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Original Article

Physiology Section

Effect of Maternal Age and Anaemia on Auditory Brainstem Response of Preterm Infants in a Tertiary Care Hospital of Kolkata, West Bengal: A Cross-sectional Study

SONALI MAJUMDAR (DAS)[1], HIYA BHATTACHARYA[2], MALAY KUMAR DASGUPTA[3]

ABSTRACT

Introduction: Adolescent pregnancy and maternal anaemia have a detrimental effect on infant growth and development. They are associated with greater risk of premature births and Low Birth Weight (LBW). Wave Interpeak Latencies (IPLs) of infant Auditory Brainstem Response (ABR) indicate the degree of maturation of brainstem auditory pathways among preterm infants. Previous studies indicated that preterm infants show prolonged wave IPLs. Whether maternal parameters like age and haemoglobin level contributes to the changes in infant ABR is debated.

Aim: To study the effect of maternal age and anaemic status on Brainstem Evoked Response Audiometry (BERA) changes among preterm infants.

Materials and Methods: An observational, descriptive study of cross-sectional design was undertaken in the Neurophysiology laboratory of Department of Physiology, RG Kar Medical College and Hospital, Kolkata from December 2019 to December 2022. Total of 119 mother-preterm infant dyads were included. Click BERA was performed on the babies aged between three months to one year. Absolute and IPLs of wave I, III and V were obtained. Mothers were assigned anaemic status {Haemoglobin (Hb) level <9 gm/dL} based on the information in their antenatal card. Student's t-test, Fischers-exact test, one way ANOVA test were used for data analysis. A p-value less than 0.05 was considered significant.

Results: Out of 76 adolescent mothers (age between 10-<18 years), 43 (56.6%) were anaemic. Out of 43 adult mothers (with age ≥18 years), 33 (76.7%) were anaemic. Mothers were divided into four groups, namely adolescent anaemic (n=43) and adolescent non anaemic (n=33), adult anaemic (n=33) and adult non anaemic (n=10). Distribution of data with respect to education years, social class and occupation among four mothers' group was comparable (p-value >0.05). Preterm infants born to both anaemic adult (Hedges g=2.51) and anaemic adolescent mothers [Hedges g=1.06] showed dyssynchronous shortening of wave latencies compared to non anaemic counterparts (p-value <0.05). Magnitude of difference with respect to infant ABR for non anaemic adolescent mothers vs non anaemic adult counterparts was large (Hedges g=1.05) with p-value <0.05. While maternal anaemia showed either shortening or prolongation of IPLs, adolescent maternal age was related with prolongation of the wave I-V. Effect size of maternal anaemia on infant ABR was more than for adolescent maternal age.

Conclusion: Maternal anaemia may exaggerate abnormal maturation of the brain stem pathways in preterm infants irrespective of maternal age.

Keywords: Audiometry, Birth, Evoked, Potential, Premature

INTRODUCTION

Adolescent pregnancy and maternal anaemia have a detrimental effect on infant growth and development [1]. Auditory brainstem response (ABR) is used to infer neuronal maturity among preverbal children [2]. India reported the highest number of preterm births in year 2020 [3]. Prematurity with LBW was the most common risk factor accounting for 57% of infants with hearing loss [4].

Brainstem Evoked Response Audiometry (BERA) test measures time taken by impulse generated within the cochlea to reach brainstem [5]. Preterm infants show prolonged central and peripheral conduction time compared to term infants [6].

Conflicting views also exist regarding the effect of maternal parameters on development of preterm infants if mother's Socio-economic Status (SES) is accounted for. Some researchers conclude that maternal age correlates positively with child development even after matching for SES [7-10]. Others contend that there is no difference in infant health outcomes with respect to maternal age and nutrition [11,12].

Limited studies have been done in India but the results have been variable [6,13-16]. Maternal history was inadequate in a few studies for further interpretation [6,13] whereas another study concluded that preterm birth alone does not lead to delayed Brainstem Auditory Evoked Potentials (BAEPs) changes at term age [15]. A part of the study was conducted by the same group of authors where the BAEP data of 250 children was collected with history of speech and language delay while 120 children had normal language milestones [13].

Thus, the present study aimed to find the effect of maternal age and antenatal haemoglobin concentration on ABR of preterm infants using Click BERA. This information may help in better interventions to optimise language and speech outcomes among affected infants.

MATERIALS AND METHODS

An observational, descriptive study of cross-sectional design was undertaken in the Neurophysiology laboratory of Department of Physiology, RG Kar Medical College and Hospital, Kolkata, Bengal, India. The study was approved by Institutional Ethical Committee. Drug Controller General of India (DCGI) registration number is ECR/322/Inst/WB/2013. Trial Registration number is CTRI/2019/05/019226. The study was conducted from December 2019 to December 2022.

