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Risk Factors for Hearing Loss in Infants: A Systematic Review

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ABSTRACT

Background & Objective: Hearing loss as a sensory disorder is among the most common developmental disorders. Based on the universal neonatal screening results, the incidence of hearing deficit is 1–3 per 1000 live births in the well-baby nursery population and 2–4 in 100 newborns in the intensive care community. The aim of this study was to highlight the main risk factors for hearing loss based on the existing evidence.

Materials & Methods: We searched all observational studies related to risk factors of hearing loss from 1990 to 2019 in PubMed, Scopus, Web of Science, Science direct, and google scholar search engines. Quality of the included studies was evaluated by the STROBE checklist. Totally, 17 observational studies met our inclusion criteria.

Results: In most of the reviewed studies, the relations between hearing loss in infants and some maternal and neonatal variables such as ventilatory support, craniofacial anomalies, hyperbilirubinemia, meningitis, Apgar scores, sepsis, asphyxia, stay in intensive care units, respiratory distress syndrome, and pulmonary surfactant were statistically significant.

Conclusion: Our results indicated that ventilator support, craniofacial anomalies, low birth weight, and hyperbilirubinemia were the main statistically significant risk factors for hearing-loss.

Keywords: Infants, Hearing Loss, Systematic Review

Introduction

Hearing is the ability by which the neonate is related to the world of voice and language. Oral language connects humans with one another, and develops the capability to share their thoughts, experiences, and views in search for new knowledge (1).

Hearing deficit is one of the most widespread developmental disorders, and deafness is the most common sensory disorder. Based on the universal neonatal screening results, the incidence of hearing deficit is 1–3 per 1000 live births in the well-baby nursery population and 2–4 in 100 newborns in the intensive care community (2-7).

Hearing loss is known as one of the most common sensory disorders in newborns, with an estimated incidence varying from 0.5 to 5 per 1000 cases reported from different countries worldwide (3). Previous studies have shown remarkable differences in hearing impairment between developed and developing countries so that an incidence of 2 to 4 per 1000 births for congenital bilateral hearing impairment is reported in developed countries, while the rate estimated for the developing countries is higher and not lower than 6 per 1000 live births (8).

Based on the existing evidence, the occurrence of permanent congenital hearing loss in neonates admitted to neonatal intensive care unit (NICU) is 10 to 20 times higher than in the general population (9). The incidence of hearing loss is approximately 28 times the prevalence of congenital phenolics, 20 times higher than hemoglobinopathy, 8 times that of hypothyroidism, and 5 times that of systolic fibrosis, making it the most common congenital defect in neonates (10).

Though the definition of hearing deficit and hearing loss may vary in different categorization systems hearing loss is categorized into profound (> 95 dB HL), severe (71–95 dB HL), moderate (41–70 dB HL), and mild (21–40 dB HL). In fact, deafness is the term reserved for profound hearing loss (11). The thresholds of 1527–1538 are expressed in dB on the hearing level scale (dB HL) (7).

Many previous researches such as the studies of Meyer et al., **(9)** Yoshinaga-Itano **(12)**, and Yoshikawa et al., **(13)** were conducted to examine risk factors associated with hearing loss. However, these studies have some controversial results. Some of the previous studies addressed the need to continue to determinate additional risk factors for hearing loss. It may even be stated that hearing loss risk factors in developed countries have actually decreased because of the proper counseling programs and advanced medical care. Indeed, in developed countries infants are not exposed to extra environmental factors which may be present in many developing countries, that can increase the risk of hearing loss in infants. Although there are many studies on the risk factors of hearing loss in most developed countries, little research is available in developing countries, including countries in the Middle East **(8)**. Many previous studies have shown that more than 50% of deaf infants have no known risk factors **(3, 14-18)**.

About half of children with permanent congenital hearing loss have one of the following risk factors: NICU admission, perinatal infection, family history of hearing loss, LBW or VLBW, asphyxia, head and facial deformity, jaundice and chromosomal abnormality **(19)**. Also, hyperbilirubinemia was the risk factor for hearing loss. The second main risk factor was Apgar scores of 0–4 at 1 min, followed by TORCH infections. To our knowledge, there is no comprehensive or systematic review about hearing loss risk factors in newborns and infants. Indeed, knowledge of which risk factors are more probable to cause hearing loss in infants can be helpful in planning for follow-up implementation of preventive measures based on modifiable risk factors. **(13)**. The main objective of this systematic review was to review the existing evidence and synthesize the results of related studies to determine the main risk factors of hearing impairment in infants.

