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Original Research Article

Prediction of hearing impairment by indirect hyperbilirubinemia in neonates

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ABSTRACT

Background: Hearing is a special sense and one of the most important components of communication. The ability to communicate and acquiring skills largely depends on the ability of hearing. Hearing impairment can have a substantial influence on a child's speaking ability, language development and social skills. Early detection and timely initiation of treatment for childhood hearing loss is very crucial as inadequate auditory input during first few years of life irreversibly delays the language skills for communication and reading. This study aimed to predict the frequency of hearing impairment in neonates with indirect hyperbilirubinemia.
Methods: This was a cross-sectional study conducted at the Neonatal intensive care unit (NICU) and Special care neonatal unit (SCANU) of Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh during the period from January 2020 to December 2021. In this study, we included 85 hospitalized neonates with hyperbilirubinemia based on the selection criteria.
Results: The mean age of the patients was 5.6 (±1.6) days. Pre-term babies were 63.5% and 36.5% were termed babies. Among all patients, 49.4% and 43.5% of patients had indirect bilirubin levels from 15 to<20 mg/dl & 20 to<25 mg/dl respectively. Among 11 hearing-impaired neonates, 3 (27.2%) had mild to moderate impairment, 6 (54.5%) had moderate to severe impairment and 2 (18.1%) had severe to profound hearing impairment. Sepsis, ototoxic drugs and indirect hyperbilirubinemia were independent predictors of hearing impairment.
Conclusions: This study concluded that indirect hyperbilirubinemia of≥15 mg/dl in preterm and≥20 mg/dl in term neonates is an important predictor of hearing impairment in neonates.

Keywords: Hearing impairment, Hyperbilirubinemia, Neonates, Prediction

INTRODUCTION

Hearing is a special sense and one of the most important components of communication. This communication is the cornerstone of education and learning. The ability to hear is essential for learning new skills and for communicating. Hearing impairment can have a substantial influence on a child's speaking ability, language development and social skills. According to WHO (2021), over 5% of the world's population or approximately 430 million people have disabling hearing loss, among them 34 million (7%) are children and around 60% of hearing loss in children can be prevented.[1] The prevalence of hearing loss in children is greatest in South Asia, Asia Pacific and Sub-Saharan Africa and only South East Asia covers one-third of the world's hearing-impaired population.[2] According to the estimation of the Government of Bangladesh, hearing impairment is the second most common form of disability in Bangladesh which is causing economic, social, educational and vocational problems and in this aspect, children are mostly affected here.[3] The prevalence of disabling hearing loss among Bangladeshi people of all ages is 9.6 percent.[4] Hyperbilirubinemia affects about

80% of neonates and severe bilirubin poisoning can harm the nervous system, especially in preterm babies.[5] According to a study by Boskabadi et al, sensorineural hearing loss in infants with hyperbilirubinemia was 4.8% and bilirubin levels showed a strong predictive ability for the prognosis of sensorineural hearing loss in epileptic newborns.[6] Indirect hyperbilirubinemia develops in newborns as a result of high bilirubin preload and inadequate bilirubin clearance. The auditory brain pathways are specifically preferred by bilirubin.[6]

Innovations in hearing screening have led to the development of more sensitive and accessible tools that can reliably and consistently measure hearing shortly after birth. Traditional behavioral methods for screening for hearing in children are insufficient and unreliable. At present, the recommended hearing screening techniques are Otoacoustic emission (OAE) testing or auditory steady-state response (ASSR) and sometimes a combination of both. Transient evoked otoacoustic emissions (TEOAEs) is a simple, non-invasive test for cochlear hearing loss in newborn babies and children who are unable or unwilling to cooperate during hearing tests.

A low-level sound is emitted by the cochlea, based on the concept that outer hair cells within the cochlea can generate force in response to incoming sounds. The sensitivity and specificity of OAE are 95% and 91% respectively.[7] Auditory steady-state response (ASSR) is an evoked potential test that can accurately measure auditory sensitivity than other hearing test methods which can be used to screen every sick and preterm newborn hearing. ASSR identifies children early with accurate hearing assessment which can lead to earlier and more accurate hearing aid settings such as cochlear implants. [8] ASSR tests can effectively predict behavioral hearing thresholds in children with a history of sensorineural hearing loss and neonatal hyperbilirubinemia.[9]

Hearing impairment has a serious and catastrophic impact on the health of the newborn. Significant hearing impairment occurs among 1 to 3 per 1000 live births and this number is up to 2 to 4% in the neonatal intensive care unit.[10] Parents underestimate hearing problems in their children, but they can detect hearing loss earlier if it involves speech-related frequencies.[11] Parental suspicion of hearing loss is not enough to identify mild hearing loss.[12] Regretfully, this hearing loss is identified too late to prevent unintentional and irreversible damage.

