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Original Research Article

EFFECT OF MATERNAL AGE AND ANEMIA ON AUDITORY BRAIN STEM RESPONSE OF PRETERM INFANTS IN TERTIARY CARE HOSPITAL

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ABSTRACT

Background: The auditory brainstem response (ABR) is a vital neurophysiological test for assessing auditory function from the cochlea to the brainstem. Preterm infants are particularly vulnerable to auditory dysfunction due to their underdeveloped auditory pathways. Maternal factors, such as age and anemia, may influence ABR outcomes in these high-risk populations. This study investigates the combined effects of maternal age and anemia on ABR results in preterm infants.

Materials and Methods: This prospective observational study was conducted at Govt medical college and its associated hospital, Jammu over two years. A total of 120 preterm infants born before 37 weeks of gestation were enrolled. Maternal data, including age and hemoglobin levels, were collected. ABR testing was performed within the first 28 days of life using standard protocols. The study analyzed wave latencies and interpeak intervals in relation to maternal age and anemia severity, using ANOVA and multiple linear regression for statistical evaluation.

Results: ABR latencies differed significantly across maternal age groups. Infants of advanced maternal age had longer wave I latency (1.92 ± 0.13 ms vs. 1.85 ± 0.14 ms in adolescents, $p = 0.031$), wave III latency (4.25 ± 0.19 ms vs. 4.15 ± 0.22 ms, $p = 0.025$), and wave V latency (6.32 ± 0.26 ms vs. 6.24 ± 0.25 ms, $p = 0.046$) compared to other groups. Severe maternal anemia was associated with longer wave I latency (2.01 ± 0.18 ms vs. 1.81 ± 0.12 ms in no anemia, $p = 0.011$), wave III latency (4.34 ± 0.24 ms vs. 4.05 ± 0.18 ms, $p = 0.023$), and wave V latency (6.41 ± 0.37 ms vs. 6.13 ± 0.22 ms, $p = 0.014$). Regression analysis indicated that maternal age and anemia were significant predictors of ABR latencies, with β coefficients for maternal age ranging from 0.12 to 0.25 and for maternal anemia ranging from 0.15 to 0.30 ($p < 0.05$).

Conclusion: Maternal age and anemia significantly affect ABR outcomes in preterm infants. Advanced maternal age and severe anemia are associated with delayed ABR latencies, indicating potential auditory and neurodevelopmental issues. These findings underscore the need for early and comprehensive assessments in preterm infants, taking maternal factors into account to guide effective interventions.

Keywords: Auditory Brainstem Response, Preterm Infants, Maternal Age, Maternal Anemia, Neonatal Audiology.

INTRODUCTION

The auditory brainstem response (ABR) is a critical neurophysiological test used to evaluate the function and integrity of the auditory pathway, specifically from the cochlea to the brainstem. The ABR measures the electrical activity generated by the auditory nerve and brainstem in response to sound stimuli, such as clicks or tone bursts, and is commonly used in both clinical and research settings to assess hearing and neurological function

in newborns, particularly in high-risk populations such as preterm infants.[1] ABR is non-invasive and objective, making it an essential tool for early detection of hearing impairments and neurological disorders that could affect auditory processing and subsequent language and cognitive development.[1]

In newborns, especially those born preterm, ABR may show delayed wave latencies or reduced wave amplitudes due to the incomplete development of the auditory system. Preterm infants are more susceptible to auditory dysfunction because of their underdeveloped cochlea, auditory nerve, and brainstem pathways. These developmental delays can manifest as prolonged ABR latencies or abnormal waveform patterns, which are indicative of delayed neural conduction along the auditory pathway.[2] As a result, the ABR test serves as an early marker for potential auditory and neurodevelopmental issues, allowing for timely interventions to mitigate the long-term effects of hearing loss.[2]

Preterm birth is a major risk factor for auditory dysfunction and other developmental delays. Approximately 10% of all births worldwide are preterm, with preterm infants experiencing a higher prevalence of hearing impairment compared to term infants.[3] Studies suggest that the incidence of hearing impairment among preterm infants varies from 2% to 15%, with more severe cases seen in extremely premature infants.[4] Given the vulnerability of this population, understanding the factors that influence ABR outcomes is crucial to improving early diagnostic and therapeutic approaches.[3,4]

