

## Hearing Threshold of Auditory Brainstem Response in Term Neonates with Hyperbilirubinemia

Fatemeh Eghbalian<sup>1</sup>, Farhad Farahani<sup>1</sup>, Amirreza Monsef Esfehiani<sup>1</sup>, Ehsan Mazloumi<sup>1</sup>, Manoochehr Karami<sup>2</sup>, Mohammad Jafari<sup>1</sup>

1. Hearing Disorders Research Center, Hamadan University of Medical Sciences, Hamadan, Iran
2. Modeling of Noncommunicable Diseases Research Center, Hamadan University of Medical Sciences, Hamadan, Iran



### ABSTRACT

**Background:** Neonatal jaundice is a common cause of premature neonatal hearing loss and is a major cause of childhood deafness, especially in developing countries. The aim of this study was evaluating Hearing threshold of Auditory Brainstem Response (ABR) in term neonates admitted with hyperbilirubinemia at a range of exchange transfusion and near exchange transfusion.

**Methods:** This cross-sectional study was performed on 134 healthy term infants admitted due to hyperbilirubinemia in the neonatal care unit of Besat Hospital in Hamadan from March 2017 to September 2017. All neonates were evaluated by Otoacoustic Emission (OAE) and ABR after admission in neonatal ward and after treatment by intensive phototherapy or blood exchange. Data were collected and analyzed through SPSS software and using Chi-square and Mann-Whitney tests. The significance level was considered at 0.05 for all statistical tests.

**Results:** The mean weight of newborns was  $3000 \pm 350$  gr and the mean of gestational age was  $39 \pm 2$  weeks. Bilirubin concentration of the infants was  $36.9 \pm 9.2$  mg/dL. There was a significant difference between hearing loss on auditory brainstem response in term neonates according to hyperbilirubinemia in blood exchange range ( $P = 0.001$ ). However, there was no significant difference between hearing loss on auditory brainstem response in term neonates according to the gestational age, sex and phototherapy ( $P > 0.05$ ).

**Conclusion:** Our findings indicated that high bilirubin levels in the range of exchange transfusion can be an important risk to the auditory system, which without creating kernicterus, can interfere with auditory tests.

**Keywords:** Hyperbilirubinemia, Auditory Brainstem Response, term Neonate exchange transfusion

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\*Correspondence: Fatemeh Eghbalian; Email: eghbalian\_fa@yahoo.com

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## Introduction

**J**aundice is a common problem during the neonatal period and can cause serious problems, such as Kernicterus. Neonatal hyperbilirubinemia is a common clinical problem in first days. Nearly 60% of term neonates and 80% of preterm neonates are expected to present with neonatal jaundice (1).

Indirect bilirubin, a major cause of neonatal jaundice, is highly neurotoxic. The auditory pathway is one of the most sensitive parts of the central nervous system to bilirubin-induced toxicity (2-5).

Hearing plays a major role in intelligence evolution. Early diagnosis and initiation of supportive care in early infancy can reduce the severity of these problems (4, 6-9). Studies have shown that auditory pathway and snail ways, especially external hair cells and brainstem damages in hyperbilirubinemia result in hearing loss (2, 3, 5-8, 10-19). Hearing impairment is one of the most common congenital anomalies, if not identified promptly causes delay in growth, speech, cognition and disrupts language learning and perception in children. In less than 6 months old patients with rapid diagnosis of the disease and early intervention, speaking and understanding have shown no difference compared to healthy children (8, 10-18).

Regarding the variable range of clinical symptoms of kernicterus and lack of relevant testing to evaluate the complications of hyperbilirubinemia, an effective and noninvasive way to evaluate the side effects of jaundice is ABR. This method examines the condition of the auditory nerve and the brain's auditory pathways (2-5, 20). In this study, we evaluated hearing threshold of auditory brainstem response in term infants who were admitted with hyperbilirubinemia at the level of blood transfusion and near exchange transfusion.