Inclusion criteria: Preterm infants were defined as born before 37 completed weeks of gestation [2]. Babies who were three months

to less than one year from their birth date, admitted to Neonatal Intensive Care Unit Infants, attending Sick Baby Clinic for follow-up in Department of Paediatric Medicine, R.G. Kar MCH, Kolkata were included in the study.

Exclusion criteria: Severely ill and restless infants, lack of parental consent, babies having congenital abnormalities (external auditory canal atresia both unilateral/bilateral, craniofacial anomalies), chromosomal disorders, history of birth trauma, metabolic disorders and intracranial infections, family history of hearing loss; suffering from external and or middle ear disease, upper respiratory tract infection; showing absent BERA waves (I and V) were excluded.

Sample size calculation: About 27.7% of teenage mothers have preterm births [17].

$N \geq Z^2 \times (1-\alpha) \times P \times Q / L^2$

$\geq 1.96 \times 1.96 \times (1-0.05) \times 28 \times 72/7 \times 7$

≥158 mother-child dyads

Where Z=1.96, α=0.05, P=28, Q=72, absolute error, L=7,

N=sample size

Initially, 160 mother-infant dyads were included by purposive sampling.

Parameters Studied

Brainstem Evoked Response Audiometry (BERA): Click BERA was applied with the help of Neuro-MEP4, Ivanovo, Russia [15,16]. Click BERA was performed during natural sleep of the babies using specified sound stimulus ("click"). COVID-19 safety protocol was strictly followed. After applying electrolyte jelly, the active, ground and reference electrodes were placed following the 10-20 rule. Click sound of 70 dB Sound Pressure Level (SPL), rarefaction polarity at 11.1 Hz using 30-1000 Hz filters for tested ear and masking of 30 dB SPL for contralateral ear was given by applying headphones. Two recordings (each containing 2000 averaged responses) per ear was taken for reproducibility [18,19]. Prominent BERA waves among preterm infants are waves I, III and V. Absolute wave I, III and V latencies; and wave I-III, I-V and III-V IPLs were measured. Unlike absolute latencies, indicate Central Conduction Time (CCT) [2].

Socio-demographic profile: Maternal parameters like age, education years and occupation were based on self-reported history. Information about maternal Hb in the first trimester of pregnancy and maternal weight was retrieved from antenatal clinic card. Self-reported age of menarche, year of marriage, interval between school leaving and child birth was used to corroborate maternal age. Social class was estimated using the Modified BG Prasad scale 2020 [20]. Data regarding the gestational age and birth weight of infants were obtained from discharge certificate and maternal history. Due to unavailability of mothers, insufficient data 119 mother-preterm infants pairs were ultimately included. Due to COVID-19 restrictions, further sampling and data collection was hampered.

Mothers were explained about the study in vernacular language and informed consent was taken from adult mothers. Consent was taken from adolescent mothers and from accompanying adult guardian.

- Mothers between 10 to <18 years of age were termed adolescent.
- Mothers ≥18 years were considered adults [21].
- Mothers with Hb=9 gm/dL were termed as non anaemic while those with Hb <9 gm/dL were grouped as anaemic [22].

STATISTICAL ANALYSIS

Data was expressed as mean and Standard Deviation (SD). Student's t-test, Fischers-exact test, one way ANOVA test and post-hoc test were used for comparison. Effect size was calculated using Hedges g (biased and unbiased) and expressed with 95% Confidence Interval (CI). Mean g>0.8 was considered large [23]. Statistical analysis was done using Graph-pad Quickcalc software California, USA, (version 9.3.1). Results with p-value <0.05 and effect size >0.8 were accepted as statistically and clinically relevant.

RESULTS

The study was conducted among 119 mother-infant dyads. Out of 119 infants, 76 were born to adolescent mothers and 43 to adult mothers. Out of 76 adolescent mothers, 43 (56.6%) were anaemic while 33 (43.4%) were non anaemic. Out of 43 adult mothers, 33 (76.7%) were anaemic while 10 (23.3%) were non anaemic. The mean gestational age of preterm infants (n=119) at birth was 30.46±2.87 weeks and their mean birth weight was 1.81±0.34 kgs. With respect to gender, 62 out 119 preterm infants were male infants (52%).

