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Editorial

Immediate Kangaroo Mother Care (iKMC) – An Advance Approach for Better Survival of Premature Neonates

Prof. Md. Mahbubul Hoque

Every year fifteen million newborn in the world are born premature, of which more than one million of them die due to complication of prematurity. According to Bangladesh demographic Health Survey 2022, neonatal mortality rate was 20 per thousand live birth, and prematurity or low birth weight contribute about 32% of total neonatal mortality. Several interventions have been proven as effective to improve survival of low birth weight neonates, such as antenatal corticosteroid, exclusive breast feeding, early management of sepsis, kangaroo mother care (KMC).

KMC is a transformative innovation in the care of preterm or low birth weight (LBW) infants and has been shown to reduce risk of neonatal mortality by 40%. KMC involves continuous and prolonged skin to skin contact with support for exclusive breastfeeding and timely discharge from NICU to lower level, close monitoring and follow up. In the ensuing years, continued research has shown that KMC is a life-saving intervention for preterm infants. Despite long standing evidence on positive impact of KMC on maternal and newborn health outcome, the implementation of KMC has shown itself to be a persistent challenge with many barriers to mothers and newborns being care for together from birth.

According to WHO-2015, Kangaroo mother care can be started when a low birth weight baby become stable (normal vitals, pink in room air or with 40% oxygen, no prolonged or frequent apnoea, no congenital anomaly or surgical problem).

Approximately 45% of neonatal deaths occur within 24 hours after birth and 80% during the first week of life; thus, the majority of deaths among infants with low birth weight typically occur before kangaroo mother care can be initiated.

The effect of initiating kangaroo mother care immediately after birth on physiological stabilization has been evaluated and skin-to-skin contact that was

initiated soon after birth in infants with low birth weight resulted in earlier stabilization than conventional care. Immediate KMC (iKMC) for small and preterm newborn has revealed lower infection rates, reduced hypothermia, better feeding and increased rate of survival.

Now for all preterm or low birthweight babies including very small and sick WHO recommends starting KMC as soon as possible after birth. If needed there should require fundamental change in the way of neonatal care. In addition we can provide family and small baby together without any period of separation and establish mother neonatal intensive care unit (M-NICU), M-SCANU and family centered care.

So the initiation of iKMC improves the outcomes of premature neonates and an advance approach for better survival of premature neonates.

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Original Article

Insights into the Practice of Kangaroo Mother Care: Experiences from a Tertiary Care Neonatal Unit in Bangladesh

Liton Chandra Saha¹, Rinky Rani Saha², Nishat Jahan³, Maksudur Rahman⁴, Md. Mahbubul Hoque⁴, Mahfuza Shirin⁴, M Monir Hossain⁵

Abstract

Background: Kangaroo Mother Care (KMC) is an evidence-based intervention proven to improve survival and health outcomes in low-birth-weight and preterm neonates. Despite its global success, challenges persist in its implementation and acceptance in resource-limited settings like Bangladesh.

Objective: This study aimed to explore maternal experiences, neonatal outcomes and barriers to KMC implementation in a tertiary neonatal unit in Bangladesh.

Methods: A cross-sectional descriptive study was conducted on 148 neonates and their mothers at a tertiary neonatal unit in Bangladesh from January to December 2023. Data on neonatal characteristics, weight progression over three follow-ups and maternal feedback were collected using structured questionnaires. Quantitative data were analyzed using SPSS, with descriptive statistics summarizing key findings.

Results: The mean birth weight of neonates was 1488.7 ± 315.1 grams, with a mean gestational age of 32.2 ± 2.2 weeks. The average KMC duration was 7.0 ± 1.6 hours per day. Neonatal weights significantly improved over follow-ups, with mean weights of 2029.0 ± 336.8 grams, 2940.0 ± 801.3 grams and 4784.2 ± 1916.4 grams, respectively. Maternal feedback was positive, with 77.7% reporting improved bonding, 68.9% increased breastfeeding confidence and 89.9% willing to recommend KMC. Challenges included difficulty managing KMC at home (39.2%).

Conclusion: KMC was found to significantly improve neonatal health outcomes and maternal experiences. However, addressing challenges such as socio-cultural barriers and logistical issues is essential for wider adoption. Strengthened healthcare support and community engagement can optimize KMC implementation in resource-limited settings.

Keywords: Kangaroo Mother Care, low-birth-weight, maternal experiences, neonatal outcomes, preterm.

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Introduction

Preterm birth and low birth weight are leading causes of neonatal mortality worldwide, with the burden disproportionately affecting low and middle-income countries like Bangladesh.¹ Limited access to

advanced neonatal care including incubators and specialized facilities exacerbates these challenges leaving many families with few viable options for improving neonatal survival and health.² Kangaroo mother care (KMC) an evidence-based low-cost

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intervention has emerged as a powerful alternative to conventional neonatal care, particularly in resource-limited settings.³

KMC involves prolonged skin-to-skin contact between the mother and the baby, exclusive breastfeeding and early discharge with follow-up care.⁴ Recognized by the World Health Organization as a lifesaving practice, KMC has been shown to reduce neonatal mortality, promote weight gain, improve breastfeeding rates and strengthen maternal-infant bonding.^{5,6} Beyond its health benefits KMC fosters emotional well-being in mothers and empowers them to actively participate in their infant's care.⁷ Despite these advantages, widespread adoption of KMC faces several barriers, including a lack of awareness, cultural misconceptions, inadequate training for healthcare providers and logistical challenges in implementing KMC.⁸

In Bangladesh, where neonatal mortality rates remain high, KMC represents a critical opportunity to improve outcomes for preterm and low-birth-weight infants.⁹ However, successful implementation relies heavily on maternal adherence and the support provided by healthcare systems.⁵ Mother's experiences and perceptions of KMC play a central role in its effectiveness, as factors such as emotional readiness, confidence in breastfeeding and access to support services can influence their ability to sustain the practice.¹⁰

This study aimed to explore the practice of KMC in a tertiary neonatal unit in Bangladesh, focusing on maternal experiences, neonatal outcomes and barriers to implementation. By evaluating baseline neonatal characteristics, weight progression during follow-ups and maternal feedback on KMC, the study seeks to generate actionable insights for improving KMC programs. It also aimed to identify key enablers and obstacles to KMC adoption, offering evidence-based recommendations for policymakers and healthcare providers.

The findings from this research will highlight the feasibility and impact of KMC in resource-limited settings, emphasizing its role as a practical, cost-effective solution for addressing neonatal health challenges. By systematically documenting maternal and neonatal experiences, the study underscores the importance of integrating KMC into routine neonatal care and strengthening support systems to ensure its broader acceptance and sustainability.

Materials and Methods

This cross-sectional descriptive study was conducted at the neonatal unit of Bangladesh Shishu Hospital and Institute from January to December 2023. A total of 148 neonates and their mothers were enrolled through purposive sampling. Eligible participants included preterm or low-birth-weight neonates who were clinically stable and suitable for Kangaroo Mother Care (KMC). Mothers who consented to participate in the study and were willing to practice KMC were included, while neonates with severe complications or mothers unable to provide KMC due to medical or personal reasons were excluded.

Data were collected using structured interviews, observation checklists and patient records. Maternal demographic information, neonatal clinical parameters (such as birth weight and gestational age) and details of KMC practice (duration per day and overall adherence) were recorded. Mothers were interviewed to gather feedback on their experiences, challenges and perceptions of KMC, with a focus on emotional bonding, breastfeeding confidence and perceived neonatal health improvements.

Key variables included birth weight, gestational age at initiation of KMC, duration of KMC per day and follow-up weights at one, two and three months. Weight measurements were taken using a calibrated digital scale and maternal feedback was documented through structured questionnaires. Challenges in implementing KMC, such as difficulties at home, lack of privacy and maternal fatigue, were noted during follow-up interviews. To ensure the quality of data collection, all healthcare providers involved in the study were trained in KMC protocols and the interviews were conducted by experienced researchers fluent in the local language.

Informed consent was secured from all participating mothers. Mothers were counseled on the benefits of KMC and necessary support was provided throughout the study period to ensure adherence and address any concerns. Data were anonymized and confidentiality was strictly maintained. Quantitative data were analyzed using SPSS statistical software and descriptive statistics such as means, standard deviations and percentages were used to summarize baseline characteristics, neonatal outcomes and maternal feedback.

Results

In this study total 148 neonates was as participants at the neonatal unit in Bangladesh Shishu Hospital

and Institute from January to December 2023. Their mean birth weight was 1488.7 ± 315.1 grams, Gestational age 32.2 ± 2.2 weeks and practiced KMC for an average of 7.0 ± 1.6 hours per day (Table-I). The highest participation was observed in December (12.8%) and January (12.2%), while the lowest was in September (3.4%), indicating variations in KMC practices throughout the year (Figure-1). At the 1st follow-up, the average weight was 2029.0 ± 336.8

Table-I

Baseline characteristics of the study population (N = 148)

Variable	Mean $\pm$ SD	Minimum	Maximum
Birth weight (grams)	1488.7 ± 315.1	885	2700
Gestation age (weeks)	32.2 ± 2.2	28	37
KMC duration (hours)	7.0 ± 1.6	2	12

grams. By the 2nd follow-up, the average weight increased to 2940.0 ± 801.3 grams and at the 3rd follow-up, a significant weight gain was observed, with an average of 4784.2 ± 1916.4 grams (Table-II). Most of the mothers had positive experiences with KMC, with 77.7% reporting improved bonding and

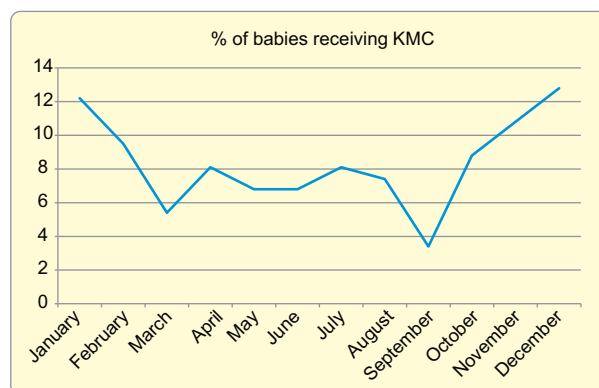


Figure-1: Percentage of babies receiving KMC in SCABU month wise (N = 148)

68.9% gaining confidence in breastfeeding. While 60.1% initially hesitated, they later embraced KMC and 89.9% were willing to recommend it. Supportive experiences like improved maternal emotional well-being (64.2%) and encouragement from healthcare staff (74.3%) played a key role. Despite this, 39.2% faced challenges managing KMC at home (Table-III). There is notable decrease in neonatal morbidities after the implementation of Kangaroo Mother Care (KMC) among 148 neonates. Hypothermia reduced

Table-II

Weight progression over follow-ups (N = 148)

Follow-up	Mean $\pm$ SD	Minimum weight (grams)	Maximum weight (grams)
1st follow-up	2029.0 ± 336.8	1400	3300
2nd follow-up	2940.0 ± 801.3	1640	5100
3rd follow-up	4784.2 ± 1916.4	1800	7800

Table-III

Maternal experiences and feedback on KMC (N = 148)

Experience*	Frequency	Percentage
Positive experience with bonding	115	77.7
Initial hesitancy but later acceptance	89	60.1
Difficulty managing KMC at home	58	39.2
Confidence in breastfeeding post-KMC	102	68.9
Willingness to recommend KMC to others	133	89.9
Improved emotional well-being (mother)	95	64.2
Encouragement and support from healthcare staff	110	74.3
Perceived improvement in neonatal health	125	84.5

*Multiple response

from 56 cases (37.8%) to 12 cases (8.1%), hyperthermia from 18 cases (12.2%) to 5 cases (3.4%), and hypoglycemia from 40 cases (27.0%) to 10 cases (6.8%). Similarly, hyperglycemia declined from 15 cases (10.1%) to 4 cases (2.7%), apnea from 34 cases (22.9%) to 9 cases (6.1%), sepsis from 42 cases (28.4%) to 15 cases (10.1%), and feeding difficulties from 65 cases (43.9%) to 18 cases (12.2%) (Table- IV).

