In our study we found it one patient (12.5%). A report published that kFLT3-ITD or point mutations have been identified in 15-30% of pediatric AML patients. This mutation indicates a poorer prognosis.[12] Several other cytogenetic abnormalities have been suggested by multiple studies like Inv(16)(p13;q22), MLL rearrangements, Aberration of 7q,5. We did not observe these abnormalities in this study may be due to the small sample size.

This analysis revealed among the 89 patients with acute leukemia, 91% of patients started receiving treatment. About 4.5% of patients presented with advanced disease and had an early death. The other 4.5% of patients refused to do it. Refusal or abandonment is mostly due to considering malignancy is a grave disease, taboo & other personal reasons, and seeking treatment from abroad. Our results are similar to Ferdousi et al.[31] BSMMU also found that 43% of their study population refused and 11% abandoned treatment midway. Financial inability is the main reason for this refusal.[26] In acute leukemia patient's overall survival was found at about 51.7% of patients and expired in about41.55% of patients. About 10% of patients reported relapse and 6.75% are lost to follow-up. In case of ALL, 90% of patients started treatment, but 5% of patients refused treatment, and 5% of patients had an early death. Among them, alive 54% of patients, and 39% of patients expired. Among AML 100% patient started treatment& 80% completed treatment. But until a recent follow-up, only 40% survived and were on regular follow-up. About 53% of patients expired and 13.33% lost for follow-up. Death occurs mainly due to advanced disease at diagnosis, disease progress, sepsis, myelosuppression, and others. American Cancer Society estimates that improved' treatment made higher overall survival, in case of ALL was 90% & AML was 64%.[21] Only one patient had relapsed and started relapse treatment protocol but failed to survive. The relapse rate is expected and comparable to available data from neighboring countries.[41,42]

Ross et. al[54] studies suggested a down syndrome child is at higher risk for developing leukemia, nearly a 20-fold rise than other individuals.[55] ACCO said AML is much more common in Down syndrome children than in ALL, especially below 5 years of age.[55] In our study we had 2 Down syndrome patients suffering from Acute leukemia, one ALL and one AML both were below 5 years of age.

Conclusion

This study found that Acute Leukemia was the most common childhood cancer. The most common age group was 0-4 years. Infantile leukemia was found in 5.6% of cases. Morphologically FAB L-2 & Immunophenotypically Pre-B-ALL was the commonest ALL. In case of AML, both morphologically & immunophenotypically AML-M3 (APML) was the most common. Cytogenetic analyses revealed most children presented with no cytogenetic abnormalities. About 91% of patients started receiving treatment and refusal rate is only 4.5% which is mostly due to considering malignancy as a grave disease, taboo & others. Overall survival was 51.7% of cases and expired in 41.6% of cases, and

6.7% of cases were lost to follow-up. About 10% of patients reported relapses.

Recommendation

As many common childhood malignancies are curable there is a need to have a dedicated pediatric cancer registry for assessing the magnitude of the problem in our country.

Conflicts of interest

Conflict of interest relevant to this article was not reported.

References

1. National Cancer Institute. Childhood Cancers. Available from: https://www.cancer.gov/types/childhood-cancers [accessed March 2022]
2. Siegel Lamellar KD, Fuchs HE, Jemal A. Cancer Statistics. *CA: A Cancer Journal for Clinicians* 2021;**71**:7-33.
3. Ferlay J, Shin HR, Bray F, Forman D, Mathers C, Parkin DM. Estimates of worldwide burden of cancer in 2008: GLOBOCAN 2008.*Int J Cancer* 2010; **127**: 2893-917.
4. Magrath I, Steliarova-Foucher E, Epelman S, Ribeiro RC, Harif M, Li CK, et al. Paediatric cancer in low-income and middle-income countries. *Lancet Oncol* 2013;**14**:e104-16.
5. MOHFW. National cancer control strategy and Pan of action 2009-2015. Bangladesh: Directorate General of Health Services, Ministry of Health and Family Welfare; 2008.
6. Hussain S, Zaman M. National Cancer Control Strategy and Plan of Action 2009-15. Available from: https://dghs.gov.bd/bn/licts_file/images/Strategy/2009_NationalCancerControlStrategy 2009-15.pdf [cited 29 March 2022].
7. Hossain MS, Ferdous S, Karim-Kos HE. Breast cancer in South Asia: a Bangladeshi perspective. *Cancer Epidemiol* 2014;**38**:465-70.
8. Hossain MS, Iqbal MS, Khan MA, Rabbani MG, Khatun H, Munira S, et al. Diagnosed hematological malignancies in Bangladesh - a retrospective analysis of over 5000 cases from 10 specialized hospitals. *BMC Cancer* 2014;**14:**438.
9. The Daily Star. Cancer affects 13,000 children in Bangladesh every year: experts. Feb 24, 2018. Available from: https://www.thedailystar.net/health/paediatricians-at-an-international-conference-says-cancer-affects-13000-children-in-bangladesh-every-year-experts-1539418 [cited 8 Feb 2022].
10. Rahman S, Otim M, Almarzouqi A, Rahman S. Setting Priorities in Childhood Cancer in Low-Income Countries Using Nominal Group Technique: Experience from an International Childhood Cancer Forum Exercise in Bangladesh. *Asian Pacific Journal of Cancer Prevention* 2019;**20**:97-103.
11. World child cancer. Country profile: Bangladesh. UK, 2022. [Internet] last updated Nov 2020. Available from: https://worldchildcancer.org/bangladesh/#:~:text=It's%20estimated%20that%20 around% 209%2C000,these% 20children%20ever%20access% 20it [cited 22 Feb, 2022].
12. Carroll WL, Bhatla T. Acute lymphoblastic leukemia. In: Lanzkowsky P, Lipton J, Fish JD, editors. Lanzkowsky's Manual of Pediatric Hematology and Oncology. 6th ed. USA: Elsevier;2016:367-410.
13. Linabery AM, Ross JA. Trends in childhood cancer incidence in the US (1992–2004). Cancer: Interdisciplinary. *Int J Am Cancer Soc* 2008;**112**:416-32.
14. Desandes E, Clavel J, Berger C, Bernard JL, Blouin P, de Lumley L, et al. Cancer incidence among children in France,1990-1999. *Pediatr Blood Cancer* 2004; **43**:749-57.
15. Stack M, Walsh PM, Comber H, Ryan CA, O'Lorcain P. Childhood cancer in Ireland: A Population-based Study. *Arch Dis Child* 2007;**92**:890-97.
16. Spix C, Eletr D, Blettner M, KaatschP.Temporal trends in the incidence rate of childhood cancer in Germany 1987-2004. *Int J Cancer* 2008;**122**:1859-67.
17. Bao PP, Zheng Y, Gu K, Wang CF, Wu CX, Jin F, et al. Trends in childhood cancer incidence and mortality in urban Shanghai, 1973-2005. *Pediatr Blood Cancer* 2010;**54**:1009-13.
18. Swaminathan R, Rama R, Shanta V. Childhood cancers in Chennai, India, 1990-2001: incidence and survival. *Int J Cancer* 2008;**122**:2607-11.
19. Wiemels J. Perspectives on the causes of childhood leukemia. *ChemBiol Interact* 2012;**59**:196.
20. Arora RS, Eden T, Kapoor G. Epidemiology of childhood cancer in India. *Indian J Cancer* 2009;**46**:264e73.
21. Ward E, DeSantis C, Robbins A, Kohler B, Jemal A. Childhood and adolescent cancer statistics, 2014. *CA: A Cancer Journal for Clinicians* 2014;**64**:83-103.
22. Rodriguez-Galindo C, Friedrich P, Morrissey L, Frazier L. Global challenges in pediatric oncology. *Current Opinion in Pediatrics* 2013;**25**:3-15.

23. Khasru AA. Childhood Cancer: A Situation Analysis and Challenges, Bangladesh Perspective. *BJCH* 2018;**41**:140-42.

24. Hossain M, Begum M, Mian M, Ferdous S, Kabir S, Sarker H, et al. Epidemiology of childhood and adolescent cancer in Bangladesh, 2001-2014. *BMC Cancer* 2016;**16:**104.

25. Kamrul Hasan. Childhood cancer treatment remains inadequate. Dhaka Tribune [Internet]. 16 Feb 2017. Available from: https://www.dhakatribune.com/bangladesh/2017/02/16/childhood-cancer-treatment-remains-inadequate [cited 30 Dec 2021].

26. Islam A, Eden T. Brief report on pediatric oncology in Bangladesh. *South Asian J Cancer* 2013;**2:**105-06.

27. Howard SC, Metzger ML, Wilimas JA, Quintana Y, Pui CH, Robison LL, Ribeiro RC. Childhood cancer epidemiology in low-income countries. *Cancer* 2008;**112**:461-72.

28. World Bank. Indicator for childhood cancer. 2020. Available from: http://data.worldbank.org/indicator/SH.DYN.MORT [Accessed 14 Jan 2022]

29. Registrar General of India. Summary Report on Causes of Death: 2001 2003 in India. New Delhi, India: Office of the registrar general and ministry of home affairs; [cited on Oct 2021] Available from: http://www.cghr.org/wordpress/wp-content/uploads/Causes_of_death_2001-03.pdf.

30. Gupta S, Morris S, Suraweera W, Aleksandrowicz L, Dikshit R, Jha P. Childhood Cancer Mortality in India: Direct Estimates From a Nationally Representative Survey of Childhood Deaths. *Journal of Global Oncology* 2016;**2**:403-11.

31. Ferdousi S, Nahar K, Moslem MM, Elahi EQ, Islam A. Incidence and outcome of childhood cancer in Bangladesh armed forces. *Bangladesh Armed forces Med J* 2021;**54**:19-27.

32. Global Cancer Data: GLOBOCAN 2018. IARC; Geneva, Switzerland. updated12 Sep 2018. [Last accessed Dec 2022]. Available from: https://www.uicc.org/news/global-cancer-data-globocan-2018#:~:text=What%20is%20GLOBOCAN%3F,for%20all% 20cancer %20sites%20 combined

33. Jabeen S, Haque M, Islam MJ. Profile of Paediatric Malignancies: A Five Year Study. *J Dhaka Med Coll* 2010;**19**:33-38.

34. Baade P, Youlden D, Valery P, Hassall T, Ward L, Green A, et al. Trends in the incidence of childhood cancer in Australia, 1983-2006. *British Journal of Cancer* 2010;**102**:620-26.

35. Ba-Saddik IA. Childhood cancer in Aden, Yemen. *CancEpidemiol* 2013;**37**:803e6.

36. Mousavi SM, Pourfeizi A, Dastgiri S. Childhood cancer in Iran. *J PediatrHematolOncol* 2010;**32**: 376e82.

37. Abuidris DO,Ahmed ME, Elgaili EM, Arora RS. Childhood cancer in Sudan: 1999-2007. *Trop Doct* 2008;**38**:208-10.

38. Al-Sheyyab M, Bateiha A, Kayed SE, Hajjawi B. The incidence of childhood cancer in Jordan: A population-based study. *Ann Saudi Med 2003*;**23**:260-63.

39. Hossain MJ, Xie L. Sex disparity in childhood and young adult acute myeloid leukemia (AML) survival: Evidence from US population data. *Cancer Epidemiol* 2015;**39**:892-900.

40. Bethesda, MD: National Cancer Institute. Key Statistics for Childhood Leukemia. Available from: https://www.cancer.org/cancer/leukemia-in-children/about/key-statistics.html [cited Jan 2022]

41. Madhumathi DS, Prasannakumari, JayadevaNaik, Appaji L, Arunakumari B, V LD. Optimised panel for characterisation of pediatric ALL in a tertiary cancer centre from a developing country: Initial experience with literature review. *Int J Human Pathol Res* 2015;**1**:1-10.

42. Fadoo Z, Nisar I, Yousuf F, Lakhani LS, Ashraf S, Imam U, et al. Clinical features and induction outcome of childhood acute lymphoblastic leukemia in a lower/middle income population: A multi-institutional report from Pakistan. *Pediatric Blood Cancer* 2015;**62**:1700-1708.

43. Iqbal Z. Molecular Genetic Studies on 167 Pediatric ALL Patients from Different Areas of Pakistan Confirm a Low Frequency of the Favorable Prognosis Fusion Oncogene TEL-AML1. *Asian Pacific J Cancer Prevent* 2014;**15**:1.

44. Tipu HN, Muhammad MB, Altaf C, Noman M, Malik HS. The spectrum of acute leukemias and aberrant markers expression based on flow cytometry in a tertiary care center. *Pak Armed Forces Med J* 2018;**68**:450-54.

45. Khan S, Mir A, Khattak B, Rehman A, Zeb A. Childhood Leukemias in Khyber Pakhtunkhwa and Afghan Children Visiting to Hayatabad Medical Complex Hospital. *Arch Can Res* 2017;**5**:149.

46. rózek K, Heinonen K, Bloomfield CD. Clinical importance of cytogenetics in acute myeloid leukemia. *Best Pract Res Clin Haematol* 2001;**14**:19-47.

47. Nucifora G, Rowley JD. The AML1 and ETO genes in acute myeloid leukemia with a t(8;21). *Leuk Lymphoma* 1994;**14**:353-62.

48. Lazic J, Tosic N, Dokmanovic L, Krstovski N, Rodic P, Pavlovic S, Janic D. Clinical features of most common fusion genes in childhood acute lymphoblastic leukemia. *Med Oncol* 2010;**27**:449-53

49. deThé H, Chomienne C, Lanotte M, Degos L, Dejean A. The t(15;17) translocation of acute promyelocytic leukemia fuses the retinoic acid receptor alpha gene to a novel transcribed locus. *Nature* 1990;**347**:558-61.

50. Kim M, Lee SA, Park HI, Oh EJ, Park CW, Lim J, et al. Two distinct clonal populations in acute promyelocytic leukemia, one involving chromosome 17 and the other involving an isochromosome 17. *Cancer Genet Cytogenet* 2010;**197**:185-88.

51. Gamerdinger U, Teigler-Schlegel A, Pils S, Bruch J, Viehmann S, Keller M, et al. Cryptic chromosomal aberrations leading to an AML1/ETO rearrangement are frequently caused by small insertions. *Genes Chromosomes Cancer* 2003;**36:**261-72.

52. Nucifora G, Rowley JD. The AML1 and ETO genes in acute myeloid leukemia with a t(8;21). *Leuk Lymphoma* 1994;**14**:353-62.

53. Burjanivova T, Madzo J, Muzikova K, Meyer C, Schneider B, Votava F, et al. Prenatal origin of childhood AML occurs less frequently than in childhood ALL. *BMC Cancer* 2006;**6**:100-7.

54. Ross JA, Spector LG, Robison LL, Olshan AF. Epidemiology of leukemia in children with Down syndrome. *Pediatr Blood Cancer* 2005;**44**:8-12.

55. Margolin J, Rabin KR, Steuber CP, Poplack, DG. Acute lymphoblastic leukemia. In: Pizzo PA, Poplack DG, editors. Principles and Practice of Pediatric Oncology. 6th ed. Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins; 2010:518- 565.

ORIGINAL ARTICLE

Outcome of Bubble CPAP in Neonate with Respiratory Distress

Sabrina Afrin[1], Mahfuza Shirin[2], Farid Ahmed[3], Mohammad Abdullah Al Mamun[4]

Abstract

Background: *Continuous Positive Airway Pressure (CPAP) is a well-established mode of respiratory support in newborns. Bubble CPAP (bCPAP) is safe, efficacious and easy to use in preterm and term neonates with mild to moderate respiratory distress.*

Objectives: *To find out the outcome of bCPAP in neonate with respiratory distress.*

Methods: *This cross sectional study was conducted over 6 months in Bangladesh Shishu Hospital & Institute. Total 108 term and preterm neonates were enrolled who were presented with respiratory distress. Neonate with type II respiratory failure, congenital heart disease and structural malformations of lung and GI tract causing respiratory distress at birth and neonate needed intubatuin at birth were excluded. Detailed information were obtained in each case. Thorough clinical examinations were done. Relevant investigation reports were collected. All the information were recorded. Statistical analysis was done by using SPSS version 23.*

Results: *In this study the mean age was found 43.3±43.1 hours with range from 2 to 204 hours. Majority 62(57.4%) patients were male and male female ratio was 1.3:1. Two third (66.7%) patients had birth weight ≥2500 gm, 14(12.9%) had <1499 gm and 22(20.4%) patients had birth weight 1500-2499 gm. Majority (59.3%) patients belonged to gestational age between 37-41 wks, followed by 27(25%) belonged between 33-36 wks and 17(15.7%) belonged between 28-32 wks. Among the enrolled cases 18(16.7%) were RDS, 18(16.7%) were PNA, 14(13%) were PPHN, 9(4.3%) were MAS, 6(5.6%) were TTN, 13(12%) were congenital Pneumonia, 15(13.9%) were Pneumonia, 10(9.3%) were Sepsis and 5(4.6%) were Laryngomalacia. Among 108 patients who were put on bCPAP, 85(78.7%) patients were weaned and 23 (21.3%) were failed and needed mechanical ventilation. Out of 85 weaned patients hundred percent were survived and got discharge. Out of 23 failed cases 16(69.6%) cases were died and 7 (30.4%) cases were survived and got discharge.*

Conclusion: *It is concluded from this study that bCPAP is an effective way of management of neonates with respiratory distress due to various causes. Patients who were failed in bCPAP, died more in final outcome.*

Keywords: *Bubble CPAP, outcome, respiratory distress.*

DS (Child) HJ 2022;38(1):27-33
DOI: https://doi.org/10.3329/dshj.v38i1.66998

1. Registrar in-Charge, Bangladesh Shishu Hospital & Institute, Sher-e- Bangla Nagar, Dhaka- 1207.
2. Associate Professor, Bangladesh Shishu Hospital & Institute, Sher-e- Bangla Nagar, Dhaka- 1207.
3. Professor and Head, Department of General Peadiatrics, Bangladesh Shishu Hospital & Institute.
4. Associate Professor, Department of Paediatric Cardiology, Bangladesh Shishu Hospital & Institute, Sher-e- Bangla Nagar, Dhaka- 1207.