Adolescent mothers were younger (mean13.8 vs 24.7 years), had lesser weight (mean 42.4 vs 44.7 kgs) but higher Hb (mean 9.96 vs 9.15 g/dL) as against the adult mothers, p-value <0.05. Mean education years (7.31 vs 7.21 years), percentage of homemakers (76.3% vs 62.8%) and working mothers (13.3% vs 18.6%), mothers belonging to poor social class (86.7% vs 81.4%) and middle class (23.7% vs 33.2%) were similar, p-value >0.05 [Table/Fig-1].

Maternal parameters	Adolescent mothers	Adult mothers	p-value
Age (years) (Mean±SD)	13.8±2.84	24.7±4.3	<0.001
Mean education years (Mean±SD)	7.31±4.15	7.21±4.16	0.89
Social Class:			
• V (Poor), n (%)	67 (86.7%)	35 (81.4%)	0.41
• III and IV, Middleclass n (%)	9 (13.3%)	8 (18.6%)	
Occupation:			
• Homemaker, n (%)	58 (76.3%)	27 (62.8%)	0.14
• Working mothers, n (%)	18 (23.7%)	16 (37.2%)	
Antenatal weight (kgs) (Mean±SD)	42.4±4.24	44.7±1.12	<0.001
Antenatal Haemoglobin concentration (gm/dL) (Mean±SD)	9.96±1.28	9.15±1.67	<0.001

[Table/Fig-1]: Shows the socio-demographic profile of adolescent and adult mothers. Social class was estimated using the Modified BG Prasad scale 2020 [20]

Mothers were divided into 4 groups based on age and anaemic status.

- Group 1: Anaemic adolescent mothers (n=43);
- Group 2: Non anaemic adolescent mothers (n=33);
- Group 3: Anaemic adult mothers (n=33); and
- Group 4: Non anaemic adult mothers (n=10).

Anaemic mothers had lower weight (mean 39.9 vs 47.2 kg) and haemoglobin (mean 8.46 vs 9.9 g/dL) vs non anaemic mothers [Table/Fig-2,3].

Parameters	Mothers with anaemia n=76	Mothers without anaemia n=43	p-value
Age (years) (Mean±SD)	19.51±4.04	18.99±3.11	0.404
Education (years) (Mean±SD)	7.23±3.95	7.71±3.11	0.434
Social Class:			
• V (Poor), n (%)	68 (89.47%)	50 (79.37%)	0.1523
• III and IV, Middleclass	8 (10.53%)	13 (20.63%)	
Occupation:			
• Homemaker, n (%)	57 (75%)	38 (60.32%)	0.07
• Working mothers, n (%)	19 (25%)	25 (39.68%)	
Antenatal weight (in kgs) (Mean±SD)	39.9±3.27	47.2±2.2	<0.001**
Antenatal Hb concentration (In gm/dL) (Mean±SD)	8.46±1.3	9.9±1.66	<0.001**

[Table/Fig-2]: Shows the socio-demographic profile of mothers with and without anaemia (p-value with help of Student's t-test for quantitative and Fischers-exact test for qualitative variables).

Maternal parameters	Group 1 (n=43)	Group 2 (n=33)	Group 3 (n=33)	Group 4 (n=10)	p-value	After Post-hoc test p-value
Age (years) (Mean±SD)	14.14±3.76	13.46±1.93	24.87±4.32	24.53±4.29	<0.001	1 vs 2, p>0.05 1 vs 3, p<0.05* 1 vs 4, p<0.05* 2 vs 3, p<0.05 2 vs 4, p<0.05* 3 vs 4, p>0.05
Mean education years (Mean±SD)	7.33± 3.94	7.29±4.36	7.12±3.97	8.12±3.64	0.76	
Social class:						
• V (Poor), n (%)	40 (92.8%)	27 (81.8%)	28 (93.33%)	7 (70%)	0.17	
• III and IV, Middleclass	3 (7.2%)	6 (18.2%)	5 (6.67%)	3 (30%)		
Occupation:						
Homemaker, n (%)	35 (81.9%)	23 (70.6%)	22 (72.2%)	5 (50%)	0.043*	1 vs 2, p>0.05 1 vs 3, p>0.05 1 vs 4, p<0.05* 2 vs 3, p>0.05 2 vs 4, p>0.05 3 vs 4, p>0.05
Working mothers, n (%)	8 (18.1%)	10 (29.4%)	11 (27.8%)	5 (50%)		
Antenatal Weight (in Kgs) (Mean±SD)	42.59±4.59	42.22±3.95	37.22±1.95	52.1±0.438	<0.001**	1 vs 2, p>0.05 1 vs 3, p<0.05* 1 vs 4, p<0.05* 2 vs 3, p<0.05* 2 vs 4, p<0.05* 3 vs 4, p<0.05
Antenatal Hb concentration (In gm/dL) (Mean±SD)	8.5±1.07	9.82±1.5	8.42±1.53	9.98±1.82	<0.001**	1 vs 2, p<0.05* 1 vs 3, p>0.05 1 vs 4, p<0.05* 2 vs 3, p<0.05* 2 vs 4, p>0.05 3 vs 4, p<0.05

[Table/Fig-3]: Socio-demographic profile of adolescent mothers and adult mothers with and without anaemia (p-value with help of one way ANOVA test and post-hoc test).