Materials and Methods

Our study aimed to find all observational articles that assessed and evaluated the factors which probably cause auditory deficiency in newborns from 1990 to 2020. Our interesting inquiry in this systematic review was"What are those environmental and demographic agents significantly related to auditory deficiency or hearing impairment in newborns as a consequence?"

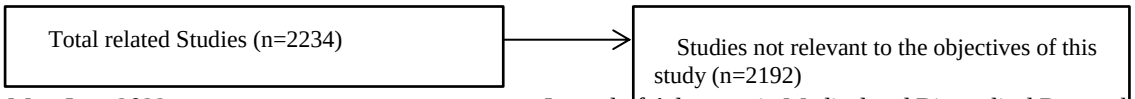
PubMed, Scopus, Web of Science, Science direct and also google scholar search engines were searched for published articles and reports related to the study question. Reference of obtained studies and transactions of related seminars were also searched manually. The search strategy includedinfant AND hearing loss OR hearing impairment OR hearing deficit AND risk factor.

Moreover, articles were entered if they studied the risk agents more likely to cause auditory deficiency in newborns as the consequence; measured any environmental and demographic factors for auditory deficiency in newborns as exposure; were designed in an observational method; and were in different languages. In addition, the evaluation of the quality of the articles was made as follows: released articles in indexed and peer review journals were considered to be the sign of the quality of these articles. Moreover, the quality of the articles published in non-indexed journals, reports, and books published by UN agencies (WHO, UNESCO, UNICEF) and the proceedings of seminars was evaluated by epidemiologists and pediatricians by the STROBE checklists (Strengthening the Reporting of Observational Studies in Epidemiology).

Indeed, the titles and abstracts of the articles were studied by two reviewers independently, a pediatrician and an epidemiologist. Studies and reports likely to be irrelevant by these two reviewers were excluded from the study. The number of excluded studies and their titles were recorded. Then, the full texts of articles and reports were retrieved and referred to two independent teams of reviewers including Pediatricians and Obstetricians. Each group separately pulled out the replies to the research question from the contents of the article and wrote down the essential notes. If there was any discrepancy, the original text of the article was assessed by the study administrator, and necessary decisions were made.

Results

In the first phase of the search, 2234 reports and articles were found based on the searched keywords, of which 2192 titles were irrelevant to our topic and were excluded. After precise evaluation of the 42 remained studies, 17 articles fully met our inclusion criteria. Figure 1 illustrates the process of searching and selecting the articles.



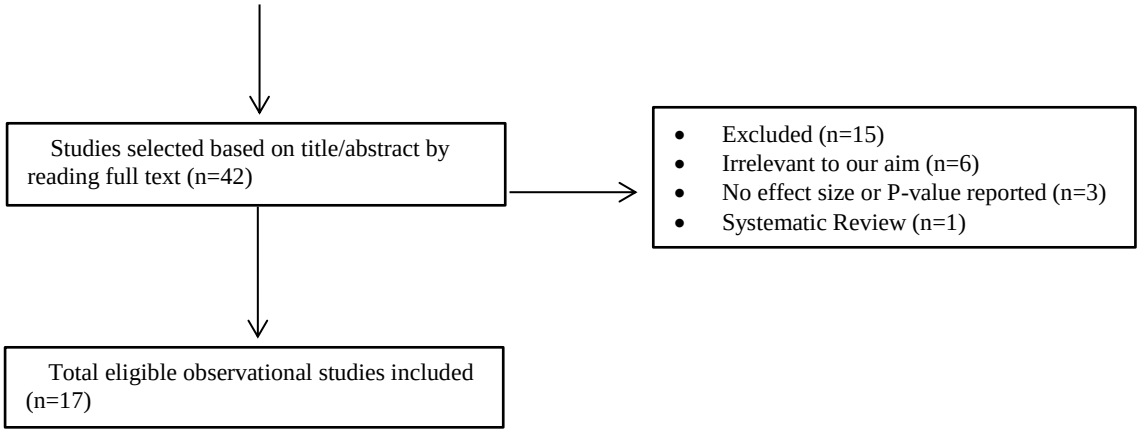


Figure 1. Flowchart of the studies selection

Reports and studies compiled into this systematic review had been published between 1990 and 2019. Nine of the 17 selected researches were prospective cohort studies. Seven and one of the other 11 studies were cross-sectional and retrospective cohort studies, respectively. The characteristics of each selected study including country of study, design, population, time length, sample, statistical model, outcome, odds ratio, and significance values of investigated risk factors are detailed in Table 1.