Correspondence to: Dr. Sabrina Afrin, Registrar in charge, Bangladesh Shishu Hospital & Institute, Sher-e- Bangla Nagar, Dhaka- 1207. Cell: +88 01711070748**,** E-mail: safrin.k59@gmail.com
Received: 7 February 2022; **Accepted**: 17 April, 2022

Introduction

Respiratory distress occurs in 0.96-12% of life birth and is responsible for about 20% of neonatal mortality.[1] It is the most common presenting problem of newborn encountered within the first 48-72 hours of life and remains the primary indication for admission to neonatal intensive care unit to combat respiratory failure.[1]

Continuous Positive Airway Pressure (CPAP) is a well-established mode of respiratory support in newborns. Advancement in technology, increasing survival of extremely preterm newborns and better understanding of various respiratory diseases led to new evidence in this field over last decade.[2] Other than RDS, during post-extubation, apnoea of prematurity CPAP may be useful in conditions that result in alveolar collapse or airway narrowing. It relieves the signs of cardiac failure due to patent ductus arteriosus. Similarly, it is often used in the management of pneumonia, transient tachypnea of newborn, postoperative respiratory management, pulmonary edema and pulmonary hemorrhage. In meconium aspiration syndromes (MAS), application of CPAP can be beneficial by resolving the atelectatic alveoli due to alveolar injury and secondary surfactant deficiency.[3]

It can be applied via a face mask, nasopharyngeal tube, or nasal prongs, using a conventional ventilator, bubble circuit or a CPAP driver. Bubble CPAP is one of the lowcost nasal CPAP delivering systems, with underwater seal. CPAP delivered by underwater seal causes vibration of the chest due to gas flow under water; and these vibrations simulate waveforms produced by high frequency ventilation.[4]

Gregory et al[5] first pioneered the use of bCPAP in Neonatology with their landmark paper in the 70s in Columbia. bCPAP differs from conventional CPAP in that in bCPAP the expiratory limb is placed under water and oscillatory vibrations are transmitted into the chest resulting in waveforms similar to those produced by high-frequency ventilation.[6]

Conventionally neonates with respiratory distress are managed by respiratory support with positive pressure ventilation (delivered usually by mechanical ventilator) and surfactant replacement therapy.[7] In study of Verder et al[8] in 1994, remarkably reduced the need for mechanical ventilator from 85% to 41% in the neonate. In the developed world mechanical ventilator and CPAP machines are the mainstays of respiratory support in neonates but these machines are too expensive and many resources constrained in low socioeconomic countries.[7] The effectiveness of locally adapted bCPAP has been documented.[9,10] bCPAP is a simple and cost effective respiratory support system (RSS) which consists of products that are easily available and health care provider can easily be trained to make and use this RSS.[9] bCPAP is as effective as the other forms of CPAP, and can reduce the CPAP failure rate and the length of hospital stay.[11] bCPAP prevents the alveolar collapse and ensures gas exchange throughout the respiratory cycle and allows the lung inflation to be maintained. It can be effectively given through the nasal prongs which eliminate the need for the endotracheal intubation.[12]

bCPAP circuits consisted of inspiratory limb, the interface (nasal prongs) and the proximal part of the expiratory limb. The proximal end of the inspiratory limb connects the humidified oxygen source (wall piped oxygen) through the interface to the baby.[9] These tubes are carefully secured with an adhesive plaster to ensure that the length immersed in water remains constant.[9] The bCPAP generator is a cylindrical, transparent bottle filled to predetermined level with distilled water. The expiratory limb of the circuit is immersed in this bottle and the depth of the immersion in centimeters below the water surface correspond to the desired bCPAP in cm H_2O usually between 5 cm to 8 cm of H_2O.[9] This provides positive pressure in the whole respiratory cycle, increases the functional residual capacity of lungs and lowers work of breathing.[10] Ultimately, bCPAP reduces the need for mechanical ventilation, morbidity, mortality.[13] Many studies have been shown that locally manufactured bCPAP system showed promising results.[14] bCPAP is more acceptable because of its simplicity, low cost and yet a powerful and effective technique of respiratory support, particularly suitable for neonatal units with limited resources.[15] But there is a paucity of studies on bCPAP in Bangladesh. In this study, we intend to observe outcome of bCPAP in the management of neonates with respiratory distress.

Materials and Methods

This Cross-sectional study was conducted in the Department of Neonatal Medicine, Bangladesh Shishu (Children) Hospital and Institute, Dhaka, Bangladesh from April 2017 to September 2017. Neonate with respiratory distress admitted at the department of Neonatology in Bangladesh Shishu (Children) Hospital & Institute were enrolled. Inclusion criterias were both term and preterm neonates presented with respiratory distress having two or more of the findings- respiratory rate >70/min, Grunting respiration, cyanosis, moderate or severe intercostals, supraclavicular, suprasternal retractions, oxygen saturation in pulse oxymeter <85%. Exclusion criteria were neonate with type II respiratory failure, congenital heart disease and structural malformation of lungs and GI tract causing respiratory distress at birth and neonate needed intubatuin at birth.

After obtaining written informed consent from parent/guardian, relevant information was recorded in predesigned proforma which includes particulars of the patient such as age on admission, sex, birth weight, gestational age and mode of delivery. Then examination findings such as weight, length, OFC, heart rate, respiratory rate, temperature, CRT, conciousness status, pallor, jaundice, cyanosis, dehydration, chest retraction, tone, primitive reflexes were also noted. Oxygen saturation was seen by using pulse oxymetry. Requirement of inotrop was recorded. Investigation findings such as RBS, CXR and ABG were also recorded. After fulfillment of enrollment criteria patients were put into bCPAP and monitoring was done clinically, with pulse oxymetry and ABG for requirement of change in settings, to see failure and outcome. Weaning was done in absence of respiratory distress (Minimal or no retraction and respiratory rate between 30 and 60 per min) and SpO_2>90% with PEEP <5 cm of H_2O and FiO_2 <50%. Failure of bCPAP was considered when neonate remained hypoxic with SpO_2<87% with FiO_2 >70% and PEEP >7cm of H_2O, had severe retractions on PEEP >7cm of H_2O, PO_2<60 mmHg, PCO_2>60 mm Hg and pH <7.25 on maximum acceptable settings, had prolonged (>20 seconds) or recurrent apneas (>2 episodes within 24 hours associated with bradycardia) requiring bag and mask ventilation, had severe metabolic acidosis or shock requiring inotropic support (dopamine and or dobutamine) >20ìg/kg/min. Those who were weaned were observed for final outcome whether those were survived and discharged or died. Those who failed bCPAP were identified and their outcome was noted. Factors responsible for failure were also noted. Permission was taken from ethical review committee, Bangladesh Institute of Child Health.

Statistical analyses were carried out by using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The mean values were calculated for continuous variables. The quantitative observations were indicated by frequencies and percentages. Chi-Square test and Fisher's exact test was used to analyze the categorical variables, shown with cross tabulation. Unpaired t-test and paired t-test was used to analyze the continuous variables. P values <0.05 was considered as statistically significant.

Results

Total 108 neonates were enrolled. Majority (45.4%) patients belonged to age ≤24 hours. The mean age was found 43.3±43.1 hours with range from 2 to 204 hours. Among them majority (57.4%) patients were male and 46(42.6%) patients were female. Male female ratio was 1.3:1. Regarding birth weight of the study patients, it was observed that two third (66.7%) patients had birth weight ≥2500 gm, 14(12.9%) had <1499 gm and 22(20.4%) patients had birth weight 1500-2499 gm. Regarding gestational age, it was observed that majority (59.3%) patients belonged to gestational age between 37-41 weeks, followed by 27(25%) between 33-36 weeks and 17(15.7%) between 28-32 weeks of gestation. It was also observed that majority (58.3%) patients were delivered by LUCS and 45(41.7%) were by NVD. (Table I). Among the neonates with respiratory distress who needed bCPAP support 18(16.7%) had RDS, 18(16.7%) had PNA, 15(13.9%) had Pneumonia and 14(13.0%) had PPHN (Table II).

Table I
Distribution of the study patients by age, sex, birth weight, gestational age and mode of delivery

Variables	Number	Percentage	
Age (in hour)			
≤24	49	45.4	Mean ±SD:
25-48	23	21.3	43.3 + 43.1
49-72	15	13.9	Range
>72	21	19.4	(min-max):
Sex			2-204
Male	62	57.4	
Female	46	42.6	
Birth weight (gm)			
<1499	14	12.9	
1500-2499	22	20.4	
≥2500	72	66.7	
Gestational Age (wk)			
28-32	17	15.7	
33-36	27	25.0	
37-41	64	59.3	
Mode of delivery			
NVD	45	41.7	
LUCS	63	58.3	

Table II
Distribution of the study patients according to diagnosis (n=108)

Diagnosis	Number	Percentage
RDS	18	16.7
PNA	18	16.7
PPHN	14	13.0
MAS	9	8.3
TTN	6	5.6
Cong. Pneumonia	13	12.0
Pneumonia	15	13.9
Sepsis	10	9.3
Laryngomalacia	5	4.6

Table III
Distribution of the study patients according to outcome of bCPAP (n=108)

Outcome of bCPAP	Number	Percentage
Wean	85	78.7
Failure	23	21.3

Table III shows outcome of bCPAP of the study patients, it was observed that out of 108 patient more than three fourth (78.7%) patients were found successfully weaned and 23(21.3%) were failed.

Table IV shows neonatal variables like age, sex, birth weight and gestational age which were not statistically significant (p>0.05) when compared with outcome of bCPAP.

Table V shows out of 23 failure cases who were put into mechanical ventilation, 16(69.6%) cases were died and 7(30.4%) cases were survived and got discharge. All (100.0%) patients were survived and got discharge in weaned group. The difference was statistically significant (p<0.05) between two groups. That means among the patients who were failed in bCPAP, died more in final outcome.

Table IV
Association of neonatal variables with outcome of bCPAP (n=108)

Variables	Outcome of bCPAP		p value
	Wean Mean (±SD)	Failure Mean (±SD)	
Age	56.11±44.58	71.83±48.42	0.14^{ns}
Sex (Male/Female)	49/3658/42 %	13/10 56/44 %	1.0^{ns}
Birth weight	2461.17±616.84	2417.39±578.12	0.76^{ns}
Gestational age	36.47±3.44	36.52±3.72	0.95^{ns}

ns = Not significant

Table V
Association between outcome of bCPAP with final outcome (n=108)

Final outcome	Weaned (n=85)		Failed (n=23)		p value
	n	%	n	%	
Discharge	85	100.0	7	30.4	0.001[s]
Death	00	0.0	16	69.6	

s= significant
p value reached from chi square test

Discussion

In this study it was observed that majority (45.4%) patients belonged to age ≤24 hours. The mean age was found 43.3±43.1 hours with range from 2 to 204 hours. Similar observation was found Soomro et al[16] study they reported that the mean age of enrolled infants was 1.35±0.60 days.

In this study it was observed that majority (57.4%) patients were male and 46(42.6%) patients were female. Male female ratio was 1.3:1. Similar result was found different studies, in study of Arora et al.[17] study observed that 66% were males and 34% were female. Soomro et al[16] study also observed that 70(57.9%) were males and 51(42.1%) were female.

In this study majority (59.3%) patients belonged to gestational age between 37-41 wks, followed by 27(25%) belonged between 33-36 wks and 17(15.7%) belonged between 28-32 wks of gestation.

In this series it was observed that majority (58.3%) patients belonged to LUCS group and 45(41.7%) belonged to normal delivery group. Arora et al[17] study found 30(17.6%) patients belonged to LUCS group and 140(82.4%) belonged to NVD group. Sharba et al[18] study observes 23(54.7%) patients in success group and 12(57.1%) in failed CPAP group were delivered by LUCS. The difference was not statistically significant (p>0.05) between two groups.

In this study it was observed that 18(16.7%) had RDS, 18(16.7%) had PNA, 15(13.9%) had Pneumonia and 14(13.0%) had PPHN. So, according to this study, the most common causes for starting bCPAP in neonate with respiratory distress are RDS, PNA, PPHN, pneumonia, congenital pneumonia, MAS, TTN, sepsis and laryngomalacia. Sethi et al[4] observed, the most common disease for starting bCPAP was RDS (80%) followed by pneumonia (17%), TTNB (0%) and MAS (2%). In Soomro et al[16] study 96 (79.3%) had subcostal recession and 81 (66.9%) had typical X-ray findings of RDS. Mathai et al[19] observed the most common disease for starting b-CPAP was RDS (n = 32) followed by pneumonia (n = 8), TTNB (n = 6) and Apnoea (n =4). In my study PNA is as equally responsible as RDS for causing respiratory distress in neonate. But in other studies, only RDS is the major cause. This may be due to irregular ANC, poverty, illiteracy, negligence, delay in intervention etc.

In this study it was observed that more than three fourth (78.7%) patients were weaned successfully and 23(21.3%) were failed. These 23 patients were put into mechanical ventilator out of which 7 were survived and got discharge and 16 were died finally. The patients who were weaned successfully, among them 100% survived and got discharged. Soomro et al[16] observed that overall 77 (63.6%) preterm infants were successfully weaned off from bCPAP. Arora et al[17] observed 118(69.4%) patients were found successfully weaned and 52(30.6%) were failed. Mathai et al[19] showed overall survival rate of the study population was 94%. Sethi et al[4] observed that 51 patients were put on bCPAP and out of them 60% were weaned successfully while other were intubated and was considered in failure group. Sharba et al[18] observed that 42 (66.67%) newborns were survived and weaned successfully from CPAP and 21 (33.33%) failed to weaned from CPAP and turn to mechanical ventilation.

Here neonatal variables like age, sex, birth weight and gestational age were not statistically significant (p>0.05) when compared with outcome of bCPAP. Soomro et al[16] found the mean age was 1.32±0.5 days in failure group and 1.36±0.6 days in success group. The difference was not statistically significant (p>0.05) between two groups. Soomro et al[16] had similar observation that 42(54.5%) were male in

failure group and 46(59.7%) in success group. The difference was not statistically significant (p>0.05) between two groups. Arora et al[17] observed, 78(66.1%) were male in success group and 34(65.4%) in failure group.

Regarding final outcome of the study patients, it was observed that majority (78.7%) patients were improved and 23(21.3%) needed mechanical ventilation. So, bCPAP is very much effective for the neonates with respiratory distress who fulfill the enrollment criteria. Because, it improves oxygenation and decreases chest retraction, tachypnoea and granting respiration by decreasing work of breathing.

Sharba et al[16] observed that 42 (66.67%) newborns were survived and weaned successfully from CPAP and 21 (33.33%) failed to weaned successfully from CPAP and turn to mechanical ventilation.

In current study, it was observed that, out of 23 failure cases that were put into mechanical ventilation, 16(69.6%) cases were died and 7(30.4%) cases were survived and got discharge. All (100.0%) patients were survived and got discharge in weaned group. The difference was statistically significant (p<0.05) between two groups. That means among the patients who were failed in bCPAP, died more in final outcome. Koti et al[12] showed 1(2.4%) patient died in weaned group and 5(35.7%) in failed group. The difference was statistically significant (p<0.05) between two groups. Sharba et al[18] also observed 2(4.7%) patients were died in weaned group and 16(76.19%) in failed group. The difference was statistically significant (p<0.05) between two groups.

Conclusion

It is concluded from this study that bCPAP is an effective way of management of neonates with respiratory distress due to various causes. Patients who were failed in bCPAP, died more in final outcome.

References

1. Neonatal morbidity and mortality: Report of the National Neonatal-Perinatal Database. *Indian Pediatr* 1997;**34**:1039-42.
2. Gupta N, Saini SS, Murki S, Kumar P, Deorari A. Continuous Positive Airway Pressure in Preterm Neonates: An Update of Current Evidence and Implications for Developing Countries. *Indian Pediatr* 2015;**52**:319-28.
3. Goldsmith JP. Continuous positive airway pressure and conventional mechanical ventilation in the treatment of meconium aspiration syndrome. *J Perinatol* 2008;**28**:S49-55.
4. Sethi A, Mehta NJ, Surti BM, Gamit D, Tada N. Safety and effectiveness of bubble continuous positive airway pressure in neonates with respiratory distress and its failure factors. *Natl J Med Res* 2015;**5**:202-06.
5. Gregory GA, Kitterman JA, Phibbs RH. Treatment of the idiopathic respiratory distress syndrome with continuous positive airway pressure. *N Engl J Med* 1971;**284**:1333e1340.
6. Lee KS, Dunn MS, Fenwick M, Shennan AT. A comparison of underwater bubble CPAP with ventilator derived CPAP in premature neonates ready for extubation. *Biol Neonate* 1998;**73**:69-75.
7. Kamath BD, Mac Guire ER, Mc Clure EM, Goldenberg RL,Jobe AH. Neonatal Mortality from Respiratory Distress Syndrome: Lessons for Low-Resource Countries. *Pediatrics* 2011;**127**:1139-46.
8. Verder H, Robertson B, Greisen G, Ebbesen F, Albertsen P, Lundstrom K, et al. Surfactant therapy and nasal continuous positive airway pressure for newborn with respiratory distress syndrome. *N Engl J Med* 1994;**331**:1051-55.
9. Kaur C, Sema A, Beri RS, Puliyel JM. A simple circuit to deliver Bubble CPAP. *Indian Pediatr* 2008;**45**: 312-14.
10. Chan KM, Chan HB. Te use of Bubble CPAP in preterm infants: Local experience. *HK J Paediatr* 2007;**12**:86-92.
11. Wang TF, Dang D, Liu JZ, Du JF, Wu H. Bubble CPAP for Preterm Infants with Respiratory Distress: A Meta-analysis. *HK J Paediatr* 2016;**21**:86-92.
12. Koti J, Murki S, Gaddam P, Reddy A, Reddy MDR. Bubble CPAP for respiratory distress syndrome in preterm infants. *Indian Peditr* 2010;**47**:139-43.
13. Courtney SE, Pyon KH, Saslow JG, Arnold GK, Pandit PB, Habib RH. Lung recruitment and breathing pattern during variable versus continuous flow nasal continuous positive airway pressure in preterm infants: an evaluation of three devices. *Pediatr* 2001;**107**:304-08.
14. Koyamaibole L, Kado J, Qovu JD, Colquhoun S, Duke T. An evaluation of bubble-CPAP in a neonatal unit in a developing country: Effective respiratory support that can be applied by nurses. *J Trop Pediatr* 2006;**52**:249-53.

15. Sahni R. Bubble CPAP: Can We Predict Success or Failure?. *Indian Pediatr* 2010;**47**:129-30.

16. Soomro T, Tikmani SS. Success of Bubble CPAP in treatment of respiratory distress syndrome in preterm Infants. *J Gen Pract* 2016;**4**:1-4.

17. Arora V, Gediya SG, Jain R. Outcome of premature babies with RDS using bubble CPAP. *Int J Contemp Pediatr* 2017;**4**:939-42.

18. Sharba SAZ, Umran RMR, Jumaa A. Bubble Nasal CPAP in the Management of Respiratory Distress Syndrome (One Year Experience in Low Resources Unit). *Medical Journal of Babylon* 2013;**10**: 809-16.

19. Mathai SS, Rajeev A, Adhikari KM. Safety and effectiveness of bubble continuous positive airway pressure in preterm neonates with respiratory distress. *Med J Armed Forces India* 2014;**70**:327-31.