Multiple group comparisons showed that they differed significantly with respect to age, weight and haemoglobin. Distribution of data with respect to education years, occupation (except column 1 vs 4) and social class among the four mothers' group was similar, p-value >0.05. Mothers were mostly homemakers by profession, belonging to poor social class and had left studying at middle school. Infant ABR for adolescent vs adult mothers showed significantly delayed wave III and I-III latencies, right ear but effect size <0.8 [Table/Fig-4].

Infant ABR for anaemic vs non anaemic mothers revealed shorter wave I-III but delayed III-V latency, right ear [p-value <0.05; effect size >0.8]. Significantly faster wave I-III, left ear and III latency, right ear was observed but effect size <0.8 [Table/Fig-5]. Prolonged wave I-V IPLs, right ear was found among infants of non anaemic adolescent vs adult mothers [p-value <0.05; Hedges g=1.35] [Table/Fig-6]. Infant ABR for anaemic adolescent vs adult mothers revealed significantly faster wave V and III-V latency, right ear but effect size <0.8 [Table/Fig-7].

With reference to [Table/Fig-5], ABR changes among preterm infants born to adolescent mothers with anaemia were similar to adolescent mothers without anaemia except shortening of wave I-III IPLs for both ears and smaller wave I-V inter peak latency, right ear [p<0.05; effect size >0.8]. Shorter absolute wave III latency for both ears was observed (p-value <0.05) but effect size not large [Table/Fig-8].

Infant ABR of anaemic vs non anaemic adult mothers displayed shorter wave I-III IPLs and wave III latency but longer wave V latency and III-V IPLs, right ear [p-value <0.05, effect size >0.8] [Table/Fig-9].

Effect size of clinical relevance (p-value <0.05 and mean Hedges g >0.8) for infant ABR with respect to maternal age and anaemic status (decreasing order) with each column (n=10) showing mean Hedges g (unbiased) with 95% CI [Table/Fig-10].

All columns except column 5 showed effect on infant ABR for anaemic vs non anaemic mothers. Effect size for column 1-7 was non overlapping with that for columns 8, 9 and 10.

Infant ABR showed dyssynchronous shortening of IPLs for all groups of anaemic/adult anaemic mothers compared to non anaemic controls.

With respect to column 1 and 2, there was prolonged wave III-V and wave V latencies while column 8 and 9 depicts shortening of wave I-III IPLs and wave III latencies for right ear of infants born to anaemic vs non anaemic adult mothers. Column 6 shows delayed wave III-V IPLs and column 10 depicts faster I-III IPLs for infants of anaemic /non anaemic mothers.

But for infants born to anaemic vs non anaemic adolescent mothers, there was delay in both the central and peripheral wave IPLs for right ear and longer peripheral conduction time for left ear. Column 3 and 4 reveal delay in wave III-V and wave I-III IPLs for right ear of infants while column 7 shows delayed wave I-III IPLs, left ear.

	Left ear			Right ear			
‡BAEP parameters (Mean±SD)	Adolescent mothers (n=76)	Adult mothers (n=43)	p-value Hedges g	BAEP parameters (Mean±SD)	Adolescent mothers (n=76)	Adult mothers (n=43)	p-value Hedges g (biased)
Wave I	1.91±0.2	1.9± 0.19	0.79	Wave I	1.88±0.11	1.81±0.34	0.10
Wave III	4.38±0.4	4.34±0.55	0.65	Wave III	4.34±0.39	4.17±0.39	0.0242*, -0.4358
Wave I-III	2.47±0.3	2.44± 0.37	0.63	Wave I-III	2.5±0.25	2.36±0.37	0.0155*, - 0.4687
Wave V	6.48±0.46	6.54±0.45	0.49	Wave V	6.43±0.5	6.38±0.39	0.57
Wave I-V	4.59±0.53	4.64±0.49	0.61	Wave I-V	4.54±0.54	4.55±0.31	0.30
Wave III-V	2.1±0.43	2.2±0.5	0.25	Wave III-V	2.09±0.44	2.21±0.39	0.14.