Table-IV
Effect of kangaroo mother care (KMC) on neonatal morbidities (N = 148)

Morbidity	Before KMC n(%)	After KMC n(%)
Hypothermia	56 (37.8)	12 (8.1)
Hyperthermia	18 (12.2)	5 (3.4)
Hypoglycemia	40 (27.0)	10 (6.8)
Hyperglycemia	15 (10.1)	4 (2.7)
Apnea	34 (22.9)	9 (6.1)
Sepsis	42 (28.4)	15 (10.1)
Feeding difficulties	65 (43.9)	18 (12.2)

Discussion

This study sheds light on the neonatal outcomes, maternal experiences and barriers to the implementation of Kangaroo mother care (KMC) in a tertiary neonatal unit in Bangladesh. The findings are consistent with global and regional studies, highlighting the efficacy of KMC while addressing the unique challenges in resource-limited settings.

Our findings demonstrated significant weight progression among neonates over the follow-up period. By the third follow-up, the mean weight had increased to 4784.2 ± 1916.4 grams, indicating the effectiveness of KMC in promoting growth and health. Similar trends were observed in earlier studies, such as those by Seidman et al., which reported KMC's ability to enhance neonatal growth by improving thermal regulation and breastfeeding practices.¹¹ Additionally, Sjömar et al., emphasized that KMC creates a favorable environment for neonates, particularly for low-birth-weight and preterm infants.¹²

The study highlighted overwhelmingly positive maternal experiences, with 77.7% of mothers reporting improved emotional bonding and 68.9% expressing increased breastfeeding confidence. This aligns with findings by Aziz et al., who noted that KMC fosters maternal

empowerment and reduces anxiety.¹³ Furthermore, the willingness of 89.9% of mothers to recommend KMC to others reflects its acceptability and perceived value. However, challenges such as managing KMC at home (reported by 39.2% of mothers) highlight socio-cultural and logistical barriers, consistent with observations by Khan et al., who identified lack of privacy and family support as significant obstacles in continuing KMC post-discharge.¹⁴

Healthcare staff support was a pivotal enabler, reported by 74.3% of mothers. Their guidance not only encouraged KMC adoption but also alleviated initial fears. This finding resonates with research by Mehjabeen et al., who emphasized the role of skilled healthcare workers in ensuring the fidelity of KMC implementation.¹⁵ The emotional well-being improvements reported by 64.2% of mothers also underscore the dual benefits of KMC for both neonates and caregivers, echoing findings by Hunter et al.¹⁶

Several barriers to successful KMC implementation were identified, including socio-cultural norms, lack of awareness and inadequate hospital infrastructure. Ariff et al.¹⁷ similarly documented these challenges, suggesting that tailored community-based interventions are necessary to address such barriers. Addressing these issues through targeted educational campaigns and infrastructure improvements is critical for sustainable implementation.

The outcomes of this study align with the global literature on KMC. For instance, Conde-Agudelo et al., documented significant reductions in neonatal mortality and morbidity through KMC.¹⁸ Similarly, Blencowe et al., highlighted the intervention's potential to reduce preterm birth complications, particularly in low- and middle-income countries.⁴ However, challenges unique to Bangladesh, such as cultural resistance and lack of healthcare resources, necessitate localized solutions.

This study underscores the need for comprehensive training programs for healthcare providers to enhance their ability to counsel and support mothers practicing KMC. Strategies such as creating dedicated KMC spaces in hospitals, as suggested by Mehjabeen et al.¹⁵ could address infrastructural barriers. Community-based follow-up programs, as highlighted by Seidman et al., could further strengthen adherence to KMC post-discharge.¹¹

The study highlights the consistent practice of KMC throughout the year, reflecting its acceptance among caregivers despite initial challenges. Furthermore, the intervention significantly improved neonatal health outcomes, including reductions in morbidities such as hypothermia, sepsis, and apnea. These findings emphasize the need for sustained efforts to enhance KMC accessibility and adherence for long-term benefits.¹⁸

The reduction in neonatal morbidities observed in our study highlights the effectiveness of Kangaroo Mother Care (KMC). Hypothermia decreased from 37.8% to 8.1%, comparable to findings by Conde-Agudelo et al.¹⁹ who reported similar reductions in low-resource settings. Feeding difficulties declined from 43.9% to 12.2%, echoing studies by Seidman et al., where KMC enhanced breastfeeding practices. Apnea cases reduced from 22.9% to 6.1%, consistent with Blencowe et al.²¹ emphasizing improved respiratory outcomes through skin-to-skin contact. These findings reaffirm KMC's role in improving neonatal health.

The study's strengths include its detailed evaluation of both maternal and neonatal outcomes and its focus on identifying barriers to KMC implementation. However, the reliance on a single tertiary care setting limits generalizability. Additionally, the use of self-reported data introduces the potential for recall bias. Future studies could explore longitudinal designs to assess the long-term impact of KMC and include diverse healthcare settings for broader applicability.

A study with a longer follow-up period is needed for assessing the safety of the restricted fluid to be used in reducing duration of respiratory support. Further multicenter studies including larger samples should be done for more appropriate findings.

Conclusion

In conclusion, this study reaffirms KMC as an effective and sustainable intervention for improving neonatal health and maternal experiences. It highlights the importance of addressing barriers to ensure its wider adoption in resource-limited settings. By focusing on maternal support, healthcare system strengthening and community engagement, KMC can significantly contribute to reducing neonatal mortality and morbidity in Bangladesh, aligning with global health priorities.

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Original Article

Impact of an Infection Control Bundle in Reducing Nosocomial Infections in Neonates Admitted in NICU of a Tertiary Referral NICU: A Quality Improvement Initiative Project

Ismat Jahan¹, Mohammad Nur Nobil Zahid², Md Arif Hossain³, Debashish Shaha⁴, Rumpa Mani Chowdhury⁴, Mohammad Kamrul Hassan Shabuj¹, Sadeka Choudhury Moni¹, Md. Abdul Mannan⁵, Sanjoy Kumer Dey⁵

Abstract

Background: Sepsis is a leading cause of neonatal mortality in low-resource settings. As facility-based births become more common than before, the proportion of neonatal deaths due to hospital-onset sepsis has increased

Objective: To find out the impact of quality improvement strategies to reduce multidrug resistance nosocomial sepsis and death in NICU.

Methods: This was Quality improvement project in a neonatal intensive care unit in Bangabandhu Sheikh Mujib Medical University where a quality improvement project was implemented. All the necessary steps of quality improvement including team establishment, problem identification, fishbone analysis, process map were conducted. A multifaceted infection prevention and control (IPC) bundles were implemented. Outcome data on healthcare-associated sepsis including culture proven sepsis, and death were collected for 6 months prior to intervention and 6 months after bundle implementation and then analysed.

Results: A total of 192 neonates were enrolled in the current study as 87 cases in pre-intervention phase and 105 cases in post-intervention phase. The two groups were comparable in terms of gender, birth weight, gestational age and mode of delivery. There was significant reduction in MDR nosocomial infection incidence rate after implementation of our infection prevention bundle, as 50/87 (57 %) episodes in Pre intervention phase compared to 35/105 (33%) in post intervention period ($p < 0.001$). There was significant difference in overall mortality rates between the two phases were 43/87 (49%) and 31/105 (29.5%) pre and post intervention respectively (p value < 0.001). Gram negative bacteria were the most commonly isolated micro-organisms (97.2 % versus 93.1 % in phase-I and II respectively), Klebsiella was the leading causative pathogen throughout the study period Candida infection was observed with seasonal variation. Run chart depicted declining trend of MDR sepsis rate over 12 months duration.

Conclusion: A simple IPC bundle can reduce multi drug resistance sepsis and death of hospitalized neonates in high-risk, low-resource settings.

Keywords: Health care associated infection, newborn, neonatal intensive care unit, nosocomial sepsis, quality improvement

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Introduction

Globally, in the year 2015, approximately 2.7 million neonatal deaths occurred, accounting for 46% of

under-5 child mortality.¹ Almost all (99%) neonatal deaths occur in low- and middle-income countries (LMICs) and about one-fifth deaths are attributable to

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neonatal infection.² Septicemia, the most common hospital acquired infection in neonates, occur 3–20 times more frequently in LMICs than high income countries.³ The reason behind the burden of neonatal sepsis in LMICs are manpower shortage, crowded neonatal ward, increasing antimicrobial resistance, and suboptimal infection prevention and control (IPC) practices.^{3,4} A study was conducted in this NICU of Bangabandhu Sheikh Mujib Medical University and found that the sepsis is an independent risk factor of death.⁵ Another retrospective study in the same setting reported that the leading causes of drug-resistant bacterial sepsis in NICU are *Acinetobacter*, *Klebsiella*, and *Escherichia coli* with high prevalence of MDR and XDR organisms. Death was significantly higher among MDR and XDR sepsis when outcome was compared with nondrug resistance counterpart.⁶

Late onset sepsis and hospital acquired sepsis causes prolonged hospitalization, increased costs and is associated with poor neurodevelopmental outcome in later life.⁷ A number of published literature demonstrated substantial reduction of infection following quality improvement initiative.^{8,9} The basis of quality improvement initiative is mainly an implementation of infection prevention and care bundles aimed at reducing exposure to pathogens and enhancing the microbiome.^{10,11} Infection

prevention and control bundles composed of simple, relatively low-cost but high impact interventions,^{12,13} might reduce the incidence of blood stream infection and death in NICU.¹⁴

The objective of the study to assess the effectiveness of infection prevention and control (IPC) strategies in a tertiary care NICU setting. To implement our strategy, we intended to determine the incidence of hospital-acquired neonatal sepsis and to compare infection rate, MDR and XDR sepsis and death due to sepsis in pre and post intervention period in NICU, BSMMU.

Materials and Methods

This was a quality improvement study consist of pre-intervention, intervention and post-intervention period, conducted in the Department of Neonatology, Bangabandhu Sheikh Mujib Medical University (BSMMU) from July 2023 to June 2024 (12 months from IRB approval).

All sick newborn admitted in NICU ≥ 3 days with suspected hospital acquired infection were included in this study.

This study segregated into pre intervention period (baseline initial 5 months), 1 months of IPC bundle implementation (IPC training and practice change period), and 6 months of post-intervention assessment, analysis and report writing period (Figure-1).

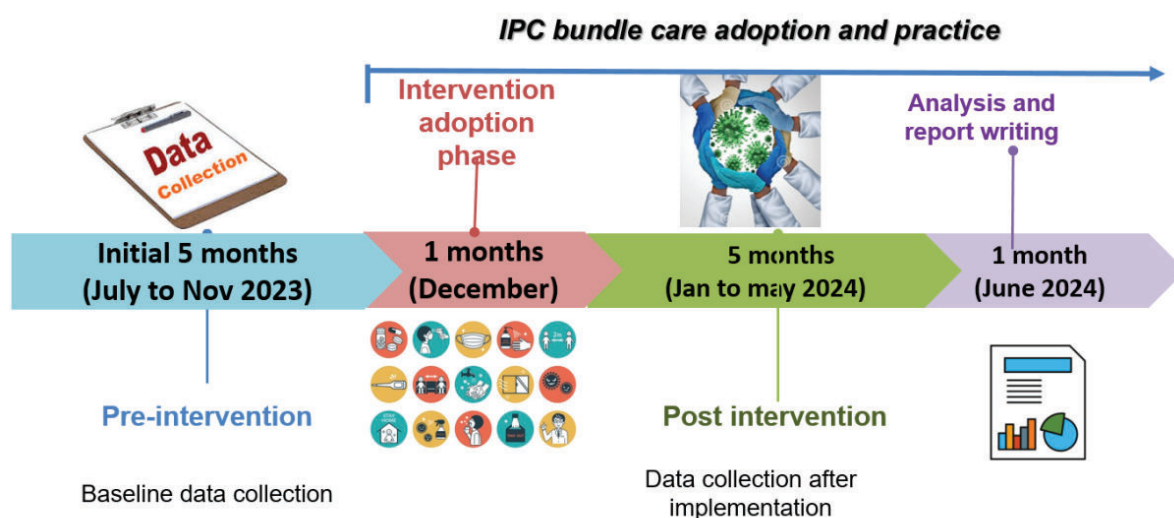


Figure-1: Time line of the project

NICU BSMMU, is a 31 bedded tertiary care referral neonatal care unit in Dhaka, Bangladesh, which provide service for both inborn and outborn admission. There are approximately 600-700 admissions per year. The average newborn-to-nurse ratio is 4-5:1. The department provides the highest level of care available in a public hospital in Dhaka, Bangladesh and has adequate medical devices. Nosocomial infection due to multi drug resistance organism is a major problem leading to half of death among admitted sick newborn.