ORIGINAL ARTICLE

Epidemiological Profile of Typhoid Fever Cases Admitted in A Tertiary Care Hospital at Dhaka City

Rabi Biswas[1], Md Rafiqul Islam[2]

Abstract

Background: *Enteric fever is a major public health problem in many developing countries including Bangladesh, where sanitation and public health standards are poor.*

Objectives: *To study the socio-demographic, some of the epidemiological features and knowledge about typhoid vaccine of the hospitalized children with typhoid fever.*

Methods*: This cross-sectional descriptive study was conducted in Bangladesh Shishu Hospital & Institute over a one year period from January to December, 2019. All diagnosed cases of Typhod fever admitted in Bangladesh Shishu Hospital & Institute, Dhaka fulfill the inclusion criteria were the study subjects. The informations were collected in a predesigned and pretested questionnaire which included sociodemographic data, family background and knowledge about Typhoid vaccine.*

Results: *A total of 86 children were enrolled in this study who were diagnosed to have typhoid fever during one year period. More than 90% of patients were aged between 1 and 10 years. Majority (90%) of the parents of affected children were unaware about availability of effective vaccine against typhoid fever. An association between literacy status, socioeconomic status, level of personal hygiene and occurrence of typhoid fever was found.*

Conclusion: *Public health interventions to minimize human carrier contact, improved personal hygienic measures and typhoid vaccination will help to reduce the morbidity and mortality of this global health problem.*

Keywords: *Typhoid fever, public health, children, Dhaka city.*

DS (Child) HJ 2022;38(1):34-38
DOI: https://doi.org/10.3329/dshj.v38i1.66999

Introduction

Typhoid fever is a commonly encountered systemic disease caused by the gram negative bacteria Salmonella enterica serover typhi[1], is both waterborne and foodborne, with an annual incidence approaching 1% in disease-endemic areas.[2-4] Salmonella infection is a major health problem globally specially in the developing countries of the tropics and subtropics, where sanitation and public health standards are poor.[5] Typhoid fever is endemic in the South-east Asian countries.[6,7] Above 22 million new cases occur each year around the world while 90% of the sufferers are from the South-East Asia. Reported deaths from typhoid fever accounts to around 2,16,000 per year.[8-11]

1. Associate Professor, Department of Paediatric Endocrinology and Metabolic Disorders, Bangladesh Shishu Hospital & Institute, Dhaka.
2. Assistant Professor, Department of Paediatric Endocrinology and Metabolic Disorders, Bangladesh Shishu Hospital & Institute, Dhaka.

Correspondence to: Dr. Rabi Biswas, Associate Professor, Department of Paediatric Endocrinology & Metabolic Disorders, Bangladesh Shishu Hospital & Institute, Sher-e-Bangla Nagar, Dhaka. Cell: +8801715287817, E-mail: rabibiswasdr@gmail.com

Received: 11 January 2022; **Accepted**: 9 May 2022

In Bangladesh, typhoid fever is a round the year problem which sometimes take epidemic proportions.[9,12] Enteric fevers are not a notifiable disease throughout Bangladesh and hence the correct incidence is not known. From the public health point of view the reason behind such occurrence are unsafe water supply, defective sewerage system and unhygienic food handling practice.[9,11,13-15]

There is a wide spectrum of clinical presentation and with the emergence of multidrug resistant typhoid now a days, the treatment has become still more complex. Its danger doesn't end when symptoms disappear as patient may turn into carrier state which may be a chronic one in which condition the person is excreting the bacilli for several years.[16] A combination of mass vaccination and improvement of water supplies has been suggested as a method to control epidemics in typhoid fever.[6-9]

We describe the epidemiological profile of typhoid fever from a tertiary care Pediatric hospital in Dhaka city, Bangladesh.

Materials and Methods

This is a hospital based cross-sectional descriptive study. It was conducted in Bangladesh Shishu Hospital & Institute [former Dhaka Shishu (Children) Hospital] to see the epidemiological profile of typhoid fever cases from January 2019 to December 2019. All cases of Typhod fever diagnosed by suggestive clinical picture and blood culture positive for Salmonella typhi organisms and/or Widal test +ve (Salmonella typhi O and H agglutinin titres > 1:80 and > 1:160 were considered to be significant)[16] admitted in a selected paediatric medicine unit of Bangladesh Shishu Hospital & Institute, Dhaka fulfill the inclusion criteria were the study subjects. The cases of enteric fever treated on OPD basis were not included in this study. There were total 86 cases of enteric fever admitted during this period. The informations were collected in a predesigned and pretested questionnaire which included sociodemographic data, family background and knowledge about Typhoid vaccine. The interview was taken by doctors from the attendants of the patients at the time of hospital stay after taking their informed consent.

Results

Total number of proved enteric fever cases admitted during the study period was 86. Age wise distribution showed that highest number of patients 51.2% were in 1-5years age group (pre-school children). A significant number were >5-10 years age group (Table I). Out of 86 cases, 62.8% patients were males and 37.2% were females. Male to female ratio was 1.7:1. Majority (67.4%) of the patients reside in urban area and rest 32.6% patients are in rural area.

Table I
Distribution of cases according to age

Age in year (N=86)	Patients (%)
<1 year	3(3.5)
1-5 years	35(40.7)
>5-10 years	44(51.2)
>10 years	4(4.7)

Distribution of literacy status and enteric fever cases (Table II) showed hat as literacy status increased, risk of getting enteric fever infection decreased.

Table II
Distribution of cases according to educational status of mother of the patients

Educational status	No. of patients (%)
Illiterate	38(44.18)
Primary	20(23.25)
High school	12(13.95)
S.S.C.	7(8.13)
Higher secondary school	6(6.97)
Graduate and higher	3(3.48)
Total	86(100.00)

Distribution of cases according to socioeconomic status showed that out of 86 cases, majority of patients 62.8% were from middle income group another 23.2% from poor group. Only 14% patients belonged to higher income group (Table III).

Table III
Distribution of cases according to socioeconomic status of the family

Monthly income (Taka)	No. of patients (%)
Poor group (<15,000)	20(23.2)
Middle income group (15,000-30,000)	54(62.8%)
Higher group (>30,000)	12(14)
Total	86(100.00)

Out of 86 respondents, 65.70% patients had poor personal hygiene and only 7.0% had good hygiene. It has been found that, as standard of personal hygiene were increased, there were less chances of enteric fever disease (Table IV).

Table IV
Levels of personal hygiene and enteric fever

Levels of personal hygiene	Total No (%)
Good	10(7.0)
Average	26(27.3)
Poor	50(65.7)
Total	86(100.00)

The distribution of enteric fever patients according to housing conditions showed that majority 58.1% had Semi Pacca and Kaccha house. Majority 79.1% had safe source of drinking water at home. Out of 86 cases, nearly two-third patients 65.1% are sanitary latrine user (Table V).

Table V
Distribution of cases according to housing conditions, source of drinking water and sanitation facilities

Housing condition	Patients (%)
Type of house	
Semi Pacca & Kaccha	50(58.1)
Pacca	36(41.9)
Source of drinking water at home	
Unsafe (Unboiled WASA &ponds water)	18(20.9)
Safe (Boiled WASA, tube well & filter water)	68(79.1)
Sanitation facilities	
Sanitary latrine user	56(65.1)
Non-sanitary latrine user	30(34.9)
Total	86(100.00)

Distribution of cases according to knowledge about Typhoid vaccine showed that only 9.3% parents were aware of availability of a vaccine against typhoid fever (Table VI).

Table VI
Distribution of cases according to knowledge about Typhoid vaccine

Know about vaccine	No. of patients (%)
Yes	8(9.3)
No	78(90.7)
Total	86(100.00)

Out of 86 patients, 97.7% were responded very well to treatment and recovered. None of the patients was died. Only two patients were discharged against medical advice and we failed to know their outcome.

Discussion

Out of 86 enteric fever cases, more than 90% were in the age group between 1-10 years, highest in >5-10 years age group (51%) and 41% in 1-5 years age group, as it is shown in other studies, where peak incidence is reported to occur in children 5-15 years of age; however, in regions where the disease is highly endemic, children <5 years of age may have among the highest infection rates.[4,17-20] The possible causes for enteric fever being common in this age group include their mobility, consumption of unhygienic food and water in schools. These observations were consistent with various studies.[21,22]

Males outnumbered the females giving M:F ratio of 1.7:1. This might be due to our cultural background where male is more likely to report to hospital, at same time more likely to contract infection outside the house. This finding was comparable with other studies.[23,24]

Among 86 patients, 38 mother (44.2%) were illiterate and 48 mothers (55.8%) were literate. A definite association was found between literacy status and occurrence of enteric fever. Enteric fever was more common among illiterate and low educational status people as is usually associated with ignorance, poverty and poor personal hygiene. This observation was consistent with study done by Corner RJ et al.[25]

The present study showed a higher number of typhoid cases are detected in lower socioeconomic status group. Several studies[23,25,26] also support the finding that enteric fever was more common in lower socioeconomic group. The low socioeconomic status usually goes parallel with poor standard of living and poor personal hygiene making persons more prone for enteric fever.[27]

Around 2/3rd (65.7%) of cases had poor personal hygiene. As standards of personal hygiene increased, risk of enteric fever decreased. Several studies support this finding.[13,15-17]

In housing conditions, about 2/3rd (65.7%) of patients had kaccha and semi pacca house. A study done by Gasem et al[28] also had similar observation. It is important that whether the house is pacca or kaccha, cleaniness is important as dirty and poor housing condition is associated with increased fly population and in turn enteric fever.

Although majority (79.1%) had source of safe drinking water at home and using sanitary latrine (65.1%), the school going children are more exposed to unsafe water at the restaurants and schools, which causing more exposed to typhoid infection as shown in a study that enteric fever was associated with lack of clean and safe water. This study has documented that knowledge of the parents regarding availability of vaccine against typhoid fever is very poor.[15] In this study, only 9% of the mothers know about it. It remains as an important factor for high prevalence of typhoid fever in our country.

Conclusion

Thus present study found majority of patients of typhoid were in 1-10 years (school children and adolescents) age group. Enteric in children occurs more in poor literacy, socioeconomic and personal hygiene status group of population.

Recommendations

1. The specific age group like school going children should be identified as high risk group and imparted health education towards prevention of enteric fever, especially regarding vaccine against typhoid.
2. Improving educational status of people and in cases of children, educational status of parents especially mothers should be increased regarding food and water borne diseases.
3. Purification of drinking water supplies at restaurants as well as promotion of food and personal hygiene should be improved.

References

1. Kliegman RM, St. Geme J. Nelson Textbook of Pediatrics, 21st ed. New Delhi: Elsevier Saunders; May, 2019. P.1186-90.
2. Keddy KH, Klugman K, Hansford CF, Blondeau C, Bouveret le Cam NN. Persistence of antibodies to the *Salmonella* typhi Vi capsular polysaccharide vaccine in South African school children ten years after immunization. *Vaccine* 1999;**17**:110-13.
3. Simanjuntak CH, Paleologo FP, Punjabi NH, Darmowigoto R, Soeprawoto, Totosudirjo H, et al. Oral immunisation against typhoid fever in Indonesia with Ty21a vaccine. *Lancet* 1991;**338**:1055-59.
4. Sinha A, Sazawal S, Kumar R, Sood S, Reddaiah VP, Singh B, et al. Typhoid fever in children aged less than 5 years. *Lancet* 1999;**354**:734-37.
5. Park K. Textbook of preventive and social medicine. 26th ed. Jabalpur: Banarsidas Bhonet Publishers; May, 2021.P.178-81.
6. Gupta MC, Mahajan BK. Text book of preventive and social medicine. 4th ed. New Delhi: Jaypee; 2013.P.202-5.
7. Crump JA, Mintz ED. Global trends in typhoid and paratyphoid fever. *Clin Infect Dis* 2010;**50**:241-46.
8. Crump JA, Luby SP, Mintz ED. The global burden of typhoid fever. *Bull World Health Organ* 2004;**82**:346-53.
9. Ochai RL, Acosta CJ, Danovaro-Holliday MC, Baiqing D, Bhattacharya SK, Agtini MD, et al. A study of typhoid fever in five Asian countries: disease burden and implication for controls. *Bull World Health Organ* 2008;**86**:260-68.
10. Pandey KK, Srinvasan S, Mhadevan S. Typhoid fever below five years. *Indian Pediatr* 1990;**27**:153-56.
11. Parry CM, Hein TT, Dordon D, White NJ, Fanar JJ. Typhoid fever. *N Engl J Med* 2002;1770-82.
12. Parry CM, Threlfall EJ. Antimicrobial resistance in typhoidal and nontyphoidal salmonellae. *Curr Opin Infect Dis* 2008;**21**:531-38.
13. Rahman M, Siddique AK, Tam FC, Sharmin S, Rashid, H, Iqbal A, et al. Rapid detection of early typhoid fever in endemic community children by the TUBEX 09-antibody test. *Diagn Microbiol Infect Dis* 2007;**58**:275-81.
14. World Health Organization. Department of Vaccines and Biologicals. Background document: the diagnosis, treatment and prevention of typhoid fever. Geneva, Switzerland. 2003.P.19-23.
15. Ananthnarayan R, Jayaram Panikar CK. Textbook of Microbiology. 11th ed, April 2021.P. 279-89.

16. Saha SK, Ruhul Amin M, Hanif M, Islam M, Khan WA. Interpretation of the Widal test in the diagnosis of typhoid fever in Bangladeshi children. *Ann Trop Paediatr* 1996;**16**:75-78.

17. Samal KK, Sahu CS. Malaria and Widal reaction. *JAPI* 1991;**39**:74-76.

18. Kuppuswami B. Manual of Socioeconomic scale (Urban), Manasayan, 32, Netaji Subhash Marg, New Delhi, 1981, 6.

19. Letter from office of Assistant Labour Commissioner, Solapur, issued to Solapur Janata Sahakari Bank, Letter no. ACL/index/2845, Assistant Labour Commissioner, dated 1-3-2002.

20. Brooks WA, Hossain A, Goswami D, Sharmeen AT, Nahar K, Alam K, et al. Bacteremic Typhoid fever in Children in an Urban Slum, Bangladesh. *Emerging Infectious Disease* 2005;**11**:326-29.

21. Mangal HN, Joshi KC, Gupta DP. Prevalence of Enteric fever in Jaipur. *Indian J Med Res* 1967,**55**: 219-23.

22. Saha S, Saha S, Das RC, Faruque ASG, Salam MA, Islam M, Saha SK. *Am J Trop Med Hyg* 2018; **99**(3 Suppl):20-25.

23. Sood SC, Taneja PN. Typhoid fever, Clinical picture and diagnosis. *Ind J of Child Health* 1961;**10**:69-76.

24. 24. Khosla SN , Miglani S , Sabharwal U , Khosla A. Incidence of carrier state in treated patients of typhoid fever. *JAPI* 1995;**43**:189-90.

25. Corner RJ, Dewan AM, Hashizume M. Modelling typhoid risk in Dhaka Metropolitan Area of Bangladesh: the role of socio-economic and environmental factors. *Int J Health Geogr* 2013;**12**:1-15.

26. Date KA, Newton AE, Medalla F, Blackstock A, Richardson L, McCullough A, et al. Changing Patterns in Enteric Fever Incidence and Increasing Antibiotic Resistance of Enteric Fever Isolates in the United States, 2008-2012. *Clin Infect Dis* 2016;**63**:322-29.

27. Rasaily R, Dutta P, Saha MR, Mitra U, Lahiri M, Pal SC. Multi-drug resistant typhoid fever in hospitalised children. Clinical, bacteriological and epidemiological profiles. *Eur J Epidemiol* 1994;**10**:41-46.

28. Gasem MH, Dolmans WM, Keuter MM, Djokomoeljanto RR. Poor food hygiene and housing as risk factors for typhoid fever in Semarang, Indonesia. *Trop Med Int Health* 2001;**6**:484-90.

ORIGINAL ARTICLE

Effectiveness of Aloe Vera Gel in Management of Superficial Burn in Children

Md. Saif Ullah[1], Md. Mazharul Alam[2], Kazi Md. Noor-ul Ferdous[3]

Abstract

Background: *Aloe vera has been used traditionally for healing burn and inflammation. Though, the evidence for the effectiveness of aloe vera for healing burn is not sufficient.*

Objective: *The aim of this study was to assess the effectiveness of aloe vera gel in management of superficial burn in children.*

Methods: *This retrospective study was taken place in the Department of Burn and Reconstructive Surgery, Bangladesh Shishu Hospital & Institute, Dhaka and other two privet clinics at Dhaka, from September, 2019 to March, 2022. Total 47 patients with superficial partial thickness burn was included in the study.*

Results: *In this study, majority (48.94%) patients were belonged to the age group of ≤24 months. The mean age was found 38.9±26.31 months. The current study observed that almost two third (61.70%) patients were male. In our study, majority (63.83%) patients stayed hospital for 1-5 days. In the present study, mean (±SD) pain relief time was 3.56±1.24 days and mean (±SD) wound healing time was found 8.19±1.6 days. The current study observed that only 3(6.38%) patients had found wound infection. In current study showed that mean treatment cost was found 76.46±31.88 Taka.*

Conclusion: *Aloe vera gel facilitated early pain alleviation, wound healing, and cost-effective superficial burn treatment in children. Therefore, it can be utilized to treat superficial burns in children to get better results.*

Keywords: Aloe vera gel, children, superficial burn.

DS (Child) HJ 2022;38(1):39-43
DOI: https://doi.org/10.3329/dshj.v38i1.67002

Introduction

Alo vera is being used for centuries for "cosmetic, medicinal, and nutraceutical purposes" due to its antioxidant properties.[1] It has 75 potentially active ingredients, including amino acids, carbohydrates, lignin, saponins, vitamins, enzymes, minerals, and salicylic and other acids.[2] The extract of aloe vera gel allowed for quicker healing of burns and restored the vascularity of burn tissues. These effects could be the result of a number of mechanisms, such as an increase in the production of collagen and the rate of epithelialization brought on by the ability of acemanan (mannose-6 phosphate) to stimulate fibroblasts, as well as an anti-inflammatory, antimicrobial, and moisturizing effect (Maenthaisong et al. 2007).[3] One of the main benefits of using aloe vera gel in many nations is the healing of burn wounds.[4-5] Burns have been identified as one of the most damaging types of child damage in terms of functional, social, and psychological impact.[6-9] Burns

1. Associate Professor, Division of Paediatric Surgery, Bangladesh Shishu Hospital & Institute, Dhaka.
2. Assistant Professor, Department of Paediatric Surgery, Mainamoti Medical College & Hospital, Cumilla, Bangladesh.
3. Associate Professor, Division of Paediatric Surgery, Bangladesh Shishu Hospital & Institute, Dhaka.

Correspondence to: Dr. Md. Mazharul Alam, Assistant Professor, Department of Paediatric Surgery, Mainamoti Medical College & Hospital, Cumilla, Bangladesh. 01717062971, E-mail: mazharcemec3@gmail.com

Received: 25 April 2022; **Accepted**: 30 May 2022

are a major cause of public health concern and are an international issue.[10] In 2000, there were 238,000 fire-related fatalities worldwide, 95% of which were in low- and middle-income nations.[11] Aloe vera has been shown by Davis RH[12] to relieve pain, inflammation, arthritis, and wounds. His conductor-orchestra theory of aloe vera considers how all of its biologically active components work together to deliver the maximum amount of desired effects with little to no toxicity. Athavale et al[13] evaluated the percentage decrease of wound healing with aloe vera gel dressing and contrasted its efficacy with that of traditional dressing (normal saline and povidone iodine). According to the study's findings, aloe vera gel is very successful in treating chronic ulcers and accelerates wound healing, which shortens hospital stays. Aloe vera gel was not linked to any adverse reactions or infections. According to Varaei et al[14], local burn wound pain was measured using a visual analogue scale 10 minutes before to changing the dressing and 24, 48, and 72 hours afterwards using 2% nitrofurazone ointment and aloe vera gel. Thus, dressing pain intensity considerably decreased over the course of 72 hours in both locations, but aloe vera gel was able to lessen pain more quickly than nitrofurazone. The cause might be the carboxypeptidase found in aloe vera gel, which interacts with bradykinin, a potent cause of acute inflammatory pain.[15] Aloe vera use is also reasonably priced. Aloe vera is thought to function by boosting the turnover, production, and cross-linking of collagen in the healing wound.[16-18] By inhibiting leukocyte adherence and the activities of Transforming Necrosis Factor and Interleukin-6, it may also suppress the inflammatory process.[19] However, the effectiveness of aloe vera gel in management of superficial burn in children has not been previously studied in depth. Therefore, the current study was conducted to evaluate the effectiveness of aloe vera gel in management of superficial burn in children.