[Table/Fig-4]: BAEP parameters among preterm infants of adolescent mothers and adult mothers.
*p-value <0.05 Statistically Significant; †Hedges g >0.8; ‡BAEP: Brainstem auditory evoked potential

‡BAEP parameters (Mean±SD)	Left ear			Right ear			
	Anaemic mothers (n=43)	Non anaemic mothers (n=43)	p-value Hedges g	BAEP parameters (Mean±SD)	Anaemic mothers (n=43)	Non anaemic mothers (n=43)	p-value Hedges g
Wave I	1.97±0.37	1.92±0.12	0.401	Wave I	1.93±0.29	1.99±0.23	0.2908
Wave III	4.36±0.66	4.55±0.44	0.12	Wave III	4.22±0.51	4.59±0.45	<0.001**, -0.769
Wave I-III	2.39±0.51	2.64±0.32	0.0079*, -0.58	Wave I-III	2.29±0.4	2.61±0.26	<0.001**, -0.948†
Wave V	6.65±0.74	6.59±0.38	0.63	Wave V	6.66±0.55	6.48±0.33	0.069
Wave I-V	4.67±0.74	4.75±0.37	0.5278	Wave I-V	4.56±0.35	4.68±0.22	0.060
Wave III-V	2.3±0.7	2.2±0.41	0.4212	Wave III-V	2.44±0.53	1.89±0.39	<0.001**, 1.182†

[Table/Fig-5]: Depicts the ABR changes among preterm infants born to mothers with and without anaemia.
*p-value <0.05 statistically significant; †Hedges g >0.8; ‡BAEP: Brainstem auditory evoked potential; **p<0.001 highly significant

‡BAEP parameters (Mean±SD)	Left ear			Right ear		
	Preterm infants of adolescent mothers non anaemic (n=33)	Preterm infants of adult mothers non anaemic (n=10)	p-value	Preterm infants of adolescent mothers non anaemic (n=33)	Preterm infants of adult mothers non anaemic (n=10)	p-value Hedges g
Wave I	1.9±0.14	1.93±0.25	0.628	1.95±0.16	2.02±0.3	0.33
Wave III	4.57±0.28	4.54±0.6	0.82	4.58±0.5	4.6±0.4	0.90
Wave I-III	2.67±0.21	2.61±0.42	0.54	2.63±0.17	2.58±0.35	0.53
Wave V	6.63±0.2	6.75±0.55	0.29	6.58±0.27	6.38±0.39	0.07
Wave I-V	4.7±0.17	4.79±0.57	0.42	4.8±0.13	4.55±0.31	p<0.001**, 1.05†
Wave III-V	2.06±0.24	2.21±0.57	0.23	2.0±0.38	1.78±0.39	0.1185; 0.057

[Table/Fig-6]: Depicts the ABR changes among preterm infants born to non anaemic adolescent and adult mothers.
*p<0.05 Statistically significant; †Hedges g >0.8; ‡BAEP: Brainstem auditory evoked potential; **p<0.001 Highly Significant

‡BAEP parameters (Mean±SD)	Left ear			Right ear		
	Preterm infants of anaemic adolescent mothers (n=43)	Preterm infants of anaemic adult mothers (n=33)	p-value	Preterm infants of anaemic adolescent mothers (n=43)	Preterm infants of anaemic adult mothers (n=33)	p-value Hedges g
Wave I	1.96±0.37	1.98±0.36	0.81	1.92±0.19	1.93±0.38	0.8811
Wave I-III	2.31±0.5	2.46±0.52	0.20	2.29±0.43	2.28±0.37	0.91
Wave III	4.27± 0.64	4.44±0.68	0.26	4.22±0.66	4.22±0.35	1.00
Wave V	6.52±0.73	6.78±0.75	0.13	6.44±0.84	6.87±0.25	0.0058*, -0.69
Wave I-V	4.6±0.85	4.74±0.63	0.43	4.56±0.17	4.55±0.53	0.907
Wave III-V	2.25±0.68	2.34±0.715	0.5777	2.22±0.75	2.65±0.3	0.0027*, -0.756

[Table/Fig-7]: Depicts the ABR changes among preterm infants born to adolescent and adult mother (both the groups of mothers suffering from anaemia).
*p-value <0.05 Statistically significant; †Hedges g >0.8; ‡BAEP: Brainstem auditory evoked potential

