Impact and benefits of early hearing screening

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2 WHAT CAUSES PERMANENT CHILDHOOD HEARING IMPAIRMENT? ANALYZING THE PROPORTIONS ATTRIBUTED TO THE AETIOLOGY

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ABSTRACT

Introduction

The generally accepted attributed proportions concerning the aetiology of permanent childhood hearing impairment (PCHI) (50% hereditary, 25% acquired and 25% unknown) are often quoted. We studied the evidence for these attributed proportions, in a period of increasing interest for causes of PCHI and growing diagnostic possibilities.

Methods

Population-based study and a systematic review. Inclusion criteria: Children born between 2003 and 2005, resident in the Netherlands at birth, known to an Audiology Center with PCHI at the age of 3-5 years. The causes of PCHI were determined, prospectively by detection of congenital cytomegalovirus on dried blood spots and/or genetic diagnostic investigations in addition to data from medical records. Systematic review with 3 terms (hearing loss, infant and etiology) and limited to articles published after January 1997 until July 2009. Main outcome measures: (weighted) proportions attributed to the aetiology following diagnostic investigations.

Results

In the study-population (n=185) a hereditary cause was found in 38.9%, acquired hearing loss in 29.7%, miscellaneous cause in 7.1% and the cause remained unknown in 24.3%. The systematic review of the literature (n=9) resulted in a weighted mean of 30.4% hereditary, 19.2% acquired and 48.3% unknown causes of PCHI.

Discussion

The systematic review and the results of the population-based study revealed little support for the generally accepted attributed proportions.

INTRODUCTION

Following introduction of newborn hearing screening programs throughout the world the awareness in parents and professionals for the aetiology of permanent childhood hearing impairment (PCHI) increased. Understanding the aetiology is important not only with respect to treatment options, but also for predicting the developmental prognosis and recurrence risk in future siblings and family members.

Numerous studies have been performed with regard to the aetiology of PCHI. These studies have lead to a better understanding of hereditary and acquired causes of hearing loss. However, because of cultural differences and methodological reasons, the reported proportions attributed to the different aetiological causes differ greatly. In general it is assumed that the cause of PCHI could be hereditary in 50% (of which 70% is non-syndromic), is non-genetic in 25% and is unknown in 25%.[7;8;42] This proportions figure is frequently cited in papers to date but, despite the recent progress in diagnostic possibilities, not often replicated without thorough diagnostic investigations.

We set out to study the aetiology of PCHI in young children in a nationwide study in the Netherlands (DECIBEL-study: Developmental Evaluation of Children: Impact and Benefits of Early hearing screening strategies Leiden) to determine the proportions attributed to the different aetiologies. Secondly a systematic review of the literature was performed searching for the latest insights concerning the aetiology of PCHI. The data on the aetiology of PCHI, collected in our DECIBEL-study in young children, were compared to the weighted proportions attributed to the different aetiologies found in the systematic review. In this way we attempted to reach a conclusion on the distribution of various causes of PCHI.

METHOD

Data on the proportions attributed to the aetiology of PCHI were generated in the DECIBEL-study and in a systematic review.

PCHI is defined as a permanent conductive or sensorineural bilateral hearing impairment of ≥40dB in the better ear. The aetiology of PCHI was classified in the following manner: When a genetic cause was identified the case was classified as hereditary hearing loss. Children with a positive family history, which can be regarded as suggestive of a hereditary cause, even when an underlying genetic cause is not identified, were also included in this category. A positive family history was defined as the presence of PCHI in a first, second or third degree relative. In cases in which risk factors for PCHI as defined by the Joint Committee on Infant Hearing (JCIH) had been present [43], a congenital infection had been or could be proven or hearing impairment

was acquired after the perinatal period, PCHI was classified as acquired. The perinatal risk factors included admission to a neonatal intensive care unit for more than 5 days, assisted ventilation, exposure to ototoxic medication and hyperbilirubinemia that required exchange transfusion. When diagnostic investigations did not reveal a relevant cause, the cause of PCHI was classified as unknown. An identified cause was given priority above the presence of a risk factor or a positive family history.

DECIBEL-STUDY

STUDY POPULATION

Data were collected in a nationwide study. Following approval by the Medical Ethics Committee of the Leiden University Medical Center, all Audiology Centers in the Netherlands (n=22) agreed to collaborate in the identification of children with PCHI. The inclusion criteria for children for this study were: born in the Netherlands between 1 January 2003 and 31 December 2005 and documented PCHI at the age of 3, 4 or 5 years. Children were invited by mail by the Audiology Center to participate in the DECIBEL-study. To generate representative results three birth cohorts were studied (2003, 2004 and 2005).

