

Title: Age of Identification of Sensorineural Hearing Loss and Characteristics of Affected Children: Findings from Two Cross-sectional Studies in Saudi Arabia

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Abstract

Objectives: To identify the average age of identification (AOI) and characteristics of Saudi children with sensorineural hearing loss (SNHL).

Methods: Two cross-sectional studies were undertaken. Study A: the medical records of 1166 children aged 0-10 years old who visited the audiology clinics in four hospitals in Riyadh and Dammam during 2015 were reviewed. Study B: 174 carers of children aged 0-12 years who visited the audiology clinics in four hospitals in Riyadh during a three-month period were surveyed.

Results: The mean AOI with SNHL in children was 3.2 years (SD= 2.6 years) and 3.1 years (SD= 2.5 years) with 14% and 16% not identified until after primary school age for Studies A and B, respectively. The presence of SNHL was positively associated with parental consanguinity, positive family history of SNHL, history of chemotherapy treatment, brain pathology and prior parental concern regarding their child's hearing.

Conclusion: AOI of SNHL among Saudi children is deemed high in relation to the likely age of onset, with about 15 in 100 children identified after school age. Childhood hearing screening programmes (at birth and at school entry) should be considered in order to intervene earlier.

Key words: Hearing Loss; Children, Saudi Arabia, Age, Characteristics

Acronyms: Hearing Loss, HL; World Health Organization, WHO; Sensorineural Hearing Loss, SNHL; Conductive Hearing Loss, CHL; Kingdom of Saudi Arabia, KSA; Universal Neonatal Hearing Screening, UNHS; School Entry Hearing Screening, SEHS; High Income Countries, HIC; Joint Committee on Infant Hearing, JCIH; Standard Deviation, SD; Neonatal Intensive Care Unit, NICU; Unilateral Hearing Loss, UHL; Age of Identification, AOI; United Kingdom, UK; United States of America, USA.

1. Introduction

One to three in a thousand live births have permanent sensorineural hearing loss (SNHL) [1, 2]. Those who receive early identification and intervention can develop language and social skills equivalent or similar to those of their peers without hearing loss (HL) [3, 4 & 5]. Those who do not can have substantially impaired language acquisition, speech perception, social/emotional wellbeing, and academic performance [6, 7].

Consequently, universal hearing screening programmes, at birth and at later ages, have been recommended in order to achieve early identification [8]. Countries that implemented universal neonatal hearing screening (UNHS) programmes have reported a reduction in the age of identification (AOI) of SNHL. For instance, the median AOI with SNHL in the United Kingdom (UK) has been reduced from 18 months before the implementation of UNHS to 49 days after the implementation [9]. Similarly, it has been reported that UNHS identified 71% of the infants with SNHL before the age of 3 months in the United States of America (USA) [10]. This compares to a previous median AOI of 30–36 months [2].

Although it has been demonstrated that UNHS dramatically decreases the AOI with SNHL, several factors make the detection of all children with SNHL by the UNHS impossible, even in cases of high sensitivity. First, it is well recognized that many cases of hereditary SNHL do not manifest at birth. In other words, a child may have normal hearing at birth (and thus pass the UNHS), but may develop SNHL over time. Second, some types of congenital SNHL are progressive in nature [11]. Thus, a child might have slight/mild SNHL at birth (and, thus, pass the UNHS, because this targets only moderate and worse degrees of SNHL) but then experience deteriorating hearing over time. Third, acquired SNHL, such as SNHL that results from childhood infectious diseases, does not exist at birth [11]. Another important point that has been highlighted is the high rate of children who fail the first step of the UNHS programme but also fail to follow-up for further investigation (ranging from 3.7– 65%) [12].

For that reason, many countries, including the UK and the USA, have additional screening programmes, such as universal school-entry hearing screening (SEHS) [13, 14].