Written informed consent was obtained from the neonate's mother or legal guardian in Bangla.

After enrollment baseline data of pre-intervention period cohort was obtained. The project started with documenting data of pre-intervention period over a period of 5 months. Demographic data (gestational age, birth weight, APGAR at 5 minutes), Maternal data (Pregnancy induced hypertension, diabetes mellitus, maternal infection and antenatal corticosteroid) were collected from clinical files. Any morbidity in terms of perinatal depression, culture proven nosocomial sepsis, MDR sepsis during NICU stay were documented. Outcome of the pre-intervention period were collected from the clinical records.

Blood cultures were obtained on all neonates with clinically suspected nosocomial sepsis after 3 days of NICU stay, defined as fever or hypothermia, tachycardia or bradycardia, hypoglycemia, respiratory difficulty, new-onset seizures, lethargy, poor feeding, abdominal distention, vomiting, or poor perfusion. Positive blood cultures were classified as blood stream infection (BSI) with pathogen.

Classification of multiple episodes of suspected sepsis: For neonates evaluated for suspected sepsis more than once, we assigned their infectious status to the most severe category. For example, if the first blood culture was sterile but a 2nd blood culture grew a pathogen, the infant was categorized as having a BSI with pathogen. A new episode of suspected sepsis was defined as a blood culture that was obtained ≥ 7 days after a prior blood culture (regardless of the results of the prior culture).¹⁵ One blood culture was obtained on all neonates with clinically suspected sepsis at the time of symptom onset. Urine and cerebrospinal fluid cultures were collected as per unit protocol. Typically, a second blood culture was obtained if a patient developed a new episode of

suspected sepsis. Blood culture bottles were inoculated with 0.5 - 1.0 ml of blood and incubated in the Bactec blood culture system. Organisms isolated were tested for antibiotic susceptibilities using the VITEK Compact 2 identification and antibiotic susceptibility test automated machine.

Development of quality improvement team and unit specific IPC interventions: Following project approval a quality improvement team was formed involving principal investigator, Neonatology and microbiology faculties, and representatives from residents, nurses and support staff. Literature review on potentially effective infection control measures were reviewed. All the steps of quality improvement projects were duly addressed (Figure-2). Fish bone analysis and Pareto chart were done as a part of quality improvement project activities.

Our proposed IPC bundle included the following strategies

- (1) periodic infection prevention control training for NICU service provider
- (2) weekly infection control update meeting involving microbiology team
- (3) enhanced NICU environmental cleaning
- (4) digital displaying of infection control measures (hand washing, hand rubbing)
- (5) carrier detection
- (6) supervised daily NICU activities of service providers with positive feedback

Education and dissemination of IPC bundle: Education and dissemination of IPC bundle care among residents, nurses, mothers and other health care providers were conducted. This educational program were conducted through face to face session. Power-point presentation, practical demonstration and video demonstration were delivered among NICU health care professionals.

Implementation of IPC bundle care: IPC bundle was implemented on enrolled newborn with suspected hospital acquired infection after taking informed written consent. Newborns with major congenital anomaly and imminent death were excluded. Enrolled newborn were monitored for development of morbidity in terms of perinatal depression, Culture proven sepsis during neonatal stay in the NICU.

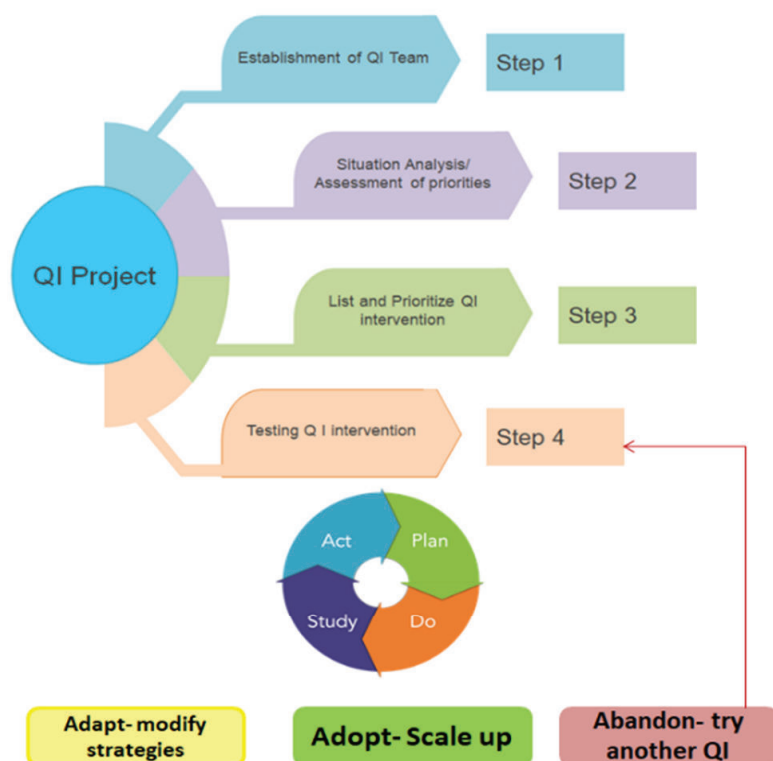


Figure-2: Steps of quality improvement study

Monthly rates of mortality and nosocomial infection with MDR organism were documented. Both the pre and post intervention groups were compared for demographic, maternal, morbidities, death and sepsis outcomes. Fishbone analysis was conducted to find out the high impact intervention to reduce infection. Pareto chart was drawn. Monthly run chart was reported depicting death rate and nosocomial infection per month. Data were analyzed using IBM SPSS software package version 22 (IBM Corp, Armonk, New York, USA). Comparisons between groups for categorical variables was performed using the χ^2 -test. Student's t-test was used to compare two groups for normally distributed quantitative data. The Mann-Whitney test was used to compare quantitative data between the groups that are not normally distributed. Odds ratio (OR) was used to calculate the ratio of the odds and 95% confidence interval (CI) of an event occurring in one risk group to the odds of it occurring in the nonrisk group. The significance of the obtained results was judged at the 5% level.

Results

A total of 192 neonates were enrolled in the current study as 87 cases in pre-intervention phase and 105

cases in post-intervention phase. The two groups were comparable in terms of gender, birth weight, gestational age and mode of delivery as shown in Table-I.

There was significant reduction in MDR nosocomial infection incidence rate after implementation of our infection prevention bundle, as 50/87 (57 %) episodes in preintervention phase compared to 35/105 (33%) in post intervention period ($p < 0.001$) (Table-II). There was significant difference in overall mortality rates between the two phases 43/87 (49%) and 31/105 (3) pre and post intervention respectively (p value < 0.001).

Gram negative bacteria were the most commonly isolated micro-organisms (97.2 % versus 93.1 % in phase-I and II respectively), *Klebsiella* was the leading causative pathogen throughout the study period followed by *Acinetobacter*, *Enterobacter* and *Serratia*. *Candida* infection was observed with seasonal variation. Emerging organism also found eg. *Barkholderiacapacia* (Table- III).

Run chart depicted declining trend of MDR sepsis rate over 12 months duration in figure 3. Run chart indicating infection control bundle can be adopted as a quality improvement project in NICU.

Table-I
Baseline characteristics of enrolled infants (N=192)

Characteristics	Pre intervention phase (before IPC) n=87	Post intervention (after IPC) n=105	P value
Gestational Age in week mean±sd	33±2.7	34±3.2	0.25
Birth weight in gram mean±sd	1516±538	1647±618	0.52
Gender			
Male n (%)	43(49.4)	60(57)	0.79
Female n (%)	44(50.6)	45(43)	
Mode of delivery			
LSCS n (%)	71(82)	80(76)	0.97
NVD n (%)	16(18)	25(24)	

LSCS-Lower segment caesarian section, NVD- Normal vaginal delivery, IPC- Infection prevention and control

Table-II
MDR sepsis and outcome among enrolled infants (N=192)

Characteristics	Before intervention (Before IPC), n=87	After intervention (After IPC), n=105	P value
MDR sepsis n (%)	50 (57)	35 (33)	<0.001
Length of NICU in days mean±sd	36±17	33±16	0.6
Mortality, n (%)	43(49)	31 (30)	<0.001

MDR- Multidrug resistance, sd- standard deviation

Table-III
Organisms isolated from blood in enrolled newborn (N=192)

Pathogen	Pre intervention n= 87	Post intervention n=105
Positive cultures n (%)	55(61)	41(39)
Gram negative organisms		
Klebsiella	17/55(31%)	29/41(71%)
Acinetobacter	9/55 (16%)	6/41(14%)
Serratia	8/55(14%)	4/41 (10%)
Enterobacter	5/55 (9%)	1/41 (2.4%)
E. coli	2/55 (3.6%)	0
Barkholderiacapacia	2/55(3.6%)	1/41 (2.4%)
Candida species	12/55 (22%)	2/41 (5%)

MDR Multidrug resistance

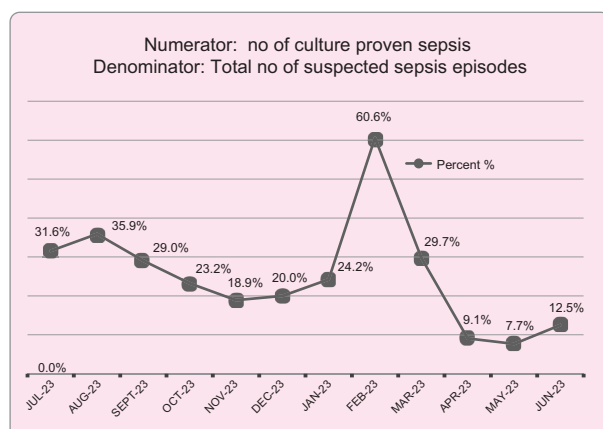


Figure-3: Run chart showing trend of MDR sepsis during the study period, N=192

Discussion

This quality improvement project explored the effectiveness of an infection control bundle at a tertiary level NICU in Bangladesh. The bundle of interventions were consisting of periodic infection prevention control training for NICU service provider, weekly infection control update meeting involving microbiology team, enhanced NICU environmental cleaning, digital displaying of infection control measures (hand washing, hand rubbing), Periodic microbiologic surveillance and supervised daily NICU activities of service providers with positive feedback. The overall frequency of infection with multidrug resistance organism declined after the infection prevention and control bundle implementation program during the study period.

The findings of this study provide understanding of the epidemiology of drug-resistant bacteria at this NICU. Furthermore, the pattern of infectious agents (high rate of sepsis due to *Pseudomonas aeruginosa* and *Acinetobacter baumannii*) was distinct to the spectrum at NICUs in the high-income countries. Similar findings were observed in Philippine where the authors reported four of the most common nonenteric pathogens: *A. baumannii*, *P. aeruginosa*, *Stenotrophomonas maltophilia*, and *A. faecalis* in their study.¹² The high frequency of nonenteric gram-negative bacilli and the high rates of drug resistance strongly imply that nosocomial transmission, rather than mother-to-child transmission during delivery.