STUDY DESIGN

Parents of children participating in the DECIBEL-study gave written consent to (1) check relevant information from medical specialists, (2) perform a PCR for congenital CMV and/or (3) carry out genetic diagnostic investigations (molecular and clinical).

The medical correspondence was checked for information on earlier aetiological diagnostic investigations and prenatal, perinatal or postnatal risk factors for hearing loss. This covered among others, congenital infections, admission to a neonatal intensive care unit and causes of acquired hearing losses (trauma/meningitis/chemotherapy). Additional information was collected by parental questionnaires which covered questions concerning pregnancy, delivery, development, medical history and family history.

Dried neonatal blood samples (DBS) were retrieved from the Dutch National Institute for Public Health and Environment (RIVM) for real-time Polymerase Chain Reaction (PCR) on congenital cytomegalovirus (CMV) infection. In the Netherlands a blood sample is routinely taken from all newborns during the first week of life for screening for metabolic, endocrine and other disorders. The remaining blood is stored as DBS on Guthrie cards for 5 years. Using DBS is a practical and reliable method for diagnosing congenital CMV infection later in life, since DBS can be stored for very long periods without loss of sensitivity.[44] The parents of the participants and their family doctors were personally informed about the results of CMV DNA detection.[45]

Consent for genetic diagnostic investigations in children participating included a photo-protocol used to screen for dysmorphisms in the child. The photo-protocol included a frontal and a profile total body photo and details of the face, hands and feet. The photos were taken by the parents. The choice of specific molecular genetic diagnostic investigations was based on the available medical correspondence, parental questionnaires and the presence or absence of dysmorphisms. When diagnostic investigations had been performed previously, and the available information did not show any additional atypical finding, molecular genetic diagnostic investigation was not carried out. When no earlier diagnostic investigation had been done and when there was no positive family history of hearing loss molecular genetic diagnostic investigations for DFNB1 (connexin-26) and Pendred syndrome were performed. The reason for carrying out diagnostics for DFNB1 was based on the high carrier frequency in the population. The reason Pendred syndrome was investigated was based on carrier frequency, the highly progressive character of the hearing loss, the necessary care to prevent abrupt deterioration and to be able to predict future medical problems concerning thyroid function. In the case of a positive family history or dysmorphisms an individualized plan was made. (e.g. dominant hearing loss, Usher syndrome or Waardenburg syndrome). The parents of the participants and their family doctors were personally informed about the results of genetic investigations.

STATISTICAL ANALYSIS

Descriptive statistics were used to summarize data from the DECIBEL-study in numbers and proportions attributed to the aetiology. All statistical tests were carried out using SPSS version 16.0 (SPSS Inc., Chicago, IL, USA).

SYSTEMATIC REVIEW

To date guidelines for systematic reviews are often restricted to randomized trials. When reviewing observational studies (including those on aetiology) a challenge is faced because of the heterogeneity of study designs and inherent biases. The quality scoring of observational studies is also controversial because scores (constructed in an ad hoc fashion) may lack demonstrated validity.[46] For this review we chose to use recommendations from the proposed checklist for reporting observational studies.[47] We applied exclusion rules to control for heterogeneity. We excluded studies with a low quality assessment (based on the appropriateness of studies concerning the objective of the review and stratification of the study-population) and we decided to limit the data-presentation to descriptive information for each study and present only sample-size weighted proportions.

LITERATURE SEARCH

The literature-databases PubMed, Web of Science and PsychInfo were searched for articles, published between January 1997 and July 2009. This time-frame was chosen because the most frequently found genetic cause to date, the mutation in the *Gap junction protein, beta 2 (GJB2)* resulting in DFNB1, was discovered in 1997.[48] The search strategy used for Pubmed is shown in Table 1. (Limits: English and Dutch language). The other databases were searched using similar terms and limits.

