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Original Article

Evaluation of the Effect of Non-Invasive Ventilation on the Hearing Outcomes in Newborns

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Abstract ***Purpose:*** This study aimed to investigate whether non-invasive ventilation (NIV) in neonates admitted to the neonatal intensive care unit (NICU) is associated with an increased risk of hearing impairment. ***Materials and Methods:*** A retrospective cohort study was conducted including 798 neonates admitted to the NICU at Karabük University Faculty of Medicine Training and Research Hospital between 1 January 2020 and 31 December 2023 who met the inclusion criteria. Infants were categorised into two groups: those who received non-invasive ventilation and those who received either supplemental oxygen or no ventilatory support. Hearing outcomes were assessed using auditory brainstem response (ABR) screening and brainstem evoked response audiometry (BERA). ***Results:*** There were no statistically significant differences between the groups in terms of birth weight or gestational age. Apgar (Appearance, Pulse, Grimace, Activity, Respiration) scores were significantly lower in infants who received NIV. A higher proportion of female infants received NIV. Although NIV was associated with an increased rate of failure in the initial ABR screening (ABR1), this association was not observed in subsequent ABR assessments (ABR2) or in BERA testing. ***Conclusion:*** NIV is associated with transient abnormalities in early auditory screening; however, this effect does not persist in confirmatory testing. These findings suggest that NIV does not confer a sustained risk of hearing impairment in neonates.

Key words Auditory brainstem response; BERA; Neonatal intensive care unit; Non-invasive ventilation; Hearing screening

Introduction

In recent years, the use of non-invasive ventilation (NIV) in neonatal intensive care unit (NICU) has increased substantially, as it has become a preferred alternative to mechanical ventilation (MV), which is associated with higher rates of respiratory morbidity.[1,2]

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However, NIV modalities may generate elevated noise levels, raising concerns regarding potential auditory effects in newborns. For example, it has been reported that approximately two-thirds of infants receiving bubble nasal continuous positive airway pressure (nCPAP) are exposed to noise levels of up to 90 dB.[3] Although MV is recognised as a risk factor for neonatal hearing impairment, it remains unclear whether NIV carries a comparable risk.[4]

While numerous studies have investigated the effects of MV on neonatal auditory outcomes in NICU populations, to the best of our knowledge, only one study has directly compared hearing outcomes between infants receiving NIV and those receiving no ventilatory support.[5]

Therefore, the aim of this study was to compare hearing screening outcomes between neonates treated with non-invasive ventilation and those who received no ventilatory support, and to evaluate whether NIV is associated with an increased risk of hearing impairment.

Materials and Methods

This study was conducted at Karabük University Faculty of Medicine Training and Research Hospital, a tertiary-level NICU. Data were obtained retrospectively from the hospital's electronic medical record system. When necessary, families were contacted by telephone to verify or complete missing information. During the study period, a total of 930 neonates were admitted to the NICU. Following application of the eligibility criteria, 798 infants were included in the final analysis.

Inclusion Criteria

Neonates admitted to the NICU between 1 January 2020 and 31 December 2023 were eligible for inclusion. Additional inclusion criteria were: absence of genetic or syndromic disorders, completion of hearing screening tests, availability of complete clinical data, no inter-hospital transfer, and documented parental consent.

Exclusion Criteria

Infants were excluded if they were admitted outside the specified study period, had known genetic or syndromic conditions, died before completion of hearing assessment, had incomplete medical records, were transferred to another institution, or lacked parental consent.

Study Groups

Participants were divided into two groups: those who received NIV and those who received no ventilatory support. The choice of respiratory support modality was made in accordance with the Turkish Neonatology Society guidelines.[6,7] In our unit, nasal intermittent positive pressure ventilation (NIPPV) is the preferred NIV modality, as it has been associated with a reduced incidence of bronchopulmonary dysplasia compared with nCPAP.[8]

Definitions

Sepsis was defined as a clinical syndrome in which compatible clinical and laboratory findings were present, together with microbiological isolation of a causative organism.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. Ethical approval was obtained from the Ethics Committee of Karabük University Faculty of Medicine on 27 February 2023 (decision number: 2023/1243).