Maternal age is one of the factors that may influence the auditory development of preterm infants. Both advanced maternal age (≥35 years) and adolescent motherhood (<20 years) have been associated with increased risks of preterm birth, intrauterine growth restriction, and other pregnancy complications.[5,6] These conditions may negatively impact fetal brain and auditory development, potentially leading to abnormal ABR results in the newborn. While maternal age has been studied extensively in relation to pregnancy outcomes, its specific impact on the auditory system and ABR results in preterm infants is less well understood.[6]

Maternal anemia, defined as a hemoglobin concentration below 11 g/dL during pregnancy, affects roughly 38% of pregnant women globally.[7] Iron deficiency anemia, in particular, can result in hypoxia or reduced oxygen supply to the fetus, which may impair brain and neural development.[8] This lack of oxygen can disrupt the development of key auditory structures such as the cochlea, auditory nerve, and brainstem, potentially leading to delayed or abnormal ABR responses in preterm infants. Despite these potential associations, few studies have directly explored the impact of maternal anemia on ABR outcomes in preterm newborns.[7,8]

Given the high prevalence of preterm births and the potential for maternal factors like age and anemia to influence auditory development, this study aimed to assess the combined effects of these factors on ABR results in preterm infants. By focusing on these maternal variables, the study seeks to contribute to a deeper understanding of the early determinants of auditory function in this vulnerable population, with the goal of informing clinical practices for early diagnosis and intervention in auditory impairments.

MATERIALS AND METHODS

Study Design

This study was a prospective observational study conducted in the department of Physiology at govt medical college and its associated hospitals for a period of 2 years between July 2021 and June 2023. The primary objective was to investigate the effect of maternal age and maternal anemia on the auditory brainstem response (ABR) in preterm infants.

Study Population

The study population included preterm infants born at less than 37 weeks of gestation and admitted to the neonatal intensive care unit (NICU). Infants were enrolled consecutively based on specific inclusion and exclusion criteria. The inclusion criteria consisted of infants born preterm (<37 weeks of gestation), with available auditory brainstem response (ABR) testing results within the first 28 days of life, and maternal hemoglobin levels measured during the third trimester of pregnancy. Exclusion criteria included infants with congenital hearing loss or other known auditory disorders confirmed through initial screening, major congenital anomalies, or neurological disorders. Additionally, infants born to mothers with pre-existing conditions such as chronic hypertension, diabetes, or preeclampsia, which could affect fetal development, were excluded from the study.

Sample Size

A total of 120 preterm infants meeting the inclusion criteria were enrolled in the study. The sample size was calculated based on a power analysis to detect a significant association between maternal factors (age and anemia) and ABR outcomes, assuming a 5% significance level and 80% power.

Data Collection

Maternal data were collected from medical records and included maternal age, which was grouped into two categories: advanced maternal age (≥35 years) and adolescent mothers (<20 years). Maternal anemia was defined according to World Health Organization (WHO) criteria as a hemoglobin concentration of <11 g/dL in the third trimester. The severity of anemia was further classified into mild (9–10.9 g/dL), moderate (7–8.9 g/dL), and severe (<7 g/dL) anemia.[9] Infant data included gestational age, which was determined based on the mother's last menstrual period or early ultrasound scans, and birth weight, which was measured immediately after delivery. Auditory brainstem response (ABR) tests were conducted within the first 28 days of life using

standard protocols. The ABR was performed using Neuro-Audio SmartEP® system (USA), with click stimuli presented at 35 dB nHL in both ears. Key variables recorded included wave I, III, and V latencies, as well as interpeak intervals I-III, III-V, and I-V. Delayed wave latencies, greater than the normal range for corrected gestational age, were considered indicative of auditory dysfunction.[1]

ABR Procedure

The ABR testing was performed in a soundproof room with the infant in a natural sleep state or under mild sedation when necessary. Surface electrodes were placed on the scalp (vertex) and on both earlobes or mastoids. The stimuli consisted of alternating polarity clicks delivered at a rate of 21.1 clicks per second. The recordings were averaged over 2,000 stimulus presentations, and responses were analyzed by a pediatric audiologist blinded to the maternal data.

Statistical Analysis

Statistical analyses were performed using SPSS version 22.0. Descriptive statistics summarized the maternal and infant characteristics, with continuous variables (e.g., ABR latencies) expressed as means and standard deviations, and categorical variables (e.g., maternal anemia severity) presented as frequencies and percentages. For group comparisons, the study population was divided based on maternal age (adolescent, advanced, or normal reproductive age) and the presence or absence of maternal anemia. ABR wave latencies and interpeak intervals were compared between these groups using ANOVA test. Multiple linear regression models were constructed to assess the independent effects of maternal age and anemia on ABR outcomes, adjusting for potential confounding factors such as gestational age, birth weight, and sex of the infant. A p-value of <0.05 was considered statistically significant.