As hearing-related disability in babies often remains un-noticed, the most obvious consequence of hearing impairment that occurs is difficulty in speech and language acquisition and this disability will have a detrimental impact on their overall literacy and other social issues. Early detection and timely initiation of treatment for childhood hearing loss is very crucial for the development of communication and social skills, academic achievement and boost of self-esteem.[13] Therefore, this study aimed to predict the frequency of hearing impairment in neonates with indirect hyperbilirubinemia.

METHODS

Study type

This was a cross-sectional study.

Study place

The study was conducted at Neonatal intensive care unit (NICU) and Special care neonatal unit (SCANU) of Bangladesh Shishu Hospital and Institute, Dhaka, Bangladesh.

Study duration

The study period during the period from January 2020 to December 2021.

Inclusion criteria

In the study, we included 85 hospitalized neonates with hyperbilirubinemia based on the selection criteria. The criteria to be eligible for enrollment as our study participants were: a) Term neonates up to 7 days old having Indirect hyperbilirubinemia of≥20 mg/dl; b) Preterm neonates up to 10 days old having Indirect hyperbilirubinemia of≥15 mg/dl and c) Parents of neonates who were willing to participate.

Exclusion criteria

The exclusion criteria were set as a) Neonates with gestational age<30 weeks or birth weight<1200 gm, b) Neonates with history of hearing impairment in the family, syndromic baby, multiple anomalies and perinatal asphyxia (hypoxic ischemic encephalopathy stage II and III) and c) Neonates with any history of acute illness (e.g., renal or pancreatic diseases, ischemic heart disease, etc.).

Data collection procedure

After obtaining written consent from the parent, the investigator conducted a face-to-face interview with the mother or caregivers to record the history of the newborns. Gestational age was determined by mothers' recall of LMP and by the new Ballard scoring system. Weight was measured by an electronic weighing scale by keeping the baby undressed and before feeding by the neonatal nurse.

The medical records of the newborns were reviewed to identify antenatal, natal and postnatal risk factors. Clinical examination was done in the search for risk factors such as ear anomalies or syndromic features. Newborns who met the inclusion criteria were screened with TEOAE first. Both ears were screened individually.

For those who failed the TEOAE screening test, a second screening test with ASSR was done in both ears before discharge. ASSR was performed in ENT and Head-Neck Cancer Hospital and Institute.

Parents were informed that if their baby did not pass screening, they would be informed of prompt follow-up. Before discharge, parents of hearing-impaired babies were counseled for follow-up testing and advised for consultation with an otolaryngologist for the subsequent measures to be taken.

Statistical analysis

All data were recorded systematically in preformed data collection form. Quantitative data was expressed as mean and standard deviation and qualitative data was expressed as frequency distribution and percentage. Categorical data of the patients were analyzed by Mann-Whitney U test and Fisher Exact test to find out the association between hyperbilirubinemia and hearing impairment.

A logistic regression model was adopted to find out different independent variables of hearing impairment. A p value<0.05 was considered as significant. Statistical analysis was performed by using SPSS 23 (Statistical Package for Social Sciences) for Windows version 10. Ethical clearance was obtained from the Ethical Review Committee (ERC) of Bangladesh Shishu Hospital and Institute to undertake the study.

RESULTS

Table 1 shows the distribution of patients' age at enrollment. In the age group 2-4 days, 22 (25.9%) neonates were in this group, while 57 (67.1%) were in the 5-7 days age group. The mean age of the patients was 5.6 (±1.6) days. The pie chart shows that among the 85 patients, 64 (75.3%) were male while 21 (24.7%) were female. The male and female ratio was 3:1 in our study.

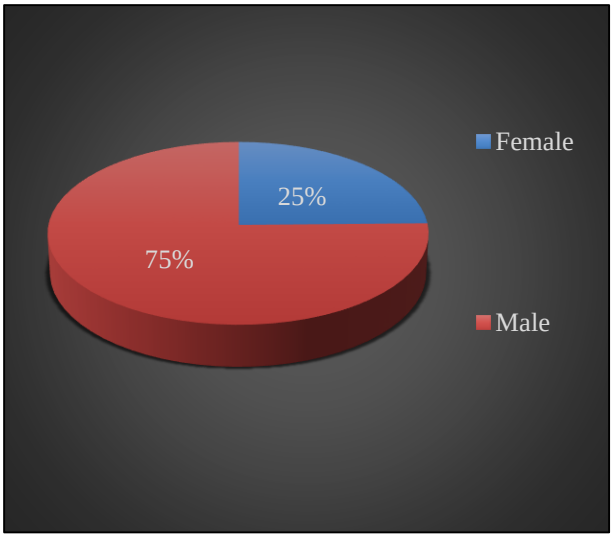

Figure 1: Distribution of patients by gender (n=85).