The implementation of hearing screening programmes for children in Middle East countries is very limited, perhaps due to other economic priorities and low levels of awareness of the seriousness of childhood SNHL [15]. The Kingdom of Saudi Arabia (KSA) is an interesting case in point. It is considered a high-income country [16], has a prevalence of childhood SNHL ranging from 1–4/1000 live births [17, 18 & 19], and has among the most well-developed audiology services in the Middle East that provide all necessary audiology services, including the cochlear implant [20]. However, the implementation of the UNHS in KSA was limited to children born in a small number of hospitals located in the main cities until 2016, when the first phase of the UNHS started [21]. Until now, there has been no nationwide covering of the UNHS, and screening programmes for older children, such as SEHS, have not implemented.

To our knowledge, no data are available in the public domain about AOI of SNHL in children in KSA. Several studies investigated the prevalence of SNHL in children in KSA but not the age at which the affected children were identified [17, 18, 19 & 22]. The availability of information about the current AOI of SNHL in Saudi children would allow for evaluating the success of the UNHS, which has been initiated in KSA, in reducing the AOI, similar to what has been reported in other countries. Additionally, it would show a possible need for periodic hearing screening programmes for children.

It is also important to look at the common risk factors to SNHL in Saudi children. This would allow to planning for hearing screening programmes that target children who are at risk to SNHL, in case it appears that the implementation of further national children hearing screening such as the SEHS, if needed, is not feasible because of lack of staff, lack of sources, etc.

Causes for childhood SNHL are either congenital or environmental factors. In countries with well-developed health services, genetic abnormalities, which account for at least 50% of SNHL cases worldwide, are considered the main risk factor to childhood SNHL. However, environmental factors such as childhood infectious diseases, which account for approximately 25% of SNHL cases worldwide, are considered the main risk factors for childhood SNHL in low-income countries where health services are not well developed [23, 24]. In KSA and other

countries in the Middle East, the high practise of consanguinity [25, 26, 27 & 28] may result in increasing the cases of genetic SNHL [29].

Previous studies of the risk factors for childhood SNHL in KSA found that consanguinity and infectious diseases are common [17, 30, 31, 32 & 33]. The most recent study was 15 years ago [17], and it is possible that the profile of risk factors has since changed following changes in health services and public health awareness, which are improving rapidly in KSA [34].

The first aim of this research was to provide initial data on the AOI of SNHL in Saudi children, to inform the evidence base for implementing and evaluating national hearing-screening programmes. The second aim was to take a fresh look at potential risk factors for childhood SNHL in Saudi children.

2. Material and methods

This paper reports the findings of two studies. Study A used a cross-sectional design that gathered medical records data from all children who visited several audiology clinics in two main cities—Riyadh (the capital city) and Dammam (a major city in the Eastern region)—during 2015. Study B used a self-report survey of carers of a different group of children with SNHL. Both studies gathered information on the AOI and characteristics of children. Whereas Study A provided a larger sample size than Study B, Study B was able to provide more information about the characteristics of children with SNHL due to limitations in what is documented in medical records. Consequently, Study A focused more on the AOI whereas Study B focused more on risk factors.

2.1 Study A

In this cross-sectional study, all hospitals/centres with audiology clinics, which are known to the authors, in different regions of KSA were contacted (there was no reliable information

about the total number and locations of audiology clinics in KSA). Of the contacted hospitals/centres, 11 were invited to participate. Those 11 hospitals, which are located in different regions of KSA (middle, eastern, and western), were selected because of their use of electronic medical records for their patients. Three hospitals did not respond, and four hospitals declined participation for reasons related to workload or inability to release patient data for research purposes. Subsequently, four hospitals/centres were included in the study; three in Riyadh (the capital city) and one in Dammam (a major city in the Eastern region).

For the purpose of the study, audiologists in each audiology clinic retrospectively reviewed the electronic medical records of all children aged 0–10 years (from birth to last year of primary school) who attended their clinics during the year 2015 ($n=1224$). Some of those children were attending for their first audiology appointment and some for follow up. Extracted information for this study included age at the day of data collection, gender, results of hearing tests, degree and type of HL if it exists, AOI with SNHL or mixed hearing loss (MHL), and any other past/present medical condition that may be related to HL.