Materials and Methods

This retrospective study was taken place in the Department of Burn and Reconstructive Surgery, Bangladesh Institute of Child Health (BICH), Dhaka Shishu (Children) Hospital and other two privet clinics at Dhaka, from September, 2019 to March, 2022. Total 47 patients' data collected from hospital records who admitted with superficial partial thickness burn involving <20% of TBSA (total body surface area) admitted within 24 hours during the study period and treated with aloe vera gel. Hospital records confirmed that, burn involving special areas (face, palm, sole, and perineum), burn associated other injuries, electric and chemical burn, patients with known allergy to aloe vera gel were excluded. An informed written consent of the guardians were taken before starting the treatment. Statistical analysis was carried out using the Statistical Package for Social Sciences version 23.0 for Windows (SPSS Inc., Chicago, Illinois, USA). The quantitative observations were indicated by frequencies and percentages.

Results

In this study, majority (48.94%) patients were belonged to the age group of ≤24 months. The mean age was found 38.9±26.31 months. The current study observed that almost two third (61.70%) patient were male (Table I). Majority (63.83%) patients stayed hospital for 1-5 days (Table II). Mean (±SD) pain relief time was 3.56±1.24 days and mean (±SD) wound healing time was found 8.19±1.6 days (Table III). Fig.-1 demonstrates the distribution of the study population according to wound infection using Aloe vera gel. The current study observed that only 3(6.38%) patients had wound infection. Mean treatment cost was found 76.46±31.88 Taka (Table IV).

Table I
Demographical characteristics of the study people (N=47)

Characteristics		n	%
Age (months)	≤24	23	48.94
	25-60	15	31.91
	>60	9	19.15
	Mean ±SD	38.9±26.31	
Gender	Male	29	61.70
	Female	18	38.30

Table II
Distribution of the study population according to hospital stay (N=47)

Hospital stay (day)	n	%
1-5	30	63.83
6-10	17	36.27

Table III
Distribution of the study population according to pain relief time and wound healing time using Aloe vera gel (N=47)

Characteristics	Mean ±SD	Range (min-max)
Pain relief time (day)	3.56±1.24	1-6
Wound healing time (day)	8.19±1.6	4-11

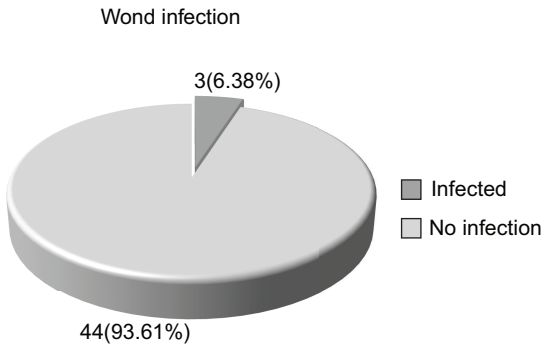


Fig.-1 *Distribution of the study population according to wound infection using Aloe vera gel (n=47)*

Table IV
Distribution of the study population according to treatment cost (N=47)

	Mean ±SD	Range (min-max)
Treatment cost (Taka)	76.46±31.88	30-180

Discussion

This study observed that majority (48.9%) patients were belonged to age ≤24 months. The mean age was found 38.9±26.31 months. Jozsa et al[20] reported most of the studied children were <5 years of age. Up to 50% of children under the age of 11 get sunburns, which are the most frequent and avoidable kind of burns.[21] Children of five years of age or younger most frequently get scald burns, which are frequently caused by spilling hot liquids while cooking.[22] The current study observed that almost two third (61.70%) patients were male. In the study of Shahzad et al[23], 68.0% patients were male in aloe group. In our study, majority (63.83%) patients stayed hospital for 1-5 days. In this present study, mean (±SD) pain relief time was 3.56±1.24 days and mean (±SD) wound healing time was found 8.19±1.6 days. In a study conducted in Bangladesh by Alam et al[24], mean pain relief time was found 2.60±1.27 days and the mean wound healing time was found 5.15±1.56 days. Thamlikitkul et al[25] used Aloe fresh mucilage in 38 patients with thermal burn and found that the healing process was accelerated significantly. In 1995, Visuthikosol et al[26] published the results of a research on 27 patients who had partial thickness burn wounds that were either dressed with gauze soaked in Aloe vera gel or left untreated. They noticed that patients who received aloe treatment had considerably faster wound healing times (11.19 days). The aloe-treated patients' wound healing times were dramatically shortened (18.9 days) in the study of Akhtar and Hatwar[27]. Shahzad et al[23] in their study found that the time taken for partial thickness burns to heal was significantly shorter with aloe vera compared to control group (11±4.18 days vs. 24.24±11.16 days). Walash et al[28] compared the effectiveness of aloe vera gel dressing to traditional dressing on the recovery process and pain levels in burn patients. Compared to the control group, the research group experienced a quicker healing process, less discomfort, and a shorter hospital stay after using an Aloe Vera gel dressing. The current study observed that only 3(6.38%) patients had wound infection. This fining is similar to the study of Alam et al[24], where the rate of wound infection was 5%. According to Shahzad et al[23], the sole mechanism supporting the ongoing usage of silver sulphadiazine in burn injuries is its antibacterial action. The topical administration of SSD may result in leukopenia, renal damage, or both. In reality, while treating major wounds, severe negative effects have been noted.[25,29,30] In the study of Walash et al[28], while 48% of the control group's patients exhibited signs of wound infection during the last two evaluations, all trial participants were free of these symptoms throughout the fifth and sixth assessments. In current study showed that mean treatment cost was found 76.46±31.88 Taka which is very cost effective compared to chemical products.

Conclusion

Aloe vera gel facilitated early pain alleviation, wound healing, and cost-effective superficial burn treatment in children. Therefore, it can be utilized to treat superficial burns in children to get better results. This research recommends using aloe vera gel to treat children's superficial burns, and the outcomes were encouraging. Further study is required with larger sample size in the fascinating topic of burn wound treatment for better understanding.

References

1. Vaidya ADB, Devasagayam TPA. Current status of herbal drugs in India: An overview. *Journal of Clinical Biochemistry and Nutrition* 2007;**41**:1-11.
2. Surjushe A, Vasani R, Saple DG. Aloe vera: A short review. *Indian journal of dermatology* 2008;**53**:163.
3. Maenthaisong R, Chaiyakunapruk N, Niruntraporn S, Kongkaew C. The efficacy of aloe vera used for burn wound healing: A systematic review. *Burns* 2007; **33**:713-18.
4. Reynolds T, Dweck AC. Aloe vera leaf gel: A review update. *J Ethnopharmacol* 1999;**68**:3-37.
5. Marshall JM. Aloe vera gel: What is the evidence? *Pharm J* 1990;**24**:360-62.
6. Crawley-Coha T. Childhood injury: A status report, part 2. *J Pediatr Nurs* 2002;**17**:133-36.
7. Taal LA, Faberb AW. Posttraumatic stress and maladjustment among adult burn survivors l-2 years postburn. *Burns* 1998;**24**:285-92.
8. Macarthur C. Evaluation of Safe Kids Week 2001: prevention of scald and burn injuries in young children. *Injury Prevention* 2003;**9**:112-16.
9. Drago DA. Kitchen scalds and thermal burns in children ûve years and younger. *Pediatrics* 2005; **115**:10-16.
10. Zaidi MM, Abusetta A, Brogowski K, Agrawal PL, Franka MR. Analysis of burned children treated in the Burns and Plastic Surgery Center, Tripoly Libya, in the Year 1992. *Ann Medit Burns Club* 1993;VI.
11. Peden MM, McGee K, Krug E. Injury: A leading cause of the global burden of disease, 2000. World Health Organization; 2002.
12. Davis RH. Aloe vera: A scientific approach, Published by Vantage Press, Inc.1997. Available from: https://scirp.org/reference/referencespapers.aspx?referenceid=996367
13. Athavale VS, Khandalkar SN, Mahawar M, Shtty I, Lad A. A comparative study between aloe vera gel dressing and conventional dressing in chronic wounds. *Int Surg J* 2017;**4**: 3427-32.
14. Varei S, Aedakili FM, Irani OS, Ranban H. The effect of aloe vera gel and nitrofurazone on dressing related pain of superficial burn wounds. *World J Plast Surg* 2017;**6**:254-56.
15. Yagi A, Kabbash A, Mizuno H, Moustafa SM, Khalifa TI, Tsuji H. Radical scavenging glycoprotein cyclooxygenase-2 and thromboxane A2 synthase from aloe vera gel. *Planta Med* 2003;**69**:267-71.
16. Chithra P, Sajithlal GB, Chandrakasan G. Inûuence of Aloe vera on collagen turnover in healing of dermal wounds in rats. *Indian J Exp Biol* 1998;**36**:896-901.
17. Chithra P, Sajithlal GB, Chandrakasan G. Inûuence of Aloe vera on collagen characteristics in healing dermal wounds in rats. *Mol Cell Biochem* 1998; **181**:71-76.
18. Chithra P, Sajithlal GB, Chandrakasan G. Inûuence of Aloe vera on the healing of dermal wounds in diabetic rats. *J Ethnopharmacol* 1998; **59**:195-201.
19. Duansak D, Somboonwong J, Patumraj S. Effects of Aloe vera on leukocyte adhesion and TNF-alpha and IL-6 levels in burn wounded rats. *Clin Hemorheol Microcirc* 2003;**29**:239-46.
20. Jozsa G, Vajda P, Garami A, Csenkey A, Juhasz Z. Treatment of partial thickness hand burn injuries in children with combination of silver foam dressing and zinc-hyaluronic gel. *Medicine* 2018;**97**:e9991.
21. Yin S. Chemical and common burns in children. *Clinical pediatrics* 2017;**56**(5_suppl):8S-12S.
22. Herndon DN. *Total Burn Care*. 5th ed. Elsevier. 2017 Oct 10:1-812.
23. Shahzad MN, Ahmed N. Effectiveness of Aloe Vera gel compared with 1% silver sulphadiazine cream as burn wound dressing in second degree burns. *J Pak Med Assoc* 2013;**63**:225-30.
24. Alam MM, Hossan MA, Islam F, AM N, Nahiduzzan DM, Chakroborthy D. Effect of Aloe Vera Gel and 1% Silver Sulphadiazine cream in the treatment of superficial burn in children: A comparative study. *Journal of MAR Pediatrics* 2022;**2**. Available from: https://www.medicalandresearch.com/assets/articles/documents/DOCUMENT_20220831124839.pdf
25. Thamlikitkul V, Bunyapraphatsara N, Riewpaiboon W, Theerapong S, Chantrakul C, Thanaveerasuwan T, et al. Clinical trial of aloe vera Linn. for treatment

of minor burns. *Siriraj Medical Journal* 2017;**43**: 313-16.

26. Visuthikosol V, Chowchuen B, Sukwanarat Y, Sriurairatana S, Boonpucknavig V. Effect of aloe vera gel to healing of burn wound a clinical and histologic study. *J Med Assoc Thai* 1995;**78**:403-09.
27. Akhtar MA, Hatwar SK. Efficacy of aloe vera extract cream in management of burn wound. *Journal of Clinical Epidemiology* 1996:49:S24.
28. Walash AM, Shehata OEKA, El-Sol AEl-SH. Efficacy of dressing by aloe vera gel on healing and pain among burned patients. *Am J of Nursing Res* 2019;**7**:1028-40.
29. Atiyeh BS, Costagliola M, Hayek SN, Dibo SA. Effect of silver on burn wound infection control and healing: Review of the literature. *Burns* 2007;**33**:139-48.
30. Klasen HJ. A historical review of the use of silver in the treatment of burns. II. Renewed interest for silver. *Burns* 2000;**26**:131-38.

ORIGINAL ARTICLE

Acute Kidney Injury Following Paediatric Cardiac Surgery: Experience of A Paediatric Cardiac Center of Bangladesh

Mohammad Makbul Hossain[1], Sabarin Ahamed[2], Khalifa Mahmud Tarik[3], Dewan Md. Al Amin[4]

Abstract

Background: *Acute kidney injury following cardiac surgery in children is a relatively common phenomenon. The risk ranges from 15% to 64% with a mortality rate of 10% to 89% for those who need dialysis.*

Objective: *To identify the occurrence of acute kidney injury following cardiac surgery in children, as well as its consequences and treatment options.*

Methods: *This study was conducted in the pediatric cardiac recovery center at Bangladesh Shishu Hospital & Institute from January 2019 to December 2020. Using the KDIGO (kidney disease improving global outcome) criteria, 50 children having cardiac surgery were assessed for the occurrence of AKI. Children were divided into two groups. The AKI group consists of 20 patients, whereas the non-AKI group consists of 30 patients. Age, sex, cardiac illness, past operations, RACHS-1 (Risk adjustment for congenital Heart surgery) and pre and post-operative creatinine levels were noted. Fisher's exact test was used to determine whether or not AKI was associated with categorical factors, while the Mann-Whitney U-test was used to see whether or not AKI was associated with continuous variables.*

Results: *Mean age of study population was 4.50±4.03 years for those who did not develop AKI and 7.55±5.79 years for those who did. Male constituted a majority in both groups. Despite the fact that patients with AKI were more acidotic at baseline, lower bicarbonate levels were not linked to an increased risk of AKI (p=0.89). Neither group had higher or lower pressure than the other. Time spent in bypass and cross-clamping was comparable across AKI and non-AKI patients. Patients with AKI did not have a higher risk of developing extracellular fluid excess than non-AKI patients. There was no significant difference between the groups in terms of the average time spent on mechanical ventilation or total hospital stay in days (p=0.17 and p=0.62, respectively). Duration of stay in the cardiac recovery increased for patients who had AKI (p=0.02). The mortality rate among the AKI patients was 20% (4/14). In the control group without AKI, there was one death (3.33%) (p 0.0001).*

Conclusion: *AKI is common complication of paediatric cardiac surgery. Prolong times spent on mechanical ventilation in the ICU and in the hospital have all been linked to AKI.*

Keywords: *Acute kidney injury (AKI), cardiac injury, cardiac surgery.*

DS (Child) HJ 2022;38(1):44-48
DOI: https://doi.org/10.3329/dshj.v38i1.67003

1. Associate Professor and Head, Department of Paediatric Cardiac Anesthesia & ICU, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
2. Medical Officer (Gynae and Obs.), Shaheed Suhrawardy Medical College and Hospital.
3. Senior Consultant and Head, Department of Paediatric Cardiac Surgery, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
4. Medical Officer, Department of Paediatric Cardiac Anesthesia & ICU, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.

Correspondence to: Dr. Mohammad Makbul Hossain, Associate Professor and Head, Department of Paediatric Cardiac Anesthesia & ICU, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh. Cell: 01983562006, E-mail: mmhossainlubna@yahoo.com

Received: 9 February 2022; **Accepted**: 25 May 2022

Introduction

After cardiac surgery, children had a 15-64% chance of developing AKI, with a 10-89% mortality rate among dialysis-dependent patients.[1-2] Acute kidney injury is associated with a worse hospital course an increased risk of infections and a higher death rate (AKI).[3] Several studies have shown variable rates of AKI prevalence, which is likely due to the syndrome being defined in different ways. The two most used classification schemes are the Risk Injury Failure Loss End-stage renal disease (RIFLE) system developed by the Acute Kidney Injury Network and the pediatric modified version of this system, pRIFLE.[4] The most up-to-date and commonly recognized definition of kidney disease is the one endorsed by the Kidney Disease: Improving Global Outcomes group. One of the main challenges of treating AKI is that it is not detected until 24-48 hours after the first insult, when the creatinine level has already increased by 50%. This means that patients undergoing heart surgery sometimes go unnoticed for days after they have suffered from AKI.[5]

Various studies have used alternative serum and urine indicators for the early detection of AKI. Serum cystatin-C and urine NGAL (Neutrophil gelatinase associated lipocalin) are two that have gained attention as potential functional indicators.[6] Hence, cystatin-C is an effective functional biomarker of damage, since it may identify AKI earlier than creatinine and with greater specificity and sensitivity. Renal ischemia and reperfusion damage, maladaptive inflammatory response, oxidative stress, microemboli, and alterations in tubular cell metabolism are all potential causes of AKI after heart surgery.[7] Despite the fact that several risk factors for AKI have been discovered, only a small number are really under the control of the individual patient. Some studies have distinguished between pre-operative and post-operative complications. In addition to preoperative risk factors including age at repair and surgical complexity, intraoperative risk factors include bypass duration, hypotensive episodes and prolong operation time.[3] Medications that may damage the kidneys, as well as the existence of systemic and wound infections are concerns to think about after surgery.[1] This study was performed to learn more about the causes, effects, and challenges of treating acute renal impairment in children after cardiac surgery. So this study was done to discuss the frequency of acute kidney injury following heart surgery in children, as well as its consequences and treatment options.

Materials and Methods

Fifty children who had heart surgery in 2019 and 2020 were analyzed for the occurrence of AKI according to the KDIGO criteria. The pediatric cardiac recovery center at Bangladesh Shishu Hospital & Institute was where all children were sent after surgery. Children were divided into two groups. The AKI group consists of 20 patients, whereas the non-AKI group consists of 30 patients. Age, sex, cardiac illness, past operations, RACHS-1 (Risk adjustment for congenital Heart surgery) and pre and post-operative creatinine levels were noted. No newborns were included in this analysis. To do descriptive statistics, we used the mean and standard deviation for continuous variables, while counts and percentages were used for categorical ones. Fisher's exact test was used to determine whether or not AKI was associated with categorical factors, while the Mann-Whitney U-test was used to see whether or not AKI was associated with continuous variables.

Results

Demographic distribution of the study subjects shows that in non-AKI group mean age was 4.50±4.03 years whereas in AKI group it was 7.55±5.79. However, in both group majority were male (Table I).

Table I
Demographic distribution

Demographic distribution	Non-AKI N (%)	AKI N (%)	p value
Mean age	4.50 ± 4.03	7.55 ± 5.79	0.03
Gender			
Male	20 (66.67)	15 (75)	0.005
Female	10(33.33)	5(25)	

Thirty percent of patients had repair for tetralogy of Fallot, 20% had VSD closure, 14% had a Fontan operation, 12% had pulmonary valve repair, and 10% had ASD closure with AV canal defect repair 4% (Table II).