The mean gestational age during pre-intervention and post intervention period were 33 ± 2.7 and 34 ± 3.2 respectively. Similar gestational age (34.7 weeks) was documented by Gill CJ et al study¹². The mean birth

weights before and after IPC bundle implementation were 1516 ± 538 and 1647 ± 618 gram respectively. The mean birth weight was found higher than the index study in Gill C J and colleague's QI project conducted during 2003 and 2004.¹²

There was significant reduction in MDR nosocomial infection rate after implementation of our infection prevention bundle, as 50/87 (57 %) episodes in Pre intervention phase compared to 35/105 (33%) in post intervention period ($p < 0.001$) (Table II). A quality improvement study conducted in Zambian NICU, they found fewer than half of episodes of suspected sepsis (549/1344, 40.8%) were associated with a positive blood culture and the proportion of neonates with a positive blood culture was inversely associated with birth weight category.¹⁵

There was significant difference in overall mortality rates between the two phases 43/87 (49%) and 31/105 (30%) pre and post intervention respectively (p value < 0.001). Similar findings of decline in overall mortality (NICU 1: relative risk, 0.5; 95% confidence interval, 0.4–0.6; NICU 2: relative risk, 0.8; 95% confidence interval, 0.7–0.9) was reported by Gill CJ et al where they implemented infection prevention bundle (composed of introduction of locally produced alcohol based hand rub, IPC training and checklists)) in 2 different NICUs in Philippines.¹² In a study conducted in Zambia also reported the comparable findings in terms of mortality. Their hospital associated mortality was lower during the intervention than baseline period (18.0% vs 23.6%). Total mortality was lower in the intervention than prior periods.¹⁵

In the current study, gram negative bacteria were the most commonly isolated micro-organisms (97.2 % versus 93.1 % in phase-I and II respectively), *Klebsiella* was the leading causative pathogen throughout the study period followed by *Acinetobacter*, *Enterobacter* and *Serratia*. *Candida* infection was observed with seasonal variation. Emerging organism also found eg. *Bacillus cereus*. In a QI study conducted in 2 different NICUs in Philippines reported *Klebsiella* species, *Enterobacter* species, *Pseudomonas* species, and *Alcaligenes faecalis* as the dominating organisms. In contrast to the present study, fungemia was uncommon in their settings. They also found in approximately the same proportions as those found in the colonization surveys.¹² In Zambian study, most positive blood cultures yielded a pathogen (409/549, 74.5%), predominantly *Klebsiella pneumoniae* (289/409, 70.1%).¹⁵

Many studies have examined the effect of a single infection prevention measure (e.g. staff education or introduction of alcohol hand rub) on colonization and neonatal sepsis, few studies have assessed the impact of a bundle of IPC interventions. Moreover, previous reports have mainly focused on the control of outbreaks in LMIC NICUs and have often lacked detail on the interventions used for the prevention of infection.¹⁶ The current quality improvement project intended to assess the efficacy of bundle interventions on MDR sepsis and sepsis related death during NICU stay. Weekly infection control meeting was a unique part in the current study which allows the center to discuss on the challenges and way forward. Antibiotic policy was changed according to the local antibiogram. This policy supports the findings from a QI study conducted in Senegal and they reported changing the antibiotic prescribing policy led to a dramatic reduction in antibiotic use in newborns at risk for infection (100% in Period 1 vs 51% in Period 2; $P < 0.0001$).¹³

The limitations of the present study are lack of reporting on the colonization status and lack of manpower did not allow to monitor the overall activity based on daily checklist specially monitoring of hand hygiene compliance and maintenance of asepsis during procedures. Moreover, inter current seasonal variation during the study period can be an important confounding variable.

Reducing the burden of multi drug-resistant nosocomial infections in NICU settings of any LMIC must be a priority to combat death due to potentially preventable disease. Additional ongoing, multi-site quality improvement project should be conducted to understand the barriers of implementing these infection control and prevention bundle and to identify and eliminate the source of environmental pathogen and to explore the cost effectiveness of the measures included in the bundle in resource limited settings in Low and middle income countries.

Conclusion

This quality improvement initiative demonstrates that strengthened infection-control interventions are feasible and appear to be effective in resource limited settings. The epidemiology of neonatal sepsis at this NICUs is characterized by nosocomial sepsis with high rate of multi-drug-resistant gram-negative bacilli, with correspondingly high rates of culture proven MDR sepsis and sepsis related death. Seasonal high occurrences of candida infection and uncommon

organism *Barholderiacapacia* seems to be an emerging threats.

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Conflict of interest: None

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Contribution of authors: Ismat Jahan, Mohammad Nur Nobi Zahid contributed to the conception and data collection. Md Arif Hossain, Debashish Shaha, Rumpa Mani Chowdhury, helped with the analysis and interpretation of data, and drafting of the article. Sadeka Choudhury Moni, Md. Abdul Mannan, Sanjoy Kumer Dey have revised it critically and helped in data interpretation and analysis.

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Original Article

Congenital Hypothyroidism Screening in Term Neonates Using Umbilical Cord Blood TSH Values – Experience in a Tertiary Care Hospital of Bangladesh

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Abstract

Background: Congenital hypothyroidism (CH) remains one of the most common preventable causes of mental retardation among children. Screening for congenital hypothyroidism is a cost-effective strategy to prevent mental retardation in the population. Measuring umbilical cord blood TSH levels is an attractive and practical method for screening for CH.

Objective: The aims of this study were to use cord blood TSH levels as a marker for screening for CH and observe the incidence of CH.

Methods: This observational cross-sectional, hospital-based study was conducted over one year from January 2023 to December 2023 at the department of paediatrics and neonatology, Ashulia Women and Children Hospital (AWCH), Dhaka. All term neonates, who fulfilled the inclusion criteria, born during the study period were included and screened according to the standard CH screening protocol. After birth, cord blood specimens were collected and tested. TSH was measured by the Perkin Elmer ELISA machine. The data were analyzed using SPSS version 20.0 (IBM Corp., Armonk, NY).

Results: Umbilical cord blood was collected at the time of delivery from 1,782 full-term neonates, and TSH levels were estimated. Neonates who had a CBTSH value of ≥ 20 mIU/L were recalled on the 7th to 10th days of life for a full thyroid profile. The male to female ratio was 0.9:1. The mean birth weight was 2800 gm. CBTSH values ranged between 1.28 and 100 mIU/L. A total of 97 neonates were recalled for repeat testing. Eventually, one of the neonates was confirmed to have hypothyroidism on repeat testing. The incidence of CH in this study was 1 in 1,782. There is a significant association between high CBTSH levels (≥ 40 mIU/L) and NVD, maternal hypertension, maternal preeclampsia, eclampsia, and fetal distress.

Conclusion: In this study the incidence of CH was 1 in 1,782. There is a significant association between high CBTSH levels and NVD, maternal hypertension, maternal preeclampsia, eclampsia, and fetal distress.

Keywords: CBTSH, screening for congenital hypothyroidism, TSH.

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Introduction

Congenital primary hypothyroidism is one of the most prevalent preventable causes of intellectual disability

globally, affecting 1 in 2,000 to 1 in 4,000 babies. Clinical signs and symptoms are frequently mild or absent at birth. Typical symptoms include delayed

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passage of meconium, constipation, extended jaundice, feeding difficulties, decreased activity, and increased sleep. Myxedematous facies, large fontanelles, macroglossia, a swollen abdomen with an umbilical hernia, and hypotonia are common findings on physical examination. The age of initiation of treatment is inversely related to the intelligence quotient (IQ).¹

Over the past three decades, extensive newborn screening programs for the detection of CH during the neonatal period have been established in developed nations,^{2,3} and have rapidly gained traction in the developing countries as well.⁴⁻⁸ Compared to the T4 screen, the primary TSH screen is more sensitive and specific for the diagnosis of primary congenital hypothyroidism.⁴ Blood samples are typically taken at 5-6 days of life for screening programs, but since many babies are released early, cord blood samples are also utilized as an alternative.⁸⁻⁹

In developing countries like Bangladesh, recalling discharged neonates for repeat testing is particularly challenging. The cord blood thyroid stimulating hormone (CBTSH) estimation method offers several benefits, including ease of collection, non-invasiveness, and low follow-up loss rates. Additionally, since the results are available before the mother's discharge from the hospital, repeat sampling can be done as soon as possible, which is crucial for initiating treatment as soon as needed. For this reason, several Asian nations have chosen to adopt this approach.⁸⁻⁹

There are limited studies on cord blood TSH values in Bangladeshi literature.¹⁰ Ashulia Women and Children Hospital started cord blood TSH screening in 2016. The purpose of this study was to evaluate the TSH level in cord blood as a screening tool for congenital hypothyroidism and to observe the incidence of CH.

Materials and Methods

This observational cross-sectional, hospital-based study was conducted from January 2023 to December 2023 at the Institute of Woman and Child Health (IWCH) and Ashulia Women and Children Hospital (AWCH), Dhaka which is a tertiary care 250 bedded hospital in a semi-urban industrialized area of Bangladesh. After approval by the hospital ethical committee, informed consent was obtained from either of the parents. All term neonates without congenital anomalies, born in the designed period were included and screened for CBTSH levels.

Detailed antenatal and maternal medical history was taken after inclusion. The infant was inspected upon birth. The baby's weight was measured and plotted in the CDC growth chart. Less than the 10th percentile of birth weight was considered as small for gestational age (SGA), the 10th to 90th percentiles were classified as appropriate for gestational weight (AGA), and greater than the 90th percentile was classified as large for gestational age (LGA). Gestational age was determined from maternal menstrual history and by using the Ballard score.

All preterm neonates (<37 completed weeks) and babies with congenital anomalies were excluded from the study. Fetal distress was identified by a poor APGAR score at birth necessitating resuscitation interventions, thick meconium-stained amniotic fluid, and/or abnormal fetal cardiac tracing during intrapartum monitoring were also excluded.

After birth, two ml of cord blood specimens were collected and analyzed. TSH was measured by the Perkin Elmer ELISA machine. TSH was measured from the cord blood samples of 1,782 newborns and included in the study. A newborn with CBTSH less than 20mIU/L was considered normal, while CBTSH 20mIU/L or more than 20mIU/L was labeled as high. On the seventh to tenth days of life, all neonates with a cord blood TSH value of 20mIU/L or more than 20mIU/L were contacted again for a complete thyroid profile, which included TSH, FT4, and T3.

Different cut-offs for CBTSH levels, ranging from 20 to 90 mIU/L, have been utilized in various investigations. For our study, we employed the lower cut-off value for CBTSH of 20 mIU/L or more than 20mIU/L, similar to the systematic review and meta-analysis was done by Anne and Rahiman et al.¹¹ The CBTSH result <10 mIU/L is considered normal, 10-20 mIU/L is considered borderline, and >20 mIU/L is considered abnormal, according to Devi AR and Noushad et al. and Raj S and Baburaj et al.¹¹⁻¹³

The data were analyzed using the statistical package for the social sciences (SPSS) version 20.0 (IBM Corp., Armonk, NY). A p-value of less than or equal to 0.05 was considered significant.

Results

After exclusion, a total of 1,782 term newborns were included in the study. Table-I shows a distribution of CBTSH in term neonates. Amongst 1,782 term

newborns, CBTSH of <5mIU/L was found in 493 babies with a percentage of 28%, while CBTSH of 5 to <10mIU/L was observed in 819 neonates, representing the highest proportion at 46%. CBTSH of less than 20mIU/L was found in a total of 1,685 neonates, while CBTSH of more than 20mIU/L of CBTSH was found in a total of 97 term neonates, accounting for 5%. Table-II shows the mean CBTSH value of the study population which was 9.52mIU/ml.

Table-I
Distribution of CBTSH level in the term neonate (N=1,782)

Distribution of CBTSH level (mIU/L)	Number	Percentage
<5	493	28
5-<10	819	46
10-<15	289	16
15-<20	84	5
≥20	97	5

Table-II
Mean and median value of CBTSH amongst the study population (n=1782)

Characteristics	CBTSH Level mIU/L
Total number of study population	1782
Mean	9.52
Median	8.10
Mode	5.70
Standard deviation (SD)	±7.94

Table-III shows the demographic data of the study population with normal (<20mIU/L) CBTSH and high (≥20mIU/L) CBTSH. Amongst 1,782 term neonates, 97 neonates had high CBTSH levels, accounting for 5.4%. In neonates with normal CBTSH values, males accounted for 44.8% and females 55.2%. Among neonates with high CBTSH, 52.6% were male, and 47.4% female. Seventy eight percent (78%) of AGA and 21.9% of SGA had normal CBTSH, while high

CBTSH was found in 75% and 25% of AGA and SGA respectively. No LGA baby was found to have high CBTSH.

Regarding mode of delivery, in neonates with high CBTSH, delivery by NVD was 49.5%, AVD was 27.8% and LUCS was 22.6%.