Of the four included hospitals/centres, two currently have newborn hearing screenings for all newborn babies, which started in 2006 (8.6 years before data collection); one has targeted hearing screening for babies in the Newborn Intensive Care Unit (NICU), which started in 2010 (5 years before data collection); and the fourth has no hearing screening. Information on whether the included children were screened for SNHL at birth was not available.

The children with HL were seen in these audiology clinics, usually either because of referrals from the screening programmes or referrals from general practitioners or ear, nose, and throat physicians. Children with SNHL/MHL are followed regularly in the audiology clinics (at least every 6–12 months), whereas children with conductive hearing loss (CHL) are usually referred back to the physicians for further management.

Types of HL were defined as follows: SNHL was defined as abnormal air and bone conduction thresholds (>20 dB HL) without an air-bone gap (≤ 10 dB HL); MHL was defined as an

abnormal air conduction and bone conduction threshold with an air-bone gap (>10 dB HL); and CHL was defined as abnormal air-conduction thresholds (>20 dB HL) with normal bone-conduction thresholds (≤ 20 dB HL) [35]. Because MHL has a sensorineural element, which is irreversible even if the conductive element has been treated/resolved [35], children with MHL were included in the SNHL group for the purposes of this analysis. Additionally, for the purpose of the analysis, children with CHL were merged with children with normal hearing in one group (the reference group).

In cases for which pure tone audiometry was used, the degree of HL was calculated by averaging the thresholds of the frequencies 0.5, 1, and 2 kHz [35]. In cases for which auditory brainstem responses were measured, the air-conduction threshold of wave V was used to determine the degree of HL. This was the same approach used by audiologists working at the participating hospitals.

Based on the British Society of Audiology's classification, the degrees were defined as follows: mild HL ranging from 20–40 dB HL, moderate HL ranging from 41–70 dB HL, severe HL ranging from 71–95 dB HL, and profound HL >95 dB HL [36]. For bilateral HL, the thresholds of the better ear were used, whereas for unilateral HL, the thresholds of the worse ear were used.

2.2 Study B

In this cross-sectional survey, carers of children aged 0–12 years (from birth to teenaged) who attended the audiology clinics in four hospitals/centres in Riyadh (three of which were the same hospitals included in Study A) during a three-month period (September to November 2016) were recruited ($n=190$). Audiologists in each clinic informed the carers about the study, provided them with the information sheet, and obtained written consent to participate. Participants completed a questionnaire (see supplementary material), which was developed based on the risk factors for SNHL listed by the Joint Committee on Infant Hearing (JCIH) [37].

Questions about specific factors thought to have an association with SNHL in Saudi children, such as consanguinity and family size [38], were also included. The final question asked about the child's current hearing test results was answered by the audiologists from the child's medical records to provide the objective diagnosis.

Ethics approval was provided by ethics committees at the University of Southampton in the UK (identification numbers 20827 and 23832) and at the participating hospitals/centres in KSA.

2.3 Data Analysis

Statistical analysis was performed using IBM SPSS Version 24. Summary statistics were described using means, standard deviations (SD), and percentages. Univariable logistic regression analysis was performed for each risk factor to SNHL to estimate the magnitude of the association. Multivariable logistic regression modelling was performed including factors that showed statistically significant association with SNHL in the univariable analysis. SNHL as an outcome was compared against a reference category composed of a combination of CHL and no diagnosis of HL. A statistical significance cut-off value of $p=0.05$ was used for all the analyses.

3. Results

3.1 Study A

The electronic medical records of 1224 children were reviewed. Of those, 1166 were included in the study, and 58 were excluded because of inconclusive hearing test results. The children's ages ranged between 0.1–10.4 years (mean = 3.7 years, SD= 2.6 years). Males represented 60% (n = 703) and females represented 40% (n = 463) of the sample.

Information on the number and percentages of children identified with different types and degrees of HL are provided in Table 1.

Table 1 to be placed here please

The mean AOI with SNHL was 3.2 years (SD = 2.5 years) and the median was 2.5 years (Interquartile range= 1.1, 5). Children were distributed into four groups according to the AOI with SNHL (0-1, 1-3, 3-6 & >6+ years).