Table II
Types of surgery (N=50)

Types of surgery	Percentage
ASD closure	10
VSD closure	20
TOF repair	30
Fontan procedure	14
Pulmonary valve repair	12
Mitral valve repair	10
AV canal defect repair	4

Surgical characteristics of patients shows that bypass time in non-AKI group was 2.52±0.80 mins whereas in AKI group it was 2.75±0.59 mins (Table III).

Table III
Surgical characteristics of patients

Patients surgical status	Non-AKI	AKI	p value
RACHS	2.52 ± 0.80	2.75 ± 0.59	0.12
Bypass time (mins)	131.88 ± 85.64	133.67 ± 34.04	0.24
Cross clamp time (mins)	80.04 ± 45.15	75.30 ± 28.60	0.92

Most patients (52%) had a RACHS-1 score of 2, as seen in Fig.-1.

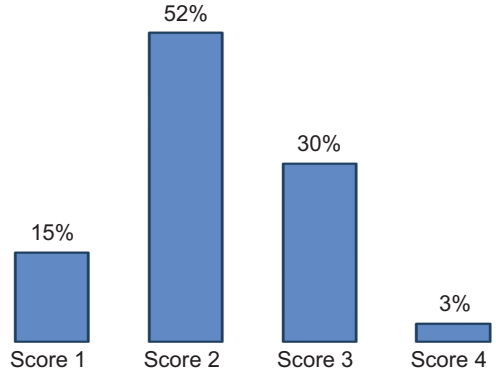


Fig.-1 *RACHS-1 score status*

Although patients with AKI tended to be more acidotic initially, we found no correlation between low bicarbonate levels and an increased risk of AKI. Blood pressure measurements showed no significant differences in terms of mean systolic and diastolic readings across the groups. Our patients with AKI did not have a higher risk of experiencing extracellular fluid overflow than our non-AKI patients, therefore this was not a major concern for them (Table IV).

Table IV
Clinical and biochemical status of patients

Clinical and biochemical status of patients	Non-AKI	AKI	p value
Hemoglobin	15.19 ± 1.46	10.81 ± 1.93	<0.0001
EF			
<60	20 (66.67%)	5(25%)	1.00
>60	10(33.33%)	15 (75%)	
Use of contrast	9 (30%)	3 (15%)	0.20
Creatinine pre-op	0.39 ± 0.15	0.81 ± 1.38	0.31
Bicarbonate	31.45 ± 2.92	20.66 ± 3.15	0.78
SBP	104.40 ± 11.97	106.55 ± 12.35	0.43
DBP	61.69 ± 10.25	58.86 ± 8.41	0.71
Creatinine post-op	0.37 ± 0.14	2.27 ± 1.86	<0.0001
Lactic acid	2.88 ± 1.55	7.00 ± 6.91	0.04

Table V
Management and treatment outcome of the patients

Treatment & outcome	Non-AKI	AKI	p value
Hospital days	9.84 ± 9.79	10.79 ± 7.85	0.62
Ventilation days	1.60 ± 1.92	2.57 ± 2.93	0.17
Length of PICU days	2.56 ± 1.44	4.00 ± 2.66	0.02
Peritoneal dialysis	-	1(5%)	-
Death Rates	1 (3.33%)	4 (20%)	<0.0001

No significant differences were seen in either on mechanical ventilation or days spent in the hospital between the two groups (p=0.17 and 0.62, respectively). A longer PICU stay was seen for individuals with AKI (p = 0.02). Twenty percent (4/14; 4) of the AKI patients that were treated ultimately passed away. When compared to the group without AKI, there was only one mortality (3.33%) (p=0.0001). Of the AKI patients, one individual needed 48 hours of peritoneal dialysis (Table V).

Discussion

Congenital Cardiac Heart surgery following AKI is a frequent complication and it's been linked to higher death rates in both adults and children. Our study's overarching objective was to use the KDIGO criteria to determine the prevalence of AKI after heart surgery in pediatric patients hospitalized to Bangladesh Shishu Hospital & Institute at PICU. According to KDIGO criteria, the incidence of AKI in cardiac surgery patients was 9.3 percent, which is lower than the 15 to 64 percent seen in other published research. The prevalence of AKI in children after cardiac surgery varies with study population age and terminology utilized. Although we employed the KDIGO criteria in this investigation, additional well defined instruments such as the pRIFLE (pediatric Risk, Injury, Failure, Loss of function, and End-stage renal disease) criteria and the AKIN (acute kidney injury network) criteria have been used to diagnose AKI in children. The AKIN criteria were the most specific, whereas the pRIFLE criteria were the most sensitive, according to a comparison conducted by Lex et al[8] in pediatric patients. KDIGO criteria, they said, were similarly nuanced. We decided for the KDIGO since it has been shown to be effective in the pediatric critical care population.[9] Nephropathy may be caused by congenital heart defects (CHDs), which have been known about for quite some time. If patients with cyanotic heart disease do not undergo prompt correction, they are more likely to develop AKI and perhaps chronic renal disease. Alterations in renal blood flow and intraglomerular hemodynamics may impact renal function in the context of hypoxia, secondary polycythemia and aberrant arterial venous shunts.[9] Age is a significant risk factor for acute kidney injury (AKI) after heart surgery. A greater post-operative lactate level, indicative of hypoperfusion, was shown to be an independent risk factor for AKI, as was the case in the research by Cardoso et al[10] lending credence to the idea of hypoperfusion as a suggested cause of AKI. Patients who went on to develop AKI had a higher preoperative serum creatinine level, although this difference was not statistically significant (p=0.32). We could not find statistical significance in the mean RACHS-1 category. A higher RACHS-1 score has been linked to a lower risk of postoperative AKI.[11] Although not all investigations have shown this to be the case.[12] Possible explanations include a lack of instances that fall into the "high risk" (RACHS-1-category) group, as shown in.[3,4] Hemoglobin levels before surgery are one of the modifiable parameters documented in the literature as independent predictors of AKI.[13] According to the previous research[12], our results showed that individuals with preoperative anemia had a higher risk of developing AKI. Those who had low hemoglobin while not having cyanotic cardiac disease were at a higher risk for developing AKI. Therefore, treating anemia before to heart surgery in this population may mitigate postoperative AKI. Consistent with previous research, we discovered that AKI is linked to a higher risk of death and illness.[14]

Several studies have shown that CPB times longer than 120 minutes are associated with an increased risk of developing postoperative acute kidney injury.[1,12] Acute kidney injury (AKI) risk rises in tandem with CPB duration, which has been hypothesized to be associated with worsening ischemia and escalating inflammation. Patients with a CPB time >130 minutes in our population did not differ in their risk of developing AKI. Nevertheless, the length of cross-clamping or the percentage of ejection fraction at baseline were both shown to be unreliable predictors of AKI. In contrast to previous research that has indicated a correlation between nephrotoxic drugs such aminoglycosides, NSAIDs, and ACE inhibitors and an elevated risk of AKI, our study revealed no such link.[15] Frequent checks on plasma levels were done to avoid potentially hazardous accumulations of nephrotoxic medications. It is vital to appropriately estimate fluid volume status before providing any therapy since hyper or hypovolemia may result from an inaccurate evaluation. Weight gain of more than 7-10%, in addition to other signs of hypervolemia, showed that the patient had been overloaded with fluids. In our research population, we found no indication that fluid excess had a significant impact in the onset of AKI or its related mortality rates. This may be a result of using loop diuretics when absolutely required. We

acknowledge that the results may have been affected by the lack of information regarding the use of inotropes, the volume of intraoperative blood loss, the amount of blood loss through the chest tube and the correction of cyanosis with hemoglobin. Nevertheless, there are difficulties in consistently quantifying all of these aspects due to the retrospective nature of the study.

Conclusion

AKI is common complication of pediatric cardiac surgery. Prolong mechanical ventilation in the ICU and in the hospital have all been linked to AKI. To improve the cardiopulmonary bypass techniques, improve renal perfusion and eradicate the causative risk factors are necessary for prevention of AKI in pediatric patients.

References

1. Li S, Krawczeski CD, Zappitelli M, Devarajan P, Thiessen-Philbrook H, Coca SG, et al. Incidence, risk factors, and outcomes of acute kidney injury after pediatric cardiac surgery: a prospective multicenter study. *Crit Care Med* 2011;**39**:1493-99.
2. Schneider J, Khemani R, Grushkin C, Bart R. Serum creatinine as stratified in the RIFLE score for acute kidney injury is associated with mortality and length of stay for children in the pediatric intensive care unit. *Crit Care Med* 2010;**38**:933-39.
3. Morgan CJ, Zappitelli M, Robertson CMT, Alton GY, Sauve RS, Joffe AR, et al. Risk factors and outcomes of acute kidney injury in neonates undergoing complex cardiac surgery. *J Pediatr* 2013;**162**:120-27.
4. Kellum JA, Lameire N. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (Part 1). *Crit Care* 2013;**17**:204.
5. Greenberg JH, Zappitelli M, Devarajan P, Thiessen-Philbrook HR, Krawczeski C, Li S, et al. Kidney outcomes 5 Years after pediatric cardiac surgery: the TRIBE-AKI study. *JAMA Pediatr* 2016;**170**:1071-78.
6. Basu RK, Wong HR, Krawczeski CD, Wheeler DS, Manning PB, Chawla LS, et al. Combining functional and tubular damage biomarkers improves diagnostic precision for acute kidney injury after cardiac surgery. *J Am CollCardiol* 2014;**64**:2753-62.
7. Devarajan P. Update on mechanisms of ischemic acute kidney injury. *J Am SocNephrol* 2006;**17**:1503-20.
8. Lex DJ, Toth R, Cserep Z, Alexander SI, Breuer T, Sapi E, et al. A comparison of the systems for the identification of postoperative acute kidney injury in pediatric cardiac patients. *Ann Thorac Surg* 2014;**97**:202-10.
9. Cordina RL, Celermajer DS. Chronic cyanosis and vascular function: implications for patients with cyanotic congenital heart disease. *Cardiol Young* 2010;**20**:242-53.
10. Cardoso B, Laranjo S, Gomes I, Freitas I, Trigo C, Fragata I, et al. Acute kidney injury after pediatric cardiac surgery: risk factors and outcomes. Proposal for a predictive model. *Rev Port Cardiol* 2016;**35**:99-104.
11. Aydin SI, Seiden HS, Blaufox AD, Parnell VA, Choudhury T, Punnoose A, et al. Acute kidney injury after surgery for congenital heart disease. *Ann Thorac Surg* 2012;**94**:1589-95.
12. Park SK, Hur M, Kim E, Kim WH, Park JB, Kim Y, et al. Risk factors for acute kidney injury after congenital cardiac surgery in infants and children: a retrospective observational study. *PLoS ON*E 2016; **11**:e0166328. DOI: 10.1371/journal.pharm.0166328.
13. Kim WH, Park MH, Kim HJ, Lim HY, Shim HS, Sohn JT, et al. Potentially modifiable risk factors for acute kidney injury after surgery on the thoracic aorta: a propensity score matched case-control study. *Medicine* 2015;**94**:e273. DOI:10.1097/MD.0000000000000273
14. Watkins SC, Williamson K, Davidson M, Donahue BS. Long-term mortality associated with acute kidney injury in children following congenital cardiac surgery. *Paediatr Anaesth* 2014;**24**:919-26.
15. Bove T, Monaco F, Covello RD, Zangrillo A. Acute renal failure and cardiac surgery. *HSR Proc Intensive Care Cardiovasc Anest*h 2009;**1**:13-21.

REVIEW ARTICLE

Processing and Use of Radiation Sterilized Human Amniotic Membrane Allografts as Biological Dressings of Wounds in Children: A Review

Swapan Kumar Chakraborty[1], Harun-Or-Rashid[2], Donald James Gomes[3]

Abstract

Radiation sterilized human amniotic membrane allografts are used as biological dressing of wounds in rehabilitative surgery. The amniotic membrane is used in many different clinical situations such as: heat burn, chemical burns, diabetic wound/ diabetic foot ulcer, leprotic ulcer, abdominal wall reconstruction, pterigium removal site, peripheral corneal ulcer, in the management of pressure sore, etc.Non-viable lyophilized/oven-dried radiation sterilized amniotic membrane allografts could be processed for utilization as temporary biological dressing of wounds. The allografts used clinically should not be the carriers of germs or a source of infection. Human chorio-amniotic membranes collected for processing as tissue allografts to be used as biological dressings were reported to be contaminated with microorganisms such as species of Staphylococcus, Micrococcus, Bacillus and Pseudomonas.However, oven dried (40°C) or freeze dried (-50°C) human amniotic membranes were found to be sterilized by irradiation with the dose of 25 kiloGray (kGy) of gamma radiation.Careful screening and selection of tissue donors, proper processing and gamma radiation sterilization of human amniotic membranes minimize the risk of disease transmission to recipients through allografts.

***Keywords**: Human amniotic membrane, gamma radiation, sterilization.*

DS (Child) HJ 2022;38(1):49-55
DOI: https://doi.org/10.3329/dshj.v38i1.67004

Introduction

Davis et al[1] in 1910 and Sabella et al[2] in 1913 reported the clinical use of foetal membranes for transplantation. The application of human amniotic membranes has been increased, in time, to many areas of surgical treatments.[3] The amniotic membranes have been used in burns,[4,5] in the treatment of venous ulcers[6], as a physiological wound dressing,[7,8] for leg ulcers,[9-11] otolaryngologic, head and neck surgery,[12,13] pelvic surgery,[14,15] etc. Human amniotic membrane grafts are used preferably as temporary biological dressings because of its unique characteristics and properties. No immunogenic rejection phenomenon does occur after the application of amniotic membrane grafts on the wound.[16,17] Healing effect of the foetal membranes when used for treating different surgical and skin defects are thought to be either due to their content

1. Chief Scientific Officer and Director, Scientific Information Unit, Atomic Energy Research Establishment, Ganakbari, Savar, Dhaka, Bangladesh.
2. Ex DG, Atomic Energy Research Establishment, Ganakbari, Savar, Dhaka, Bangladesh.
3. Professor, Department of Microbiology, University of Dhaka, Dhaka 1000, Bangladesh.

Correspondence to: Dr. Swapan Kumar Chakraborty, Chief Scientific Officer and Director, Scientific Information Unit, Atomic Energy Research Establishment, Ganakbari, Savar, Dhaka, Bangladesh. Cell: 01715305967, E-mail:chakraborty swapankumar@yahoo.com

Received: 3 March 2022; **Accepted**: 26 May 2022

of some antibacterial, angiogenic or other biochemical factors, or to the biomechanical characteristics of the foetal membranes as such.[18]

The amniotic membraneallografts prevent local inflammatory response[19] and its antimicrobial properties reduce risk of post-operative infection.[20] The transplanted membrane may perform as a structural barrier to impede proliferation of fibrous tissue and thus decrease scarring.[21,22]

Microbial contamination of human tissue allografts

The risk of infectious disease transmission with human tissue allografts is a major concern in tissue banking practice. Microorganisms can be introduced into the grafts during tissue collection, processing and storage, but even if all these procedures are done under aseptic conditions, the possibility of bacterial and viral disease transmission of donor origin cannot be excluded.[23] In order to minimize the risk of disease transmission through allografts, several steps should be undertaken by tissue banks, including careful donor-screening, proper tissue processing and sterilization of tissue allografts.[23]

Islam et al[24] and Begum et al[25] reported bacterial isolates obtained from human amniotic membranes and one of the bacterial isolates was reported to be highly radio-resistant. Chakraborty et al (2012)[26] and Chakraborty et al (2015)[27] reported association of microorganisms with human chorio-amniotic membranes. Chakraborty et al[26] isolated bacterial contaminants from all the studied 34 post-delivery chorio-amniotic membranes collected from labor rooms of hospitals and the contaminants were identified as *Staphylococcus aureus*, *S. cohnii*, *S. epidermidis*, *S. sciuri*, *Micrococcusroseus*, *Bacillus* sp., *B. megaterium*, *Pseudomonascepacia* and *P. diminuta*.

Sterilization of tissue allografts with ionizing radiation

Radiation sterilization of medical materials on a commercial scale was applied for the first time in the middle of the 1950s with less than 10% of medical products sterilized by ionizing radiation in the 1970s, and nearly 50% at the period of report by Dziedzic-Goclawska et al[23] with an increasing tendency. The International Atomic Energy Agency (IAEA) in Vienna promotes and supports the use of ionizing radiation for sterilization purposes. IAEA has elaborated and issued many guidelines and standards applicable for radiation sterilization.[28] The Agency's promotion and support resulted in the development of national programmes on tissue banking and application of ionizing radiation for the sterilization of tissue allografts. Tissue banks were created in many countries of the Asia Pacific region under the auspices of IAEA.[23]

The killing effect of radiation may be due to direct effect or indirect effect. The direct action of radiation involves the interaction between ionizing radiation and critical biological molecules, which results in excitation, lesion and scission of polymeric structure such as DNA.[29] The indirect effect of radiation is due to biochemical changes within the organism. The interaction of ionizing radiation with water molecules within living cells leads to the production of short-lived free radicals and peroxy radicals. These radiolytic products interact with biological molecules including DNA; hence inactivating the reproduction process. This indirect effect of radiation normally occurs as an important part of the total chain of reactions of ionizing radiation.[30,31] The indirect effect is more prominent and very much influenced by environmental factors including oxygen, water content, medium, temperature and chemicals present during irradiation.[32-34] Chakraborty et al[35] reported the influence of irradiation medium and initial viable cell numbers on the gamma radiation sterilization of the bacterial isolates recovered from human amnion membranes and bones. The sterilization efficacy of ionizing radiation lies in its good penetrability inside the matter and its high killing efficiency of microorganisms.[23] Ionizing radiation is effective in the inactivation of microorganisms in the bulk of any material without associated problems of heat exchange, pressure differences or hindrances by diffusion barriers.[36] Chakraborty et al[26] studied the effect of gamma radiation on the sterility quality of tissue allograftsand found that human amniotic membrane allografts irradiated with a dose of 25 kiloGray (kGy) ofgamma radiationwere sterilized.

Transmission of hepatitis C virus (HCV) by non-sterilized cadaveric tissue allografts has been described, while allografts irradiated with a dose of 17 kGy did not evoke infections of the graft recipients.[37] There is no data on the sensitivity of hepatitis B virus (HBV) to ionizing radiation;

however, the virus is known to be resistant to heat sterilization.[23]

Most of the studies on the effectiveness of ionizing radiation to inactivate viruses were done on the inactivation of human immunodeficiency viruses (HIV), particularly in blood plasma. The dose required to eliminate all active HIV-1 from the particular tissues depends on the amount of virus originally present (initial contamination).[23] It has been postulated that the dose of irradiation needed to reduce the viral load by 1 $\log_{10}$ is 4 kGy[38] or even 5.6 kGy[39]. Fideler et al[40], using polymerase chain reaction (PCR), found that in order to inactivate HIV in fresh frozen bone-patellar ligament allografts, a dose in the range of 30-40 kGy was required. The sensitivity of HIV to ionizing radiation is reported to depend on the temperature during irradiation. The inactivation of the virus titre of 5 to 6 $\log_{10}$ was achieved at doses of 50 to 100 kGy in frozen (-80ºC) plasmas and at the dose of 25 kGy at 15ºC.[41] Dziedzic-Goclawska et al[23] reported that prions, responsible for Creutzfeldt-Jacob disease (CJD) in humans, are extremely resistant to most of the chemical and physical sterilizing/disinfecting agents including ionizing radiations.