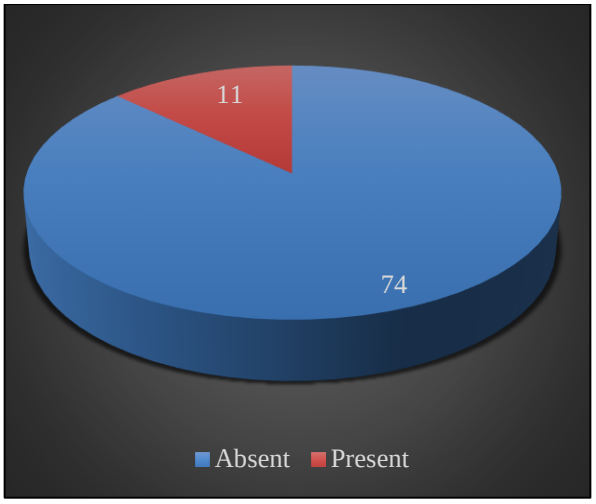

Figure 2: Distribution of patients by hearing impairment (n=85).

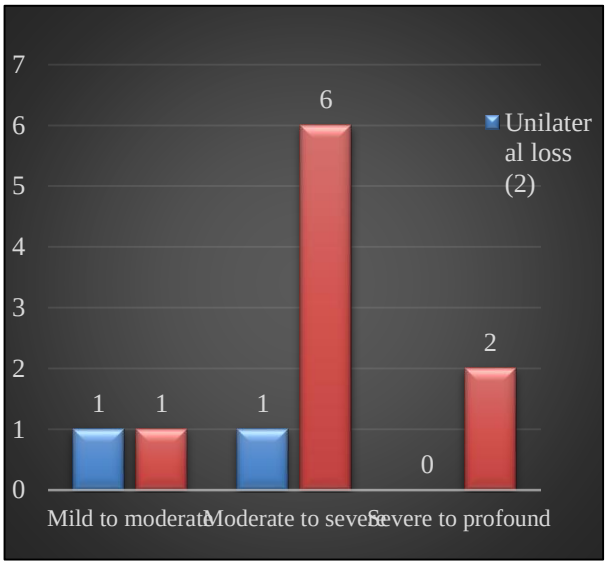

Figure 3: Grades of hearing impairment (n=11).

Table 2 shows the distribution of the patients based on gestational age. Among 54 (63.5%) pre-term babies 15 (17.6%) had a gestational age of 33-34 weeks and 39 (45.9%) had a gestational age of 35-37 weeks. On the other hand, 31 (36.5%) were termed babies. No neonates were found between gestational age 30-32 weeks. Birth weight distribution of the patients showed that 49 (57.6%) had low birth weight while 36 (42.2%) had normal weight. The mean birth weight of the patients was 2390.1 (±466.4) gm. No neonates were found between birth weights 1200-1499 gm.

Table 3 showed the indirect serum bilirubin level of the patients where 42 (49.4%) patients had indirect bilirubin levels from 15 to<20 mg/dl and 37 (43.5%) patients had indirect bilirubin levels from 20 to<25 mg/dl. The mean indirect bilirubin level of the patients was 20.2 (±3.5) mg/dl. Table 4 shows that sepsis was found in 22 (25.8%) patients while 4 (4.7%) were TORCH pathogen positive.

ABO incompatibility was present in 15 (17.6%) patients and exchange transfusion was done in 8 (9.4%) patients. Among all patients, 29 (34.1%) patients received Ototoxic drugs.

Figure 2 showed that hearing impairment was present in 11 (12.9%) patients while 74 (87.1%) patients had no hearing loss. Table 5 shows that among 85 patients, 70 (82.4%) patients passed the Transient Evoked Otoacoustic Emissions (TEOAE) test while 15 (17.6%) were referred for Auditory Steady-State Response (ASSR) test. ASSR revealed that 2 (2.4%) patients had unilateral hearing loss while 9 (10.6%) patients had bilateral hearing loss. Figure 3 shows that among 11 hearing-impaired neonates, 3 (27.2%) had mild to moderate impairment, 6 (54.5%) had moderate to severe impairment and 2 (18.1%) had severe to profound hearing impairment. Table 6 shows that among 11 hearing-impaired cases, 90.9% were preterm babies and 9.1% were term babies. No significant statistical difference was observed between the groups regarding gestational age (p=0.050). Sepsis was significantly higher in patients with hearing impairment (54.5%) compared to patients without hearing impairment (21.6%) (p=0.030).