‡BAEP parameters (Mean±SD)	Left ear			Right ear		
	Preterm infants of adolescent mothers with anaemia (n=43)	Preterm infants of adolescent mothers without anaemia (n=33)	p-value Hedges g	Preterm infants of adolescent mothers with anaemia (n=43)	Preterm infants of adolescent mothers without anaemia (n=33)	p-value Hedges g
Wave I	1.96±0.37	1.9±0.14	0.38	1.92±0.19	1.95±0.16	0.467
Wave III	4.27±0.64	4.57±0.28	0.0142* -0.0607	4.22±0.66	4.46±0.17	0.045* -0.614
Wave I-III	2.31±0.5	2.67±0.21	p<0.001** -0.938†	2.29±0.43	2.63±0.17	p<0.001** -1.062†
Wave V	6.52±0.73	6.63±0.2	0.40	6.44±0.84	6.58±0.27	0.36
Wave I-V	4.6±0.85	4.7±0.17	0.50	4.56±0.57	4.8±0.13	0.02* -0.865†
Wave III-V	2.25±0.68	2.06±0.24	0.129	2.22±0.75	2.0±0.38	0.128

[Table/Fig-8]: Shows the ABR changes of preterm infants born to adolescent mothers with anaemia and without anaemia.
*p-value <0.05 Statistically significant: †Hedges g >0.8; ‡BAEP: Brainstem auditory evoked potential; **p<0.001 Highly significant

DISCUSSION

There are numerous studies regarding the relation between maternal parameters and infant development. Maternal SES is known to adversely affect infant health outcomes. Risk of premature birth and LBW is more in case of mothers who have poor access to healthcare, education and nourishment [10,11]. Mothers were divided into four groups, namely adolescent anaemic (n=43) and adolescent non anaemic (n=33), adult anaemic (n=33) and adult non anaemic (n=10). Distribution of data with respect to education years, social class and occupation among four mothers' group was comparable (p-value >0.05).

Distribution of data relating to antenatal weight revealed that adolescent mothers had lesser mean weight vs adult mothers p-value <0.001. With respect to antenatal Hb concentration, adolescent mothers had greater mean Hb concentration compared to adult mothers, p-value <0.001.

The findings were similar to previous studies [10,24,25]. Fulpagare PH et al., reported that less number of adult mothers registered their pregnancy with antenatal care services while Siddiqui MZ et al., concluded that they were more likely to be anaemic [24,25].

On the contrary, based on National Family Health Survey-IV, it was inferred that teenage mothers were more likely to be anaemic compared to adults [10]. Anaemic mothers had lower weight and haemoglobin vs non anaemic mothers. The findings were similar to other studies [1,10]. Mothers' groups were similar with respect to SES but differed in mean weight and haemoglobin,

‡BAEP parameters (Mean±SD)	Left ear			Right ear		
	Preterm infants of anaemic adult mothers (n=33)	Preterm infants of non anaemic adult mothers (n=10)	p-value	Preterm infants of anaemic adult mothers (n=33)	Preterm infants of non anaemic adult mothers (n=10)	p-value Hedges g
Wave I	1.98±0.36	1.93±0.25	0.68	1.93±0.38	2.02±0.3	0.49
Wave III	4.44±0.68	4.54±0.6	0.67	4.22 ±0.35	4.6±0.4	0.0058* -1.07†
Wave I-III	2.46±0.52	2.61±0.42	0.41	2.28± 0.36	2.58±0.35	0.025* -0.83†
Wave V	6.78±0.75	6.75±0.55	0.90	6.87± 0.25	6.38±0.39	p<0.001** 1.52†
Wave I-V	4.74±0.63	4.79±0.57	0.82	4.554 ± 0.531	4.55±0.31	0.98
Wave III-V	2.34±0.72	2.21±0.57	0.60	2.65± 0.3	1.78±0.39	p<0.001** 2.51†

[Table/Fig-9]: Shows the ABR changes among infants born to adult mothers (with anaemia and without anaemia).
*p-value <0.05 statistically significant; †Hedges g >0.8; ‡BAEP: Brainstem auditory evoked potential; **p<0.001 Highly Significant

	BAEP parameters of preterm infants (ear) Born to mothers- adult(ad)/adolescent (ado); anaemic (an)/non anaemic (nan)									
	Column 1	Column 2	Column 3	Column 4	Column 5	Column 6	Column 7	Column 8	Column 9	Column10
	Wave III-V (rt)	Abs. wave V (rt)	Wave III-V (rt)	Wave I-III (rt)	Wave I-V (rt)	Wave III-V (rt)	Wave I-III (lt)	Wave I-III (rt)	Abs. Wave III (rt)	Wave I-III (rt)
Hedges g (unbiased)	Ad an/nan mother	Ad an/nan mothers	Ado an/nan Mother	Ado an/nan mothers	Nan A do/ ad mother	An/nan mothers	Ado an/nan mothers	Ad an/nan mothers	Ad an/nan mothers	An/nan mothers
95% CI upper limit	3.17	2.06	1.64	1.57	1.59	1.63	1.46	-0.32	-0.48	-0.53
Mean	2.48	1.49	1.14	1.08	1.05	1.17	0.976	-0.83	-1	-1
95% CI lower limit	1.84	0.94	0.66	0.6	0.72	0.61	0,5	-1.35	-1.53	-1.4