Selection of tissue donors

Tissues could be procured from both living and cadaveric donors. Tissues from living donors mainly fall into two categories, namely amniotic membranes and bones obtained after surgical procedures. Tissues from cadaveric donors (*e.g.*, skin, bone, cartilage, tendon etc.) are obtained under sterile or non-sterile conditions.[42] The main goal of the tissue bank is to provide safe and high quality tissue grafts to the patients. Therefore, each potential donor must be evaluated through a careful review of the donor's medical and sexual history, physical examination and laboratory screening. Generally, the ideal donor is a young, healthy adult under 55 years of age.[42] Donor selection is based on a review of social and medical history, physical examination, autopsy results (if performed) and blood tests. Donors are excluded if any elements of past social, sexual and medical history indicate the risk of HIV (human immunodeficiency virus), hepatitis B and C, or jaundice of unknown etiology, infectious diseases including tuberculosis, malignant diseases, presence or suspicion of neurodegenerative symptoms including dementia, the use of pituitary derived hormones, systemic connective tissue diseases (*e.g.*, lupus erythematosus, rheumatoid arthritis), chronic steroid treatment, exposure to toxic substances and exposure to irradiation at the site of tissue donation.[23]

Serological as well as microbiological examinations are needed to fully screen donors. The minimum testing accepted universally includes VDRL (Venereal Disease Research Laboratory test)/RPR (rapid plasma reagin), hepatitis B surface antigen, hepatitis C antibodies, HIV antibody and microbiological (culture) testing of small donor tissue samples or swabs. Other tests can be done selectively when indicated such as: CMV (cytomegalovirus) test, hepatitis B core antibody, histopathological examination, antigen testing for HIV using antibody or polymerase chain reaction (PCR) and HTLV (Human T-lymphotrophic virus) I and II.[42]

Collection and preservation of tissues

Tissues are collected aseptically in airtight sterile containers and transported to the tissue processing laboratory in an insulated container that can keep the tissues at a temperature of 4ºC for at least 12 hours (h). Normally ice slabs or dry ice are placed in the container to keep the temperature low. Chorio-amniotic membranes collected after delivery should be kept completely immersed in sterile normal saline in a plastic container and stored in a refrigerator (4ºC) for not more than 24 h.[42]

Processing of radiation sterilized human amniotic membranes for use in rehabilitative surgery

The procedure of processing of radiation sterilized human amnion membrane allografts for use in rehabilitative surgery is described elsewhere.[26,43] Post-delivery human chorio-amniotic membranes from clinically suitable donors are collected aseptically in sterile normal saline and temporarily preserved in the freezer. The frozen tissues are first thawed and then the amnion is separated aseptically from the chorion using sterile surgical instruments. The amniotic membranes are washed several times with sterile normal saline using an electric orbital platform shaker to remove blood and tissue debris. The membranes are then aseptically cut into pieces, stretched on surgical gauge and mounted on surface sterilized (70% ethanol) plastic frames and dried overnight at 40ºC temperature in an electric controlled oven. The dried membranes are then cut under a laminar air flow into pieces and each piece

of amniotic membrane is then packaged in triple layer with polyethylene packages, labeled, vacuum sealed, and then irradiated with gamma radiation at the dose of 25 kiloGray (kGy). The irradiated membranes are preserved at refrigerating temperature. The sterility of the irradiated membranes is determined by sterility testing using microbiological culture media, and then the sterile membranes are supplied to hospitals/clinics for use in rehabilitative surgery.[26,43]

Effect of processing and radiation sterilization on the biomechanical properties of tissue allografts

Chakraborty et al (2007)[44] studied the effect of oven drying (40ºC), freeze drying (-50 ºC) and gamma irradiation (25kGy) on the tensile strength of human amnion membranes. When the tensile strength of the amnion membranes was measured without rehydration of dried samples, it was found to be increased at different stages of processing including oven dried (7.93% increase), freeze dried (6.38% increase), oven dried-gamma irradiated (7.57% increase) and freeze dried-gamma irradiated (6.97% increase) as compared to that of the controls. Rehydration of dried and irradiated membranes resulted in a decrease in tensile strength. After rehydration in normal saline for 5 minutes, the retention of tensile strength by oven dried-irradiated and freeze dried-irradiated amnion membranes was respectively about 70% and 61% of that of controls.

Clinical uses and effectiveness of radiation sterilized amniotic membranes

Human amniotic membrane is used in many different clinical situations such as: superficial burns,[17, 45] mixed burns,[46] leprotic ulcer,[47,48] chemical and thermal burns,[49] deep corneal ulcers,[50] in the management of pressure sore[51] etc. It is reported to reduce pain, decrease electrolyte, fluid and protein loss, and promote epithelialization.[9] It is also reported to prevent local inflammatory response and decrease corneal haze.[19] Bari et al[52] reported a prospective study of 40 patients with deep and deep dermal burns in which radiation sterilized (25 kGy) human amniotic membranes were used. Nessa et al[43] reported the use of oven dried (40ºC) and gamma radiation sterilized (25kGy) human amniotic membranes in the treatment of 168 patients with heat burn, acid burn, diabetic wound/diabetic foot ulcer, leprotic ulcer, abdominal wall reconstruction, chemical (acid) burn (corneal surface Rt), chemical (lime) burn, pterigium removal site, peripheral corneal ulcer, and orbit reconstruction in hospitals/ clinics in 2008 in Bangladesh. For utilization as temporary biological dressing of wounds, non-viable lyophilized/oven-dried radiation sterilized amniotic membrane grafts could be processed.[17]

Use of amniotic membrane allografts in the treatment of burns in children

Khan et al[17] reported treatments of children with superficial burns using radiation sterilized amniotic membranes as biological dressing. The authors mention that the amnion grafts were very easily applied to the wounds and the patients did not feel pain during repeated dressings. No side effect was also noticed after the application of grafts and all the patients healed satisfactorily without any post operative complication. Chakraborty et al[46] reported management of mixed (superficial and deep) burn in children with allogeneic amnion and autogeneic skin grafting. Shahid et al[53] reported the use of radiation sterilized amniotic membrane as local burn wound coverage and demonstrate that amniotic membrane is a suitable and effective biological dressing in reducing patient's morbidity when compared with non-biological medicated tulle (sofratulle). Ullah et al[54] reported the use of radiation sterilized amniotic membranes in the treatment ofa total of 370 patients (mean age 2.76 years) with superficial partial thickness burn. The authors[54] mention that amnion dressing suppresses bacteria in the wound as well as reduces infection. Amnions have good adherent characteristics, which reduces infection as well as reduction of oozing of plasma from the wound.[54]

Burn injuries are one of the most devastating physical and psychological injuries that a person can suffer.[55] From 1981 to 1990 it was the second most common surgical problem in paediatric age group in the department of pediatric surgery, Dhaka Shishu Hospital.[56] Ullah et al[54] reported the use of radiation sterilized amniotic membranes in the treatment of a total of 370 patients with partial thickness burn. The authors mention that amnion dressing suppresses bacteria in the wound as well as reduces infection. Amnions have good adherent characteristics, which reduces infection and also reduce oozing of plasma from the wound. It has a role on burnt pain reduction, frequency of dressing change, rate of healing, cost, and duration of hospital

stay. Ullah et al[54] conclude that amniotic membrane is one of the effective biological skin substitutes used in burn wounds, with efficacy of low bacterial counts, has advantages of reducing loss of protein, electrolytes and fluids, decreasing the risk of infection, minimizing pain, accelerated wound healing and good handling properties. It is readily available and does not present immunological problem and allergy response. It is cost effective and very helpful for developing countries.

Conclusion

The facility of preservation of oven dried and radiation sterilized human amniotic membranes in a refrigerator, makes it possible to build up a large stock of allografts for use as biological dressing of wounds. Processing and preservation of radiation sterilized tissue allografts in a tissue bank can ensure ready availability of tissue allografts for safe clinical use.

References

1. Davis JS. Skin transplantation with a review of 550 cases at the John Hopkins Hospital. *JHH Report* 1910;**15**:307 (cited from Farazdaghi M, Adler J, Farazdaghi SM. Electron microscopy of human amniotic membrane. In: Phillips GO, Nather A, Strong DM, von Versen R, editors. Advances in Tissue Banking vol. 5, World Scientific Publishing Co Pte Ltd, Singapore, 2001;P.149-71).
2. Sabella N. Use of foetal membranes in skin grafting. *Med Rec NY* 1913;**83**:478 (cited from Farazdaghi M, Adler J, Farazdaghi SM. Electron microscopy of human amniotic membrane. In: Phillips GO, Nather A, Strong DM, von Versen R, editors. Advances in Tissue Banking vol. 5, World Scientific Publishing Co Pte Ltd, Singapore, 2001;P.149-71).
3. Farazdaghi M, Adler J, Farazdaghi SM. Electron microscopy of human amniotic membrane. In: Phillips GO, Nather A, Strong DM, von Versen R, editors. Advances in Tissue Bankingvol.5, World Scientific Publishing Co Pte Ltd, Singapore, 2001;P.149-71.
4. Kirschbaum SM, Hernandez H. Use of amnion in extensive burns. Proc. Third Int. Cong. Plastic Surg. Excerpta Medica, Amsterdam 1963 (cited from Farazdaghi M, Adler J, Farazdaghi SM. Electron microscopy of human amniotic membrane. In: Phillips GO, Nather A, Strong DM, von Versen R, editors. Advances in Tissue Banking vol. 5, World Scientific Publishing Co Pte Ltd, Singapore, 2001;P.149-71).
5. Quinby WC, Jr., Hoover HC, Scheflan M, Philmon TW, Sumner AS, Conrado CB. Clinical trials of amniotic membranes in burn wound care. *Plastic Reconstructive Surg* 1982;**70**:711-16.
6. Ward DJ, Bennett JP, Burgos H, Fabre J. The healing of chronic venous leg ulcers with prepared human amnion. *Br J Plastic Surg* 1989;**42**:463-67.
7. Colocho G, Graham WP, Green AE, Matheson DW, Lynch D. Human amniotic membrane as a physiologic wound dressing. *Arch Surg* 1974;**109**:370-73.
8. Gruss JS, Jirsch DW. Human amniotic membrane a versatile dressing. *J Can Med Assoc* 1978;**118**:1237-46.
9. Trelford JD, Trelford-Sauder M. The amnion in surgery, past and present. *Am J Obstet Gynecol* 1979;**134**:833-45.
10. Faulk WP, Matthews RN, Stevens PJ, Bennett JP, Burgo H, His BL. Human amnion as an adjunct in wound healing, *Lancet* 1980;1158 (cited from Farazdaghi M, Adler J,Farazdaghi SM. Electron microscopy of human amniotic membrane. In: Phillips GO, Nather A, Strong DM, von Versen R, editors.Advances in Tissue Bankingvol. 5. World Scientific Publishing Co Pte Ltd, Singapore 2001;P.149-71).
11. Ward DJ, Bennett JP. The long term results of the use of human amnion in the treatment of leg ulcers, *Br. J. Plastic Surg*. 1984;**37**:191-93.
12. Zohar Y, Talmi YP, Finkelstein Y, Shvili Y, Sadov R, Laurian N. Use of human amniotic membrane in otolaryngologic practice *Laryngoscope* 1987;**97**:978-80.
13. Talmi YP, Finkelstein Y, Zohar Y. Use of human amniotic membrane as a biologic dressing. *Euro J Plastic Surg* 1990;**13**:160-62.
14. Rennekamff HO, Dohrman P, Fory R, Fandrich F. Valuation of amniotic membrane as adhesion prophylaxis in a novel surgical gastrochisis model. *Invest Surg* 1994;**7**:187-93.
15. Gharib M, Ure BM, Klose M. Use of amniotic grafts in the repair of gastrochisis. *Pediatr Surg* 1996;**11**:96-99.
16. Akle CA, Adinolfi M, Welsh KI, Leibowitz S, McColl I. Immunogenicity of human amniotic epithelial cells after transplantation into volunteers. *Lancet* 1981;**2**:1003-05.
17. Khan AR, Aziz MA, Ullah MS, Nessa A, Chakraborty SK, Miah MM. Radiation sterilized amnion membrane grafts in the management of superficial burn in children. *Dhaka Shishu (children) Hospital Journal* 2002;**18**;:52-54.

18. Panakova E, Koller J. Utilization of foetal membranes in the treatment of burns and other skin defects. In: Phillips GO, Strong DM, von Versen R, Nather A, editors. Advances in Tissue Banking vol. 1, World Scientific Publishing Co Pte Ltd, Singapore 1997; P. 165-81.

19. Choi YS, Kim JY, Wee WR, Lee JH. Effect of application of human amniotic membrane on rabbit corneal wound healing after excimer laser photorefractive keratectomy. *Cornea* 1998;**7**: 389-95.

20. Talmi YP, Sigler L, Inge E. Antibacterial properties of human amniotic membranes. *Placenta* 1991;**12**:285-88.

21. Shimazaki J, Shinozaki N,Tsubota K. Transplantation of amniotic membrane and limbal autograft for patients with recurrent pterigium associated with symblepharon. *Br J Ophthalmol* 1998;**82**:235-40.

22. Tseng SCG, Li DQ, Ma X. Suppression of transforming growth factor beta isoform, TGF-â receptor type II and myofibroblast differentiation in cultured human corneal and limbal fibroblasts by amniotic membrane matrix. *J Cell Physiol* 1999;**179**:325-35.

23. Dziedzic-Goclawska A, Stachowicz W. Sterilization of tissue allografts. In:Phillips GO, Strong DM, von Versen R, Nather A, editors. Advances in Tissue Banking vol. 1, World Scientific Publishing Co Pte Ltd, Singapore 1997;P.261-21.

24. Islam MS, Begum R. Microbiological and radiation sensitivity studies of bacterial isolates obtained from human amniotic membranes. In: Phillips GO, Kearney JN, Strong DM, von Versen R, editors. Advances in Tissue Banking vol. 3, World Scientific Co Pte Ltd, Singapore, 1999;P.457-62.

25. Islam MS, Begum R. A highly radio-resistant bacterial isolate from human amnion membranes, In: Phillips GO, Kearney JN, Strong DM, von Versen R, editors.Advances in Tissue Banking vol. 3, World Scientific Co Pte Ltd, Singapore, 1999;P.463-67.

26. Chakraborty SK. Microorganisms associated with donor tissues and the impact of physico-chemical treatments on the clinical applicability of tissue allografts. PhD Thesis, Department of Microbiology, Faculty of Biological Sciences, University of Dhaka, Dhaka 1000, Bangladesh, 2012.

27. Chakraborty SK, Rashid H, Gomes DJ. Status of contamination, and isolation and identification of microorganisms from some human donor chorio-amniotic membranes and femoral head bones. Internal Report, *SIU-**3***, March 2015, Chief Editor: Dr. Md. Sirajul Islam, Director, SIU, Published by Scientific Information Unit, Atomic Energy Research Establishment, Ganakbari, Savar, Dhaka.

28. Mukherjee RN. IAEA standards applicable for sterilization. In: Morrisey RF, Prokopenko YL, editors. Sterilization of Medical Products Johnson and Johnson, Polyscience Publication Inc., Morin Heights, Canada 1991;P.117-24.

29. Yusof N. Effect of radiation on microorganisms-Mechanism of radiation sterilization. In: Phillips GO, Nather A, Strong DM, von Versen R, editors. Advances in Tissue Banking vol.5, World Scientific Publishing Co Pte Ltd, Singapore, 2001;P.342-57.

30. Antoni F. The effect of ionizing radiation on some molecules of biological importance. In: Manual on Radiation Sterilization of Medical and Biological Materials. *IAEA Technical Reports Series* 1973;**149**:13-36.

31. Coggle JE, Biological effects of radiation, Wykeham Science Series, London 1973; p. 150 (cited from Yusof N. Effect of radiation on microorganisms-Mechanism of radiation sterilization. In: Phillips GO, Nather A, Strong DM, von Versen R, editors. Advances in Tissue Banking vol. 5, World Scientific Publishing Co Pte Ltd, Singapore, 2001;P.342-57).

32. Tallentire A. Aspects of microbiological control of radiation sterilization. *J Rad Ster* 1973;**1**:85-103.

33. Gardner JF, Peel MM. Introduction to Sterilization and Disinfection, Churchill Livingstone, Edinburgh, 1986 (cited from Yusof N. Effect of radiation on microorganisms-Mechanism of radiation sterilization. In: Phillips GO, Nather A, Strong DM, von Versen R, editors. Advances in Tissue Banking vol. 5, World Scientific Publishing Co Pte Ltd, Singapore, 2001;P.342-357).

34. Whitby JL. Microbiological aspects relating to the choice of radiation sterilization dose. *Rad Phys Chem* 1993;**42**:577-80.

35. Chakraborty SK, Rashid H, Deen NS, Gomes DJ. Effect of suspending medium and bacterial load on the gamma radiation sterilization of some bacterial isolates from human amnion membrane. *Bangladesh J Medical Science* 2011;**17**:57-62.

36. Christensen EA, Kristensen H, Miller A. Radiation sterilization. In: Russell AD, Hugo WB, Ayliffe GAJ, editors. Principles and Practice of Disinfection, Preservation and Sterilization 2nd edn. Blackwell Science, Oxford, 1992 (cited from Dziedzic-Goclawska A, Stachowicz W. Sterilization of tissue allografts. In: Phillips GO, Strong DM, von Versen R, Nather A, editors. Advances in Tissue Banking vol.1, World

Scientific Publishing Co Pte Ltd, Singapore 1997; P.261-321).

37. Conrad EU, Gretch D, Obermeyer K, Moogk M, Sayers M, Wilson J, Strong DM. The transmission of hepatitis C virus through tissue transplantation. *J Bone & Joint Surg* 1995;**77**:214-24.

38. Conway B, Tomford WW, Mankin H, Hirsch MS, Schooley RT. Radiosensitivity of HIV-1. Potential application to sterilization of bone allografts. *AIDS* 1991;**5**:608-09.

39. Conway B, Tomford WW. Radiosensitivity of human immunodeficiency virus type 1. *Clin Infect Dis* 1992;**14**:978-79.

40. Fideler BM, Vangsness CT, Moore T, Li Z, Rasheed S. Effects of gamma irradiation on the human immunodeficiency virus. *J Bone & Joint Surg* 1994;**76**-A:1032-35.

41. Hiemstra H, Tersmette M, Vos AH, Over J, Van Berkel MP, De Bree H. Inactivation of HIV by gamma radiation and its effect on plasma and coagulation factors. *Transfusion* 1991;**31**:32-39.

42. Multi-Media Distance Learning Package on Tissue Banking, Module 4, Phillips GO. coordinating editor, p. 4-5, 10-11, 16-17, IAEA/NUS Regional Training Centre, IAEA/NUS International Training Centre, National University of Singapore, Singapore.

