Section: Miscellaneous

Original Research Article

A CASE-CONTROL STUDY TO ASSESS THE EFFECT OF GESTATIONAL ANAEMIA ON THE AUDITORY FUNCTION OF NEONATES

Toms Joseph Thuruthumaly[1], Amrutha Mary Zachariah[2], Vikram Gowda NR[3], Jacob Abraham[4], Vinod Jose Kakkanatt[5], Alex Mathew[6]

[1]Undergraduate Medical Student, Pushpagiri Institute of Medical Sciences and Research center, Thiruvalla, Kerala, INDIA
[2]Associate Professor, Department of Physiology, Pushpagiri Institute of Medical sciences and Research center, Thiruvalla, Kerala, India
[3]Professor & Head, Department of Physiology, Pushpagiri Institute of Medical sciences and Research center, Thiruvalla, Kerala, India.
[4]Professor & Head, Department of Paediatrics, Pushpagiri Institute of Medical sciences and Research center, Thiruvalla, Kerala, India
[5]Consultant, Department of ENT, St. Thomas Hospital, Chethipuzha, Changanacherry, Kottayam, Kerala, India
[6]Audiologist and Vestibular Therapist.

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Corresponding Author:
Dr. Amrutha Mary Zachariah,
Email: marymitha100@gmail.com

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Abstract

Background: Hearing loss in neonates in India is not very rare. Early detection and prevention of this are important as hearing is important for language development and hence affects the overall quality of one's life. Identifying the causative factors of this condition will help us to adopt suitable preventive measures. Anaemia can affect the oxygen delivery to the inner ear; a tissue highly susceptible to ischemia. This in turn may affect its function as revealed by previous studies in adults and children. Sole dependency of Foetus and neonates to mothers for nutrition raises the question of the effect of maternal Hb status on their auditory function. As there is a paucity of such studies especially in the Indian scenario, we undertook the present study. **Materials and Methods:** Our study was a hospital-based case-control study conducted to find out the association between gestational anaemia and hearing loss. Infants having a latency of Wave IV in auditory brainstem response (ABR) were selected as cases and age and sex-matched infants born in the same hospital were taken as controls. There were 19 cases and 38 controls in our study. The maternal haemoglobin (Hb) status of these infants and other relevant information which were needed to select the study subjects were obtained from hospital medical records. Hb value less than 11 gm/dl in the third trimester of pregnancy was considered gestational anaemia. **Result:** Odds of exposure to maternal anaemia in cases and controls were determined and The Odds ratio was calculated to find out the strength of the association between the two. Our study showed a possibility of auditory dysfunction in infants exposed to maternal anaemia with an odds ratio of 3.375 (CI=1.0254 to 11.1086) with a 95 % confidence level. **Conclusion:** Our study showed that there is an association between maternal anaemia and hearing loss in neonates. Further studies exploring the type of anaemia leading to hearing loss will help to evaluate the causative factors better.

INTRODUCTION

Anaemia is defined as the reduction in an absolute number of circulating red blood cells (RBCs), measured by a reduction in haemoglobin (Hb) concentration, haematocrit (Hct) or RBC count. Anaemia accounts for the most frequent disturbance of physiology in the world throughout a woman's life. WHO has defined anaemia as Hb of <11 g/dl.[1] During pregnancy, a Hb value of <11 g/dl in the first trimester, <10.5 g/dl in the second trimester, and <11 g/dl in the third trimester are taken as the cut-off values.[2] The global prevalence of anaemia in pregnancy is estimated to be approximately 41.8% and in India, it is 65–75%.[3,4]

Normal hearing in the early stages of life is a critical element for appropriate language, psychosocial, and cognitive outcomes. Hearing loss during this period can have a negative impact on the quality of life in the later years. The global prevalence of neonatal hearing loss is 0.5 to 5.0 per 1000 infants.[5] Neonatal hearing loss in India is also not that uncommon.

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Studies done in India using different hearing screening protocols have estimated neonatal hearing loss varying from 1.59 to 8.8 per 1000 live births.[6,7] This points to the need for early detection and intervention of this condition. An essential requirement for this is to find out the possible risk factors leading to hearing loss especially those which are preventable or correctable.