The use of ototoxic drugs was significantly more in patients with hearing impairment (72.7%) compared to patients without hearing impairment (28.4%) (p=0.006). Indirect serum bilirubin level was significantly higher (21.5 mg/dL) in patients with hearing impairment compared to patients without hearing impairment (19.4 mg/dL) (p=0.018). Table 7 shows a logistic regression model performed to ascertain the effects of different independent variables on hearing impairment. Sepsis (odds ratio (OR): 18.401, 95% CI: 1.571-215.554, p=0.020), ototoxic drug (OR: 10.364, 95% CI: 1.292-83.154, p=0.028) and indirect hyperbilirubinemia (OR: 1.739, 95% CI: 1.233-2.452, p=0.002) were independent predictors of hearing impairment.

Table 1: Distribution of patients by age (n=85).

Age at enrolment (days)	Frequency	%
2-4	22	25.9
5-7	57	67.1
8-9	6	7.1
Total	85	100.0
Mean±SD	5.6±1.6	

Table 2: Distribution of patients by gestational age and birth weight (n=85).

Gestational age	Frequency	%	Mean±SD
Preterm			36.2±1.6 (weeks)
33-34 weeks	15	17.6	
35-37 weeks	39	45.9	
Term			
≥38 weeks	31	36.5	
Birth weight			2390.1±466.4 (grams)
Low birth weight (1500-<2500)	49	57.6	
Normal birth weight (≥2500)	36	42.4	

Table 3: Distribution of patients by indirect bilirubin level (n=85).

Indirect bilirubin level (mg/dl)	Frequency	%
15-<20	42	49.4
20-<25	37	43.5
≥25	6	7.1
Total	85	100.0
Mean±SD	20.2±3.5	

Table 4: Distribution of patients by other risk factors for hearing impairment among hyperbilirubinemic neonates (n=85).

Risk factors	Frequency	%
Sepsis	22	25.8
TORCH	4	4.7
Rh incompatibility	5	5.9
ABO incompatibility	15	17.6

Continued.

Risk factors	Frequency	%
Exchange transfusion		
Done	8	9.4
Use of ototoxic drugs (Amikacin, Furosemide)		
Yes	29	34.1

Table 5: Distribution of patients by transient evoked otoacoustic emissions (TEOAE) and auditory steady-state response (ASSR) test (n=85).

Characteristics	Frequency	%
TEOAE		
Passed	70	82.4
Referred	15	17.6
ASSR		
Unilateral loss	2	2.4
Bilateral loss	9	10.6
Normal	4	4.7

Table 6: Association of risk factors with hearing impairment (n=85).

Characteristics	Without hearing impairment (n=74)	With hearing impairment (n=11)	P value
Gestational age			
Pre-term	44 (59.5%)	10 (90.9%)	0.050
Term	30 (40.3%)	1 (9.1%)	
Birth weight			
Low birth weight	42 (56.8%)	7 (63.6%)	0.753
Normal birth weight	32 (43.2%)	4 (36.4%)	
Sepsis			
Present	16 (21.6%)	6 (54.5%)	0.030
Absent	58 (78.4%)	5 (45.5%)	
Ototoxic drug			
Yes	21 (28.4%)	8 (72.7%)	0.006
No	53 (71.6%)	3 (27.3%)	
Indirect serum bilirubin level (mg/dl) (median (IQR))	19.4 (17.1- 21.2)	21.5 (19.7- 23.4)	0.018

Table 7: Binary logistic regression model of different independent variables to hearing impairment (n=85).

Criteria	P value	Odds ratio	95% CI
Sepsis	0.020	18.401	1.571-215.554
Ototoxic drug	0.028	10.364	1.292-83.154
Indirect hyperbilirubinemia	0.002	1.739	1.233-2.452

DISCUSSION

In our study at first, we screened 85 indirect hyperbilirubinemic neonates with TEOAE. Among them, 70 (82.4%) patients passed the Transient Evoked Otoacoustic Emission (TEOAE) test while 15 (17.6%) were referred. Diagnostic Auditory Steady-State Response (ASSR) was performed finally in the referred neonates to confirm the hearing loss. Among these 15 patients, the ASSR test revealed that 3 (3.5%) patients had unilateral hearing loss while 8 (9.4%) patients had bilateral hearing loss. In our study, hearing impairment was found in 12.9% of the indirect hyperbilirubinemia neonates. This nearly matches the result of a systematic review of nineteen studies where the incidence of hearing impairment among neonates was 6.7-14.3% at 3 months follow-up.[13] A study done by Dey et al, showed that the prevalence of hearing impairment among hyperbilirubinemic neonates was 21.9%.[14] A study conducted by Boskabadi et al, (2018) in Iran found that