Maternal risk factors revealed that amongst high CBTSH of 97 neonates, 35% had maternal hypothyroidism (was on treatment during pregnancy), 21.6% had diabetes mellitus (DM), and gestational diabetes mellitus (GDM), either treated with insulin or oral hypoglycaemic agents. Preeclampsia and eclampsia accounted for 18.5% of high CBTSH and lastly, maternal hypertension was associated with 15.5% of high CBTSH. It was observed that amongst high CBTSH, about 57.7% of the babies exhibited fetal distress.

Table-III
Comparison of demographic data between term newborns of normal and high CBTSH

Variables	Normal CBTSH, <20mIU/L (n=1685) n (%)	High CBTSH ≥20mIU/L (n=97) n (%)
Gender		
Male	755 (44.8)	51 (52.6)
Female	930 (55.2)	46 (47.4)
Birth weight according to gestational age		
AGA	1316 (78)	73 (75)
SGA	369 (21.9)	24 (25)
LGA	3 (0.1)	0 (0)
Mode of delivery		
NVD	743 (44.1)	48 (49.5)
AVD	56 (3.3)	27 (27.8)
LUCS	886 (52.6)	22 (22.6)
Maternal medical condition		
Hypothyroidism	85 (5)	34 (35)
DM, GDM	144 (8.5)	21 (21.6)
Preeclampsia, Eclampsia	81 (4.8)	18 (18.5)
Hypertension	94 (5.6)	15 (15.5)
Foetal distress	205 (12)	56 (57.7)

The distribution of demographic profiles amongst high CBTSH is shown in Table-IV. All 97 babies with high CBTSH were divided into two groups for comparison: CBTSH >20 to <40 mIU/L and CBTSH ≥40 mIU/L.

Table-IV
Comparison of demographic profile amongst raised CBTSH
 (≥ 20 mIU/L - < 40 mIU/L VS ≥ 40 mIU/L)

Variable	CBTSH: ≥ 20 to < 40 mIU/L (n=70; 72.2%)	CBTSH: ≥ 40 mIU/L (n=27; 27.8%)	Total: 97 n (%)	P-value
Birth weight (SGA)	21 (30.0)	15 (55.6)	36 (37.1)	0.039*
Mode of delivery				
NVD	34 (48.6)	14 (51.9)	48 (49.5)	0.047*
AVD	16 (22.9)	11 (40.7)	27 (27.8)	
LUCS	20 (28.6)	2 (7.4)	22 (22.7)	
Maternal hypothyroidism	27 (38.6)	7 (25.9)	34 (35.1)	0.351
Maternal DM, GDM	14 (20.0)	6 (22.2)	20 (20.6)	1.000
Maternal hypertension	7 (10.0)	8 (29.6)	15 (15.5)	0.037*
Preeclampsia, eclampsia	3 (4.3)	15 (55.6)	18 (18.6)	0.001*
Foetal distress	31 (44.3)	25 (92.6)	56 (57.7)	0.001*

*A p-value of < 0.05 considered as significant

Babies classified as SGA were statistically significant for CBTSH ≥ 40 mIU/L. Furthermore, normal vaginal delivery, maternal hypertension, maternal preeclampsia, eclampsia, and fetal distress were found to be statistically significant associated factors.

All 97 babies with high CBTSH were recalled after 7 to 10 days and repeat serum TSH, T3, and free T4 levels were tested. All babies showed normal values, except one, who had significantly high TSH (100 mIU/L) in the repeat sample. The baby was treated with oral thyroxine with adequate dosage and is on regular follow-up as per standard protocol.

Discussion

In our developing nation, congenital hypothyroidism is one of the main causes of mental retardation and still poses a significant burden on society. Due to the large population size and challenging socioeconomic background, it is quite difficult to recall newborns for screening within the first three to four days after delivery.

Since CBTSH data is available before the mother's hospital discharge, this method allows for early detection and therapy initiation, low loss-to-follow-up rates, and the possibility of obtaining repeat samples when CBTSH levels are elevated.

In our study, the mean CBTSH level was 9.52 mIU/ml, comparable to other studies where the mean TSH ranged from 6.13 mIU/ml to 10 mIU/ml.¹⁴⁻¹⁷ However, the mean CBTSH was higher than 10 mIU/ml in a few studies.¹⁵⁻¹⁷

In the present study, cord blood was available for 1,782 term infants. Among them CBTSH of < 5 mIU/L was found in 493 babies with a percentage of 27%, while 5 to < 10 mIU/L observed in 819 neonates, which were the highest proportion, accounting for 46%. CBTSH of less than 20 mIU/L was found in a total of 1,685 neonates, while 20 mIU/L or more than 20 mIU/ml of CBTSH was found in a total of 97 term neonates, accounting for 5%. Therefore, our recall rate for repeat testing was 5%, which is somewhat higher as compared to the 2.3% reported by Wu et al., who had a large cohort of 11,000 neonates.⁸ If we could consider the cut-off value to be more than 40 mIU/L, then the recall value would have fallen to 1.5%, which is comparable to Ravi Bhatia's study, where recall rates were 3 and 2%, respectively.¹⁸

There is wide variation in the normal CBTSH values, which can vary from 1 to 38.9 mIU/L.¹⁹ We used a cut-off value of 20 mIU/L, which has also been employed in studies conducted globally. In our study, only one neonate was confirmed to have CH, with a repeated TSH of 100 mIU/L, out of 1,782 neonates. The incidence of CH in our study was 1:1782 in a semi-urban, industrialized, densely populated area near Dhaka city of Bangladesh. This finding is consistent with another large cohort of 261,550 neonates by Azim et al., where in our country the incidence was 1:2126.²⁰ So far, our study is the first study in Bangladesh where the sample is directly taken

and analyzed in the same institute from a densely populated, semi-urban, industrial demographic area.

In neonates with normal CBTSH values, males accounted for 44.8% and females 55.2%. In high CBTSH neonates, the male was 52.6%, and females 47.4%. No correlation between cord blood TSH levels and gender was observed, consistent with the findings of Zion et al.²¹ 78% of AGA neonates and 21.9% of SGA neonates had normal CBTSH, while high CBTSH was found in 75% and 25% of AGA and SGA neonates, respectively.

CBTSH levels were higher (≥ 40 mIU/L) in our study in infants delivered by NVD (49.5%). Maternal preeclampsia, eclampsia, and fetal distress were found to be statistically significant associated factors (shown in Table IV).

Considering other studies around the world and neighboring limited-resource countries like ours we can use safely cord blood TSH cut of Value ≥ 20 mIU/L. However, if clinical suspicion is high, biochemical tests must be done irrespective of screen results. To make a National Newborn screening guideline for Congenital Hypothyroidism further large population-based multicenter studies are required to establish a normative cord blood TSH value in Bangladesh.

Conclusion

In this study the incidence of CH was 1 in 1,782. There is a significant association between high CBTSH levels and NVD, maternal hypertension, maternal preeclampsia, eclampsia, and fetal distress. Large, population-based, multicentre studies are required to establish normative values for cord blood TSH in Bangladesh.

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article. Soofia Khatoon, Jebunnesa, and Banani Chakraborti have revised it critically and helped in data interpretation and analysis.

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Original Article

Disease Pattern and Outcome of Newborns Requiring Continuous Positive Airway Pressure (CPAP): A Cross-Sectional Descriptive Analysis from a Paediatric Hospital in Bangladesh

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Abstract

Background: Bubble continuous positive airway pressure is a well-established, safe and easy to use device recommended for both preterm and term newborns having respiratory distress.

Objective: To observe the different disease pattern and outcome of neonatal admission requiring bubble CPAP in the level III neonatal intensive care unit.

Methods: This cross-sectional descriptive study was conducted in the neonatal ICU of Dr. M R Khan Shishu Hospital & ICH from January 2022 to December 2022. All admitted neonates who received bubble CPAP during that time were included in the study. Collected data include demographic characteristics, indications for bubble CPAP, age of initiation, weaning and discharge outcomes. Findings were reported for all term and preterm neonates.

Results: A total of 1400 neonates were admitted during the study period, of whom 62 (4.4%) got bubble CPAP. There was male predominance (55%) and mean gestational age was 36.8±2.3 weeks, mean birth weight 2662.09±633.39 gm. The most common diseases for bCPAP use among admitted neonates were pneumonia (41.9%), congenital pneumonia (14.5%), respiratory distress syndrome (8.1%) and meconium aspiration syndrome (8.1%) and others [perinatal asphyxia and congenital heart disease (24.2%)]. Majority of neonates were successfully weaned (88.7%) from bCPAP and were discharged to home (83.6%). Superficial erosion (50%) was the predominant complication related to nasal interface during the use of this device. Two patients died (3.6%) due to sepsis with DIC.

Conclusion: The most common diseases of admitted neonates requiring bCPAP were pneumonia, congenital pneumonia, perinatal asphyxia, respiratory distress syndrome and meconium aspiration syndrome. Superficial erosion was the predominant complication observed and most of the patients were discharged well.

Keywords: Clinical profile, newborn with CPAP.

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Introduction

Newborn mortality is a major contributor of under-five children death in Bangladesh. Most of this death occur

in first one week of life and more commonly in first 24 hours of age. In 2022, neonatal mortality rate in Bangladesh was 20 per 1000 live births which accounts

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two third on under-five mortality.¹The predominant causes of neonatal mortality are prematurity and its complications, perinatal asphyxia, sepsis, birth defects etc.² Most of these sick newborns got admission in neonatal intensive care units and require respiratory support, thermal care and many other supportive cares.

Among the various supports newborns need during their critical illness, continuous positive airway pressure (CPAP) is one of the commonest. continuous positive airway pressure (CPAP) is a means of providing respiratory support to neonates with either upper airway obstruction or respiratory failure. Respiratory failure constitutes either failure of ventilation or failure of lung function. The delivery of constant positive pressure to the airway of a spontaneously breathing neonate maintains adequate functional residual capacity within the alveoli to prevent atelectasis and improves oxygen and carbon dioxide exchange within the pulmonary circulation.³

There are two main types of CPAP systems. The first consists of variable flow devices, which include flow drivers such as a specific nasal prong or mask. The second type, such as bubble CPAP systems and infant ventilators, consists of a continuous flow device.⁴ In Bangladesh, bubble CPAP is very popular and there is national guideline on its use. Any term or preterm newborn with respiratory distress due to various underlying diseases such as respiratory distress syndrome, pneumonia, meconium aspiration syndrome, transient tachypnea of newborn or respiratory distress not improving with supplemental oxygen, apnea of prematurity, and post-extubation; then CPAP is indicated.⁵

The NICU of Dr. M R Khan Shishu Hospital is working with bubble CPAP since the beginning of 2022. But there was no study on this. So, so this study was aimed to observe the clinical profile of those neonates who required CPAP during a period of one year from our inception. In addition, in this study we also looked for the outcome of the studied neonates.

Materials and Methods

A retrospective single-center cross-sectional descriptive analysis was conducted to evaluate the indications and outcome of all admitted neonates requiring CPAP at the NICU of Dr. M R Khan Shishu Hospital & ICH in the period between January 2022 and December 2022.

Dr. M R Khan Shishu Hospital & Institute of Child Health is a non-profitable pediatric teaching hospital located at the center of Dhaka city. This 30 bedded neonatal intensive care unit (NICU) is a level-3 NICU having facilities for out born neonates transferred from local public and private hospitals both from inside and outside Dhaka. The annual number of admissions is around 1500.

Among the various devices used for newborns like incubator, syringe pumps, phototherapy machine, pulse oximeter, portable x-ray and blood gas analyzer, bubble CPAP machine is also in practice in this NICU. During the study period, neonates requiring CPAP and treated with four existing bubble CPAP (Fisher & Paykel), were included in the study. Data were extracted from the hospital records after a comprehensive review of the admission notes, daily progress notes, consultation notes, discharge summaries, problem lists, medication sheets, and laboratory and radiologic investigations.

Demographic characteristics include gestational age, birth weight, gender, age of admission, mode of delivery etc. The indication of CPAP was noted based on the final diagnosis such as: respiratory distress syndrome, congenital pneumonia, meconium aspiration syndrome, late onset sepsis pneumonia, perinatal asphyxia, apnea etc. Complications of CPAP and outcome in terms of improved and required ventilator were reported. Final outcome such as discharged or death were also observed.

Data were obtained in a pre-formed structured data collection sheet. Data collection was performed by two well-trained medical officers. Statistical analyses were performed using SPSS Statistics Software version 21. Data were presented as frequency distributions and percentages for categorical variables, and mean±standard deviation for continuous variables.