Hearing Assessment Protocol

At discharge, all neonates underwent automated auditory brainstem response (AABR) screening. Infants identified as belonging to high-risk groups—defined in accordance with established neonatal hearing screening guidelines[9]—including those with a family history of hearing loss, NICU stay exceeding five days, exposure to ototoxic medications, hyperbilirubinaemia requiring exchange transfusion, congenital infections (TORCH: toxoplasmosis, cytomegalovirus, herpes simplex, syphilis, and others), bacterial or viral meningitis, craniofacial anomalies, extracorporeal membrane oxygenation (ECMO) therapy, or syndromic conditions associated with hearing loss (e.g., Down, Turner, Waardenburg, Usher, Alport syndromes, and DFNA1-related disorders), as well as very low birth weight infants (<1500 g), were scheduled for follow-up testing. These infants underwent repeat ABR testing and brainstem evoked response audiometry (BERA) within six months of initial screening.

Table 1 summarises the Turkish Neonatal Association Guidelines for respiratory support in neonates, including recommendations for non-invasive and invasive ventilation. Non-invasive support (CPAP, nCPAP, NIPPV, and HHHFNC) is recommended as the initial respiratory management when appropriate, whereas invasive mechanical ventilation should be reserved for infants requiring intubation. The guidelines also emphasize minimising the duration of invasive ventilation, using lung-protective ventilation strategies, and providing non-invasive respiratory support following extubation.

Data Analysis

Data were analysed using IBM SPSS Statistics for Windows (Version 20.0; IBM Corp., Armonk, NY, USA). Normality of continuous variables was assessed using skewness and kurtosis values, and data were found to be consistent with a normal distribution.

Continuous variables are presented as mean ± standard deviation, whereas categorical variables are expressed as frequencies and percentages. Comparisons between two independent groups for continuous variables were performed using the independent samples t-test. Associations between categorical variables, including

hearing outcomes and NIV status, were evaluated using the chi-square test.

To control for potential confounders, binary logistic regression analysis was performed, incorporating variables such as NIV, sepsis, prolonged NICU stay (>5 days), exposure to ototoxic medications (vancomycin and gentamicin), as well as 1st and 5th minute APGAR scores and birth weight. Statistical significance was defined as a p-value of <0.05.

Results

The study population consisted predominantly of late preterm and term infants in both the NIV and control groups. The demographic characteristics of the patients included in the study are presented in Table 2. Infants who received NIV had significantly lower 1-minute (p=0.04) and 5-minute Apgar scores (p=0.01) than those who did not receive NIV. No significant differences were observed between the groups in terms of birth weight, gestational age, or sex distribution (all p>0.05). Among infants who received NIV, the most common treatment duration was 24-72 hours, accounting for 42.5% of cases.

The relationship between receiving NIV and failing the hearing test is analysed in Table 3. A significantly higher proportion of ABR1 failure was observed in infants who did not receive NIV (p=0.001), whereas ABR2 and BERA outcomes did not differ significantly according to NIV status (p>0.05). NIV: non-invasive ventilation; ABR: auditory brainstem response; BERA: brainstem evoked response audiometry.

Factors Associated with ABR1 Failure

Factors influencing ABR1 failure were evaluated using binary logistic regression analysis (Table 4). The overall model fit was statistically significant (χ^2=99.085, p<0.001).

The analysis demonstrated that a lower 5-minute APGAR score and prolonged NICU stay (>5 days) were independently associated with an increased risk of ABR1 failure. Specifically, each unit increase in the 5-minute APGAR score was associated with a reduced likelihood of ABR1 failure (B=-1.07; p<0.001; OR=0.34).

In contrast, a NICU stay exceeding 5 days was associated with an approximately six-fold increase in the odds of ABR1 failure (B=1.78; p=0.04; OR=5.94).

No statistically significant associations were observed between ABR1 failure and non-invasive ventilation, sepsis and vancomycin (all p>0.05).