Figure 1 shows the number of children identified with different degrees of bilateral and unilateral SNHL at different age groups. It can be seen that a considerably high percentage of children with bilateral severe/profound degrees of SNHL were not identified until after their first year of age. Only 31 (24%) of bilateral severe/profound cases were identified within their first year. The remaining 99 (76%) were identified at later ages with 24 (18%) of children not identified until after their 3rd birthday (after starting their schooling).

Other degrees of SNHL showed similar results with only a few (n = 29, 18%) of the children identified with bilateral mild/moderate SNHL during their first year of age, whereas more than half of the children were not identified until after school age (either kindergarten or primary schooling) (n = 88, 55%).

Unilateral SNHL was identified in 22 (7%) of the children identified with SNHL in our sample. Of these children, 13 (59%) were identified after school age (3+ years). One child with profound unilateral SNHL was not identified until 9 years of age.

Figure 1 to be placed here in colour for both online and print copies please

In addition to the AOI with SNHL, the presence of several predictors to SNHL (as defined by JCIH [30]) in the children in our sample and the association between these predictors and the presence of SNHL were explored. The children with CHL and those with no diagnosis of HL were merged into one group and compared to children with SNHL using univariable logistic regression analysis. Table 2 provides information on the association between each potential risk factor as an indicator and the presence of SNHL as an outcome.

Table 2 to be placed here please

Associations ($p < 0.05$) were found between the presence of SNHL and parental consanguinity, positive family history of SNHL, NICU admission for more than 5 days, treatment with chemotherapy, and the presence of a diagnosis of brain pathology/tumour. The Multivariable regression model, which takes into account all the above statistically significant factors, did not alter these results, except that the NICU admission predictor ceased to be associated with the presence of SNHL ($p = 0.08$). Consanguineous marriages have been found in 44% of the parents of children in our sample. The children of consanguineous marriages were 1.6 times more likely to have SNHL than the children of non-consanguineous marriages (95% Confidence Intervals (CI) 1.1 - 2.4, $p = 0.007$).

3.2 Study B

Of the 190 carers of children who were surveyed, 174 of their questionnaires were included and 16 were excluded due to incompleteness, giving a response rate of 92%. Children's ages ranged between 0.1–12 years (mean = 5.4 years, SD = 3.4 years). Males represented 59% ($n = 102$) of the sample, and females represented 41% ($n = 72$).

Table 1 provides information on the number and percentages of children identified with different types and degrees of HL. As can be seen, just below half of the children (46%) were identified with SNHL. Of those, 53% have severe/profound degrees of SNHL with two children (5%) were identified after primary school age (6+ years). Unilateral SNHL accounted for 8% of the children identified with SNHL.

The mean AOI with SNHL was 3.1 years (SD = 2.6 years) with a median of 2 years (Interquartile range = 0.9, 5). Carer responses showed that almost one third of the children with SNHL of any degree were identified during the first year of age (31%), whereas the majority were identified at later ages. Between 1–3 years, 33% were identified with SNHL, another 20% were identified between 3–6 years, whereas the remaining 16% were not identified until after their 6th birthday, which is after they started their primary schooling. Two

children with unilateral SNHL were identified during their first year, whereas four were identified beyond 3 years (at 5, 6, 8, and 8 years old).

Figure 2 shows the number of children identified with different degrees of bilateral and unilateral SNHL.

Figure 2 to be placed here in colour for both online and print copies please

Carers were asked about the presence of various risk factors to SNHL in their children. Table 2 lists their association with the presence of SNHL. Both univariable and multivariable logistic regression analyses of these variables showed that parental consanguinity and parental concern about the child's hearing are possible predictors for SNHL in children ($p < 0.0001$) in comparison to a reference group consisting of children with CHL and children who have no diagnosis with HL (Table 3). It has been found that 57% of the children in Study B have consanguineous parents. Children of related parents appeared to be 5 (95% CI 2.2 - 10.7) times more likely to have SNHL than children of unrelated parents, even after adjusting for other risk factors.