Overall, most of these studies have examined the association of a large number of maternal and neonatal factors with hearing loss. The main factors assessed as risk factors for hearing loss included ventilatory support, craniofacial anomalies, hyperbilirubinemia, meningitis, Apgar scores, sepsis, asphyxia, intensive care, respiratory distress syndrome, and pulmonary surfactant. The following paragraphs describe how each of these variables relates to the hearing loss.

Four of the17 studies showed statistically significant association between hearing loss in infants with ventilatory support, craniofacial anomalies, low birth weight and hyperbilirubinemia (Table 1).

Three of the 17 studies showed statistically significant association between hearing loss in infants and meningitis, Apgar scores, sepsis and asphyxia. Two studies showed significant associations between hearing loss in infants and intensive care, respiratory distress syndrome and pulmonary surfactant (Table 1).

In addition, several factors were significantly related to the hearing loss in infants in at least one of the reviewed studies. These factors were the age of onset of jaundice, exchange transfusion performed, prenatal steroid use, blood exchange, furosemide consumption, intraventricular hemorrhage, bronchopulmonary dysplasia, type of delivery, dysmorphic features, cerebral bleeding, cerebral infarction, parity, religion, age over 30 days, exclusive breast-feeding, loop diuretics, operation for retinopathy of prematurity, ototoxic drugs, developmental delay, microcephaly, family history of deafness, maternal infection, consanguinity, presence of at least one JCIH[1] risk factor, postnatal hypoxia, ototoxic exposure, forceps delivery, and isolated craniofacial anomalies.

Table 1. Studies included in the systematic review

Author(year) (reference code)	Country	Study design	Study population	Study period	Sample size	Statistical model	Outcome	Main risk factors	OR	95% CI OR	P-value
Boo N et al.,(1994) (20)	Malaysia	Prospective Cohort	Jaundiced term neonates	1984	128	Logistic regression	Hearing loss	Age of onset of jaundice (days)	0.59	0.39-0.89	0.01
								Exchange transfusion performed (no)	0.04	0.002-0.84	0.03
	Australia	Prospective Cohort	Infants with birth	1985-1990	102		Hearing loss	O_2 days >90	4.0	1.1-15.6	0.04

[1] Joint Committee on Infant Hearing

Author(year) (reference code)	Country	Study design	Study population	Study period	Sample size	Statistical model	Outcome	Main risk factors	OR	95% CI OR	P-value
			weights <I000					Max FiO, >0.90	5.6	1.2-26.9	0.03
Leslie GI et al., (1995) (21)						Conditional logistic regression		Plasma Na <125	5.6	1.1-27.8	0.03
								Max pH >7.6	5.6	1.1-89.0	0.03
								Ventilator days	-	-	0.006
Borradori C et al., (1997) (22)	Switzerland	Prospective Cohort	Preterm infants	1987-1991	547	Logistic regression	Hearing loss	Ventilatory support (day)	-	-	0.001
								Intensive care (day)	-	-	0.005
								Days in the intensive care unit (average)	-	-	0.004
Kountakis SE et al (1997) (23)	US	Prospective Cohort	Consecutive infants	1986-1990	50	Student's t-test	Hearing loss	Respiratory distress syndrome	-	-	0.03
								Craniofacial anomalies	-	-	0.4
								Bilirubin >lO µmol/L	-	-	0.2
								Days of ventilatory support (>5)	-	-	0.001
Kountakis SE et al., (2002) (24)	US	Prospective Cohort	Consecutive neonates	1993-1998	110	Chi-square test	Hearing loss	Craniofacial anomalies (ie, atresia(	-	-	0.001
								Bacterial meningitis	-	-	0.001
								Syndrome with hearing loss	-	-	0.001
								Asphyxia	-	-	0.001
Hille ET et al., (2007) (25)	Netherland	Prospective Cohort	NICU infants	1998-2002	2186	Logistic regression	Hearing loss	Birth asphyxia	1.7	1.01-2.7	0.01
								Assisted ventilation	3.6	2.1-6.0	0.001
								Prenatal steroid use	0.37	0.19-0.73	<0.001
								Pulmonary surfactant	0.33	0.17-57	<0.001
Martínez-Cruz CF et al., (2008) (26)	Mexico	Prospective Cohort	NICU infants	1990-2005	418	Chi-square test	Hearing loss	Blood exchange	8.17	4.12-16.19	<0.001
								Meningitis	4.36	1.73-10.97	0.002
								Furosemide	3.83	2.42-6.06	<0.001
								Intraventricular hemorrhage	7.10	4.34-11.60	<0.001