Search No.	
1	(hearing loss/diagnosis"[Majr] OR "hearing loss/epidemiology"[Majr] OR "hearing loss/etiology"[Majr] OR "hearing loss"[ti] OR "hearing impairment"[ti] OR ("deafness/diagnosis"[Majr] OR "deafness/epidemiology"[Majr] OR "deafness/etiology"[Majr] OR "deafness"[ti]) OR deaf[ti])
2	("infant"[MeSH Terms] OR "infant"[tiab] OR "infants"[tiab] OR pediatric[tiab] OR paediatric[tiab] OR "child"[MeSH Terms] OR "child"[tiab] OR "children"[tiab] OR "infant, newborn"[MeSH Terms] OR ("infant"[tiab] AND "newborn"[tiab]) OR "newborn infant"[tiab] OR "newborn"[tiab] OR "neonate"[tiab] OR "neonatology"[MeSH Terms] OR "neonatology"[tiab] OR "neonatal"[tiab])
3	("etiology"[ti] OR "causality"[MeSH Terms] OR "causality"[ti] OR etiologic[ti] OR aetiologic[ti] OR "aetiology"[ti] OR cause[ti] OR "causes"[ti] OR "epidemiologic factors"[MeSH Terms] OR "epidemiology"[ti] OR "epidemiology"[MeSH Terms] OR epidemiologic[ti] OR "incidence"[ti] OR "incidence"[MeSH Terms] OR "prevalence"[ti] OR "prevalence"[MeSH Terms] OR "diagnosis"[ti] OR "diagnosis, differential"[MeSH Terms] OR "diagnostic"[ti])
4	1 and 2 and 3
5	Limits: publication from 1-1-1997 until 14-7-2009, English, Dutch

Table 1 Search strategy for Pubmed

LITERATURE SELECTION

Using this search strategy we found 915 citations. Titles and abstracts were read and reviewed and included for further study independently by two researchers (AK, SM). Differences in study-selection were solved by discussion. Following the first selection 97 articles were read completely and references were searched. The following inclusion criteria were used: (1) original article, (2) bilateral permanent conductive or sensorineural hearing loss of ≥ 40dB, (3) children younger than 18 years, (4) studies performed earlier than 1997 and (5) a distribution of proportions attributed to the aetiology. Studies that focused on a subpopulation were excluded (eg. mentally handicapped). A total of 9 original articles met the inclusion criteria (Figure 1.). [4;49-56]

DATA SYNTHESIS

Information from each relevant article was noted, including country and type of study, participant characteristics (e.g. hearing threshold), sample size, type of investigations performed and aetiological

diagnostic classifications. The aetiological classification included hereditary origin (syndromic, non-syndromic and chromosomal), acquired origin and the classification unknown. Data were extracted from the relevant articles by one reviewer and double-checked with the original article by a second reviewer. For data-presentation the original articles will be listed in alphabetical order.

STATISTICAL ANALYSIS

Following the observational character of the studies included in this systematic review the characteristics of these studies were narratively synthesised. Proportions were chosen as outcome measure and overall mean proportions were calculated using sample size weighted proportions. If a study did not account for a particular aetiological classification it was not incorporated into the calculation of the mean. Finally the weighted overall mean of the studies included in the review was compared with the results found in our nationwide DECIBEL-study. All statistical tests were carried out using SPSS version 16.0. (SPSS Inc., Chicago, IL, USA).