Table 3 to be placed here please

Carers of the children who were diagnosed after the age of 3 years were asked their opinions about the reason for the seemingly late diagnosis ($n = 29$). Of those, 41% reported that their children had developed SNHL after the age of 3 years, and 31% mistakenly thought that their children were intentionally ignoring people who talked to them. Another 28% reported that they were concerned about their children's hearing before the age of 3 years, but that either there was no audiology clinic in their town (21%), or they had not been referred to an audiology clinic despite requests (7%).

Carers of children who felt their children had developed SNHL after 3 years of age ($n = 12$) were asked to comment on what caused them to feel that way. Of those, 11% reported that their children had normal hearing test results before the age of 3 years. Another 24% reported that their children went through normal language processes. The other 32% and 33% reported

that their children stopped responding to loud sounds and experienced behavioural changes after the age of 3 years, respectively.

4. Discussion

Our studies aimed at providing initial data on the AOI with SNHL in Saudi children and exploring the current characteristics of children with SNHL to identify any potential risk factors that had not been identified earlier.

4.1 Age of Identification with SNHL in Children

The median AOI of childhood SNHL was similar for Study A and B: 2.5 years and 2 years, respectively. Additionally, a wide spread of the AOI in our samples has been noticed: 75% of the median was 5 years in both studies, suggesting that some children reached school age before they have been identified with SNHL. This is much higher than the AOI recommended by the JCIH (i.e., 3 months [37]). In other high-income countries, such as the USA, the identification of childhood SNHL occurs on average before the age of 3 months [39]. Likewise, in the UK, the median AOI is 49 days [9].

It is acknowledged that the samples in Study A and Study B were driven from a few audiology clinics located in two cities in the country. Thus, the findings might not be generalizable on a national level. However, the following two points made us confidently say that the present sample represent other regions of the country as well as Riyadh and Dammam. First, patients who visit the audiology clinics included in the two studies (especially in Riyadh) come from different regions of the country because two of the included hospitals are main military and civilian medical cities that serve people live around the country. Because of the lack of audiology clinics in some regions, eligible people who live out of Riyadh are served at the audiology clinics located in Riyadh. For instance, The Security Forces Hospital in Riyadh (one of the included hospitals) is a main hospital that serves people who work for the different sectors of the Ministry of Interior with tertiary health services. Eligible people might be living

anywhere in the country where audiology clinics might not be available; for that reason, the audiology clinic at the main hospital in Riyadh accepts referrals from primary care units that follow the hospital and are located all around the country. Second, the latest report of the General Authority of Statistics in Saudi Arabia [40] stated that the average family income in Saudi is 10,723 SR and around 40% of the Saudi population have low family income. This is close to our findings, which showed that 54% (94) of the sample have low family income (<10,000 SR) (Table 3).

In an attempt to explain the high AOI of childhood SNHL in the present samples, it was difficult to tell if the identification was late or if the SNHL had developed or been acquired at late ages. This is because the age of onset of SNHL was unknown; the only information that we had was the age at which SNHL was identified/confirmed. This leads us to two explanations for this high AOI: the first is that the children in the present samples had congenital SNHL but had not been identified until older and the second is that the children might have had normal hearing at birth but developed/acquired SNHL at later ages. The first explanation is possibly true, because it is well known that most forms of hereditary SNHL are autosomal recessive in nature (80%) and cause prelingual SNHL [23]. The high practice of consanguinity in the country [25] is expected to cause autosomal recessive SNHL because consanguinity is known to have a high chance of pairing recessive alleles of SNHL [41]. The findings of our studies are consistent with this possibility of late identification because the majority of children identified with SNHL in our samples had consanguineous parents. Our findings also showed that parental consanguinity is a potential predictor to childhood SNHL. Even in Study B, where the sample size was considerably small, parental consanguinity was still shown as a potential predictor to childhood SNHL. It was difficult to tell if the late AOI (if we assume that it is late) occurred because of the absence of UNHS, or it occurred even with the implementation of UNHS, because the samples included children who might have been screened for SNHL at birth and children who were not. The exact information was not available.