43. Nessa A, Chakraborty SK, Chakma K, Hasan MZ, Miah MM. Collection, processing and gamma radiation sterilization of human amniotic membranes for use in rehabilitative surgery. Technical Report 2008 (published in 2010), AERE/ TR-14, ISSN 2074-2371, Atomic Energy Research Establishment, Ganakbari, Savar, Dhaka;P.219-22.

44. Chakraborty SK, Nessa A, Ali Y, Alam J, Haque ME, Rashid H, Gomes DJ. The effect of oven drying, freeze drying and gamma irradiation on the tensile strength of human amnion membrane. *Bangladesh J Medical Science* 2007;**13**:144-47.

45. Goebel P, Schubert W. Personal experiences with covering burns in children with amnion. *Brit Orthop Traumatol* 1990;**37**:495-98.

46. Chakraborty SK, Nessa A, Mia MM, Khan AR, Aziz MA, Ullah MS. Management of Mixed (superficial and deep) burn with allogeneic amnion and autogeneic skin grafting. *Bangladesh Journal of Medical Science* 2003;**9**:91-94.

47. Bari MM, Begum R, Chakraborty SK, Islam MS. Tissue Banking: Use of radiation sterilized amniotic membrane grafts as temporary biological dressings for the treatment of leprotic ulcers. *Acta Orthopedica Hellenica* 1995;**46**:88-93.

48. Bari MM, Begum R. Use of radiation-sterilized amniotic membrane grafts as temporary biological dressings for the treatment of leprotic ulcers. In: Phillips GO, Kearney JN, Strong DM, von Versen R, Nather A, editors. Advances in Tissue Banking vol.3, World Scientific Publishing Co Pte Ltd, Singapore, 1999;P.477-83.

49. Shimazaki J, Yang HY, Tsubota K. Amniotic membrane transplantation for ocular surface reconstruction in patients with chemical and thermal burns. *Ophthalmol* 1997;**104**:2068-76.

50. Kruse FE, Rohrschneider K, Volcker HE. Multilayer amniotic membrane transplantation for reconstruction of deep corneal ulcers. *Ophthalmol* 1999;**106**:1504-11.

51. Hoque F, Muldun S, Rahman S, Islam M. An initial study of pressure sore management with amniotic membrane dressing. In: Phillips GO, Kearney JN, Strong DM, von Versen R, Nather A, editors.Advances in Tissue Banking vol. 3. World Scientific Publishing Co Pte Ltd, Singapore, 1999;P.491-93.

52. Bari MS, Choudhury MIM, Khan AR, Nessa A. Role of human foetal membranes (amniotic membrane) in the management of burn wounds. *Annals of Burns and Fire Disaster* 2002;**15**:3-8.

53. Shahid SMA, Khan AR, Rahman MM, Lina KSN. Effectiveness of radiation sterilized amniotic membrane in reducing patient's morbidity in comparison to non biological dressing like medicated Tulle (Sofra Tulle). *IOSR Journal of Dental and Medical Sciences* 2019;**18**:44-50.

54. Ullah MS, Ferdous KMN, Mullick MMH, Alam MR, Rahman MS, Khan AR. Amnion membrane graft dressing in superficial partial thickness burn in pediatric patients. *Chattagram Maa-O-Shishu Hospital Medical College Journal* 2015;**14**: 22-25.

55. Demling RH. Burns and other thermal Injuries. In: Lawrence WW, Doherty GM. editors. Current Surgical Diagnosis and Treatment, 11th ed. New York, McGraw-Hill, 2003;P.267-69.

56. Masood AFM, Khan AR, Islam KK. Surgical problems in children-10 years survey in Dhaka Shishu (Children) Hospital. *Dhaka Shishu (Children) Hospital Journal* 1991;**7**:24-29.

DS (Child) HJ 2022;38(1):56-60 DOI: https://doi.org/10.3329/dshj.v38i1.67005

CASE REPORT

Infantile Inflammatory Bowel Disease in A 14 Month Old Bangladeshi Boy: An Unusual Presentation

Tanzila Farhana[1], Salahuddin Mahmud[2], Mashud Parvez[3], Madhabi Baidya[4], Ahmed Rashidul Hasan[5], Syed Shafi Ahmed[6]

Introduction

The term inflammatory bowel disease (IBD) is used to represent two particular disorders, Crohn's disease (CD) and Ulcerative colitis (UC). It has been pointed out that; the frequency of childhood onset inflammatory bowel disease (IBD) is increasing throughout the world. P-IBD (onset before 17 years of age) has been sub-classified based on the age of onset of the disease as neonatal onset (<28 days of life), infantile onset (<2 years of age), very early onset (<6 years of age), and early onset (<10 years of age).[1,2] The incidence of paediatric onset UC, which constitutes roughly 15% to 20% of all UC, ranges at 1to 4/ 1000000/ year in most North American and European regions.[3] A study of Canada showed the incidence of IBD increased from 9.4 per 100,000 children (95% confidence interval [CI], 8.2-10.8/ 100,000 children) in 1994 to 13.2 per 100,000 children (95% CI, 11.9-14.6/100,000 children) in 2009 (P< .0001). The incidence increased by 7.4% per year among children younger than 6 years old and 6-9.9 years old, and by 2.2% per year among children ≥10 years old.[4] Nevertheless, in the countries of Asian subcontinent like Bangladesh, VEO-IBD patients have not been extensively studied, mostly because of the rarity of this patient population. So there has been remained a scarcity of research, in order to obtain a better sense of what they respond to and what they don't. The presentations of childhood-onset IBD are more aggressive, rapidly progressive and often needed early surgical interventions as compared to the characteristics of the adult cohort.[5-7] Infantile IBD should be considered as an important differential diagnosis of any child <2 years of age presents with persistent diarrhea, abdominal pain, hematochezia, failure to thrive, and/or poor feeding. Assessing the severity of the disease greatly relies on The Pediatric Ulcerative Colitis Activity Index (Table II) is an authentic score of clinical disease activity, not required endoscopy or laboratory markers and is accessible to calculate routinely. A clinically significant response is indicated by a decline in PUCAI of at least 20 scores. Moreover in drug trials, the PUCAI score is advantageous, including

Keywords: Inflammatory bowel disease, infant, mesalazine.

1. Resident Medical Officer, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka.
2. Associate Professor, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
3. Associate Professor, Department of Pathology, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
4. Assistant Professor, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.
5. Registrar in-charge, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka,
6. Professor and Head, Department of Pediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh.

Correspondence to: Dr. Tanzila Farhana, Resident Medical Officer, Department of Pediatric Gastroenterology, Hepatology & Nutrition, Bangladesh Shishu Hospital & Institute, Dhaka, Bangladesh. Cell: +8801737257050, E-mail: tanzila.djmc@gmail.com

Received: 9 January 2022; **Accepted**: 22 February 2022

high correlation with colonoscopy. Here the authors will report case of a 14 month-old Bangladeshi boy who presented with bloody diarrhea and was finally diagnosed as Infantile IBD and treated conservatively. He showed acceptable improvement and was followed up, up to a certain period of time.

Case Report

A 14 month old boy was referred to the Department of Pediatric Gastroenterology, Hepatology and Nutrition unit of Bangladesh Shishu Hospital & Institute, having frequent passage of blood mixed loose stool for last 7 days. The frequency was about 10-12 times per day and other associated conditions were, low grade intermittent fever, occasional abdominal pain and irritability. In last 2 months preceding hospitalization, he had experienced off and on passage of loose stool mixed with mucus but no blood. His medical history indicated the ante natal, natal and post-natal period was uneventful. He was on exclusive breast feeding up to 6 months of his age later complimentary feeding was started with family foods but no allergic ones (like cow's milk, nuts etc.) was introduced. For these reason he was treated several times by different physicians without any long lasting improvement.

On the day of admission, the boy passed about 10 bowel movements a day, which was bloody and >50% of the stool volume being blood and it persisted for next 7 days. Many of the purging occurred at night. It was associated with abdominal pain as because the boy was crying during purging. On general examination, he looked irritable, mildly pale, anicteric, febrile, temperature was 100°F, heart rate was 124/min, blood pressure was 90/60 mmHg, respiratory rate was 18 breathes/min. There was no lymphadenopathy or skin lesion present. His height was 78cm (falls on 50th centile; ref. value CDC) and weight was 10 kg (falls on 10th centile; ref. value CDC).

On systemic examination, abdomen was soft, mildly distended, no rigidity, ascites, gurding or organomegaly was present. No abnormality was seen on the perianal region and other systemic examination revealed normal finding. With the aim of precluding the differential diagnosis, microbiological testing was done. Routine microscopic examination of stool showed us there was presence of plenty of pus cells along with numerous RBC and Stool for OBT found positive. Stool and Blood cultures were found no growth of any organism. Allergic testing was also performed and found normal. The results of laboratory tests are shown on *Table 1.* Immunoglobulin levels with flow cytometry were normal in range and HIV testing was also done which found negative. The abdominal Ultrasonography and Chest X-ray was normal. We also did RT PCR for COVID-19 (found negative) before performing the upper GI endoscopy and Colonoscopy.

Table I
Laboratory results

Parameters	Initial values	F/up values	Normal range/unit
Hemoglobin	9.2	9.8	11.5-14.5gm/L
WBC count	18,700	8,500	6,000-17,500 /mm^3
Platelet count	506,000	365,000	1, 50,000-4, 50,000 / mm^3
N%	45	38	28
L%	44	58	61
M%	06	03	3
E%	05	01	5
ESR	68	35	
Na+	145.0	136.5	135-156 mmol/L
K+	3.6	4.5	3.5-5.4 mmol/L
Cl^-	105.0	104.0	96-108 mmol/L
S. creatinine	64.0	-	40-110 umol/L
S. Ca++	2.1	-	2.02-2.6 mmol/L
S. Albumin	32.9	38.7	35-60 gm/L
D-Dimer	2.5	1.2	<0.5 mg/L
CRP	116.0	12.6	<5 mg/L
ANA	Negative	-	
PT	10.7	-	12 sec
F. calprotectin	890.0	95.0	<80 µg/gm
IgE	10.0	-	<29 IU/ml

Colonoscopy report showed, the mucosa of the rectum, sigmoid colon, descending colon and up to mid transverse colon was inflamed and friable. Vascular pattern was lost in the affected segment. The mucosa, vascular pattern and lumen of the rest of the colon appeared normal including the anal canal (*Figure 1a, 1b, 1c*). Biopsy specimen was taken from inflamed area of the colon and histopathological report revealed, colonic tissue presenting ulcerations, edema and acute inflammatory exudates. The lamina propria was edematous with cryptitis. Crypt abscess and diffuse mixed inflammatory cellular infiltrates predominant cells were lymphocytes, plasma cells, polymorphs and

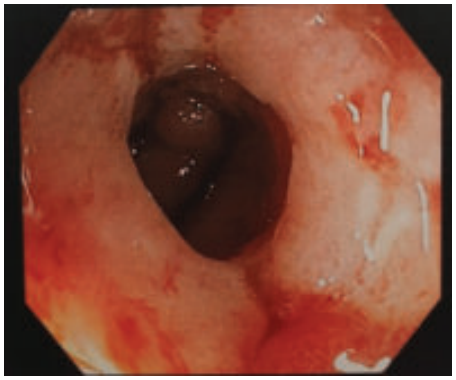


Fig.-1a *Inflamed mucosa*

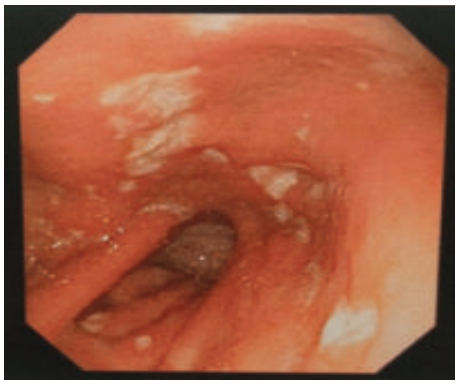


Fig.-1b *Scattered ulceration*

Fig.-1c *Large ulceration*

Fig.-1(a,b,c) *Colonoscopic view of infantile IBD*

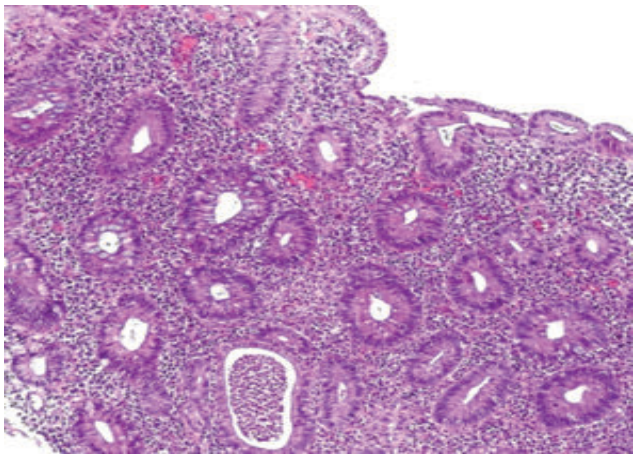


Fig.-2: *Colonic tissue, H & E stain low-power image reveal crypts abscess and cryptitis*

eosinophils (Figure-2). No architectural distortion or basal plasmacytosis was seen. Endoscopy of upper GIT revealed normal finding. Disease activity was assessed as 70 Score on the PUCAI scale (Paediatric Ulcerative Colitis Activity Index Table II). Ulcerative colitis was the final diagnosis. Treatment was planned with IV Methylprednisolone 1.5mg/kg/day for 5 days; along with broad spectrum antibiotic inj. Meropenem. We also restricted feeding initially and gradually increased the amount with continued breast milk and rice suji accordingly. From 1st week of treatment we observed gentle clinical improvements; the numbers of bowel movement were ceased, stool no longer contained blood, no night time purging, baby became playful, and fever subsided.

Table II
PUCAI score

Paediatric Ulcerative Colitis Activity Index (PUCAI)			
1. Abdominal pain		***4. No. of stools***	
No pain	0	0-2	0
Pain can be ignored	5	3-5	5
Pain cannot be ignored	10	6-8	10
2. Rectal bleeding	>8	15	
None	0	***5. Nocturnal stools***	
Small amount only in<50% stools	10	No	0
Small amount with most stools	20	Yes	10
Large amount >50%of the stool content	30	***6. Activity level***	
3. Stool consistency		No limitation	0
Formed	0	Occasional limitation	5
Partially formed	5	Severely restricted activity	10
Completely unformed	10		

PUCAI Scoring with interpretation			
<10	Remission	**10-34**	Mild disease activity
35-64	Moderate disease activity	**>65**	Severe disease activity

At this point of treatment we switched to oral prednisolone 1mg/kg/day and Mesalazine was added (40mg/kg/day). One week after discharge on his 1st follow-up visit PUCAI score was 5. General condition was good, he regained appetite. He was passing 2 bowel movements per day, which was of normal consistency with no blood or mucus. CBC, CRP, S. albumin levels showed significant improvements.

It was recommended to reduce the oral dose of Prednisolone gradually, to continue Mesalazine, to expand the range of the diet slowly added some adjunctive medications like Zinc, Folic acid, Cholecalciferol and he was scheduled for regular follow-up visit.

Discussion

It is distressing that the incidence of Pediatric IBD is inflating worldwide, having a multifactorial etiopathogenesis. Our patient presented at his 14 months of age, Sara Ebrahimi reported a neonate who presented at 7 days of life and Chie Iida reported of an infant of 3 months of age.[8, 9]

In our case symptoms were found persistent diarrhea, abdominal pain, hematochezia, irritability, and poor feeding, similarly Xin Wang and Yuan Xiao found, patients in the 0–2 y group commonly manifested systemic symptoms such as fever, weight loss, diarrhoea and limitation of activity, colonic lesions, strictures and perianal disease. [10-13] The prevalence of extra-intestinal manifestations in IBD reportedly ranges from 6% to 47%. But in our case there was no such type of involvements like perianal disease. Our patient's PUCAI score was above 65 which indicated severe form. [14-17] The laboratory findings included mild anemia, leukocytosis and thrombocytosis in CBC, a raised ESR & CRP with a normal IgE level and primary immunodeficiency panel. It was almost similar with the findings of Ahamed N [18], so that other differentials like milk protein allergy, primary immunodeficiency syndrome were excluded. At this age it has a strong connection with IL-10 receptor gene, unfortunately we didn't have access for gene analysis which can be a limitation of our study. Colonoscopic and Histopathological evidences confirmed the diagnosis of UC. We initially administered IV Methylprednisolone 1.5mg/kg/day for 5 days; along with broad spectrum antibiotic inj. Meropenem. When purging rate was declining as well as the clinical features were improving we switched over to oral prednisolone 1m/kg/day later it was tapered within 2.5 months and Mesalazine was added (40mg/kg/day), as there are many side effects such as growth disturbances, osteoporosis, immunosuppression are documented in the long term use of steroids. Our patient responded gradually with anti-inflammatory agents and antibiotics and we discharged him with the plan of regular follow-up.

Conclusion

Chronic bloody diarrhea at any age should be evaluated properly for IBD. Colonoscopy and histopathology should be done routinely to make a diagnosis. PUCAI scoring can be used to measure the severity of the disease. As the infantile IBD has a poor prognostic factor so combined therapy should be started as early as possible to prevent surgical intervention.

References

1. Crowley E, Muise A. Inflammatory bowel disease: what very early onset disease teaches us? *Gastroenterol Clin North Am* 2018;**47**:755-72.
2. Ujjal P, Moinak SS. Higher Prevalence of Monogenic Cause Among Very Early Onset Inflammatory Bowel Disease in Children: Experience From a Tertiary Care Center From Northern India. *Inflammatory Bowel Diseases* 2023;**XX**:1-7.
3. Dan Turner D, Ruemmele FM, Orlanski-Meyer E, Griffiths AM, de Carpi JM, Bronsky J, et al. Management of pediatric ulcerative colitis. *JPGN* 2018;**67**:257-91
4. Benchimol E, Mack DR, Nguyen GC. Incidence, outcomes, and health services burden of very early onset inflammatory bowel disease. *Gastroenterology* 2014;**147**:803-13.e7.
5. Moon JS. Clinical aspects and treatments for pediatric inflammatory bowel disease. *Intest Res* 2019:**17**:17-23.
6. Kelsen J, Baldessano R: The role of monogenic disease in children with very early-onset inflammatory bowel disease. *Curr Opin Pediatr* 2017:**29**:566-71.
7. Yousef Almana, Reem Mohammed: Current concepts in pediatric inflammatory bowel disease; IL10/IL10R colitis as a model disease. *International Journal of Pediatrics and Adolescent Medicine* 2019:**6**:1-5.
8. Ebrahimi S,Khademi G, Jafari SA, Nejad NZ, Norouzy A, Imani. B. Neonatal presentation of unremitting inflammatory bowel disease. *IJMS* 2018;**43:**328-31.

9. Iida C, Tatsumi A, Fujino H. Infantile Inflammatory Bowel Disease in a Three-Month-Old-Boy. *Cureus* 2021;**13**:e12743.