Ethical Considerations

The study protocol was approved by the Institutional Review Board. Informed written consent was obtained from the parents or legal guardians of all participating infants prior to enrollment in the study. The study adhered to the principles outlined in the Declaration of Helsinki for medical research involving human subjects.

RESULTS

The study included 120 preterm infants with a mean gestational age of 32.6 ± 2.5 weeks and a birth weight of 1512.3 ± 449.2 grams. Infants of adolescent mothers had slightly lower gestational ages (32.0 ± 2.6 weeks) and birth weights (1424.5 ± 473.1 grams) compared to other groups. Male infants made up 60.0% of the sample, with similar distributions across all maternal age groups. The average maternal hemoglobin level was 10.1 ± 1.3 g/dL, with adolescent mothers having the lowest levels (9.5 ± 1.2 g/dL). Mild anemia was most common (41.7%), particularly among adolescent mothers (55.2%). Severe anemia was observed in 14.2% of the cohort, with a higher prevalence in the normal age group (20.6%) compared to adolescent (6.9%) and advanced maternal age mothers (7.1%). [Table 1]

The auditory brainstem response (ABR) latencies showed significant differences across maternal age groups. Wave I latency was longest in the advanced maternal age group (1.92 ± 0.13 ms) compared to the adolescent (1.85 ± 0.14 ms) and normal age groups (1.82 ± 0.12 ms) ($p = 0.031$). Similarly, wave III ($p = 0.025$) and wave V latencies ($p = 0.046$) were significantly longer in the advanced maternal age group (4.25 ± 0.19 ms and 6.32 ± 0.26 ms, respectively) compared to the other groups. The III-V interval was significantly longer in the advanced maternal age group (2.17 ± 0.15 ms) compared to the adolescent (2.05 ± 0.14 ms) and normal age groups (2.02 ± 0.13 ms) ($p = 0.032$). Although the I-III interval showed a trend toward longer times in the advanced maternal age group, this was not statistically significant ($p = 0.057$). The I-V interval was significantly longer in the advanced maternal age group (4.46 ± 0.19 ms) compared to both the adolescent and normal age groups ($p = 0.041$). [Table 2]

Auditory brainstem response (ABR) latencies demonstrated significant variation based on the severity of maternal anemia. Infants born to mothers with severe anemia had the longest wave latencies, with a wave I latency of 2.01 ± 0.18 ms, compared to 1.81 ± 0.12 ms in the no anemia group ($p = 0.011$). Wave III ($p = 0.023$) and wave V latencies ($p = 0.014$) followed a similar trend, with severe anemia showing the longest latencies (4.34 ± 0.24 ms and 6.41 ± 0.37 ms, respectively). The I-III interval was significantly prolonged in infants with severe anemia (2.47 ± 0.18 ms) compared to those with no anemia (2.24 ± 0.13 ms) ($p = 0.036$). Although the III-V interval showed a significant difference ($p = 0.022$), it was relatively consistent across the groups. The I-V interval was longest in the severe anemia group (4.53 ± 0.24 ms), compared to 4.33 ± 0.17 ms in the no anemia group ($p = 0.025$). [Table 3]

The regression analysis revealed that both maternal age and anemia were significant predictors of ABR latencies. Maternal age was positively associated with wave latencies, with a β coefficient of 0.12 for wave I ($p = 0.041$), 0.18 for wave III ($p = 0.027$), and 0.25 for wave V ($p = 0.033$). Similarly, maternal anemia was a significant factor, showing stronger associations, with β values of 0.15 for wave I ($p = 0.023$), 0.22 for wave III ($p = 0.018$), and 0.30 for wave V ($p = 0.011$). Gestational age had a negative association with ABR latencies, particularly for wave V ($\beta = -0.20$, $p = 0.020$) and wave III ($\beta = -0.15$, $p = 0.035$). Birth weight also showed a negative relationship, significantly affecting wave III ($\beta = -0.08$, $p = 0.046$) and wave V latencies ($\beta = -0.12$, $p = 0.038$). The sex of the infant influenced

latencies as well, with male infants having longer latencies, particularly for wave V (β = 0.18, p = 0.010). [Table 4]