The second explanation for the high AOI (appearance of late-onset hereditary SNHL or acquired SNHL) is also possible because late-onset hereditary SNHL, which is progressive in most cases [23], could be related to consanguinity. A previous study in KSA reported that consanguinity was found in 81% of the cases with known progressive SNHL [38]. Additionally, the possibility of acquiring SNHL at late ages because of environmental factors is acknowledged. In Study B, just below half (41%) of the carers of children diagnosed with SNHL after the age of 3 years reported that their children had normal hearing before that age and gave different justifications for that fact (see section 3.2). These findings support the explanation that some children might have developed/acquired SNHL at late ages. Both explanations seem to apply at least in part to some children in the present samples.

Knowing that these findings were driven from Riyadh and Dammam, which host tertiary care hospitals where most audiology clinics are located, then it is highly likely that the findings will be worse in other cities where there is less access to hearing healthcare.

4.2 Risk Factors to SNHL in Children

The present research looked at the characteristics of Saudi children with SNHL. The findings confirmed the presence of some known risk factors for SNHL in children in KSA such as parental consanguinity, positive family history of SNHL, the treatment with chemotherapy and having brain pathology/tumour that has been reported previously [17, 42 & 43].

In KSA, a prevalence of 56% of consanguineous marriages has been reported [25]. This is comparable to the findings of this research in which consanguinity accounted for 44% and 57% of the whole sample in studies A and B, respectively. Additionally, 71% and 73% of the children identified with SNHL in Studies A and B, respectively, had consanguineous parents. This is close to what has been reported in another Saudi study in which 81% of children with SNHL had consanguineous parents [38]. It is also similar to what has been reported by another Gulf country (Oman) with a reported prevalence of 70% of consanguinity among parents of children with SNHL [27]. The high practice of consanguineous marriages in the country

increases the possibility of having congenital and late-onset hereditary SNHL [23, 38, 41]. This indicates that in a country such as KSA, UNHS would not be enough but rather it is recommended to have periodic hearing screening for children.

Interestingly, parental concern regarding their children's hearing was found to be one of the potential predictors to SNHL. Apparently, parents may have a suspicion about their child's hearing but, because of limited awareness about SNHL, they may blame the child for not responding. Thus, it is important to raise public awareness about the seriousness of SNHL and the importance of having children's hearing checked immediately in suspicious cases.

Conversely, although it has been reported in the literature that acquired SNHL resulting from postnatal infectious diseases is prevalent in children in KSA [31, 32 & 33], the findings of the current research showed no evidence of association between postnatal infectious diseases and the presence of SNHL. This might be explained by the small sample size in Study B.

4.3 Implications for practice

It is the right of children with SNHL to have a chance to receive intervention as early as possible especially in a country where the latest audiological re/habilitation technologies including cochlear implants are available [20]. Reducing the AOI of SNHL in Saudi children is crucial and should be considered seriously and urgently by applying childhood hearing screening programmes (at birth and at school entry), which proved its success in other countries. It is also important to test the children's hearing immediately in case of suspicion. Otherwise, late identification and intervention would negatively affect the child's language acquisition, speech perception, social and emotional wellbeing, and academic performance [6, 7]. It would also affect these children's future chances for employment and work productivity, thus posing an additional economic cost to the society [44], which could have otherwise been prevented or at least reduced.

4.4 Strengths and limitations

To the authors knowledge, these two studies were the first to explore the AOI of SNHL in Saudi children. Despite the difference in the sample sizes of the two studies, findings from both studies were similar, which ensures reliable results. In addition, the findings from Study B, which had the smaller sample size, were similar to the findings of other studies in literature.

The chance of double counting the participants in Study A was very low because three of the centres were governmental hospitals, each serving a particular population so if a patient attends the audiology clinic in one of these hospitals, it is unlikely that s/he attends the audiology clinic in the other two hospitals. In addition, audiologists assured that there had been no duplication of the same patient, even if s/he attended the clinic more than once during 2015.

Gathering information about children with HL in KSA was challenging. No databases were found regarding the number of audiology clinics in KSA, the incidence of children with SNHL in KSA, and the period of time since the child is referred from primary clinics to audiology clinics. Thus, it was impossible for us to know how representative our sample was to the general population, either in Riyadh and Dammam or in the country as a whole.