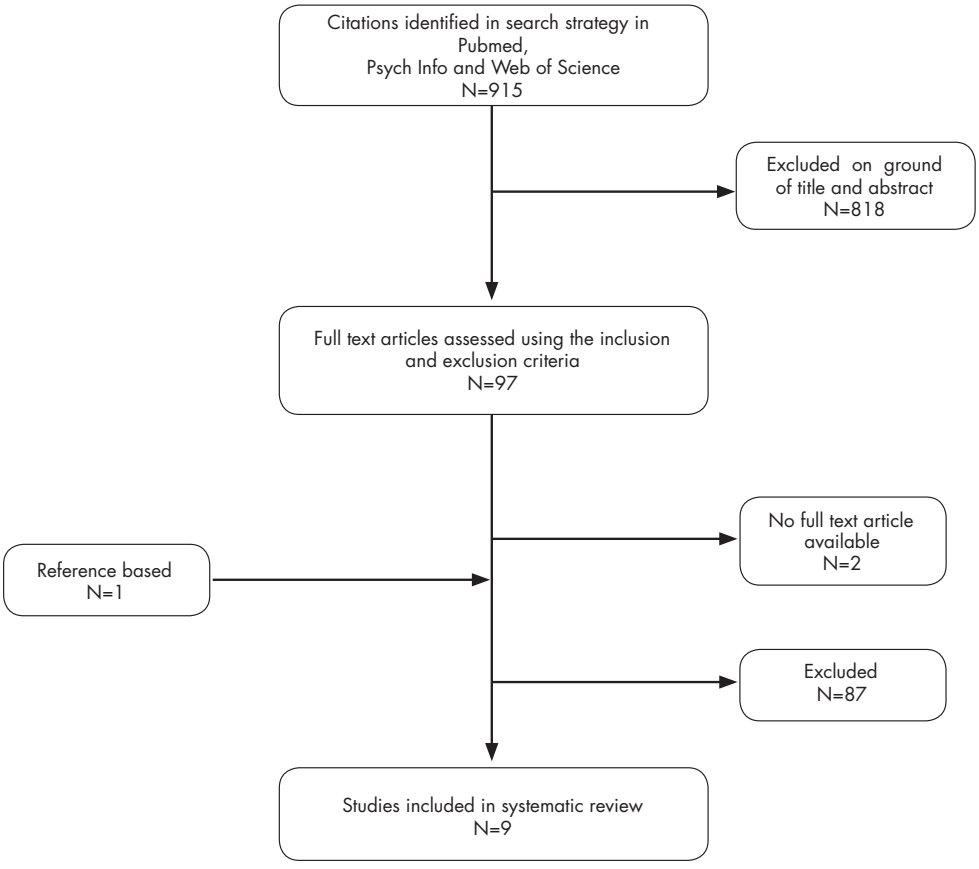

Figure 1 Flow diagram of literature search.

RESULTS

DECIBEL-STUDY

Two hundred and two children (one-third of all children identified with PCHI at the age of 3-5 years) participated in the DECIBEL-study. Of these, parents of 185 children (91.6%) gave permission for prospective diagnostic investigations or had given permission for diagnostic investigations to others previously. The data of the remaining 17 children were incomplete due to the absence of consent, no information on the presence of risk factors or only partially performed previous diagnostic investigations.

Of the children participating in the DECIBEL-study 171 Guthrie cards were available for CMV-PCR testing. CMV DNA was detected in 10 of the 171 DBS tested during this study.[45] When the results of children previously tested for congenital CMV (n=10, of which 6 were positive) were added, 16 children had a documented congenital CMV infection.

Parents of 90 of the 202 children (44.6%) participating gave permission for prospective genetic diagnostic investigations. Genetic diagnostic investigations were not performed in 26 of the 90 children for whom permission for was given since diagnostic investigations had been carried out previously and further investigations were not expected to contribute to the diagnosis (n=18) or available data were incomplete data (n=8). Genetic diagnostic investigations were performed in the remaining 64 children. In 55 children (85.9%) autosomal recessive diagnostic investigations were performed, in 7 children (10.9%) autosomal dominant diagnostic investigations, mitochondrial diagnostic investigations in 1 (1.6%) and a Single Nucleotide Polymorphism Array (SNP-array) in 1 (1.6%).

The proportions attributed to the different aetiologies, based on the diagnostic investigations performed within the DECIBEL-study (genetic and serological) and the available information gained from the medical history and records including earlier diagnostic investigations, is shown in table 2.

NUMBER OF CHILDREN (%)		MODERATE N=98	SEVERE N=43	PROFOUND N=44	TOTAAL N=185
HEREDITARY		**37 (37.8)**	**19 (44.2)**	**16 (36.4)**	**72(38.9)**
Non-syndromic					**32(17.3)**
Autosomal recessive	GJB2 homozygous	-	3	4	7
	GJB2 compound heterozygous	3	-	-	3
	Positive family history pattern	7	1	2	10
Autosomal dominant	Mutation DFNA3	-	-	1	1
	Positive family history pattern	8	1	2	11
Syndromic					**29(15.7)**
Autosomal recessive					**14**
	Campomelic dysplasia	-	1	-	1
	Cardio-Facio-Cutaneous syndrome	1	-	-	1
	Chudley McCullough syndrome	1	-	-	1
	Jervell-Lange Nielsen	-	1	-	1
	Johansen-Blizzard syndrome	-	-	1	1
	Pendred syndrome - non specified - mutation SLC26A4 - mutation SLC26A4 and EVA	 2 1	 1 3	 1	8
	Zellweger like syndrome	-	1	-	1
Autosomal dominant					**6**
	Nail-patella syndrome	1	-	-	1
	Stickler syndrome	1	1	-	2
	Townes Brocks	1	-	-	1
	Treacher Collins	1	-	-	1
	Waardenburg syndrome type1	-	-	1	1
Chromosomal					**9**
	Deletion chromosome 7	-	-	1	1
	Down syndrome	2	2	-	4
	De Grouchy syndrome	-	-	1	1
	Interstitial deletion 18q22.3q23	-	1	-	1
	Partial trisomy 8	1	-	-	1
	Turner syndrome	1	-	-	1
Positive family history non-specified		6	3	2	**11**