## Materials and Methods

This cross-sectional study was studied 134 neonates with icter who were admitted in the Neonatal ward of Hamadan Besat Hospital during 6 months (March 2017 to September 2017). Samples were selected by census method. The research protocol was approved by Hamadan University of Medical Sciences Ethics Committee (IR.UMSHA.REC.1396.197).

All neonates admitted to hospital because of Hyperbilirubinemia to undergo severe phototherapy or blood transfusion were included. Exclusion criteria included hospitalization for other reasons than hyperbilirubinemia, with the presence of any type of anomalies or syndromic phenotypes, history of any hearing impairment prior to the admission in infant or in family and any confounding factors, such as the history of asphyxia and drug use.

The data collection tool included a pre-designed checklist based on the specific objectives of the plan, including: gestational age, sex, blood transfusion status, intensive phototherapy status, OAE and ABR status after the treatment. All neonates were evaluated by OAE and ABR after being admitted in the neonatal ward and after the treatment by intensive phototherapy or exchange transfusion.

Hearing threshold of auditory brainstem response and transient evoked otoacoustic emission tests were performed in the audiology laboratory at the Besat hospital. In this study, all patients were first subjected to OAE test, then underwent ABR test.

In OAE test, a miniature earphone and microphone are placed in the ear, sounds are played and the response is measured. If the patient hears normally, an echo is reflected back into the ear canal and is measured by the microphone. When the patient has a hearing loss, no echo or a reduced echo can be measured.

For ABR test, small surface electrodes are attached to the head at several places. An earphone is placed in the ear, brief sounds are played, and the electrical signals (v signals) across the electrodes are recorded. ABR is interpreted by audiologist. The type of abnormalities in ABR is based on the numerical value obtained from the last V wave. The ABR interpretation standard is based on the db HL unit. The standard criteria for neonate is according to the Handbook of Audiometry Jack zatz (21).

Auditory with ABR is based on the intensity of the V wave in about 6 milliseconds, which have frequency band between 1-4 Khz and are classified according to Table 1.

**Table 1.** Classification of Hearing Threshold of Auditory Brainstem Response

0-25 db	Normal
25-40 db	Mild
40-55 db	Moderate
55-70 db	Moderate to Severe
70-90 db	Severe
90< db	Profound

Independent t-test was used to compare the means in normal data. Mann-Witney test was used for abnormal data. Statistical analysis was carried out through SPSS20 and  $P < 0.05$  was considered as statistically significant level.

## Results

The mean weight of newborns was  $3000 \pm 350$  gr and the mean of gestational age was  $39w \pm 2w$ . Means of age and bilirubin concentration of the infants were  $7.17 \pm 7.7$  days and  $36.9 \pm 9.2$  mg/dL, respectively. About 44% of infants were male and 55.3% were females.

As it is seen in Table 2, the majority of term neonates had no problems in the right and left ears, but 7.5% of the neonates had moderate hearing impairment of the brainstem in the left ear and 6% in the right ear. Also, OAE test was normal in all newborns and there was no auditory neuropathy in them.

**Table 2.** Hearing Threshold of Auditory Brainstem Response in the studied term neonates with Hyperbilirubinemia

	Hearing Response	Number	Percentage
Left Ear	Normal	112	83.6
	Mild	4	3
	Moderate	10	7.5
	Moderate To Severe	2	7.5
	Sever	2	1.5
	Deep	4	3
Right Ear	Normal	110	82.1
	Mild	8	6
	Moderate	4	3
	Moderate To Severe	4	3
	Sever	2	1.5
	Deep	6	4.5

Table 3 shows there was no significant difference in hearing impairment of brainstem in the hospitalized term neonates based on Sex ( $P=0.763$ ) and Gestational age ( $P = 0.082$ ). But, there was a statistically significant difference in

hearing loss on auditory brainstem according to blood exchange ( $P = 0.001$ ). However, there was no significant difference between brainstem hearing impairment in neonates according to phototherapy ( $P = 0.278$ ).

