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Original Research Article

Prevalence of aminoglycoside therapy and other determinant factors that induce hearing loss in neonates

Nassor R. Hamad[1]*, Retnosari Andrajati[2], Rina Mutiara[2], Risma Kerina Kaban[3], Rajesh Kumar Das[4]

[1]Faculty of Pharmacy, [2]Department of Pharmacy, [3]Department of Medicine, [4]Department of Epidemiology, University of Indonesia, Indonesia

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***Correspondence:**
Dr. Nassor R. Hamad,
E-mail: drnassorrashid@gmail.com

ABSTRACT

Background: Hearing loss is the most common disorder in neonates; it can be best managed if it is diagnosed at early stage of life. The global prevalence of permanent neonatal hearing loss mainly occurs in developing countries, which accounts 0.5 to 5.0 per 1000 live births. The objective of this study was to determine the prevalence of aminoglycoside therapy and other risk factors that induce hearing loss in neonates admitted at NICU at Cipto-Mangunkusumo General Hospital (CMGH).
Methods: This was a case-control study conducted among 112 neonates at Cipto-Mangunkusumo General Hospital (CMGH). Data from neonatal hearing screening were retrospectively collected from hospital electronic medical records and medical files. Only patients treated at neonatal unit from November 2018 to October 2019 were recruited.
Results: Out of 112 neonates studied, the gestational age at birth (GA) and craniofacial anomalies were considered risk factors for hearing loss since they were statistically significant ($p<0.05$). The study showed no statistical significant association in gender, birth weight, mechanical ventilation, NICU stay period (>5 days), hyperbilirubinemia (>20 mg/dl), asphyxia, and aminoglycoside therapy ($p>0.05$).
Conclusions: The prevalence of hearing loss in neonates with lower gestational age less than 37 weeks and craniofacial anomalies are significant higher compare to neonates born full term. They are more associated with 3 and 6 times increased risk of hearing loss in neonates.

Keywords: Aminoglycoside therapy, Hearing loss, Neonates

INTRODUCTION

Hearing loss is a common problem in neonates and 4th leading cause of disability globally, whereby 1-2 in 1000 live newborn are diagnosed with congenital or acquired hearing disorder.[1] Permanent hearing loss claims 0.5 to 5.0 per 1000 infants with live births worldwide. Ninety percent of these cases are from developing countries, yet the number can be even higher in low and middle-income countries.[2,3] Neonatal hearing loss is the disorder that can be best managed if diagnosed at early stage of life, say before age of six month.[2,4] Previous studies show that 2-4% of neonates who are admitted in neonatal intensive care unit (NICU) have significant bilateral hearing loss.[1]

The Joint Committee on Infant Hearing (JCIH) recommends to re-evaluate hearing in all children's who are exposed with potential risk factor which can result hearing impairment. The JCIH enumerates the risk factors as treatment with ototoxicity medications, congenital infections, craniofacial anomalies, low birth weight, hyperbilirubinemia, bacterial meningitis, low APGAR score, mechanical ventilation for at least 5 days, and presence of syndrome associated with congenital hearing loss.[4,5]

Apart from optimized 10 risk factors identified by JCIH, several more risk factors which related to hearing impairment are documented by Skoulas et al.[4] These risk factors include respiratory distress syndrome, hypoxia, intensive care unit stay more than 5 days, premature birth, maternal infection and type of birth (vaginal birth or caesarean section).[4,6]

The purpose of this study was to determine the prevalence on risk factor of hearing loss in neonates at CMGH.

METHODS

The study was conducted at paediatric department (neonatal unit) and Department of otolaryngology (Ear, Nose and Throat), Cipto Mangunkusumo General Hospital (CMGH), in Jakarta Indonesia. The ethical approval was obtained from the Ethics Committee, Faculty of medicine, University of Indonesia and Cipto Mangunkusumo Hospital, Jakarta.

Study design

The study design was case-control which used retrospectively data from neonatal hearing screening. The data was collected from hospital electronic medical records and medical files for patient treated at neonatal unit between November 2018 and October 2019.