Table 2 (PART 1) The distribution of the proportions attributed to the aetiology in young children with PCHI in the Netherlands (DECIBEL-study). Data are given in number (and percentage) of children. Categorized for severity of hearing loss: moderate 40-60dB, severe 61-90dB and profound >90dB.

NUMBER OF CHILDREN (%)		MODERATE N=98	SEVERE N=43	PROFOUND N=44	TOTAL N=185
ACQUIRED		**19 (19.4)**	**13 (30.2)**	**23 (52.3)**	**55 (29.7)**
Prenatal					18 (9.7)
Congenital infection	Cytomegalovirus	2	4	10	16
	Rubella	-	1	1	2
Peri-natal riskfactors					29 (15.7)
Asphyxia (APGAR score <5 at 5 min)		8	3	5	16
Hyperbilirubinemia requiring exchange transfusion		-	1	1	2
Ototoxic medication (Gentamycine or Furosemide)		4	1	-	5
Other perinatal riskfactors		4	2	0	6
Post-natal					8 (4.3)
	Chemotherapy	-	1	-	1
	Cholesteatoma	1	-	-	1
	Meningitis (pneumococcal)	-	-	6	6
MISCELLANEOUS					**13(7.0)**
	GJB2 heterozygous	3			3
	Cleft palate	2	-	-	2
	Ear canal atresia	4	-	-	4
	Goldenhar syndrome	2	-	-	2
	Others	1	-	1	2
TOTAL KNOWN CAUSES AND/OR RISK FACTORS		**68 (69.4)**	**32 (74.4)**	**40(90.9)**	**140 (75.7)**
TOTAL UNKNOWN CAUSES DESPITE EXTENSIVE INVESTIGATION (congenital CMV and genetic investigations)		30 (30.6)	11 (25.6)	4 (9.1)	45 (24.3)

Table 2 (PART 2) The distribution of the proportions attributed to the aetiology in young children with PCHI in the Netherlands (DECIBEL-study).
Data are given in number (and percentage) of children. Categorized for severity of hearing loss: moderate 40-60dB, severe 61-90dB and profound >90dB.

Using a combination of genetic and serological investigations and medical records an underlying cause was found in 75.7% (n=140/185). In 45 children (24.3%) it was not possible to establish an underlying cause.

Irrespective of the degrees of hearing loss a hereditary cause was found in 38.9% (n=72/185) and acquired hearing loss in 29.7% (n=55/185). Perinatal risk factors were evenly distributed over all degrees of hearing loss.

In children with profound hearing loss the cause was known most often (n=40 out of 44, 90.9%) and the contribution of known acquired hearing loss the largest (n=23, 52.3%). This was caused by the large contribution of congenital cytomegalovirus infection (n=10) and meningitis (n=6).

SYSTEMATIC REVIEW

All relevant original studies (n=9) selected for systematic review were studies conducted in Western countries (Table 3). One study from the U.K. included only Bangladeshi children living there.[50] The majority of studies included in this review recruited children with PCHI from out-patient departments (n=7) and had a retrospective character (n=9). Most studies (n=5) focused on children with both sensorineural hearing loss (SNHL) and permanent conductive hearing losses. Five studies classified hearing loss in children with a positive family history for hearing loss, as hereditary.[4;51-53;55] Two studies prospectively performed molecular diagnostic investigations, of which one performed serological testing for congenital infections as well.[50;53] In those studies the highest proportions of acquired hearing losses and hereditary hearing losses were determined (although one of them classified children with a positive family history as hereditary also). The number of children included in the studies of Fortnum [4;54] was outside the range of the number included in other studies. When overall means were calculated this was acknowledged by the weight ascribed to the studies based on the number of children included in the study-population. Based on this systematic review the aetiology of PCHI was found to be of hereditary origin in 30.4%, 19.2% could be classified as acquired hearing loss and the aetiology of PCHI was unknown in 48.3%. When the study of Bangladeshi children (consanguinity percentage 33%) was excluded, a weighted hereditary origin was found of 30.2%.