A significant positive correlation was observed between maternal anemia and various ABR variables. Wave I latency showed a moderate positive correlation with maternal anemia (r = 0.301, p = 0.017), while wave III (r = 0.353, p = 0.016) and wave V latencies (r = 0.405, p = 0.018) had even stronger correlations. Among the interpeak intervals, the I-III interval demonstrated a correlation of r = 0.258 (p = 0.033), and the III-V interval showed a correlation of r = 0.286 (p = 0.024). The I-V interval also had a significant positive correlation with maternal anemia (r = 0.334, p = 0.016), indicating that as anemia severity increased, ABR latencies and interpeak intervals tended to lengthen. [Table 5]

Table 1: Demographic and Clinical Characteristics of Study Population

Characteristics	Frequency (%)/ Mean±SD			
	Total (N=120)	Adolescent (n=29)	Advanced Maternal Age (n=28)	Normal Age (n=63)
Gestational Age (weeks)	32.6 ± 2.5	32.0 ± 2.6	32.9 ± 2.1	32.8 ± 2.4
Gender of Infant				
Male	72 (60.0%)	18 (62.1%)	16 (57.1%)	37 (58.7%)
Female	48 (40.0%)	11 (37.9%)	12 (42.9%)	26 (41.3%)
Birth Weight (g)	1512.3 ± 449.2	1424.5 ± 473.1	1526.9 ± 411.6	1484.7 ± 425.1
Hemoglobin (g/dL)*	10.1 ± 1.3	9.5 ± 1.2	10.2 ± 1.1	10.4 ± 1.3
Anemia*				
No Anemia	15 (12.5%)	1 (3.4%)	5 (17.9%)	9 (14.3%)
Mild Anemia	50 (41.7%)	16 (55.2%)	12 (42.9%)	22 (34.9%)
Moderate Anemia	38 (31.7%)	10 (34.5%)	9 (32.1%)	19 (30.2%)
Severe Anemia	17 (14.2%)	2 (6.9%)	2 (7.1%)	13 (20.6%)

*Maternal

Table 2: Comparison of ABR Results Based on Maternal Age Groups

ABR Variables	Mean±SD			p-value
	Adolescent (n=29)	Advanced Maternal Age (n=28)	Normal Age (n=63)	
Wave I Latency (ms)	1.85 ± 0.14	1.92 ± 0.13	1.82 ± 0.12	0.031
Wave III Latency (ms)	4.15 ± 0.22	4.25 ± 0.19	4.11 ± 0.18	0.025
Wave V Latency (ms)	6.24 ± 0.25	6.32 ± 0.26	6.18 ± 0.22	0.046
I-III Interval (ms)	2.31 ± 0.15	2.35 ± 0.14	2.28 ± 0.13	0.057
III-V Interval (ms)	2.05 ± 0.14	2.17 ± 0.15	2.02 ± 0.13	0.032
I-V Interval (ms)	4.35 ± 0.18	4.46 ± 0.19	4.32 ± 0.17	0.041

Table 3: Comparison of ABR Results Based on Maternal Anemia Severity

ABR Variables	Mean±SD				p-value
	No Anemia (n=15)	Mild Anemia (n=50)	Moderate Anemia (n=38)	Severe Anemia (n=17)	
Wave I Latency (ms)	1.81 ± 0.12	1.86 ± 0.14	1.91 ± 0.16	2.01 ± 0.18	0.011
Wave III Latency (ms)	4.05 ± 0.18	4.15 ± 0.22	4.26 ± 0.22	4.34 ± 0.24	0.023
Wave V Latency (ms)	6.13 ± 0.22	6.27 ± 0.26	6.33 ± 0.27	6.41 ± 0.37	0.014
I-III Interval (ms)	2.24 ± 0.13	2.31 ± 0.11	2.31 ± 0.17	2.47 ± 0.18	0.036
III-V Interval (ms)	2.18 ± 0.12	2.07 ± 0.14	2.18 ± 0.16	2.15 ± 0.17	0.022
I-V Interval (ms)	4.33 ± 0.17	4.36 ± 0.18	4.47 ± 0.19	4.53 ± 0.24	0.025

Table 4: Multivariate Regression Analysis for Factors Associated with ABR Latencies

Variables	(β, p-value)		
	Wave I Latency	Wave III Latency	Wave V Latency
Maternal Age (years)	β = 0.12, p = 0.041	β = 0.18, p = 0.027	β = 0.25, p = 0.033
Maternal Anemia (g/dL)	β = 0.15, p = 0.023	β = 0.22, p = 0.018	β = 0.30, p = 0.011
Gestational Age (weeks)	β = -0.10, p = 0.052	β = -0.15, p = 0.035	β = -0.20, p = 0.020
Birth Weight (kg)	β = -0.05, p = 0.062	β = -0.08, p = 0.046	β = -0.12, p = 0.038
Sex of Infant (M/F)	β = 0.08, p = 0.036	β = 0.12, p = 0.023	β = 0.18, p = 0.010