[Table/Fig-10]: Shows effect size in descending order (left to right) for BERA changes in preterm infants of Adolescent (Ado) and adult mothers with anaemia (an) and non anaemic (nan).
p-value <0.05 and Hedges g >0.8

p-value <0.05. The results were in accordance with previous studies [1,10,21].

Effect of adolescent vs adult mothers on infant ABR was of limited clinical relevance if mothers irrespective of haemoglobin was included. Al-Balas HI et al., found no significant correlation between maternal age and LBW with failure of the first Otoacoustic Emission (OAE) test (used for hearing loss screening) among apparently healthy newborn babies [11]. On the contrary, Kumar G et al., reported that children born to adolescent mothers were under weight and had more hospitalisation vs adult mothers [10] .

Infants ABR showed shorter wave I-III but delayed III-V latency, right ear [p-value <0.05; mean Hedges g>0.8] among anaemic vs non anaemic mothers. Based on ABR, early maturation of the peripheral nerves with delayed myelination of central auditory circuits was noted. Probably, maternal anaemia together with prematurity has deleterious effect on neuronal maturation resulting in prolonged III-V IPLs. These findings are in agreement with previous works [26-31]. Wave III and V depend on processing of central auditory pathways by which meaningful sound stimuli are identified resulting in speech ,music and object recognition [28].

Iron is essential for normal neurogenesis and Iron Deficiency (ID) accounts for >80% of cases of gestational anaemia [10]. Shukla AK et al., reported that reduced maternal serum iron was associated with low newborn iron stores. Affected infants showed delayed wave IPLs [29].

In the present study, infant ABR reveals dyssynchronous shortening of wave IPLs in case of anaemic/anaemic adult mothers vs non anaemic counterparts. For infants born to anaemic adolescent vs non anaemic controls there was delay in wave IPLs.

Third trimester of gestation is crucial for infant brain development. In preterm births, myelination of peripheral nerves is completed rapidly after birth in order to make up for lost time. Thus, prematurity itself can result in accelerated neural maturation and shorter wave I-III IPLs [30]. On the contrary, some scientists contend that injuries due to perinatal-postnatal complications can lead to abnormal infant ABR [31]. Raposo D et al., noted that intraventricular haemorrhage may cause early maturation of nerves among preterm births [32].

Delayed wave III-V IPLs may be due to adverse health outcomes that may selectively damage infant auditory brainstem [31,32]. Also wave I latency is less sensitive to damage caused by hypoxia, infections, toxins etc., and neuronal pathway responsible for wave I matures earlier. Thus, shortening of wave I latency occurs earlier compared to wave III and V [33]. Prolonged wave I-V IPLs, right ear was found among infants of non anaemic adolescent vs adult mothers [p-value <0.05; Hedges g=1].

In the present study, effect of adolescent maternal age on infant ABR was large when mean maternal Hb was >8 gm/dL. Non anaemic adolescents were thinner compared to adult mothers, p-value <0.05. Wave I-V IPLs indicate functional integrity of auditory neurons and CCT. Maternal undernutrition could lead to delayed CCT. The results are in agreement with other studies [10,12].

However Marvin-Dowle K et al., failed to find any association of LBW or preterm delivery to adolescent maternal age after adjusting for SES and maternal nutrition [34].

Faster wave V and III-V latency, right ear was found for infants of anaemic adolescent vs adult mothers (p-value <0.05) but effect size <0.8. There is simultaneous shortening of wave latencies after birth due to neuronal maturation. In present study, adolescent and adult mothers were similar with respect to SES as well as in anaemic status (p>0.05). Thus, maternal anaemia may have shrouded deleterious effect of adolescent maternal age on infants ABR. The study findings are in accordance with Seetapathy J et al., who found shortening of central ABR waves in preterm infants at three months compared to one month of age due to neuronal maturation [35].

On the contrary, population-based study reported that adolescent mothers are more likely to be underweight and anaemic during gestation.They were more likely to bear neonates with adverse developmental outcomes [10,21].