A comparison between the proportions found in the DECIBEL-study and in the systematic review, shows that thorough but relatively limited diagnostic investigations (one specific prenatal infection (CMV) and limited genetic investigations without clinical consultation) contribute to a decrease of approximately 20% in the proportion of unknown causes (Figure 2.). This is reflected by an increase of causes of acquired and hereditary origin.

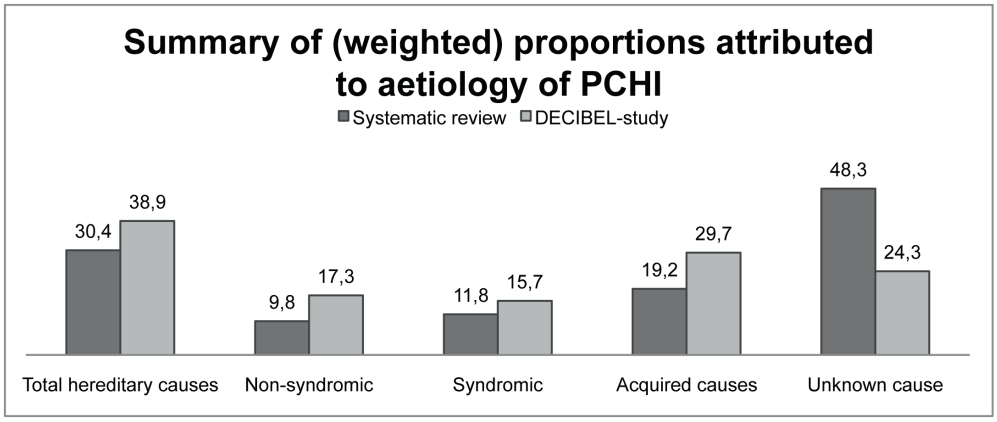

Figure 2 Summary of (weighted) proportions (%) attributed to the aetiology of PCHI.

STUDIES	COUNTRY OF STUDY	STUDY-PERIOD	STUDY-SAMPLE (PCHI-SAMPLE)	POPULATION	STUDY-TYPE	TYPE OF HEARING LOSS	IN BILATERAL PCHI			
							HEARING TRESHOLD (DB)	HEREDITARY CAUSE (%)	ACQUIRED CAUSE (%)	UNKNOWN CAUSE (%)
Admiraal, R.J.C.	Netherlands	1998-1999	55 (55)	School	R	SNHL and conductive	60	47.3	22	31
Bajaj, Y.	U.K.#	2003-2006	119 (119)	Out-patient	R/P	SNHL	40	59.6	18.5	21.8
Billings, K.R.	U.S.A.	1993-1996	301 (211)	Out-patient	R	SNHL	35	24.6	26.0	24.6
Dietz, A.	Finland	1988-2002	92 (54)	Out-patient	R	SNHL	40	40.7	16.7	42.3
Egeli, E.	Turkey	2001-2002	162 (162)	School	R/P	-	-	41.4	37.7	20.0
Fortnum, H. M.	U.K.	1997	653 (653)	School and out-patient	R	SNHL and conductive	40	39.7	16.5	40.9
Fortnum, H. M.	U.K.	1998	17160 (17160)	School and out-patient	R	SNHL and conductive	40	29.7	19.0	49.4
Nekahm, D.	Austria	2000	165 (165)	Out-patient	R	SNHL and conductive	40	33	30	36.0
Uus, K.	Estonia	1998	248 (248)	Out-patient	R	SNHL and conductive	40	36.3	29.4	34.3

Table 3 Overview of studies included in the review and the proportions attributed to the aetiology. Population: (School) school for deaf and hard-of hearing, (Out-patient) out-patient department. Study-type: (R) retrospective and (P) prospective. Type of hearing loss: (SNHL) sensorineural hearing loss, (conductive) conductive hearing loss
concerning Bangladeschi children living in th U.K.

CONCLUSION AND DISCUSSION

Neither the DECIBEL-study nor the systematic review support the assumption that 50% of PCHI could be of genetic origin, 25% of non-genetic origin and 25% has an unknown cause[7;8;42] The DECIBEL-study results in the following distribution: 40% is of hereditary origin, 30% is of acquired origin and one-fourth is of unknown cause. An extra category including miscellaneous causes (e.g. non hereditary cranio-facial anomalies such as Goldenhar syndrome and ear canal atresia) should be added to complete this proportions-figure up to 100%. The proportions in this aforementioned calculation seem to vary with the degree of hearing loss.