Table 1 Turkish Neonatal Asociation Guidelines for respiratory support

Non-invasive (nasal) ventilation	Invasive ventilation
Delivery room: CPAP support should be provided	If intubation is required: synchronised ventilation with a tidal volume target is recommended.
nCPAP: It is recommended to be performed with	HFOV can be tried as a rescue approach in babies who cannot be ventilated with tidal volume targeted synchronous ventilation.
CPAP support should be started with FiO_2 = 21-30% and PEEP = 5 cmH_2O.	It is necessary to avoid hypocarbia and hypercarbia during mechanical ventilation.
nCPAP failure criteria: PEEP≥7 cmH_2O and FiO_2 requirement>40%	It is recommended to keep the duration of mechanical ventilation as short as possible to increase the success of extubation.
NIPPV: If nCPAP failure criteria are present, spontaneous respiration is inadequate, or respiratory acidosis develops, it should be tried before intubation.	It is recommended to provide non-invasive respiratory support after weaning from mechanical ventilation.
HHHFNC: Not recommended for primary respiratory support in small premature babies who are candidates for BPD	Target oxygen saturation: recommended to be 90-94%

BPD, bronchopulmonary dysplasia; CPAP, continuous positive airway pressure; nCPAP, nasal continuous positive airway pressure; NIPPV, nasal intermittent positive pressure ventilation; PEEP, positive end-expiratory pressure; FiO_2, fraction of inspired oxygen; HHHFNC, heated humidified high-flow nasal cannula; HFOV, high-frequency oscillatory ventilation.

Factors Associated with ABR2 Failure

Binary logistic regression analysis demonstrated that neonates diagnosed with sepsis had a 92% higher odds of ABR2 failure compared with those without sepsis (Table 5).

A higher 1-minute APGAR score showed a trend towards a reduced risk of ABR2 failure; however, this association did not reach statistical significance (B=-0.68; Wald=3.43; p=0.06).

No statistically significant associations were identified between ABR2 failure and non-invasive ventilation (p=0.88), vancomycin exposure (p=0.78), gentamicin exposure (p=0.17), 5-minute APGAR score (p=0.75), or prolonged NICU stay (>5 days) (p=0.57).

Factors Associated with BERA Outcomes

As all infants diagnosed with sepsis had normal BERA results, these cases were excluded from the BERA-specific analysis. Table 6 presents the results of the analyses identifying the factors associated with BERA outcomes.

Table 2 Comparison of socio-demographic characteristics of infants with their non-invasive ventilation (NIV) status

Characteristics		**NIV status**						**Test statistics**	**P**
		Received		**Not received**		**Total**			
		Mean±SD		**Mean±SD**		**Mean±SD**			
Weight		2896.23 ± 669.61		2950.48 ± 665.15		2920.43 ± 667.75		-1.14**	0.25
Birth week		36.54 ± 3.11		36.86 ± 3.13		36.68 ± 3.12		0.68**	1.15
1st-minute APGAR score		6.53 ± 1.35		6.73 ± 1.42		6.62 ± 1.38		-2.07**	**0.04***
5th-minute APGAR score		7.67 ± 1.28		7.9 ± 1.32		7.78 ± 1.3		-2.49**	**0.01***
		n	%	n	%	n	%		
Gender	Male	251	57.7	184	42.3	435	100.0	2.07***	0.15
	Female	191	52.6	172	47.4	363	100.0		
	Total	442	55.4	356	44.6	798	100.0		
Duration of NIV	2-6 hours	6-24 hours	24-72 hours	72-96 hours	96 hours				
Total:442	N: 34	N: 132	N: 188	N: 84	N: 4				
	7.69%	29.86%	42.53%	19%	0.9%				

Percentages are based on row totals. *p<0.05; **Independent sample T-test; *** Chi-square test

Data are presented as mean ± standard deviation (SD) or number (%). Continuous variables were compared using the independent-samples t test, while categorical variables were analysed using the chi-square test.

Table 3 Comparison of non-invasive ventilation (NIV) status and hearing test outcomes (ABR1, ABR2, BERA)

Test	**Outcome**	**Received NIV (n, %)**	**No NIV (n, %)**	**Total (n, %)**	**χ^2**	**p-value***
ABR1	Passed	416 (57.2%)	311 (42.8%)	727 (100%)	11.11	0.001
	Failed	26 (36.6%)	45 (63.4%)	71 (100%)		
ABR1 Total		442 (55.4%)	356 (44.6%)	798 (100%)		
ABR2	Passed	423 (55.9%)	334 (44.1%)	757 (100%)	1.43	0.15
	Failed	19 (46.3%)	22 (53.7%)	41 (100%)		
ABR2 Total		442 (55.4%)	356 (44.6%)	798 (100%)		
BERA	Passed	430 (55.7%)	342 (44.3%)	772 (100%)	0.93	0.22
	Failed	12 (46.2%)	14 (53.8%)	26 (100%)		
BERA Total		442 (55.4%)	356 (44.6%)	798 (100%)		

Percentages are based on row totals. *p<0.05.