**Table 3.** Hearing Threshold of Auditory Brainstem Response in term neonates with high bilirubin in terms of sex, blood exchange and phototherapy

Variable	Category	Brain stem auditory Response impairment		P Value
		No	Yes	
		Number (percent)	Number (percent)	
Sex	Male	14 (24.1)	44 (75.9)	0.763
	Female	14 (13.9)	62 (86.1)	
Gestational age	Term	16 (19.3)	67 (80.7)	0.082
	Pre-term	12 (23.5)	39 (76.5)	
Blood exchange	Yes	14(70)	6 (30)	0.001
	No	14 (12.3)	100 (87.7)	
Phototherapy	Yes	24 (19.4)	100 (80.6)	0.278
	No	4 (40)	6 (60)	

## Discussion

Early detection of jaundice complications is one of the most important Issues of this disease. In indirect hyperbilirubinemia without treatment, due to lipid solubility, it can pass through the blood-brain barrier and spread into

the brain, which is a potential damage to the nervous system (1).

One of the neurological complications in these patients is the result of bilirubin aggregation in the auditory nuclei followed by hearing impairment (2-9).

In the present study, there was no statistically significant difference in hearing impairment of brainstem in hospitalized neonates based on gender and gestational age, which was consistent with the results of Nabavi *et al.* (17). According to the findings of the present study, there was a significant difference in hearing loss on auditory brainstem response in term neonates based on blood exchange which is coincided with the results of Agrawal *et al.* study on 30 infants with jaundice. They have reported that in 23% of infants, ABR wave did not appear (11).

In the study of Eghbalian *et al.*, of 24 neonates, at least one IV-V wave complex did not appear (15) and in the study of Nwaesei *et al.*, from 9 neonates with jaundice, 3 patients did not have brainstem responses before blood exchange, which appeared after blood exchange (18). In the Deorari *et al.* study, from 18 cases of term neonates with jaundice, 8 cases had no complex of IV-V, which became normal after blood exchange (14). All of these cases indicated an improvement in acute brainstem damage and acute hearing tracks poisoning following blood exchange. According to several studies, high bilirubin levels can be an important risk to the auditory system which, without causing kernicterus, make hearing tests abnormal (2, 3, 5). However, it is unclear whether this abnormal auditory state is long-term or permanent, and long-term research is required to investigate this issue (20).

The results of this study showed that there was no statistically significant difference in ABR in term neonates according to phototherapy. This result is in line with the results of Lee *et al.*, Which showed that icteric infants under intensive phototherapy had normal ABR and there was no significant difference in the latency time of the V wave compared to the control group (22). In the study of Nabavi *et al.*, 13% of the infants who underwent phototherapy because of hyperbilirubinemia had abnormal ABR, which was not significantly different from treatment with ET and phototherapy (17). In another study, there was a relationship between

hyperbilirubinemia, weight less than 1500 g, cesarean section and impaired ABR results. The most common risk factors of hearing loss are hyperbilirubinemia, asphyxia, birth weight less than 1500 g, septicemia, convulsion, and meningitis (15, 23). According to the results of similar studies, it can be said that auditory track is one of the most sensitive parts of the nervous system in relation to the toxic effect of bilirubin (5, 24). Therefore, jaundice in newborns is one of the common causes of sensory neural deafness and is a major cause of childhood deafness especially in developing countries. The indirect passage of bilirubin and its aggregation in the ventricular auditory cells cause sensory-neural hearing loss (2-19). Although the sample size of this study is acceptable like many similar studies, it is recommended that studies with greater sample size and in different neonatal age groups be considered.

## Conclusion

Hyperbilirubinemia can impair infant's hearing without causing Kernicterus. In our study, some of icteric infant who just underwent phototherapy and did not have exchange transfusion, showed hearing impairment. So, according to the results of this study, it is necessary that infants with low bilirubin levels who are not hospitalized be tested for hearing impairment and ABR and OAE tests are recommended in them.

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