Author(year) (reference code)	Country	Study design	Study population	Study period	Sample size	Statistical model	Outcome	Main risk factors	OR	95% CI OR	P-value
								Bronchopulmonary dysplasia	4.69	3.00-7.33	<0.001

Table 1. **Studies included in the systematic review (continued)**

Author(year) (reference code)	Country	Study design	Study population	Study period	Sample size	Statistical model	Outcome	Main risk factors	OR	95% CI OR	P-value
Taghdiri MM et al., (2008) (1)	Iran	Cross-sectional	NICU infants	2005-2006	834	Chi-square test	Hearing loss	Hyperbilirubinemia	-	-	0.001
								Birth weight (1500g and higher)	-	-	0.002
								Type of delivery (Cesarean section)	-	-	0.005
Coenraad S et al., (2010) (27)	The Netherlands	Prospective Cohort	NICU infants	2004-2009	103	Chi-square test	Hearing loss	Dysmorphic Features	-	-	<0.001
								Apgar 1min	-	-	0.01
								Sepsis	-	-	0.003
								Meningitis	-	-	0.01
								Cerebral bleeding	-	-	0.01
								Cerebral infarction	-	-	<0.001
Olusanya BO (2011) (28)	Nigeria	Cross-sectional	Infants aged 0–3 months attending health clinics for routine BCG immunization	2005-2008	6585	Logistic regression	Hearing loss	Parity (Multiparous)	2.31	1.11 – 4.82	0.02
								Religion (Christianity)	0.33	0.13 – 0.87	0.02
								Age over 30 days	4.68	2.36 – 9.27	<0.001
								Exclusive breast-feeding	0.09	0.01 – 0.78	0.02
								Hyperbilirubinemia	5.05	2.04 – 12.51	<0.001
Biswas AK et al., (2012) (29)	India	Cross-sectional	Infants with age range of 2 days to 6 months	2006-2009	490	Chi-square test	Hearing loss	Apgar score: 0–4 at 1 min, 1–6 at 5 min	-	-	
								Oto toxic medication	-	-	
								TORCH infections	-	-	

Author(year) (reference code)	Country	Study design	Study population	Study period	Sample size	Statistical model	Outcome	Main risk factors	OR	95% CI OR	P-value
Eras Z et al., (2014) (30)	Turkey	Retrospective cohort	Preterm infants born with a gestational Age 32 weeks and/or birth weight 1,500 g, hospitalized in the NICU	2009-2011	1360	Multinominal logistic regression	Hearing loss	Bacterial meningitis	-	-	
								Proven sepsis	5.5	1.01 - 1.63	0.01
								Mechanical ventilation ≥5 days	6.3	1.5-12.1	0.02
								Loop diuretics	12.7	4.8-25.3	<0.001
								Patent ductus arteriosus ligation	4.6	0.73 - 42.4	0.01
								Operation for retinopathy of prematurity	3.5	1.2-11.3	0.01
Mukherjee SS et al., (2013) (31)	India	cross-sectional comparative	Infants of 6 months to 1 year of age	-	127	Multiple logistic regression	Hearing loss	Ototoxic drugs	21.42	1.98 - 230.66	0.01
								Developmental delay	4.33	1.09 - 17.10	0.03
								Cranio-facial abnormality	20.13	1.37 - 298.15	0.02
								Microcephaly	6.88	1.34 - 35.14	0.02
								Family h/o deafness	41.89	2.87 - 611.01	0.006

Table 1. Studies included in the systematic review (continued)