Data are presented as n (%). Percentages were calculated within rows. Comparisons between infants who received and did not receive NIV were performed using the chi-square test.

According to the analysis, no statistically significant associations were found between BERA failure and the use of NIV (p=0.44), exposure to vancomycin (p=0.60), or gentamicin (p=0.50). Likewise, APGAR scores at 1 minute (p=0.56) and 5 minutes (p=0.84), as well as prolonged NICU stay (>5 days) (p=0.24), were not significantly associated with BERA outcomes.

Discussion

To the best of our knowledge, this study represents only the second investigation in the literature comparing hearing outcomes in neonates receiving NIV with those receiving no respiratory support.

Although concerns have been raised that non-invasive ventilation may generate elevated environmental noise levels and thereby increase the risk of neonatal hearing impairment, current evidence remains limited and inconclusive. In a study of 344 neonates, Rastogi et al reported that the risk of hearing impairment was higher among infants receiving any form of respiratory support. However, no significant difference was observed between infants treated with nCPAP and those receiving mechanical ventilation.[10] These findings are not consistent with the results of the present study.

In a retrospective cohort study conducted at Zagazig University Hospital in Egypt, including 30 preterm infants, it was reported that MV and nCPAP did not significantly differ in their effects on auditory function. However, the small sample size limits the generalisability and robustness of these findings.[11]

In the present study, hearing outcomes were evaluated in both term and preterm infants. Although non-invasive ventilation was associated with a higher rate of ABR1 failure, no significant differences were observed in ABR2

Table 4 Factors affecting ABR1failure status

	B	S.E.	Wald	P	Exp (B)	95% CI Lower	95% CI Upper
Birth weight	0.26	0.79	0.11	0.75	1.29	0.28	6.02
NIV status (Reference: Did not receive)	0.19	0.67	0.08	0.77	1.21	0.33	4.47
Vancomycin (Reference: Did not receive)	0.20	0.30	0.46	0.50	1.22	0.68	2.19
Gentamicin (Reference: Did not receive)	0.56	0.30	3.47	0.06	1.75	0.97	3.17
1st minute APGAR score	-1.07	0.34	9.63	**0.00**	0.34	0.17	0.67
5th minute APGAR score	1.78	0.88	4.09	**0.04**	5.94	1.06	33.37
Staying in NICU for more than 5 days (Reference = No)	0.50	0.77	0.42	0.52	1.65	0.36	7.44
Presence of sepsis (Reference = No)	-4.10	0.68	36.02	**0.00**	0.02	0.00	0.06

Model performance: χ^2=99.085 (p<0.001); Cox & Snell R^2=0.117; Nagelkerke R^2=0.259; overall classification accuracy=93.1%.

Note: The Hosmer–Lemeshow test was significant (p<0.001), suggesting that the model fit should be interpreted with caution.

Table 5 Factors affecting ABR2 failure status

Feature	B	S.E.	Wald	P	Exp (B)	95% CI Lower	95% CI Upper
Birth weight	0.62	0.79	0.62	0.43	1.85	0.40	8.63
NIV status (Reference: Did not receive)	-0.10	0.67	0.02	0.88	0.90	0.24	3.34
Vancomycin (Reference: Did not receive)	0.10	0.35	0.07	0.78	1.10	0.56	2.18
Gentamicin (Reference: Did not receive)	0.45	0.33	1.91	0.17	1.57	0.83	2.96
1st minute APGAR score	-0.68	0.37	3.43	0.06	0.50	0.24	1.04
5th minute APGAR score	0.23	0.70	0.11	0.75	1.25	0.32	4.91
Staying in NICU for more than 5 days (Reference = No)	-0.44	0.78	0.32	0.57	0.64	0.14	2.99
Presence of sepsis (Reference = No)	-2.54	0.51	24.54	**<0.01**	0.08	0.03	0.22

Model performance: χ^2=33.085 (p<0.001); Cox & Snell R^2=0.041; Nagelkerke R^2=0.122; overall classification accuracy=94.9%.