Studies conducted among adults were able to bring out a significant correlation between hearing loss and iron deficiency anaemia (IDA).[8,9] The exact mechanism by which anaemia can lead to hearing loss still needs clarification. The proposed mechanism in adults is that anaemia results in the reduced oxygen-carrying capacity of blood leading to ischaemic damage to the cochlea which solely depends on the labyrinthine artery for its vascular needs. In addition to this, Iron deficiency results in damage to myelin sheath by causing the degradation of lipid saturase and desaturase.[10] This has been supported by pieces of evidence from animal studies showing that anaemia alters the histopathology of the inner ear such as the reduction of spiral ganglion cells and strial atrophy, resulting in the development of SNHL.[11]

The role of IDA in neuronal dysfunction and organ maldevelopment makes it a potential risk factor for paediatric hearing loss as well. A study by Kathleen M. Schieffer demonstrated an increased chance of hearing loss in children with iron efficiency anaemia.[12] Similarly, Cecilia Algarín et al conducted a study in Chile which showed that infants who had uncorrected iron deficiency anaemia had altered myelination and increased auditory brainstem responses when tested at age four emphasizing the role of iron in myelination and thus in auditory function.[13]

Findings from these studies have triggered thoughts of the effect of gestational anaemia in auditory function. Neonates solely depend on their mothers for their nutritional needs. An adequate supply of nutrients in prenatal and postnatal periods is important for the development of various systems especially, the nervous system. Considering these facts, there is a possibility that the low iron status of the mother during the period of pregnancy can harmfully affect the auditory function of neonates. ElAlfy M S et al evaluated auditory brainstem response (ABR) in full-term neonates born to anaemic mothers in an attempt to find out the role of maternal haemoglobin status in auditory development and revealed anaemia during late pregnancy adversely affects the hearing status of new born.[14] Reduction of ribbon synapse density and dysregulation of VGLUT3, myosin VIIa, and prestin in the cochlea are seen in Guinea Pigs born to iron-deficient mothers emphasizing the effect of gestational anaemia on hearing loss.[15]

Although the previous studies indicate the association of anaemia with hearing loss, insufficient data are available regarding the effect of anaemia on the auditory function of neonates in the Indian scenario. This is especially important as anaemia is a preventable condition, early adequate interventions may lead to normal auditory development. It might also be possible to improve screening guidelines and have better insight into the role of iron on neurological and vascular function. Hence as a preliminary step, we determined to assess the effect of maternal Hb status during pregnancy on the auditory function of neonates.

MATERIALS AND METHODS

This was a hospital-based case-control study which was conducted among neonates born in a tertiary care hospital. The data collection was started in August 2022 after obtaining Ethical approval from the Institutional Ethics Committee. Permission from the hospital superintendent was also obtained to access the medical records for data collection. The sample size was calculated as 19 cases and a minimum of 19 controls using the following formula.

$$n = \frac{(Z_{\alpha}+Z_{1-\beta})^2 \times (S_1^2+S_2^2)}{(\mu 1-\mu 2)^2}$$

where n=sample size per group, Zα at 95% CI=1.96, Z 1- β at 80% power=0.84, S1=standard deviation of 1st group and S2= standard deviation of second group.

Infants showing absolute latency of wave IV in auditory brain stem response done within six weeks of age were taken as cases and neonates born in the same hospital with normal hearing in the screening test were considered as controls. Haemoglobin laboratory values (<11 g/dl) during the third trimester of pregnancy are taken as the exposure variable.

The hearing status of infants who had undergone hearing tests was collected from the Audiology department and they were categorized into cases and controls. Medical records of these infants were examined for age, gender, birth weight, complications during the postnatal period and other significant details. Controls were selected in such a way that their demographic details were similar to that of cases. All relevant information regarding mothers, like demographic details, personal history, examination details and laboratory test results were attained from the medical records of mothers.

Infants having a family history of hearing loss, perinatal complications, history of consumption of ototoxic drugs by the mother, history of maternal rubella or any other infection during the antenatal period and postnatal period were excluded from the study. The odds of exposure to gestational anaemia in cases and controls were determined and the Odds ratio was calculated to measure the strength of association between exposure and outcome.

RESULTS

Exposure to maternal anaemia in age and sex-matched cases and control were compared in our study. There were 19 cases and 38 controls. The data were entered into Microsoft Excel and the Odds ratio

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was calculated to find out the strength of the association between gestational anaemia and hearing loss.

The demographic details of the cases and controls are given in [Table 1]. The age of both groups varies from 2 to 5 weeks with a mean age of 4.2+/- 0.62 weeks for cases and 3.8+/- 0.24 weeks for controls. The birthweight and gender of the two groups also did not vary significantly. This indicates a proper matching between the two groups.