Results

A total of 1400 neonates were admitted to the NICU during the study period from January 2022 to December 2022. Of the admitted neonates, CPAP required in 62 (4.4%) patients.

Among the study population (neonates required CPAP), 55% were male and 45% were female with a male: female ratio of 1.2:1. Term neonates accounted for 74.2% of all included newborns and nearly 25.8% were born at preterm gestation. About two third of the studied neonates were delivered by LUCS (Table-I).

Table-I
Demographic variables of the studied population (n=62)

Variable	Number	Percentage
Gestational age (weeks) mean±SD	36.8±2.30	
Term	46	74.2
Preterm	16	25.8
Birth weight (g)	2662.09±633.39	
Normal birth weight	43	69.4
Low birth weight (<2500 g)	19	30.6
Gender		
Male	34	55
Female	28	45
Mode of delivery		
Vaginal	26	41.9
LUCS	36	58.1
Age on admission (hours) mean±SD	47.83±79.27	

Figure-1 shows the indications of bCPAP where respiratory distress due to early or late onset pneumonia was predominant (41.9%) followed by other causes 24.2% (e.g. perinatal asphyxia, congenital heart disease), congenital pneumonia (14.5%). Rest of the indications were respiratory distress syndrome (8.1%) in preterm neonates and meconium aspiration syndrome (8.1%) in term and post term neonates.

Table-II reflects that mean age of initiating bCPAP was 75.65±105.47 hours and mean duration in bCPAP was 4.43±3.36 days. About 11.3% patients required to shift to mechanical ventilator.

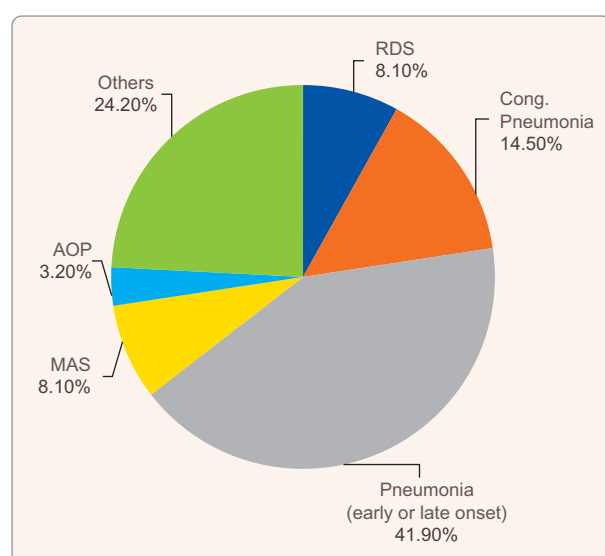


Figure-1: Indication of using bCPAP (based on final diagnosis)

Table-II
CPAP initiation and weaning

Variable	Mean ±SD
Age when initiated bCPAP (hours)	75.65±105.47
Duration in bCPAP (hours)	4.43±3.36
Required to switch to mechanical ventilator n(%)	7 (11.3)

During the use of bCPAP, complications related to nasal interface (nasal prongs) was observed. It revealed superficial erosion was the major complication (50%). Septal necrosis was found in 6.5% patients as shown in figure-2. In table-II the outcome of these CPAP babies was noted. Majority of the babies were weaned from bCPAP (88.7%) and later discharged to home (83.6%). Only 2 patients (3.6%) died during the study period.

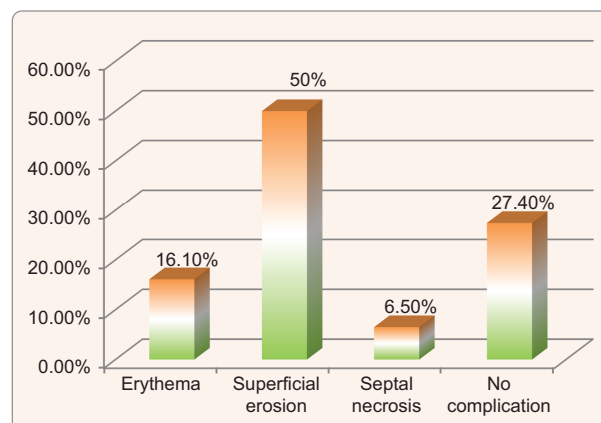


Figure-2: Complications by bCPAP interface observed during the study

Table-III
Outcome of patients who were in bCPAP (N=62)

Outcome	Number (n=62)	Percentage (%)
Weaned from bCPAP	55	88.7
CPAP failure	7	11.3
Final outcome of neonates who were successfully weaned from CPAP (n=55)		
Discharge	46	83.6
LAMA	14	12.7
Death	2	3.6

Discussion

This cross-sectional study was conducted over twelve months and during that period 4.4% neonates received bubble CPAP. The incidence may vary depending upon the setting and patient load of neonatal intensive care units of different tertiary level hospitals.

Among the study population (neonates required bCPAP), male was predominant (55%) which is consistent with a study done in Nepal⁶ (male 75%). Similarly, term neonates were found to get bCPAP more than preterm neonates in both studies respectively (Afroze S et al. 74.2% and Manandhar SR. 71%).⁶

In this study the most common disease specific indication for bCPAP use was pneumonia 41.9% (early or late) followed by other causes 24.2% (e.g., perinatal asphyxia, congenital heart disease) and congenital pneumonia (14.5%). Rest of the indications were respiratory distress syndrome (8.1%) in preterm neonates and meconium aspiration syndrome (8.1%) in term and post term neonates.

Whereas, in other study, the most common disease for starting bCPAP was congenital pneumonia 15 (23%) followed by MAS 12 (19%) and birth asphyxia 8 (13%). There were 7 (11%) babies who had respiratory distress syndrome and neonatal sepsis. Six babies (10%) were diagnosed as congenital heart disease.⁶ Mathur NB et al.⁷ postulated congenital pneumonia as the main cause of respiratory distress (68%). Congenital pneumonia was our second common indication.

As this hospital is an outborn hospital, babies mostly present within or after 72 hours of age for which the mean age of initiating b CPAP was late 75.65±105.47 hours. Outborn patients came from outside when only condition deteriorated. The mean duration in b CPAP

was 4.43±3.36 days that is in accordance with other study (95.71±36.7 hours mean around 4-5 days).⁶

This study revealed that superficial erosion (50%) was the predominant complication related to nasal interface followed by erythema (16.10%) and less commonly septal necrosis (6.5%). The studies by Yong and Nascimento suggested that nasal injury was observed in nearly all neonates instituted on CPAP and the risk was related to the duration of CPAP therapy. In the study by Nascimento, mild hyperemia was observed in 79.6% (117/147) neonates and bleeding in 19.7% (29/147) neonates.⁸⁻¹⁰ The study suggested that training and educational programs can improve the care of newborns who are on CPAP and can help prevent complications related to CPAP use. Another single center study suggested the utility of silicone gel sheeting to reduce the incidence of nasal injury.¹¹

About 88.7% patients were weaned and 11.3% patients failed to respond bCPAP therapy and required to shift to mechanical ventilator. This finding is consistent with another study conducted in a pediatric hospital in Dhaka, Bangladesh where successful weaning from CPAP was observed in 78.7% neonates and in an Indian study 86%.¹²⁻¹³

CPAP failure rate was 11.3% in our study which is lower than other studies as described in a systematic review. They mentioned that the proportion of neonates who failed CPAP and required mechanical ventilation varied from 20 to 40% (eight studies).⁸ It might be due to the early or timely initiation of b CPAP in our study population (Mean 75.65±105.47 hours and range: 29.82 hours to 181.12 hours).

Most of the patients got CPAP were discharge successfully to home and this finding matches with other study results.⁶

Conclusion

The most common diseases of admitted neonates requiring bCPAP were pneumonia, congenital pneumonia, perinatal asphyxia, respiratory distress syndrome and meconium aspiration syndrome. Majority of neonates were successfully weaned from bCPAP and were discharged to home. Superficial septal erosion was the predominant complication related to nasal interface during the use of this device.

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Review Article

Neonatal Respiratory Distress: An Overview of Management

Nargis Ara Begum¹, Sharmin Afroze², Md. Abdul Mannan³

Abstract

Respiratory distress is one of the commonest causes of hospital admission among neonates. Common conditions those lead to respiratory distress include transient tachypnea of newborn (TTN), respiratory distress syndrome (RDS), meconium aspiration syndrome (MAS), congenital pneumonia, persistent pulmonary hypertension of newborn (PPHN) etc. With the development of neonatal medicine and intensive care, the concepts and methods of managing respiratory problems in neonates have been changing continuously. Important aspects of respiratory management comprise of the use of non-invasive ventilation and various ventilation modes in order to avoid intubation, ventilation induced lung injury and other co-morbidities. Nasal CPAP (nCPAP), nasal intermittent positive pressure ventilation (NIPPV), heated humidified high flow nasal canula are some common non-invasive ventilation strategies used by neonatologists now-a-days. High frequency oscillatory ventilation is still a preferred mode of respiratory support in MAS and PPHN. Use of exogenous surfactant and caffeine for preterm newborns (born before 37 weeks) are promising adjunct to the respiratory treatment. Considering all the updates, it is challenging but crucial for clinicians to use appropriate respiratory strategies in neonates, not only to save their lives but also to ensure better short-term and long-term outcomes.

Keywords: Respiratory distress in newborn, respiratory management

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Introduction

Respiratory distress in newborn is one of the most common clinical entities observed in neonates. It is recognized as one or more signs of increased work of breathing, such as tachypnea, nasal flaring, chest retractions or grunting.¹⁻² Newborn can present with respiratory distress due to various underlying etiologies. Regardless of the cause, if not recognized and managed quickly, respiratory distress can escalate to respiratory failure and cardiopulmonary arrest that finally leads to death. Therefore, intervention with adequate respiratory support can save many lives. In the modern era of neonatology, with the institution of many new technologies and adjunctive therapies, the provision of adequate respiratory care has become very complex and challenging.² So, this review aimed

to summarize the different aspects of respiratory care available for sick neonates along with their recommendation of use in daily practice.

Burden of respiratory distress in newborn

Respiratory distress is one of the most common reasons for neonatal admission in NICU. Around 15% of term infants and 29% of late preterm infants admitted to the NICU develop significant respiratory morbidity. This incidence is even higher for babies born before 34 weeks of gestation.³ Among the various causes of respiratory distress, respiratory distress syndrome (RDS) is commonest in preterm neonates. The incidence of RDS is inversely related to gestational age. It occurs in 98% of preterm infants between 22 and 24 weeks of gestation but only 25% of those with

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birth weight between 1251 to 1500 g.^{4,5} On the other hand, neonatal pneumonia and sepsis account globally for approximately 500,000 deaths annually and almost 50% of deaths of infants within first 28 days of life.⁶ Meconium aspiration syndrome contributes to neonatal mortality by 3-5%.^{7,8} Similar to this, other respiratory conditions have significant impact on neonatal morbidity and mortality. There is no global data to find out the overall incidence of different causes. So, considering the importance to survival, timely intervention is crucial.

Different causes of respiratory distress in neonates

The causes of respiratory distress in a newborn are diverse and multisystemic. Some causes are transient, some are persistent. Cardiac cause can also present with minimal respiratory distress like pulmonary causes. The different causes for respiratory distress are listed in table-I.