Note: The Hosmer–Lemeshow test was significant (p<0.001), suggesting that the model fit should be interpreted with caution.

or BERA outcomes. Accordingly, these findings suggest that non-invasive ventilation is not associated with permanent hearing impairment (Table 3).

In a retrospective cohort study of 331 neonates admitted to the NICU, Ekmen et al reported that gentamicin exposure did not adversely affect hearing outcomes when administered for short durations (5-7 days), at extended dosing intervals (24-48 hours), and without concomitant use of other ototoxic agents such as loop diuretics.[12]

Similarly, in the present study, exposure to gentamicin, vancomycin, and furosemide was not associated with abnormal hearing test results.

In a study conducted between 2002 and 2006 at Turku University Hospital, Germany, brainstem auditory evoked potentials (BAEP) and hearing thresholds in preterm infants with a birth weight ≤1500 g and/or gestational age ≤32 weeks were evaluated using brainstem audiometry. The aim was to investigate whether the duration of CPAP influenced auditory pathway function. The authors reported that prolonged CPAP exposure was associated with increased latencies of BAEP components III (p=0.01) and V (p=0.02) in the right ear, suggesting a potential adverse effect on central auditory conduction.[13] However, follow-up assessments performed at a corrected age of one month demonstrated recovery of these prolonged latencies. This finding is consistent with previous evidence indicating that BAEP latencies decrease with maturation,[14,15] supporting the notion that such electrophysiological alterations may be transient in nature.

In line with these observations, the present study demonstrated that NIV was associated with abnormal early hearing screening results; however, this effect was not observed in subsequent ABR or BERA assessments, suggesting that the observed impairment is likely transient rather than permanent.

An additional and unexpected finding in our study was that, although neonates diagnosed with sepsis who met the inclusion criteria showed an increased risk of ABR2 failure, all subsequently demonstrated normal BERA results. This may be attributed to the relatively small number of confirmed sepsis cases, as well as the exclusion of 12 critically ill infants who required mechanical ventilation and were therefore not included in the analysis.

Limitations

This study has several limitations. First, the relatively small number of neonates with sepsis, together with variability in statistical outcomes across analyses, limited the ability to fully evaluate the potential effect of sepsis on auditory test results. Accordingly, further studies with larger sample sizes are required to clarify the relationship between sepsis and neonatal hearing outcomes.

Second, although an association between NIV and abnormal early hearing screening results was observed, this effect was not sustained in subsequent assessments. As such, data regarding the potential long-term auditory effects of NIV remain limited. More comprehensive longitudinal studies are therefore warranted to evaluate long-term hearing outcomes in this population.

Table 6 Factors affecting BERA failures

Feature	B	S.E.	Wald	P	Exp (B)	95% CI Lower	95% CI Upper
Birth weight	1.32	0.82	2.59	0.11	3.73	0.75	18.53
NIV status (Reference: Did not receive)	-0.54	0.71	0.58	0.44	0.58	0.15	2.33
Vancomycin (Reference: Did not receive)	-0.23	0.43	0.28	0.60	0.80	0.35	1.84
Gentamicin (Reference: Did not receive)	-0.29	0.43	0.45	0.50	0.75	0.32	1.74
1st minute APGAR score	0.28	0.48	0.34	0.56	1.33	0.51	3.42
5th minute APGAR score	-0.15	0.74	0.04	0.84	0.86	0.20	3.65
Staying in NICU for more than 5 days (Reference = No)	-0.95	0.81	1.37	0.24	0.39	0.08	1.90

Model performance: χ^2=22.773 (p<0.001); Cox & Snell R^2=0.028; Nagelkerke R^2=0.113; overall classification accuracy=96.7%.

Note: The Hosmer–Lemeshow test was non-significant (p=0.531), indicating an acceptable model fit.

Conclusion

This study investigating the effect of non-invasive ventilation on neonatal hearing outcomes demonstrated that NIV was associated with abnormal early hearing screening results. However, this effect was not observed in follow-up ABR or BERA testing, suggesting that the impact is transient rather than permanent. Nevertheless, well-designed prospective controlled studies with larger cohorts are required to further elucidate the potential effects of NIV on neonatal auditory function.

Declaration of Interest

The authors declare that they have no conflicts of interest.

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