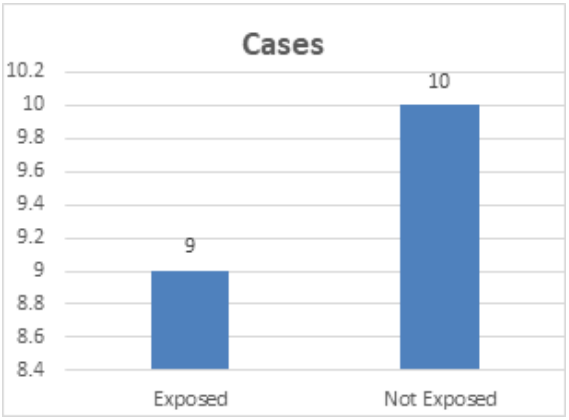

Figure 2: Number of infants with and without exposure to maternal anaemia in cases

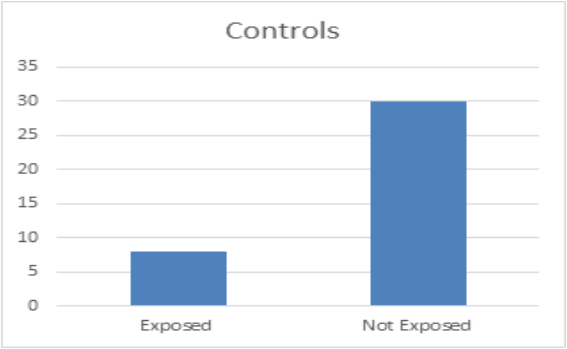

Figure 3: Number of infants with and without exposure to maternal anaemia in controls

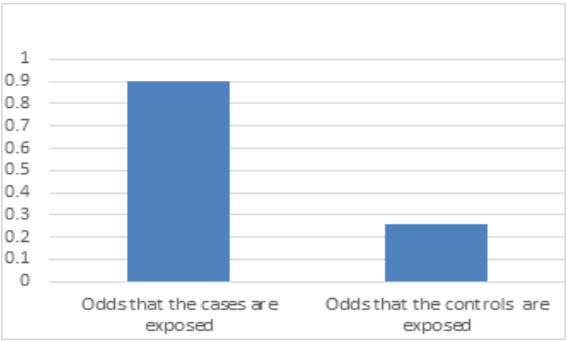

Figure 4: Odds of exposure in cases and controls

Table 1: Demographic details

Variable	Cases	Controls
Number	19	38
Gender		
Male (%)	52	49
Female (%)	48	51
Mean birth weight in Kg	3.03+/_0.27	3.05+/- O.28 [NS]

NS=not significant with P=0.17

Table 2: Risk of hearing loss in infants exposed to gestational anaemia

Exposed to maternal anaemia	Cases	controls	Odds ratio (95%CI)
Yes	9	8	3.3750 (1.0254 to 11.1086)
No	10	30	

Odds ratio when calculated to find the association between exposure to maternal anaemia and the development of hearing loss found to be 3.375 (95% CI 1.0254 to 11.1086) when cases were compared with controls.

DISCUSSION

Development and functioning of the auditory system need a suitable environment including proper blood supply and Hb status. Hence presence of anaemia can affect auditory function adversely. There are only limited studies available exploring the effect of anaemia on hearing loss. Most of the studies are done in adults, some are in children and only a few are being conducted in the infant. Studies evaluating the effect of exposure to anaemia in the prenatal period in human subjects are very rare although limited animal studies are available. Although there are studies indicating the role of anaemia in hearing loss, there are few studies evaluating the effect of maternal Hb status on the auditory function which prompted us to initiate this study. We did a case-control study where cases were infants who had unilateral or bilateral hearing loss proven by brain stem-evoked auditory response by the latency of wave V. The maternal Hb less than 11gm/dl in the third trimester is considered the exposure variable. the statistical analysis showed a positive relationship between the two with an odds ratio of 3.3750.[16,17]

Mohsen Saleh ElAlfy,[14] compared the auditory function of infants born to 50 anaemic mothers with that of normal at 48 hours and 3 months of the postnatal period and demonstrated significantly prolonged interpeak latencies in ABR. A similar finding was given in the study conducted by Cecilia 12 in Chilean infants who had anaemia in infancy and tested for auditory function at the age of four. They proposed that this might be due to the role of iron in myelination.

A H Sun et al,[11] demonstrated the development of sudden SNHL in rats fed on an iron deficiency diet.

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Contrary to this, IDA infants didn't show a delay in brain stem transmission times compared to normal guinea pigs in the study by Ozturan O.[18]

Our findings also support the role of anaemia in hearing loss. As has been proposed before, the aetiology behind this might be the high vascular dependency of the inner ear and susceptibility to ischemic damage which gets aggravated in anaemia. The role of iron in myelination and brain development could be the probable cause of auditory dysfunction. However, in our study, we could not analyze this as it was a retrospective study where the data was collected from medical records. As anaemia in late pregnancy is not routinely categorized and documented, the data showing iron status in pregnancy was lacking.