10. Kelsen JR, Cuffari C, Mamula P. Ulcerative colitis in children. 2011 Sep. [cited 2013 Feb]. Available from: URL: http://www.eMedicine .medscape.com

11. Turner D, Seow CH, Greenberg GR, Griffiths AM, Silverberg MS, Steinhart AH. A systematic prospective comparison of noninvasive disease activity indices in ulcerative colitis. *Clin Gastroenterol Hepatol* 2009;**7**:1081-88.

12. Turner D, Otley AR, Mack D, Hyams J, de Bruijne J, Uusoue K, et al. Development, validation, and evaluation of a Pediatric Ulcerative Colitis Activity Index: a prospective multicenter study. *Gastroenterology* 2007;**133**:423-32.

13. Turner D, Hyams J, Markowitz J, Lerer T, Mack DR, Evans J, et al. Appraisal of the Pediatric Ulcerative Colitis Activity Index (PUCAI). *Inflamm Bowel Dis* 2009;**15**:1218-23.

14. Turner D, Walsh CM, Benchimol EI, et al. Severe paediatric ulcerative colitis: incidence, outcomes and optimal timing for second-line therapy. *Gut* 2008;**57**:331-38.

15. Dinesen LC, Walsh AJ, Protic MN. The pattern and outcome of acute severe colitis. *J Crohns Colitis* 2010; **4**:431-7.

16. Van Limbergen J, Russell RK, Drummond HE. Deûnition of phenotypic characteristics of childhood-onset inûammatory bowel disease. *Gastroenterology* 2008;**135**:1114-22.

17. Gower-Rousseau C, Dauchet L, Vernier-Massouille G. The naturalhistoryof pediatric ulcerativecolitis: apopulation-based cohort study. *Am J Gastroenterol* 2009;**104**:2080-88.

18. Ahamed N, Khadga M, Majumder W. An eleven months old infant with very early onset Inammatory Bowel Diseases (IBD): A rare case report. *Bangladesh Med J* 2021;**50**:45-49.

ABSTRACTS FROM CURRENT LITERATURE

Antibiotic-Resistant bacteremia in young children hospitalized with pneumonia in Bangladesh is associated with a high mortality rate

Chisti MJ, Harris JB, Carroll RW, Shahunja KM, Shahid ASMSB, Moschovis PP, et al. Open Forum Infect Dis 2021;**8**:ofab260.

Background: Pneumonia is a leading cause of sepsis and mortality in children under 5 years. However, our understanding of the causes of bacteremia in children with pneumonia is limited.

Methods: We characterized risk factors for bacteremia and death in a cohort of children admitted to the Dhaka Hospital of the International Centre for Diarrhoeal Disease Research, Bangladesh (icddr,b) between 2014 and 2017 with radiographically confirmed pneumonia.

Results: A total of 4007 young children were hospitalized with pneumonia over the study period. A total of 1814 (45%) had blood cultures obtained. Of those, 108 (6%) were positive. Gram-negative pathogens predominated, accounting for 83 (77%) of positive cultures. These included *Pseudomonas* (N = 22), *Escherichia coli* (N = 17), *Salmonella enterica* (N = 14, including 11 *Salmonella* Typhi), and *Klebsiella pneumoniae* (N = 11). Gram-positive pathogens included Pneumococcus (N = 7) and *Staphylococcus aureus* (N = 6). Resistance to all routinely used empiric antibiotics (ampicillin, gentamicin, ciprofloxacin, and ceftriaxone) for children with pneumonia at the icddr,b was observed in 20 of the 108 isolates. Thirty-one of 108 (29%) children with bacteremia died, compared to 124 of 1706 (7%) who underwent culture without bacteremia (odds ratio [OR], 5.1; 95% confidence interval [CI], 3.3-8.1; $P < .001$). Children infected with bacteria resistant to all routinely used empiric antibiotics were at greater risk of death compared to children without bacteremia (OR, 17.3; 95% CI, 7.0-43.1; $P < .001$).

Conclusions: Antibiotic-resistant Gram-negative bacteremia in young children with pneumonia in Dhaka, Bangladesh was associated with a high mortality rate. The pandemic of antibiotic resistance is shortening the lives of young children in Bangladesh, and new approaches to prevent and treat these infections are desperately needed.

Antibiotic use for acute respiratory infections among under-5 children in Bangladesh: a population-based survey

Hassan MZ, Monjur MR, Biswas MAAJ, Chowdhury F, Braithwaite J, et al. BMJ Global Health 2021;6:e004010.

Introduction: Despite acute respiratory infections (ARIs) being the single largest reason for antibiotic use in under-5 children in Bangladesh, the prevalence of antibiotic use in the community for an ARI episode and factors associated with antibiotic use in this age group are unknown.

Methods: We analysed nationally representative, population-based, household survey data from the Bangladesh Demographic and Health Survey 2014 to determine the prevalence of antibiotic use in the community for ARI in under-5 children. Using a causal graph and multivariable logistical regression, we then identified and determined the sociodemographic and antibiotic source factors significantly associated with the use of antibiotics for an episode of ARI.

Results: We analysed data for 2 144 children aged <5 years with symptoms of ARI from 17 300 households. In our sample, 829 children (39%) received antibiotics for their ARI episode (95% CI 35.4% to 42.0%). Under-5 children from rural households were 60% (adjusted OR (aOR): 1.6; 95% CI 1.2 to 2.1) more likely to receive antibiotics compared with those from urban households, largely driven by prescriptions from unqualified or traditional practitioners. Private health facilities were 50% (aOR: 0.5; 95% CI 0.3 to 0.7) less likely to be sources of antibiotics compared with public health facilities and non-governmental organisations. Age of children, sex of children or household wealth had no impact on use of antibiotics.

Conclusion: In this first nationally representative analysis of antibiotic use in under-5 children in Bangladesh, we found almost 40% of children received antibiotics for an ARI episode. The significant prevalence of antibiotic exposure in under-5 children supports the need for coordinated policy interventions and implementation of clinical practice guidelines at point of care to minimise the adverse effects attributed to antibiotic overuse.

Antimicrobial resistance in shigellosis: A surveillance study among urban and rural children over 20 years in Bangladesh

Nuzhat S, Das R, Das S, Islam SB, Palit P, Haque MA, et al. PLoS ONE 17(11): e0277574.

Antimicrobial resistance against shigellosis is increasingly alarming. However, evidence-based knowledge gaps regarding the changing trends of shigellosis in Bangladesh exist due to the scarcity of longitudinal data on antimicrobial resistance. Our study evaluated the last 20 years antimicrobial resistance patterns against shigellosis among under-5 children in the urban and rural sites of Bangladesh. Data were extracted from the Diarrheal Disease Surveillance System (DDSS) of Dhaka Hospital (urban site) and Matlab Hospital (rural site) of the International Centre for Diarrheal Disease Research, Bangladesh (icddr,b) between January 2001 and December 2020. We studied culture-confirmed shigellosis cases from urban Dhaka Hospital (n = 883) and rural Matlab Hospital (n = 1263). Since 2001, a declining percentage of shigellosis in children observed in urban and rural sites. Moreover, higher isolation rates of *Shigella* were found in the rural site [1263/15684 (8.1%)] compared to the urban site [883/26804 (3.3%)] in the last 20 years. In both areas, *S. flexneri* was the predominant species. The upward trend of *S. sonnei* in both the study sites was statistically significant after adjusting for age and sex. WHO-recommended 1st line antibiotic ciprofloxacin resistance gradually reached more than 70% in both the urban and rural site by 2020. In multiple logistic regression after adjusting for age and sex, ciprofloxacin, azithromycin, mecillinam, ceftriaxone, and multidrug resistance (resistance to any two of these four drugs) among under-5 children were found to be increasing significantly ($p<0.01$) in the last 20 years in both sites. The study results underscore the importance of therapeutic interventions for shigellosis by appropriate drugs based on their current antibiogram for under-5 children. These observations may help policymakers in formulating better case management strategies for shigellosis.

Antibiotic Use for Febrile Illness among Under-5 Children in Bangladesh: A Nationally Representative Sample Survey

Nora Samir N, Hassan MZ, Biswas MAAJ, Chowdhury F, Akhtar Z, Lingam R, et al. *Antibiotics* 2021;*10*:1153.

Fever in children under five years of age is a common and predominantly self-limiting sign of illness. However, in low- and middle-income countries, antibiotics are frequently used in febrile children, although these children may not benefit from antibiotics. In this study, we explored the prevalence of, and factors associated with, antibiotic use in children under five years old with febrile illness in Bangladesh. We analysed data from the 2017–2018 Bangladesh Demographic and Health Survey to determine the prevalence of antibiotic use in children under five years of age with a febrile illness. We used a causal graph and performed a multivariable logistical regression to identify the factors associated with antibiotic use in children under five years old with febrile illness in Bangladesh. Of the 2784 children aged less than five years with fever included in our analysis, 478 (17%, 95% CI 15% to 19%) received antibiotics. Unqualified sources, including unqualified providers and pharmacies, contributed to 60% of antibiotic prescriptions in children with fever, followed by the private medical sector (29%) and the public sector (23%). The highest use of antibiotics was found in children under six months of age (25%). Children with parents who completed secondary or higher education were more likely to receive antibiotics (adjusted OR (aOR): 2.61 (95% CI 1.63 to 4.16)) than children whose parents did not complete primary education. Educational interventions promoting rational use of antibiotics and improved regulations governing over the counter purchase of antibiotics in Bangladesh may improve antibiotic dispensing practices.

INSTITUTE NEWS

Bangladesh Institute of Child Health (BICH) was the academic wing of Dhaka Shishu (Children) Hospital. It was established in 30 January 1983. It was affiliated with Dhaka University, Bangabandhu Sheikh Mujib Medical University (BSMMU) and Bangladesh College of Physicians and Surgeons (BCPS). Recently the name of BICH has been changed, its new name is Bangladesh Shishu Hospital & Institute. In this Institute different basic science departments were established in the year 2006. It has been conducting different courses e.g. FCPS (in General Paediatrics and also subspeciality like FCPS Neonatology, Paediatric Nephrology, Paediatric Haemato-oncology, Paediatric Neurology and Development, Paediatric Pulmonology, Paediatric Cardiology under BCPS), MD Residency Course in General Paediatrics and Neonatology and Nephrology under BSMMU, MD Non residency course under Dhaka University and BSMMU, MS (Paediatric Surgery) Residency Course under BSMMU, MS (Paediatric surgery) non residency course under Dhaka University, DCH course under BSMMU. The Institute is also conducting Diploma in Paediatric Nursing course under Bangladesh Nursing Council, BSc in Health Technology course under Dhaka University. It conducts 3 months certificate course in Paediatrics and 15 days Intensive course for MCPS examinee. It organizes different programme, seminars and symposium on Paediatrics. The Institute conducted its regular classes, academic activities, symposium, seminars etc. during COVID-19 pandemic.

Library facilities

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

DOI: https://doi.org/10.3329/dshj.v38i1.67007

Postgraduate Courses and Training in Paediatrics in Bangladesh Shishu Hospital & Institute

1. BSH&I has course for FCPS in General Paediatrics (2nd part): Students can be registrared twice in a year, in the month of January and July.
2. BSH&I is a recognized center by BCPS for training in FCPS (Paeditric Medicine and Surgery).
3. It is a recognized centre for course and training in different subspeciality of Paediatrics like Neonatology, Paediatric Nephrology, Paediatric Haematology and Oncology, Paediatric Pulmonology, Paediatric Neuroscience and Paeditric Cardiology.
4. There is MD Residency program in General Paediatrics, Neonatology, Paediatric Nephrology and MS Paediatric Surgery. Phase A commences in the month of March every year. There is also MD Paediatrics and MS Paediatric Surgery. Non Residency Courses commences in the month of January and July.
5. DCH course: Once in a year in the month of July.
6. Other courses conducted by BSH&I are
   - Paediatric Nursing.
   - BSc in Health Technology.
   - Three months certificate course: Every year the institute conducts 3 months certificate course in Paediatrics for general practitioners & other post graduate candidates e.g. MCPS.
   - Training programme on Essential Newborn Care for doctors and nurses, KMC (Kangaroo Mother Care) training, ETAT (Emergency Triage, Assessment and Treatment) training, IMCI (Integrated management of childhood illness), newborn and paediatric standard use of oxygen therapy for hypoxemia management etc. are conducted by BSH&I.

Contact Person : Academic Coordinator
Bangladesh Shishu Hospital & Institute
Sher-e-Bangla Nagar, Dhaka, Bangladesh.

Contact : Phone No. 55059063, 55059064, 55059051-60 Ext. 411.
E-mail: infodshjournal@gmail.com, info.bich@gmail.com

DOI: https://doi.org/10.3329/dshj.v38i1.67008

DS (Child) HJ 2022;38(1):65

Students Qualified from Bangladesh Institute of Child Health (At present BSH&I)

Student Qualified From BSH&I till July 2022

Course	Number
DCH	380
MD Pediatrics	119
MS Pediatrics	108
FCPS Pediatrics	19
MD Neonatology	11
MD Pediatric Nephrology	06
Total	643

Foreign Student qualified from BSH&I till July 2022

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

Present Students (till July 2022) of BSH&I

Name of Courses	Number of Students
MD (General Pediatrics) Phase-A	35
MD (Neonatology) Phase -A	07
MD (Pediatric Nephrology) Phase –A	03
MS Pediatric Surgery Phase-A	22
FCPS (Pediatrics) Part-II	02
MD (Pediatrics) Part III	03
FCPS (Pediatric Cardiology)	01
FCPS(Pediatrics Nephrology)	01
MS (Pediatric Surgery) Part III	02
DCH	23
MD (General Pediatrics) Phase-B	19
MD (Neonatology) Phase –B	04
MD (Pediatric Nephrology) Phase –B	03
MS Pediatric Surgery Phase-B	23
Total	148

DOI: https://doi.org/10.3329/dshj.v38i1.67011q

INSTRUCTIONS FOR AUTHORS

Dhaka Shishu (Children) Hospital Journal is the official organ of Bangladesh Shishu Hospital & Institute (BSH&I). 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 descriptions 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**.

Subscription form - National subscribers

Please include me as a subscribed
member of Dhaka Shishu (Children) Hopital Journal

Annual subscription rate: BDT 200 (Individual)
or BDT 500.00 for three years
(postal/courier service charges included)

ISSN 1013-2295
Volume.....Number -1 and 2 (year.....).

I hereby enclose an account payee cheque/ pay order/bank draft for Dhaka Shishu Hopital Journal payable to "Dhaka Shishu Hospital Journal" by Pay order/Account payee Cheque/ Bank draft no _____ of _____ bank dated _____ .

Signature _____

Name (Capital Letters) _____

Mailing Address _____

Phone : Res _____ Mob: _____

Office/Chamber _____

Fax _____ E-mail _____

(PHOTOCOPY ALLOWED)

Subscription form - National subscribers

Please include me as a subscribed
member of Dhaka Shishu (Children) Hopital Journal

Annual subscription rate: BDT 200 (Individual)
or BDT 500.00 for three years
(postal/courier service charges included)

ISSN 1013-2295
Volume.....Number -1 and 2 (year.....).

I hereby enclose an account payee cheque/ pay order/bank draft for Dhaka Shishu Hopital Journal payable to "Dhaka Shishu Hospital Journal" by Pay order/Account payee Cheque/ Bank draft no _____ of _____ bank dated _____ .

Signature _____

Name (Capital Letters) _____

Mailing Address _____

Phone : Res _____ Mob: _____

Office/Chamber _____

Fax _____ E-mail _____

(PHOTOCOPY ALLOWED)

From

Stamp

To
The Editor
Dhaka Shishu (Children) Hospital Journal
Sher-e- Bangla Nagar, Dhaka - 1207
BANGLADESH

From

Stamp

To
The Editor
Dhaka Shishu (Children) Hospital Journal
Sher-e- Bangla Nagar, Dhaka - 1207
BANGLADESH

BANGLADESH SHISHU HOSPITAL & INSTITUTE

SHER-E- BANGLA NAGAR, DHAKA-1207

Bangladesh Shishu Hospital & Institute has been modernized with sophisticated equipments for the following investigations

Pathology

1. Mythic18 Automated Haematology Analyser having 18 parameters: WBC count with 3 parts differential - RBC count, Haemoglobin percentage, HCT, MCV, MCH, MCHC, RDW, Platelet count, MPV, PDW
2. Haemoglobin Electrophoresis
3. BT, CT, PT, APTT
4. Routine urine exam, including pH, urobilinogen, bilirubin, haemoglobin and morphology of RBC in urine.
5. Routine stool exam, including reducing substances and occult blood test
6. Osmotic Fragility test
7. NESTROFT for screeing of beta thalassaemia
8. LE cell Phenomenon
9. Sputum for Eosinophils

Microbiology

1. All types of cultures and sensitivity test of aerobic and anaerobic organisms
2. Serological Test - Widal test, Febrile Antigen, ASO titre, RA Test, VDRL, HbsAg, ICT for Kala-Azar, Malaria, Filaria and Dengue
3. Cytology-
   CSF analysis with Latex agglutination test for bacterial antigens
4. Staining - gram stain, AFB stain, KLB stain
5. Skin scrapping for fungus

Biochemistry

1. Full auto biochemistry analyzer (Dade Behring)- Dimension RxL Max with random acesss test- Bilirubin, SGPT, SGOT, Alkaline Phosphatase, Urea, Creatinine, Calcium, Phosphate, Uric Acids, Protein, Albumin, Glucose, CPK, Serum Electrolytes, Serum Ferritin, CRP, ammonia, lactate
2. Semi Auto Biochemistry analyzer - Routine biochemical tests
3. Electrolyte analyzer - Na, K, Cl, TCO_2
4. Gas analyzer - Blood pH, PCO_2, PO_2, HCO_3, O_2 saturation, Base excess, Oxyhemoglobin, Carboxy hemoglobin, Methemoglobin, Deoxyhemoglobin, Oxygen binding capacity

Blood Bank

1. Blood grouping and cross matching
2. Screening test - HbsAg, HCV, HIV, VDRL, MP
3. Coomb's test - direct and indirect
4. Collection of platelet & concentrate

Histopathology : Histopathology of all surgical specimens

Cytology: FNAB of all superficial and deep masses. Cytology of all effusions

Radiology and Imaging

1. All types of plain x-ray - 24 hours service, contrast radiographic examination-Barium swallow, enema, IVU and MCU both neonates and children
2. Conventional Ultrasonography by SIEMENS Sonoline Prima Having Multi frequency, multi probe facilities. USG are performed like- brain, abdomen, eye, hipjoint and musculoskeletal system
3. Color Doppler study by SIEMENS Color Doppler Machine (Sonoline - G40), study of abdominal vessels, portal vein, renal artery, cerebral arteries, vascular malformation of neck- upper/lower limbs
4. Portable USG for very sick indoor patients
5. Colour Doppler Echocardiogram

Director
Bangladesh Shishu Hospital & Institute

Published by Bangladesh Shishu Hospital & Institute, Sher-e-Bangla Nagar, Dhaka. E-mail: info.dshjournal@gmail.com and printed at Asian Colour Printing, 130, Fakirerpool, Dhaka. Phone: 49357726, 58313186, 01851248141 E-mail: asianclr@gmail.com