Table 5: Correlation Between Maternal Anemia Severity and ABR Wave Latencies

ABR Variable	Correlation Coefficient (r)	p-value
Wave I Latency	r = 0.301	0.017
Wave III Latency	r = 0.353	0.016
Wave V Latency	r = 0.405	0.018
I-III Interval	r = 0.258	0.033
III-V Interval	r = 0.286	0.024
I-V Interval	r = 0.334	0.016

DISCUSSION

In this study, we assessed the effect of maternal age and anemia on the auditory brainstem response (ABR) of preterm infants. Our findings demonstrated significant associations between both maternal factors and delayed ABR wave latencies, indicating auditory dysfunction in preterm infants born to mothers with anemia and advanced or adolescent maternal age.

The positive correlation between maternal anemia and prolonged ABR latencies (Wave I: $r = 0.301$, $p = 0.017$; Wave V: $r = 0.405$, $p = 0.018$) suggests that maternal hemoglobin levels are crucial for normal auditory development. Anemia, especially in the third trimester, may lead to fetal hypoxia, which impairs neural myelination and synaptic transmission, particularly in the auditory brainstem pathways. Similar findings were observed in a study by ElAlfy et al., Keats et al., and Seo et al., which reported that infants born to anemic mothers had significantly delayed wave latencies, supporting our results that maternal anemia is a risk factor for abnormal ABR outcomes in preterm infants.[10,11,12]

Our analysis also revealed that advanced maternal age (≥35 years) and adolescent mothers (<20 years) were associated with longer ABR wave latencies compared to mothers of normal reproductive age. This observation aligns with studies such as that by Shi et al., and Kokorudz et al., which showed that maternal age extremes are linked to higher risks of perinatal complications, including impaired fetal growth and neurodevelopmental delays.[13,14] Physiological changes during pregnancy, including placental insufficiency and oxidative stress in older mothers, may contribute to delayed maturation of auditory pathways in preterm infants.[13] Additionally, adolescent mothers may face nutritional deficiencies and suboptimal prenatal care, exacerbating the risk of neurodevelopmental delays.[14]

The gestational age and birth weight of the infants also significantly influenced ABR outcomes. Lower gestational age and birth weight were associated with prolonged latencies ($p < 0.05$), consistent with previous literature. Preterm birth disrupts the normal myelination process, leading to slower neural conduction in the brainstem. This is supported by Angrisani et al., and Li et al., who found that preterm infants exhibit delayed auditory pathway maturation compared to term infants, with significant differences in ABR wave latencies.[15,16]

In terms of gender differences, male infants showed longer ABR latencies compared to females, especially in wave V ($\beta = 0.18$, $p = 0.010$). This gender disparity has been well-documented in auditory study by Krizman et al., with males generally exhibiting slower neural transmission in the auditory system.[17] The reasons may be multifactorial, including hormonal influences on brain development and differences in prenatal vulnerability to environmental factors.[17]

This study highlights the importance of maternal anemia and age in influencing auditory outcomes in preterm infants. The significant prolongation of ABR latencies in infants of anemic mothers, particularly those with severe anemia, suggests the need for routine prenatal screening and effective management of maternal anemia. Early interventions could help mitigate the risk of auditory dysfunction in this vulnerable population. Furthermore, the impact of maternal age underscores the necessity for targeted prenatal care for both adolescent and older mothers to minimize adverse neurodevelopmental outcomes.

Limitations

Our study's strengths include a robust sample size and the use of comprehensive ABR testing protocols to assess auditory dysfunction in a vulnerable population. However, it is important to acknowledge certain limitations, such as the reliance on maternal hemoglobin levels measured during the third trimester, which may not fully capture anemia severity throughout pregnancy. Additionally, environmental and genetic factors influencing auditory development were not controlled for, which could contribute to variations in ABR outcomes.

CONCLUSION

In conclusion, our findings underscore the importance of maternal health, particularly anemia and maternal age, in shaping auditory outcomes in preterm infants. The significant delays in ABR latencies observed in infants born to anemic mothers highlight the need for early screening and intervention to mitigate potential hearing impairments. Future research should explore long-term auditory outcomes and the potential benefits of maternal anemia management during pregnancy to prevent neurodevelopmental delays in preterm infants.

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