Future studies analysing the type of anaemia from cord blood samples may give more input.

CONCLUSION

Maternal anaemia can adversely affect the auditory function of neonates. Delayed diagnosis of hearing loss can be associated with delayed speech and language development. This often affects their literacy, academics and overall social well-being. Identifying a relationship between anaemia and hearing loss may facilitate earlier diagnosis of hearing loss and improve screening guidelines.

REFERENCES

1. Nutritional anaemias. Report of a WHO scientific group. World Health Organ Tech Rep Ser. 1968; 405:5-37.
2. Recommendations to prevent and control iron deficiency in the United States. Centres for Disease Control and Prevention. MMWR Recomm Rep. 1998 Apr 3;47(RR-3):1-29.
3. WHO/UNICEF/UNU. Iron deficiency anaemia assessment, prevention, and control: a guide for programme managers. Geneva, World Health Organization, 2001.
4. Bora, R, Sable, C, Wolfson, J, Boro, K, Rao, R. Prevalence of anaemia in pregnant women and its effect on neonatal outcomes in northeast India. J. Matern. Fetal. Neonatal Med.2014; 27(9): 887–91.
5. World Health Organization Neonatal and Infant Hearing Screening. Current Issues and Guiding Principles for Action; Proceedings of the Outcome of a WHO Informal Consultation; Geneva, Switzerland. 9–10 November 2009; Geneva, Switzerland: World Health Organization; 2010. pp. 1–39.
6. Rawat, V., Arora, R., Singh, J. et al. Incidence of hearing loss in neonates at a secondary care hospital in North India—a pilot UNHS study. Egypt J Otolaryngol 39, 120 (2023)
7. Verma RR, Konkimalla A, Thakar A, Sikka K, Singh AC, Khanna T (2021) Prevalence of hearing loss in India. Natl Med J India 34(4):216–222.
8. Chung S. D., Chen P. Y., Lin H. C., & Hung S. H. Sudden sensorineural hearing loss associated with iron-deficiency anaemia: A population-based study. Otolaryngology—Head & Neck Surgery.2014;140: 417–22.
9. Schieffer KM, Chuang CH, Connor J, Pawelczyk JA, Sekhar DL. Association of iron deficiency anaemia with hearing loss in US adults. JAMA Otolaryngol Head Neck Surg [Internet]. 2017;143(4):350–4.
10. Brown AM, Hamann M. Computational modeling of the effects of auditory nerve dysmyelination. Front Neuroanat. 2014;8:73. doi: 10.3389/fnana.2014.00073
11. Sun A. H., Wang Z. M., Xiao S. Z., Li Z. J., Zheng Z., & Li J. Y. (1992). Sudden sensorineural hearing loss induced by experimental iron deficiency in rats. ORL: Journal for Oto-rhino-laryngology and Its Related Specialties, 54, 246–250.
12. Schieffer KM, Connor JR, Pawelczyk JA, Sekhar DL. The Relationship Between Iron Deficiency Anemia and Sensorineural Hearing Loss in the Pediatric and Adolescent Population. Am J Audiol. 2017 Jun; 26(2): 155–162.
13. Algarin C., Peirano P, Garrido M., Pizarro F., Lozoff B. Iron deficiency anaemia in infancy: Long-lasting effects on auditory and visual system functioning. Pediatric Research.2003; 53: 217–223.
14. ElAlfy MS, El-Farrash RA, Taha HM, Ismail EA, Mokhtar NA. Auditory brainstem response in full-term neonates born to mothers with iron deficiency anaemia: relation to disease severity. J Matern Fetal Neonatal Med. 2020 Jun;33(11):1881-88.
15. Yu F, Hao S, Yang B, Zhao Y, Zhang W, Yang J. Mild Maternal Iron Deficiency Anemia Induces Hearing Impairment Associated with Reduction of Ribbon Synapse Density and Dysregulation of VGLUT3, Myosin VIIa, and Prestin Expression in Young Guinea Pigs. Neurotox Res. 2016 May;29(4):594-604
16. Cetin T, Yetiser S, Cekin E, Durmus C, Nevruz O, Oktenli C. Outer hair cell activity of the cochlea in patients with iron deficiency anaemia. Auris Nasus Larynx. 2004;31:389–94.
17. Hemawathiy Sundagumaran a, Jayashree Seethapathy b. Outer hair cell functioning in infants with iron deficiency anemia. International Journal of Pediatric Otorhinolaryngology. 2020; 138 : 110393.
18. Ozturan O, Henley CM, Littman TA, Jenkins HA. Iron deficiency anaemia and hearing. ORL J Otorhinolaryngol Relat Spec. 1997;59:73

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