Causes of respiratory distress are diagnosed based on history, clinical examination, radiological and laboratory findings. Such as TTN is diagnosed in term or late preterm neonates having respiratory difficulty soon after birth and has chest x-ray features of hyperinflation or prominent perihilar marking. Any preterm neonate who presents with respiratory distress within first six hours of life, having characteristic chest x-ray finding: presence of air bronchogram, reticulo-granular pattern or ground glass opacity is labelled as RDS. A term or post term neonate who is

meconium stained or has history of meconium aspiration with coarse, fluffy densities or patchy infiltrates in chest-x-ray is termed as meconium aspiration syndrome. In surgical causes, specific findings are detected in plain or contrast x-ray. Other than these tools, an important investigation is arterial blood gas analysis which also guide us in diagnosing the underlying condition as well as managing the patient.⁹

Respiratory care management for neonates

Respiratory distress is a common condition seen in neonates both in preterm and full-term neonates. Before, initiating any respiratory support, the severity of respiratory distress needs to be assessed. Downes' score (DS) and Silverman Anderson score (SAS) are commonly used for quick diagnosis of distress and assessment of its severity. DS is used for assessment of both term and preterm newborns whereas SAS has been validated only in preterm babies.¹⁰

Modalities of oxygen therapy

Regarding treatment with oxygen therapy, there are several ways such as nasal canula, oxygen hood, continuous positive airway pressure and mechanical ventilator. Among them face mask and oxygen hood is not recommended for neonates as they lead to hypercarbia and oxygen toxicity.¹¹ Among other modes of oxygen therapy, invasive ventilation is unavoidable in some situations and non-invasive ventilation may be sufficient in several neonates. Over the last few decades, non-invasive respiratory support

Table-I
Common causes of respiratory distress in newborns

Pulmonary	Extra-pulmonary	Surgical
Parenchymal		
Respiratory distress syndrome (RDS)	PDA	Tracheo-esophageal fistula
Transient tachypnea of newborn (TTNB)	CHDs	Diaphragmatic hernia
Meconium aspiration syndrome (MAS)	Metabolic acidosis	Choanal atresia
Persistent pulmonary hypertension of newborn	Sepsis	
Pneumonia	Hypoglycemia	
Pul. hemorrhage	Other systemic causes	
Pul. hypoplasia		
Extra-parenchymal		
Pneumothorax		
Pleural effusion		

has gained much popularity. Whatever, the mode of delivery is, oxygen blender is essential to ensure as it allows precise control of the oxygen concentration and prevents damage to the brain, lungs and eyes.¹¹

Monitoring a neonate while on oxygen therapy

When a patient is getting oxygen therapy by any respiratory support system, monitoring is crucial. Health care providers have to monitor the patient clinically regarding vital signs, level of consciousness, respiratory distress severity scoring and pulse oximetry. Moreover, each and all parameters set for the patient need to be checked in the device including pressures, volumes, oxygen concentration etc. Arterial blood gas and imaging can also guide us in understanding the disease progress and to plan weaning from the respiratory device.

Non-invasive ventilation: It refers to any method of providing respiratory support, where an endotracheal tube is not used. Different methods of non-invasive ventilation include continuous positive pressure ventilation (CPAP), heated humidified high flow nasal cannula (HHFNC or HFNC), nasal intermittent positive pressure ventilation (NIPPV), nasal high frequency oscillatory ventilation (nHFOV) and nasal neurally adjusted ventilator assist (nNAVA).¹²

Continuous positive pressure ventilation (CPAP)

Continuous positive pressure ventilation (CPAP) is a form of non-invasive ventilation where a positive pressure is applied in the airway of a spontaneously breathing infant throughout the respiratory cycle and thus prevents collapse of alveoli and terminal airway during expiration. In the early 1970s, Gregory et al. first described the clinical use of CPAP in preterm infants with respiratory distress syndrome.¹³ The benefits of CPAP for RDS in preterm infants are well established.¹⁴⁻¹⁵ CPAP provides distending pressure into the upper and lower airways preventing collapse in RDS.¹⁶ The World Health Organization (WHO) has recommended the use of CPAP for preterm infants with clinical signs of respiratory distress syndrome.¹⁷

Sometimes it is difficult to ascertain respiratory status in preterm babies soon after birth and to accurately predict the prognosis. Preterm babies with respiratory failure may not show signs of respiratory distress in the first hours after birth. Even babies with early respiratory distress may improve. Based on evidence and analyzing the cost-benefit ratio, WHO has recommended that, continuous positive airway

pressure (CPAP) therapy may be considered immediately after birth for very preterm infants (< 32 weeks' gestation), with or without respiratory distress. Delivery room CPAP is crucial for preterm newborns as it can significantly reduce the need for invasive mechanical ventilation, surfactant administration and potential complication like bronchopulmonary dysplasia (BPD) by providing early respiratory support in delivery room.¹⁷ So, center need to focus on delivery room CPAP for early recruitment of lungs in preterm infants.

CPAP is usually initiated at a pressure of 5 cm H₂O, flow of 5 L/min and fraction of inspired oxygen (FiO₂) of 30%. Following this, the CPAP is titrated to reduce the work of breathing, flow to obtain adequate bubbling (continuous bubbling in both phases of respiration) and FiO₂ to achieve the saturation targets (90%–95% for preterm neonates). Based on clinical judgement, CPAP is weaned gradually.¹⁸

Humidified high flow nasal cannula (HHFNC or HFNC)

High flow nasal oxygen can be initiated in preterm newborns as an alternative to CPAP. HHF delivers humidified gas at increased flow rates (3 - 8 L/min) via binasal prongs. In HFNC, inhaled gases flow higher than the inspiratory demand flow. This leads to wash out of upper airways, reduces physiological dead space, and decreases nasopharyngeal airway resistance.¹⁹ Three recent randomized controlled prospective studies showed that the efficacy and safety of HHFNC was similar in post-extubation respiratory support compared with NCPAP for infants with GA between 28 weeks and 32 weeks. There was no significant difference in mortality and morbidity comprising bronchopulmonary dysplasia, patent ductus arteriosus, and intraventricular hemorrhage. Nasal trauma was significantly reduced in HHFNC.²⁰⁻²² Moreover, a single -center study conducted upon 76 preterm neonates having RDS, suggested HHFNC to be as effective as NIPPV (nasal intermittent positive pressure ventilation) in preventing endotracheal ventilation (28.9% vs. 34.2%) in the primary treatment of RDS in preterm infants.^{23,24} Further larger and multi-center studies are required on this.

Nasal Intermittent Positive Pressure Ventilation (NIPPV)

It is another type of non-invasive ventilation where pressure is delivered at two levels [peak inspiratory

pressure (PIP) and positive end expiratory pressure (PEEP)] using a mechanical ventilator, by moderating the gas flow and orifice of the expiratory valve. Thus, it improves respiratory drive, provides higher mean airway pressure, and induces head's paradoxical reflex.²⁵ In a randomized controlled trial (RCT) comparing synchronized NIPPV with nasal CPAP in preterm neonates with RDS, neonates managed on sNIPPV had lower rates of respiratory support failure, hypercarbia, and hypoxia.²⁶

Other non-invasive respiratory support

Nasal high frequency oscillatory ventilation (nHFOV) and nNAVA (nasal neurally adjusted ventilatory assist) are two sophisticated modes of non-invasive ventilation. nHFOV combines the advantages of high frequency ventilation and nasal ventilation. By delivering a small tidal volume at supra-physiological rates, it causes better CO₂ elimination. In a meta-analysis of 8 RCTs involving 463 preterm neonates, showed that nHFOV results in a lesser likelihood of MV (RR = 0.50; 95% CI 0.36 to 0.70) and better CO₂ removal [mean difference (MD) -4.6 mmHg; 95% CI -7.9 to 1.3] when compared with nCPAP or nBiPAP.^{26,27}

Neurally-adjusted ventilatory assist (NAVA) is a relatively newer mode of ventilation in which a ventilator utilizes the electrical activity of the diaphragm (Edi) to generate appropriate breaths and assist ventilated patients. There is no specific indication for the use of NAVA in adults, children, or neonates. It can be used in all conditions where conventional ventilators are indicated.²⁸

Invasive ventilation

When a newborn either term or preterm, has no self-respiration, it is essential to put the baby in mechanical ventilator. Recent evidences highlight the importance of preserving the infant's spontaneous breathing and provide only the necessary level of support to assist ventilation better than controlling the infant's ventilation and gas exchange.²⁹ Some examples include:

Pressure support:

For a more stable and effective gas exchange, addition of the pressure generated by the infant's respiratory pump and that produced by the ventilator during synchronized ventilation result in a more consistent tidal volume and improved ventilation compared to intermittent mandatory ventilation (IMV). One study showed the additional use of PSV to SIMV can

facilitate the weaning compared to SIMV alone. Lower peak pressure levels with PSV boosted the spontaneous breaths reducing the reliance on larger SIMV breaths.²⁹⁻³¹

Volume controlled ventilation

In volume ventilation, the ventilator delivers the preset volume, using pressure over the inspiratory time that has been set. The pressure needed to deliver the volume will vary depending on the compliance. As the compliance improves with the recovery of the lungs, the pressure needed reduces and the baby 'auto weans'.²⁹

Hybrid modes of ventilation

Hybrid modes try to combine the advantages of various modes to make ventilation more physiological and gentler on the lungs. It may be SIMV/SIPPV +VG, SIMV+PS or PSV+VG.

In SIMV+VG mode, the set number of breaths will be given with the targeted tidal volume by adjusting PIP based on the previous exhaled tidal volume. Whereas in SIPPV+VG mode, every spontaneous breath triggered by the baby is supported to deliver the targeted tidal volume.

During SIMV+PS mode, the PS component does not have any mandatory ventilator rate as backup control if the baby goes into apnea. The SIMV rate needs to be set to provide adequate backup.

The advantage of PS+VG is that the baby receives the targeted tidal volume with the required pressure support but can regulate its own inspiratory time and rate. It gains more liberty to increase or decrease minute ventilation when being on flow cycled ventilation.²⁶

Faster weaning: Clinical trials have consistently shown faster weaning and shorter duration of mechanical ventilation with synchronized modes compared to IMV which is more evident among the more premature infants.²³

High frequency oscillatory ventilation (HFOV)

In neonates, HFOV is preferred when there is failure of ventilation and oxygenation while on conventional ventilation. Whereas in some centers, HFOV is used as a primary mode of ventilation for extremely preterm infants.³² HFOV is characterized by delivering tidal volumes close to or less than the anatomical dead space. Preterm infants also benefitted from small tidal volumes compensated by higher ventilation rates.

Clinical studies have shown that HFV can effectively restore lung function, and potentially limit ventilator-induced lung injury, which is considered an important risk factor for developing bronchopulmonary dysplasia (BPD).³³ Studies also suggest that, HFOV can effectively improve lung ventilation and oxygenation function, shorten ventilator treatment time, and reduce the incidence rate of air leakage for neonatal MAS.³⁴

Other therapies

Surfactant

From the previous studies and practice, it is proven that replacement therapy with exogenous surfactant preparations derived from animal sources dramatically reduced RDS-related morbidity and mortality.³⁴ Over the time, the delivery method of surfactant has changed a lot. From bolus administration to INSURE (Intubate Surfactant Extubate) and then to LISA (Less Invasive Surfactant Administration) via small catheter has made the technique easy. Studies have showed that surfactant delivery via a thin catheter to spontaneously breathing preterm infants compared with surfactant administration through an ETT was associated with a decrease risk of death or BPD, need for assisted breathing in the first 72 hours of life, severe brain bleeding, death during first hospitalization, and BPD among survivors.³⁵ Surfactant nebulization is another method that may offer a truly non-invasive option for surfactant delivery to preterm infants in the near future.³⁶

Caffeine

Caffeine is an important therapy for all preterm newborns in reducing as well as preventing apnea. The World Health Organization has recommended 20 mg/kg loading dose and a 5 mg/kg per day maintenance dose of caffeine for six weeks. The duration of caffeine administration should be based on clinical judgement. If caffeine is not available, other methylxanthines (aminophylline or theophylline) may be considered.¹⁷ Now-a-days, early treatment with caffeine in the delivery room (DR) has been proposed to decrease the need for mechanical ventilation (MV) by limiting episodes of apnea and improving respiratory mechanics in preterm infants. In a multi-center prospective study, infants with 25⁺⁰–29⁺⁶ weeks of gestational age were enrolled and randomized to receive 20 mg/kg of caffeine citrate intravenously, via the umbilical vein, or enterally, through an orogastric tube, within 10 min of birth.³⁷ Caffeine blood level was

measured at 60 ± 15 min after administration and 60±15 min before the next dose (5 mg/kg). The study results showed that intravenous and enteral administration of caffeine can be performed in the DR without interfering with infants' postnatal assistance. Some patients did not reach the therapeutic range, raising the question of which dose is the most effective to prevent MV.³⁷

Conclusion

Respiratory diseases pose a significant portion of neonatal admission in newborn care units. There is a variety of options for providing respiratory support to these patients. But timely initiation of the desired one and thoughtful decisions for maintenance of that system is crucial. This, will eventually reduce morbidity and improve outcome of the newborns.