5. Conclusions

The AOI of SNHL in Saudi children is considerably high with a relatively high percentage of children not identified until after school age. Reducing the AOI of SNHL in Saudi children is a priority to ensure that children with SNHL have a chance to receive early interventions and thus acquire normal speech, language, social/emotional and behavioural skills. This could be done by considering an implementation of periodic childhood hearing screening because UNHS would not detect children who would develop hereditary late-onset SNHL. For instance, considering SEHS is highly recommended. Additionally, it is recommended to establish public

health campaigns and genetic counselling to increase societal awareness of the potential consequences of consanguinity, including SNHL.

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Figure captions:

Figure 1 *Number of children identified with different degrees of bilateral SNHL and unilateral SNHL at different age groups (Study A)*

Figure 2 *Number of children identified with different degrees of bilateral SNHL and unilateral SNHL at different age groups (Study B)*

Table 1 Number and percentage of children identified with different types and degrees of hearing loss in Study A and Study B

Type/degree of HL	Number of children	Percentage of children	Mean age (years)	Standard deviation (years)
Study A				
HL of any type (SNHL/MHL or CHL)	533	46	4.4	2.7
SNHL/MHL	340	29	3.9	2.7
CHL	193	17	3.8	2.7
Mild SNHL/MHL	36	11	-	-
Moderate SNHL/MHL	150	44	-	-
Severe SNHL/MHL	72	21	-	-
Profound SNHL/MHL	82	24	-	-
Study B				
HL of any type (SNHL/MHL or CHL)	97	56	5.5	3.5
SNHL/MHL	80	46	5.5	3.4
CHL	17	10	6.7	3.3
Mild SNHL/MHL	8	11	-	-
Moderate SNHL/MHL	22	28	-	-
Severe SNHL/MHL	16	20	-	-
Profound SNHL/MHL	26	33	-	-

Table 2 Characteristics of children with HL and the association of the presence of SNHL/CHL with different risk factors (Study A)

	No diagnosis of HL N (%)	SNHL N (%)	CHL N (%)	Univariable regression <i>p</i> -value	Univariable Odd Ratio of SNHL ^a (95% CI)	Multivariable Odd Ratio of SNHL ^b (95% CI) <i>p</i> -value
Consanguinity	267 (58%)	167 (71%)	80 (61%)	0.008	1.6 (1.1 – 2.3)	1.6 (1.1 – 2.4) <i>p</i> = 0.006
Family history of SNHL	44 (7.4%)	78 (27%)	9 (6%)	< .0001	4.4 (2.8 – 6.9)	4.2 (2.4 – 6.1) <i>p</i> <0.0001
Admission to NICU >5 days	213 (36%)	72 (24%)	67 (37%)	0.03	0.7 (0.4 – 0.9)	0.7 (0.5 – 1.0) <i>p</i> = 0.08
Having any syndrome	62 (10%)	42 (12%)	46 (24%)	0.57	1.2 (0.7 – 2)	-
Head trauma	2 (0.3%)	2 (0.6%)	2 (1%)	0.5	2.7 (0.2 – 46)	-
Renal disease	11 (2%)	8 (2%)	7 (4%)	0.9	1.1 (0.3 – 3.7)	-
Hyperbilirubinemia^a	8 (1%)	5 (2%)	2 (1%)	0.4	1.8 (0.5 – 7.4)	-
Chemotherapy	15 (2%)	20 (6%)	2 (1%)	0.002	5.6 (1.9 – 16.7)	4.9 (1.4 – 14.7) <i>p</i> = 0.004
Craniofacial anomalies	18 (3%)	19 (6%)	34 (18%)	0.4	1.4 (0.7 – 2.7)	-
Brain pathology/tumour	10 (2%)	19 (6%)	4 (2%)	< 0.0001	7.5 (2.5 – 22.3)	7 (3 – 64) <i>p</i> <0.0001
Hypoxia	12 (2%)	8 (2%)	4 (2%)	0.65	1.22 (0.4 – 9.6)	-
Postnatal infectious disease	23 (4%)	13 (4%)	5 (3%)	0.2	1.8 (0.8 – 4)	-
Neurological disorder	19 (3%)	15 (4%)	3 (2%)	0.4	1.5 (0.6 – 4)	-