Inclusion criteria

The inclusion criteria of the selected population included very neonates who underwent hearing screening test by distortion product otoacoustic emissions and automated auditory brainstem response (DPOAE and AABR) on discharge date. Neonates who were treated with aminoglycoside drugs who were identified presenting one or more risk factors that can cause hearing loss were also included in the study.

The case group consisted of neonates diagnosed with positive hearing loss marked as “refer” result with DPOAE examination while control group were the neonates without hearing loss marked as “pass” result with DPOAE examination. Both groups were admitted to neonatal ward at CGMH. In this study, seven risk factors for hearing loss in neonates were included, the factors include: aminoglycoside therapy uses as ototoxic drug; preterm birth (gestational age at birth <36 weeks); craniofacial anomalies; hyperbilirubinemia; intensive care stay >5 days; days of ventilatory support (>5 days); low birth weight <1500 grams.

Exclusion criteria

Exclusion criteria were family history of hearing loss, maternal infection during pregnancy such as rubella, intrauterine infection such as TORCH groups, meningitis, Usher syndrome, neurofibromatosis, and Hunter syndrome.

Statistical analysis

Data were analysed using SPSS version 23 and statistical analysis was carried out using chi-square test to explore the relationship between independent variable against dependent variables. The statistical significance was defined as p value <0.05 with corresponding to 95% confidence interval (CI). The odd ratio (OR) with corresponding 95%CI was used to express the strength of the associations among the variables.

RESULTS

Total of 156 newborns data were collected between November 2018 and October 2019, 112 infants were eligible to our study. Among them, 44 neonates did not meet the inclusion criteria and were excluded from the study. The gestational age at birth ranged between 24 weeks and 41 weeks while median value was 35 weeks. The birth weight ranged from 890 gm to 4300 gm; the median value was 2107 gm.

The gestational age at birth (GA) and craniofacial anomalies were considered risk factors for hearing loss since they were statistically significant with p-value of less than 0.05. The results show that GA were 73.21% of the total cases of CGMH (p value=0.02) and craniofacial anomalies were 50% of the total premature case in Table 1 (p value=0.019). Table 2 illustrates the results where multivariate analysis crude OR 2.55; 95%CI 1.15 to 5.7 where p=0.021 for gestational age at birth and crude OR 3.68; 95% CI 1.6 to 8.4 where p=0.002 for craniofacial anomalies.

Furthermore, the study shows no statistical significant difference in gender, birth weight, mechanical ventilation, NICU stays period, hyperbilirubinemia, asphyxia, and aminoglycoside therapy (p>0.05).

DISCUSSION

Our study shows the prevalence of hearing loss in neonates treated with aminoglycoside therapy and exposed with other risk indicator during discharged at CMGH. The small gestational age at birth below 37 weeks confirmed to be a risk of hearing loss in neonates by 2-fold [in our analysis by 41/56 (73.21%) of total cases who were screened failed/refer audiometric test]. Neonatal hearing loss has consistently increased with the decrease of gestational age from (31 to 24 weeks by 1.2% to 7.5%). This finding is also consistent to other several studies which show that prematurity neonates with small GA are more vulnerable to hearing loss compared to full term baby.[7-9]

Table 1: Prevalence of risk factors of hearing loss in neonates.

Variables	Cases (refer group) (n=56)	Controls (pass group) (n=56)	Chi square	P value
	N (%)	N (%)		
Birth weight				
Less than 1500 gm	8 (16.67)	5 (8.92)	0.783	0.376
More than 1500 gm	48 (83.33)	51(91.07)		
Gestational age at birth				
Less 37 weeks (preterm)	41 (73.21)	29 (51.78)	5.4486	0.019
Above 37 weeks (full term)	15 (26.79)	27 (48.22)		
Aminoglycoside therapy				
Exposed	37 (66.07)	30 (53.58)	1.820	0.177
Non exposed	19 (33.93)	26 (46.42)		
Baby with hyperbilirubinemia >10 Umol/l				
Yes	27 (48.21)	19 (33.93)	2.361	0.124
No	29 (51.79)	37 (66.07)		
Congenital malformation (craniofacial anomalies)				
Yes	28 (50)	12 (21.43)	9.956	0.002
No	28 (50)	44 (78.57)		
Days of ventilatory support (>5 days)				
Yes	11 (19.64)	10 (17.86)	0.059	0.809
No	45 (80.36)	46 (82.14)		
ICU stay (>5 days)				
Yes	12 (21.43)	8 (14.29)	0.974	0.324
No	44 (78.57)	48 (85.71)		

Table 2: Potential risk factors for hearing loss in newborns at CMGH.