Author(year) (reference code)	Country	Study design	Study population	Study period	Sample size	Statistical model	Outcome	Main risk factors	OR	95% CI OR	P-value
Karaca ÇT et al., (2014) (32)	Turkey	Cross-sectional	Every newborn infant with one or more of defined risk factors	2009 - 2012	2284	Chi-square test	Hearing loss	Birth type (Vaginal birth)	-	-	0.02
								Maternal infection	-	-	0.01
								Consanguinity of parents	-	-	0.02

Author(year) (reference code)	Country	Study design	Study population	Study period	Sample size	Statistical model	Outcome	Main risk factors	OR	95% CI OR	P-value
Abu-Shaheen A et al., (2014) (8)	Jordan	Cross-sectional	Every newborn infant in 37 hospitals and mother-child clinics distributed across the entire country	2007-2008	63041	Logistic regression	Hearing loss	Low birth weight	-	-	0.03
								Age	2.58	1.14-6.30	<0.001
								Admission to NICU > 5 days	1.83	1.11-4.77	0.02
								Birth weight (kg)	5.63	2.62-13.88	<0.001
								Presence of at least one JCIH risk factor	1.71	1.43-4.85	<0.001
								Postnatal hypoxia	3.38	1.13-7.88	0.004
Poonual W et al., (2016) (33)	Thailand	prospective cohort study	all infants (aged 3 months) in Uttaradit, Buddhachinaraj, , and hospitals	2010-2012	13120	Multivariable risk regression	Hearing loss	Forceps delivery	1.33	1.05-5.33	0.03
								Birth weight 1,500–2,500 g	1.6	1.1-2.6	0.02
								APGAR score <6 at 5 minutes	2.2	1.1-4.4	0.02
								Craniofacial anomalies	2.5	1.6-4.2	<0.001
								Sepsis	1.8	1.0-3.2	0.04
								Ototoxic exposure	4.1	1.9-8.6	<0.001
Wroblewska-Seniuk K et al., (2018) (7)	Poland	Cross-sectional	Infants born at the university hospital in poznan	2010-2013	27935	Chi-square and kruskal-Wallis tests	Hearing loss	Isolated craniofacial anomalies	-	-	<0.05
								Hyperbilirubinemia requiring intensive phototherapy	-	-	<0.05
Araujo DM et al., (2019) (34)	Brazil	Cross-sectional	Infants between 8 and 10 months,	-	154	Chi-square and Mann-whitney tests	Hearing loss	APGIR1	-	-	<0.001
								APGIR5	-	-	0.02

Discussion

This systematic review summarized the findings of relevant studies around the world to assess the relationship of maternal and neonatal factors of hearing loss in infants. In the reviewed studies, we found a relatively high range of maternal and neonatal factors affecting hearing loss in infants.

Studies entered in this review, had been performed in various parts of the world from the North and South American countries to Europe, Africa, Southeast Asia, and the Eastern Mediterranean countries. The designs used in the reviewed studies were, in most cases, prospective cohort and cross-sectional, and the statistical models used to analyze the relationship of

dependent and independent variables were mostly logistic regression and univariate statistical tests (chi-square). Also, in most studies, the study population included children under 6 months of age, children with known risk factors, or neonates admitted to the NICU. The intended outcome in all studies was hearing loss.

According to our findings, some risk factors such as ventilatory support, craniofacial anomalies, low birth weight and hyperbilirubinemia can play a key role in the development of hearing loss, because these factors have been observed in many studies, and also the geographical scope of the studies included in this review article covered most parts of the world including developing and developed countries. Besides, conducting further studies in different regions of the World Health Organization can help with more in-depth illustration of the role and strength of each risk factor.

Craniofacial anomalies have been identified as one of the risk factors for hearing loss in 4 of the studies reviewed **(7, 23, 31, 33)**. Wroblewska-Seniuk showed that isolated craniofacial anomalies are more common in children with Conductive Hearing Loss (CHL) than other kinds of hearing loss. A lot of children with this condition have cleft palate and deformity of the auricle. Another congenital defect seen in children with CHL isDown syndrome. In Down syndrome children, every region of the neck and head can be affected and hearing loss is usually conductive secondary to the ossicular chain abnormalities or chronic middle ear disease. However, sensorineural hearing loss was diagnosed in two other children with Down syndrome and in three other cases with a mixed type of hearing deficit. Another child with the conductive hearing deficit was identified as Cornelia de Lange syndrome (CdLS). Based on the researchers' findings, both sensorineural and conductive hearing loss have been reported in children with CdLS, due to external auditory canal stenosis and serous otitis media. **(7)**.