Our DECIBEL-study has some limitations. It is unknown whether parents of children with PCHI of an unknown cause were more eager to participate in this study with prospective diagnostic investigations. This may have caused response bias. It is unsure whether the probable participation of mainly ''unknown'' causes lead to an under- or an overestimation of the true proportions attributable to certain aetiologies, however the proportion genetic versus non-genetic it is not likely to be biased. Although not all parents gave consent for prospective investigations, the proportion with positive consent was fair to moderate in the light of the population studied (young children) and the burden involved when performing diagnostic investigations. Ideally, prospectively investigating the aetiology in the total study-population would be preferred. However, since diagnostic investigations are currently becoming clinical practice reviewing previous investigations is important from ethical and practical perspective. Our DECIBEL-study presents the aetiology of PCHI based not only on earlier diagnostic investigations, family history and risk factors but also on prospective genetic and serological diagnostic investigations, leading to the best estimate of the proportions attributed to the aetiology to date.

Although some uncertainties are inherent to analyzing retrospective data, the data (prospectively) generated by molecular diagnostic investigations as well as by the PCR on congenital CMV are robust. Determining the risk factors for PCHI retrospectively, however, might have been subject to information bias, since parental questionnaires and medical correspondence were used as available data sources. This might have led to an underestimation of the attribution of perinatal risk factors in the aetiology of PCHI. Additionally an underestimation of the proportion attributed to hereditary causes might have been introduced by the use of photographs for clinical genetic evaluation of the child. We believe that examination of the child by photographs can be used as a 'screening-instrument' for dysmorphisms, but that it can never replace the physical examination by the clinician as the gold standard. There is a chance that we may have missed typical features belonging to a particular hereditary cause, which could have lead to not requesting an individualized application for molecular diagnostic investigations.

The systematic review was subject to some limitations. First the difficulty in the definition of the correct search strategy. The present strategy resulted in a large number of not-appropriate articles; a narrower search however would have lead to the loss of important literature. We were not able to define a more specific search strategy to eliminate articles focusing on one aetiologic factor, presenting combined results for uni- and bilateral hearing loss or articles not specifying the degree of hearing loss. Personal assessment of a large number of full text articles was therefore necessary.

Secondly, the inconsistency and heterogeneity in the original studies necessitated the use of strict inclusion and exclusion rules. This was caused by differences in the classification of the aetiology, the number and range of diagnostic investigations, the sample-size and the study-design. It led to variations in the reported proportions and complicated the analysis. Congenital anomalies were, for example, included in the category genetic, as well as in the category unknown syndromal or 'other'. The risk factors for PCHI as described by the JCIH were also handled in various ways. The total number of studies included prevented us from dividing the studies into subgroups for further (pooled) analysis. By presenting only the major aetiologic classification and by using weighted proportions to calculate an overall mean we tried to overcome the differences between the studies and were able to generate useful evidence.

In the DECIBEL-study an acquired cause was found in 30% of children with PCHI. It was expected that several important causes would be less prevalent because of our nationwide well-established immunization program for *haemophilus influenza*, pneumoccal disease, rubella, mumps and measles in children and the low population prevalence of CMV infection. Perinatal risk factors, however, contributed largely to this category.

The results of the DECIBEL-study draw attention to the importance of the degree of hearing loss in the proportions attributable to aetiology. In children with profound hearing loss the proportion of acquired hearing loss appears much larger than the (over all degrees of hearing loss) expected 25%. In the children with severe hearing loss diagnostic investigations might be performed (and aetiologic factors found) more frequently. A degree of hearing loss related proportion figure could be a useful tool for clinical consultation.

In summary, the results of the DECIBEL-study and the systematic review support the value of diagnostic investigations in determining the aetiology of PCHI. Even when only one specific prenatal infection (congenital CMV) and limited genetic diagnostic investigations (without clinical consultation) were performed, the cause of PCHI was identified in a substantial proportion of children. Although it was not found that hereditary causes would account for 50%, it is likely that the proportion attributed to hereditary causes will be higher when the possibilities for diagnostic investigations develop further and are more widely used in the next few years.

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