Risk factors	Crude OR				Adjusted OR			
	OR	95% CI		P	OR	95% CI		P
Birth weight (less than 1500 gm)	1.700	0.520	5.559	0.380	2.001	0.434	9.219	0.374
Gestational age at birth (below 37 weeks)	2.545	1.155	5.609	0.021	2.657	0.989	7.137	0.053
Aminoglycoside therapy	1.688	0.787	3.619	0.179	1.912	0.779	4.689	0.157
Baby with hyperbilirubinemia >20 Umol/l (Yes)	1.813	0.846	3.885	0.126	2.099	0.836	5.274	0.115
Congenital malformation (craniofacial anomalies)	3.667	1.606	8.373	0.002	6.883	2.512	18.859	0.000
Days of ventilatory support (>5 days)	1.124	0.435	2.907	0.809	0.743	0.244	2.261	0.601
ICU stay (>5 days)	1.636	0.612	4.376	0.326	1.564	0.471	5.199	0.465

In this study craniofacial anomalies has shown statistical significant difference, where 28/56 (50%) of neonate are four to six times higher at risk to develop hearing loss (p=0.002). The similar findings are shown by Bielecki et al and Neumann et al.[3,10] The conductive hearing loss was observed to be common risk factor associated with craniofacial anomalies such cleft palate. This is documented in the other previous studies to the presence of middle ear effusions because of poor tensor veli palatine function and increased Eustachian tube compliance.[11,12]

The finding of this study is supported by previous studies, which show that aminoglycoside therapy uses is the most common risk factor for sensorineural hearing loss in neonates. These drugs are one among the most common used in neonate at NICU, and is referred as ototoxic drug which can result sensorineural hearing loss by destruction of cochlear hair cells due to generation of free radicals within the inner ear. The drug toxicity results to permanent damage to sensory cells and neurons.[13-15] Even though some authors have shown no relationship between aminoglycoside uses (serum aminoglycoside level in the blood) and ototoxicity effects as we have observed in our study to be insignificant risk of hearing loss in infants.[7,16]

The neonates admitted at NICU and stay more than 5 days may be a risk factor of hearing impairment. This was not observed to be significant finding in our study. The results are different in the previous studies which have proven to be a risk indictor for hearing loss in some other authors.[7,17] The variable of low birth weight (<1500

gm) as the risk indicator did not show statistical difference between case and control groups (p=0.38). This finding is consistent with what has been reported previous studies which found no relationship between low birth weight and hearing loss, while other authors have reported complimentary relationship in very low birth and progressive or delayed-onset of newborn hearing loss remains poorly understood.[1,6,7]

Hyperbilirubinemia >20 mmol/l was not significant risk factor for hearing loss in our study. On the other hand, Boskabadi et al showed that the infant with bilirubin level >20 mg/dl were ten to fifty times higher at risk for sensorineural hearing impairment compared to non icteric infants.[12] Hyperbilirubinemia can be risk factor for hearing loss since can cause toxic effects on the nervous system by damage brainstem auditory nuclei, auditory nerve and spiral ganglion cells that can result hearing impairment.[8,12,18]

In our recently study mechanical ventilation (days of ventilatory support >5 days) were not confirmed in our statistical analysis to be a risk indictor which can lead hearing impairment to neonates. Previous studies have reported different findings that mechanical ventilation with excessive ventilatory support more than 5 days can significantly damage the peripheral segment of the hearing tract and increase chance of developing hearing loss in newborn.[10]

This study was subjected to limitations which should be taken care in understanding the findings. Small sample size as not all neonates underwent hearing screening test (pre and post-test after exposed with risk factors) and half of the neonates did not have post discharge follow up.

CONCLUSION

In conclusion, the prevalence of hearing loss in neonates with lower gestational age less than 37 weeks and craniofacial anomalies are significant higher compare to neonates born full term, and are associated with 3 and 6 times increased risk of hearing loss in neonates.

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