Hyperbilirubinemia has been introduced as a risk factor for hearing loss in some previous studies **(1, 7, 24, 28)**. In the study of Wroblewska-Seniuk et al., hyperbilirubinemia cases needing phototherapy were observed in over 50% of children with Sensorineural hearing loss (SNHL). According to their results, hyperbilirubinemia was not severe in any of the studied children so that they did not require further treatments such as exchange transfusion or they did not develop kernicterus, although this may have been due to the start of phototherapy in the early stages of the disease **(7)**. Hyperbilirubinemia is probably the cause of auditory neuropathy spectrum disorders that are due to dyssynchrony of the auditory peripheral system **(35)**. In a study conducted by Lima et al., hyperbilirubinemia was not recognized as a risk factor in univariate analysis. However, when hyperbilirubinemia was investigated in relation with the other variables, it acquired great statistical power so that it had an important role in the occurrence of hearing loss. The researchers suggested that it is essential to administer guidelines with strict control of jaundice cases, including the use of objective measures to assess the serum level of bilirubin and efficient phototherapy, representing measures to prevent hyperbilirubinemia and its outcome, jaundice **(36)**. Indeed, neonatal jaundice occurs in the first days of life, and mothers regardless of where they choose to deliver need to be more educated and aware on the early signs of this condition to initiate effective phototherapy or exchange blood transfusion when needed **(28)**.

LBW has been identified as the main risk factor for hearing loss in most of the reviewed studies **(1, 7, 32, 33)**. Premature birth and low birth weight are not necessarily the risk factors because providing curative treatment for the newborns in the intensive care units can decrease the possibility of hearing loss **(33)**. According to the existing literature, weight less than 1500g at birth (VLBW) can be associated with hearing impairment. It should be noted that this finding is not strong and it's greater or lesser significance can be related to the differences in the populations and also conditions of perinatal care **(1)**.

Hearing loss may be caused by certain hereditary as well as harmful environmental factors surrounding the pregnancy or birth. These two main factors may have delayed audiological symptom expression. There is uncertainty about which risk factors are relevant, which infants have the risk factors or will fail to attend follow-up **(32)**.

Ventilatory support has also been identified as one of the most important risk factors for hearing loss in several studies reviewed **(22, 24, 25, 30)**. Ventilatory support is used for infants in different ways. One of the common methods is mechanical ventilation. Eras et al., in Turkey showed that mechanical ventilation could significantly increase the risk of hearing loss in children **(30)**.

Based on the existing evidence, Mechanical ventilation could significantly damage the peripheral segment of the hearing tract. Also, it was stated that the length of mechanical ventilation and the duration of hospital stay could be increased in children with SNHL **(26, 37)**. Several other factors such as meningitis, Apgar scores‘ respiratory distress syndrome, sepsis, asphyxia, and pulmonary surfactant have been introduced as the risk factors for hearing loss in some studies entered into our review. Among these factors, meningitis and Apgar scores have a potential importance so that meningitis is the cause of SNHL listed in congenital hearing loss risk factors **(38)**. The Apgar scores, as a way to evaluate the health of a newborn immediately after childbirth, at 1 min were significantly lower in children with SNHL in comparison with healthy controls. In general, the Apgar scores at 5 and 10 min were also lower in the infants with SNHL. At 10 min the difference in Apgar scores between the controls and infants with SNHL

were the smallest, probably as a result of proper treatment of the newborns. In fact, low Apgar scores are an indicator of perinatal hypoxia **(39)**. Hille et al., and Vohr et al., also indicated a significant relationship between low Apgar scores and hearing loss in infants admitted to NICU infants **(25, 40)**. Several other studies also found a relationship between hearing loss and other aspects of hypoxia like prolonged mechanical ventilation **(41-43)**.

Conclusion

This study highlights the hearingloss problem among infants and its related risk factors. This review revealed that ventilatory support, craniofacial anomalies, low birth weight, and hyperbilirubinemia were the main statistically significant risk factors of hearing loss. Further studies are needed to determine that other factors assessed in each of the studies entered into this review could be considered as a predictive or risk factor for hearing loss.

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Conflict of Interest

There is no conflict of intrest.

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