Early wave I-III IPLs, both ears and I-V IPLs, right ear [p-value <0.05; effect size >0.8] was seen for infants of anaemic adolescent mothers vs non anaemic controls. The study findings were in agreement with the previous studies [10,26,27,29-32]. Possibility of hospitalisation was more for infants born to anaemic mothers [10]. Major perinatal complications affecting preterm infants include prolonged mechanical ventilation, Cytomegalovirus Infection (CMV), meningitis and periventricular haemorrhage. Mechanical ventilation and CMV decreased wave III-V IPLs while the intracranial haemorrhage shortened wave I-V IPLs with p-value <0.05 [32].

On the contrary, Choudhury V et al., reported that infants with latent iron deficiency (n=23) had significantly longer wave V, III-V and I-V IPLs compared to infants with normal iron status even after adjusting for confounders. No difference was noted for wave III and I-III IPLs among the groups [14]. Infant ABR of anaemic vs non anaemic adult mothers displayed shorter wave I-III IPLs and wave III latency but longer wave V latency and III-V IPLs, right ear [p-value <0.05, effect size >0.8]. Abnormal shortening of wave IPLs may be due to adverse impact of maternal anaemia on infant iron stores. Study findings were in agreement with previous works [26,27,31-33]. Tiwari N and Mishra V, found that mean haemoglobin of adult mothers was positively correlated with birth weight of newborn (p-value <0.001). Cord blood ferritin showed positive correlation with maternal ferritin levels, p-value <0.001 [27]. However, Choudhury V et al., found poor correlation between maternal ferritin levels and that of cord blood. Normal birth weight newborns showed significantly higher cord blood Hb when compared to LBW newborns [14].

Infant ABR showed dyssynchronous shortening of IPLs for all groups of anaemic mothers compared to non anaemic controls. There was either delayed wave III-V but faster I-III IPLs (for infants of anaemic/adult anaemic mothers) or faster CCT with shortening of wave I-III greater than wave I-V IPLs (for anaemic adolescent mothers' infants).

Effect of adolescent maternal age on infant ABR was apparent for non anaemic mothers. Influence of maternal anaemia was more than adolescent age on infant ABR. Maternal anaemia probably due to poor nutrition was related to abnormal maturation of the neuronal pathways among infants. Distribution of antenatal weight and Hb concentration revealed that adult mothers had less mean weight and mean Hb concentration compared to adolescent mothers.

Similarly, ElAfy MS et al., reported prolonged I-III, III-V, and I-V IPLs among neonates born to anaemic mothers with ID vs control, p-value <0.05 [26] Poona W et al., inferred that premature infants were more likely to be anaemic vs full-term infants, p-value <0.001 [36]. In contrast, Widiyanto J et al., found that risk of LBW babies was more for adolescent mothers than anaemic mothers (16,2 vs 6.3 times) when compared to respective controls [37]. Poona W et al., concluded that based on ABR, relative risk of infant hearing loss was more for teenage mothers (2.03 vs 1.2) against older mothers [36]. Moreno-Fernandez J et al., reported that birth weight had no effect on severity of infant anaemia p-value=0.568 [38].

In summary, with regards to infant ABR, effect of anaemic adult mothers and anaemic adolescent mothers vs non anaemic controls was large. There was dyssynchronous shortening of CCT and impact of maternal anaemia was more for wave III-V > I-III >I-V IPLs. Influence of adolescent maternal age on infant ABR was apparent among non anaemic mothers with delayed wave I-V latency. Effect of maternal anaemia on infant ABR was greater than maternal adolescent age.

Limitation(s)

The study had its limitations including small sample size and lack of follow-up. Maternal parameters were based on history and antenatal records. Not all risk factors affecting infant ABR were accounted for. Mothers and infants were not tested for serum iron levels.

CONCLUSION(S)

Maternal anaemia may exaggerate abnormal maturation of infant auditory brainstem pathways irrespective of maternal age. Effect on central fibres was more than for peripheral nerves. Effect of adolescent maternal age on infant ABR was apparent for non-anaemic mothers. Impact of maternal anaemia was found to be more in comparison to maternal adolescent age for the present study.

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PARTICULARS OF CONTRIBUTORS:
1. Associate Professor, Department of Physiology, Tamralipto Government Medical College, Tamluk, West Bengal, India.
2. Assistant Professor, Department of Physiology, Diamond Harbour Government Medical College, Diamond Harbour, West Bengal, India.
3. Professor and Head, Department of Paediatric Medicine, KPC Medical College, Jadavpur, Kolkata, West Bengal, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Sonali Majumdar (Das),
26/4, K. K. Road, Kolkata-700008, West Bengal, India.
E-mail: drsonalidas1976@gmail.com

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