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Case Report

Sirenomelia (Mermaid Syndrome): A Case Report in Bangladesh

Md. Hasan Moshir Shawon

Abstract

Sirenomelia is an extremely rare and typically fatal birth defect characterized by the partial or complete fusion of the lower limbs, genitourinary anomalies, and pulmonary malformations. The exact causes are unknown, but several risk factors have been identified, including maternal diabetes mellitus, teratogenic drugs, genetic susceptibility, vascular hypoperfusion, cocaine use, exposure to landfill water, and maternal age being less than 20 years or greater than 40 years. A preterm (35 weeker) low birth weight (2300 gm) baby was born from 30 years old non-consanguineous mother via caesarean section. The baby had fused lower limbs with 10 toes, absent external genitalia, and a single umbilical artery. The baby was passed away after 30 minutes of birth. We could not find any risk factor for sirenomelia in this case. We recommend an early routine ultrasound anomaly scan in all pregnant women particularly for early detection and termination of pregnancy as the prognosis is guarded.

Keywords: Mermaid, Sirenomelia

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Introduction

Sirenomelia, also known as mermaid syndrome, is a congenital deformity characterized by the fusion of the lower limbs, resembling the mythical mermaid.¹ Defined by Stevenson as “a limb deformity in which the normally paired lower limbs are replaced by a single midline limb,” it is named after the legendary Greek Sirens.² This rare and often fatal birth defect occurs with an incidence rate of 0.8–4 per 60,000 to 100,000 pregnancies.³⁻⁵ The exact causes are unknown, but several risk factors have been identified, including maternal diabetes mellitus, teratogenic drugs, genetic susceptibility, vascular hypoperfusion, cocaine use, exposure to landfill water, and maternal age being less than 20 years or greater than 40 years.⁶⁻⁹ It is more common in monozygotic twins and males.^{4, 10} Associated anomalies include absent or ambiguous external genitalia, imperforate anus, rectal atresia, absent urinary bladder, single umbilical artery, renal agenesis, esophageal atresia, omphalocele, pulmonary hypoplasia, cardiac defects, diaphragmatic hernia, lumbosacral/pelvic bone abnormalities, and spina bifida.¹¹ Prenatal diagnosis

can be achieved with sonography in the first trimester, identifying symptoms such as nuchal translucency, fused or single lower limb, renal agenesis, a single umbilical artery, and oligohydramnios.¹²

Case Report

A 30-year-old woman, gravida three, para two, with two healthy children aged eight and six years, was admitted for a caesarean section at 35 weeks gestation due to severe oligohydramnios and fetal distress. She had no personal or family history of diabetes and had only taken iron and folic acid supplements during pregnancy. The parents were non-consanguineous and reported no conditions or birth defects in their family history, nor was there any history of radiation exposure. An ultrasound performed at 32 weeks gestation revealed oligohydramnios. The baby did not cry within the golden minute after birth and exhibited severe birth defects, necessitating transfer to the special care and neonatal unit (SCANU) of the district hospital for better management.

The newborn was resuscitated for 20 minutes but unfortunately passed away due to cardiac and

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respiratory arrest. The newborn exhibited severe birth defects, including the fusion of the lower segment of the body below the pelvis into a single lower limb, with two feet fused posteriorly to form a single flipper-like foot with ten toes spread out in a fan-like pattern, characteristic of mermaid syndrome (Figure-1, Figure-2 and Figure-3). The foot was oriented anteriorly relative to the trunk, and external palpation suggested the presence of two femurs and two tibias. The external genitalia were absent, making it impossible to determine the sex (Figure-2). Additionally, the newborn had an imperforate anus and no urinary meatus, along with a single umbilical artery (Figure-4). The upper part of the body appeared normal. Weight of the baby was 2300 gm. Permission for autopsy was declined by the parents. On infantogram, it reveals that all thigh and leg bones are present and according to these findings the newborn can be categorized as type 1 according to the Stocker and Heifetz classification of



Figure-1: Complete morphological view of sirenomelic fetus.



Figure-2: Photograph of the groin area showing no external genitalia and absent urinary meatus.



Figure-3: Photograph showing the fused feet with 10 toes.



Figure-4: Posterior view showing fused lower limbs, imperforate anus.

sirenomelia (Figure -5). Ultrasonography report showed bilateral renal agenesis with absent urinary bladder (Figure-6).

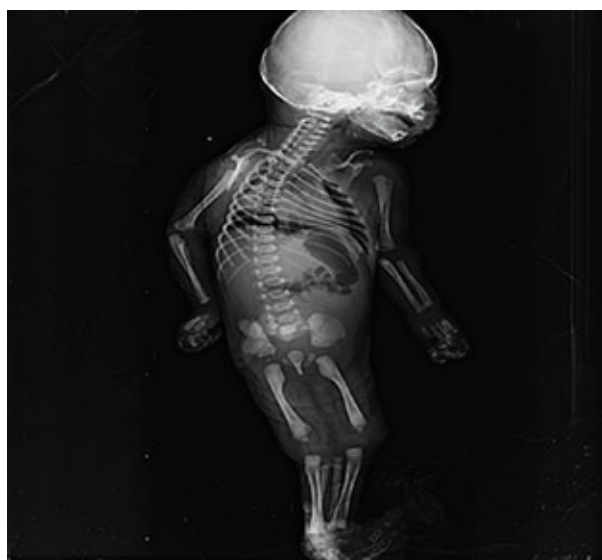


Figure-5: Infantogram showing that all thigh and leg bones are present. The newborn can be categorized as type 1 according to the Stocker and Heifetz classification of sirenomelia

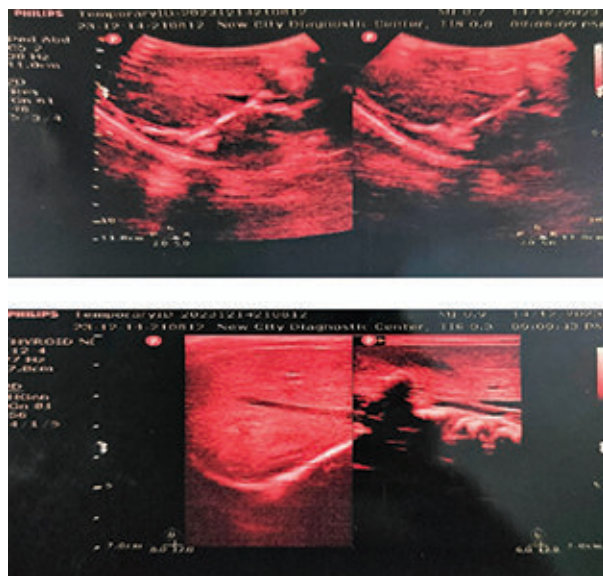


Figure-6: Ultrasonography revealed bilateral renal agenesis with absent urinary bladder.

Discussion

Sirenomelia is an extremely rare birth defect characterized by malformation of the gastrointestinal and genitourinary systems, fusion and skeletal abnormalities of the lower extremities, a single exceptional umbilical artery, and Potter's facies.¹³ It was first reported in 1542 by Rocheus et al. and later by Palfyn et al. in 1543. In 1961, Duhamel classified mermaid syndrome (sirenomelia) as type 5 caudal regression syndrome (CRS).¹⁴ However, now a days, mermaid syndrome is considered a separate entity. The presence of two umbilical arteries, non-lethal renal anomalies, non-fused lower limbs, abdominal wall defects, and abnormalities of the tracheoesophageal tree, neural tube, and heart are key features of CRS. In contrast, sirenomelia is characterized by a single umbilical artery, bilateral lethal renal anomalies, and severe oligohydramnios associated with severe pulmonary hypoplasia.¹¹

The exact etiology of sirenomelia is unknown. Researchers believe that both environmental and genetic factors may play a role in the development of this birth defect. Most cases appear sporadically, which suggests environmental factors or a new mutation. It is most likely that sirenomelia is multifactorial. In 1986, Stevenson proposed the theory of 'vitelline artery steal' to explain the development of sirenomelia. According to this theory, all patients with

sirenomelia have a large umbilical artery that branches from the abdominal aorta slightly below the celiac artery. This abnormal vascular anatomy may lead to inadequate blood supply and nutrition to the lower part of the body during embryonic development. As a result, various malformations can occur, including sacral agenesis, fusion of the lower limbs, imperforate anus, rectal agenesis, internal and external genitalia anomalies, and renal agenesis.¹⁵ Another proposed theory, based on 'defective blastogenesis', suggests that incomplete development of the caudal region and malformed lower limbs in sirenomelia result from ischemia due to defective angiogenesis during embryonic development.¹⁶ These theories highlight the complex interplay of vascular anomalies and developmental abnormalities that contribute to the unique features of sirenomelia.

The genetic basis of sirenomelia in humans remains largely unknown. While no specific chromosomal abnormalities have been identified as causing sirenomelia,³ experimental studies on mice have provided insights into potential genetic mechanisms. Experiments inducing loss-of-function (LOF) mutations in the signaling sequences of the "bone morphogenetic protein" (Bmp-7) gene or gain-of-function (GOF) mutations in the signaling sequences of the "retinoic acid" (RA) gene have resulted in phenotypes similar to those observed in humans with sirenomelia. These include the fusion of lower limbs and severe pelvic malformations.¹⁷

Poorly controlled maternal diabetes is indeed a recognized risk factor for sirenomelia,¹³ although it only accounts for a small percentage of cases (approximately 0.5%–3.7%) reported in diabetic mothers.¹⁸ The teratogenic effect is thought to be related to increased production of free oxygen radicals in maternal diabetes, which can interfere with normal embryonic development, potentially leading to anomalies like sirenomelia.^{3, 4, 7, 16} It's notable that in many reported cases, maternal diabetes mellitus was not present, indicating that other factors may also contribute to the development of this birth defect. Additionally, maternal age below 20 years or above 40 years has been identified as another risk factor for sirenomelia.¹⁹ This suggests that maternal age-related factors may also play a role in the incidence of this rare condition, although the exact mechanisms are

not fully understood.

The recurrence pattern of sirenomelia is a topic of ongoing research and debate. Orioli et al. reported no familial recurrence in their study.⁸ However, other studies have reported cases of true recurrence of sirenomelia within families, indicating a potential genetic component.^{20, 21}

The most widely used sirenomelia classification system is that proposed by Stocker and Heifetz¹⁸ (Table I); therefore, our case was assigned to category 1 (one).

Diagnosing sirenomelia through antenatal ultrasound can be achieved as early as 14 weeks of gestational age.²² Key ultrasound findings consistent with sirenomelia include nuchal translucency, the presence of a fused or single lower limb, renal agenesis, and a single umbilical artery.¹² During the second trimester, diagnosing sirenomelia becomes more challenging due to the development of oligohydramnios, which is often associated with renal agenesis or dysgenesis. Color and power Doppler ultrasound can aid in the diagnosis by showing a single greater vitelline artery. This artery typically originates from the proximal aorta, enters the iliac vessels without branching within the fetal pelvis, and connects to the umbilical cord ventrally. These specific Doppler findings can help differentiate sirenomelia from other conditions and assist in accurate prenatal diagnosis.²³

As sirenomelia is a serious birth defect and incompatible with life due to pulmonary hypoplasia and renal failure resulting from renal agenesis, medical termination of pregnancy is admissible. Approximately 50% of cases of sirenomelia result in live births, but most affected newborns do not survive beyond the first few days of life. In clinical practice, decisions regarding the management of pregnancies affected by sirenomelia involve careful consideration of medical ethics, parental wishes, and the anticipated outcomes for both the fetus and potential newborn.⁴

Conclusion

Sirenomelia remains a lethal condition with multisystem involvement which makes this condition incompatible with life. Research in this area is lacking due to isolated cases occurring every year worldwide. More research is needed to obtain a better understanding of the etiology and pathophysiology in order to prevent future cases and/or develop antenatal/postnatal treatments to improve outcome.

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Guideline for Manuscript Preparation and Submission, Bangladesh Journal of Newborn Health (BJNH)

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This journal is published half yearly in the month of January and July. The types of articles accepted for publication include original research articles, review articles, editorials and case reports.

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