4.8% of the infants with severe hyperbilirubinemia had sensorineural hearing loss.[6] Fouladinejad et al, in his study documented 3.1% of the hyperbilirubinemic neonates with hearing loss.[15] Among the hearing-impaired cases, 90.9% were preterm babies and 9.1% were term babies. No significant statistical difference was found between the groups regarding gestational age (p=0.050). Studies showed low gestational age was significantly associated with failed TEOAE.[16,17] Another study revealed that small for gestational-age neonates had a higher risk of hearing loss than appropriate for gestational-age neonates.[18]

Very low birth weight alone may not have a severe impact on hearing, it is commonly associated with one or more other risk factors that can alter hearing.[19] Studies suggested that cochlear immaturity in preterm neonates and middle ear effusion due to prolonged tracheal intubation are the main causes of hearing impairment in low-birth-weight newborns.[20,21]

Boskabadi et al, (2018) demonstrated a significant relationship of bilirubin levels in icteric infants with and without hearing loss (p<0.001). He showed a higher risk of developing hearing loss with increased severity of hyperbilirubinemia.[6]

In this study, serum indirect bilirubin level was significantly higher (21.5 mg/dl) in patients with hearing impairment compared to patients without hearing impairment (19.4 mg/dl) (p=0.018). Similarly, a study by Dey et al, conducted on 264 newborns revealed that newborns with hyperbilirubinemia who require phototherapy or exchange transfusion are at increased risk of hearing impairment.[14]

Sepsis was found in 22 (25.8%) patients which was significantly more in patients with hearing impairment (54.5%) compared to patients without hearing impairment (21.6%) (p=0.030). Poonual et al, demonstrated that the following risk factors were independently linked to hearing loss, APGAR score<6 at 5 minutes (risk ratio (RR): 2.2, 95% CI: 1.1–4.4), craniofacial anomalies (RR: 2.5, 95% CI: 1.6–4.2), sepsis (RR: 1.8, 95% CI: 1.0–3.2), ototoxic exposure (RR: 4.1, 95% CI: 1.9–8.6) and birth weight 1,500–2,500 gm (RR: 1.6, 95% CI: 1.1–2.6).[22]

Ototoxic drugs (Aminoglycoside, Furosemide) were received by 29 (34.1%) patients in this study. Use of ototoxic drugs was significantly more in patients with hearing impairment (72.7%) compared to patients with normal hearing (28.4%) (p=0.006). Similarly, Hameed and Malih (2019) showed ototoxic drugs used in neonates were significantly associated with failed TEOAE screening (p=0.004), which is also in agreement with the results of So TY (2009) who documented that bolus doses of ototoxic drugs specially Aminoglycosides is highly related to neonatal hearing loss.[23] Al-Meqbel and Al-Baghli in their study showed hyperbilirubinemia, premature birth and ototoxic medication were significantly associated with hearing loss.[24] A study done by Mannan et al, (2014) found small for gestational age, birth weight<1500 gm, neonatal ototoxic medication, sepsis and hyperbilirubinemia to be an independent risk factor for abnormal hearing screening results (p<0.01).[25]

In the current study, a logistic regression was performed to work out the effects of different independent variables on hearing impairment. Sepsis (odds ratio [OR]: 27.639, 95% CI: 1.916-398.796, p=0.015), ototoxic drug (OR: 13.391, 95% CI: 1.410-127.225, p=0.024) and hyperbilirubinemia (OR: 1.689, 95% CI: 1.195-2.389, p=0.003) were independent predictors of hearing impairment.

This was a single-center study. We did not do any long term follow up and did not know other possible interference that may happen in the long term with these patients.

CONCLUSION

In this study, we concluded that indirect hyperbilirubinemia of ≥15 mg/dl in preterm and≥20 mg/dl in term neonates is an important predictor of hearing impairment in neonates. Indirect hyperbilirubinemia in neonates, particularly at severe levels, has been associated with an increased risk of hearing impairment. Early identification and treatment of hyperbilirubinemia are necessary to prevent potential hearing defect. Even though not all neonates with elevated bilirubin levels have hearing difficulties, the results emphasize the importance of thorough bilirubin level monitoring and timely interventions. Further study can be conducted to validate the findings of this study.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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