^a SNHL/MHL compared against a reference category composed of a combination of CHL and no diagnosis with HL in univariable logistic regression

^b Multivariable logistic regression for the variables which were statistically significant association with SNHL in the univariable analysis, consanguinity, family history of SNHL, Admission to NICU >5 days, Chemotherapy and brain pathology/tumour

Table 3 Characteristics of children with HL and the association of the presence of SNHL/CHL with different risk factors (Study B)

	No diagnosis with HL N (%)	SNHL N (%)	CHL N (%)	Univariable regression <i>p</i> -value	Univariable Odd Ratio of SNHL ^a (95% CI)	Multivariable Odd Ratio of SNHL ^b (95% CI) <i>p</i> -value
Maternity infectious diseases	1 (1%)	0	1 (6%)	-	-	-
Low birth weight <2 Kg	13 (17%)	8 (10%)	2 (12%)	0.4	0.5 (0.1 – 2.3)	-
Hypoxia	10 (13%)	8 (10%)	1 (6%)	0.7	0.7 (0.2 – 3.4)	-
Hyperbilirubinemia	19 (25%)	16 (20%)	4 (24%)	0.3	1.9 (0.6 – 6)	-
Admission to NICU	22 (29%)	20 (25%)	3 (18%)	0.5	1.5 (0.5 – 5)	-
Post-natal infectious disease	4 (5%)	4 (5%)	0	0.6	1.2 (0.3 – 203)	-
Syndromes	7 (9%)	5 (6%)	6 (35%)	0.6	0.6 (0.1 – 3)	-
Craniofacial anomalies	0	7 (9%)	4 (24%)	0.3	2.5 (0.5 – 13)	-
Neurological diseases	5 (7%)	7 (9%)	0	0.4	11.3 (1.1 – 118)	-
Developmental delay	10 (13%)	13 (16%)	6 (35%)	0.5	1.7 (0.4 – 7)	-
Language delay	33 (43%)	33 (41%)	10 (59%)	0.1	0.5 (0.2 – 1.3)	-
Head trauma	7 (9%)	6 (8%)	1 (6%)	0.2	0.3 (0.04 – 1.9)	-
Chemotherapy	1 (1%)	4 (5%)	0	0.5	2.5 (0.2 – 35)	-
HL-induced medication	4 (5%)	10 (13%)	2 (12%)	0.7	1.4 (0.2 – 8)	-
Consanguinity	33 (43%)	58 (73%)	8 (47%)	< 0.0001	6.4 (2.4 – 17)	4.9 (2.2 – 10.7) <i>p</i> <0.0001
Family history	9 (12%)	16 (3%)	4 (24%)	0.8	1.1 (0.4 – 3.4)	-
Parent concern	28 (38%)	72 (90%)	13 (77%)	<0.0001	23.8 (6 – 88)	15 (6 – 40) <i>p</i> <0.0001
Teacher concern	10 (14%)	7 (9%)	3 (19%)	0.9	1 (0.2 – 4.5)	-
Mother university education	43 (56%)	38 (48%)	8 (47%)	0.7	0.8 (0.3 – 2.4)	-
Father university education	45 (58%)	41 (51%)	9 (53%)	0.3	0.6 (0.2 – 1.6)	-

Mother employment	24 (31%)	25 (31%)	4 (24%)	0.3	1.8 (0.6 – 5.7)	-
Smoking at home	26 (34%)	22 (28%)	6 (35%)	0.08	0.4 (0.1 – 1.1)	-
Low family monthly income	44 (57%)	50 (63%)	14 (82%)	0.6	0.8 (0.3 – 2)	-

^a SNHL/MHL compared against a reference category composed of a combination of CHL and no diagnosis with HL in univariable logistic regression

^b Multivariable logistic regression for the variables which were statistically significant association with SNHL in the univariable analysis, Consanguinity and parent concern