

## Research Article

# Study of association of family history and consanguinity with congenital hearing loss

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### ABSTRACT

**Background:** Knowledge about the association of family history and consanguinity with congenital hearing loss is vital in order to prevent occurrence of such morbidity in future generations. The aim of the study was to find the strength of association between family history and consanguinity and congenital hearing loss.

**Methods:** A case control study was done using 50 congenitally deaf children and 50 children with normal hearing. A detailed history was taken from the parents with regard to family history of hearing loss and consanguinity.

**Results:** In the case group, 28% children had a family history of hearing loss and in the control group; none had a family history of hearing loss. In the case group, 48% of the children had parents with consanguinity. In the control group, 28% of the children had parents with consanguinity.

**Conclusions:** Family history and consanguinity play significant role in children having congenital hearing loss. Hence, avoidance of consanguineous marriages and pre-marital genetic counselling can prevent congenital hearing loss.

**Keywords:** Congenital, Hearing loss, Family, History, Consanguinity

## INTRODUCTION

Congenital hearing loss is a major morbidity and affects the life of the child as well as the family. The congenital deafness affects the language and speech development in the child and thus affects the child's education as well. Usually the congenital deafness is bilateral. Occasionally the congenital deafness is unilateral. In such a situation, it becomes difficult for early detection by the family. The advantage of early detection is that the child can be helped with hearing aid or cochlear implantation at the earliest and it can regain near normal speech and language development.

The period from birth to 5 years of life is critical for the development of speech and language; therefore, there is

need for early identification and assessment of hearing loss and early rehabilitation in infants and children. It was observed that children whose hearing loss was observed and managed before 6 months of age had higher scores of vocabulary, better expressive and comprehensive language skills than those diagnosed and managed after 6 months of age emphasising the importance of early identification and treatment.<sup>1</sup>

The causes of permanent childhood hearing loss are divided into hereditary in 50%, acquired in 25% and unknown in 25%.<sup>2</sup> The congenital hearing loss may be part of a syndrome with additional features affecting the skin, eyes, limbs etc. A family history and consanguinity of parents is often a cause for genetic disorders. If the hearing couple is consanguineous or comes from a highly

inbred community, the subsequent offspring have close to a 25 percent probability of deafness because of the high likelihood of autosomal recessive inheritance.<sup>3</sup> Hence, this study was conducted to study the depth of association between family history and consanguinity and congenital deafness.

**Objective**

To find the strength of association between family history and consanguinity and congenital hearing loss.

**METHODS**

This is a prospective case control study conducted at the department of otolaryngology of Navodaya Medical College, Raichur, Karnataka, India. The case control ratio was 1:1. The case group consisted of 50 deaf children of age group 6 months to 5 years who visited our Out Patient Department for complains of hearing loss. Each child under went detailed ear, nose and throat examination including otoscopy and audiological tests. The audiological tests done were Distraction test (for children of 6 to 24 months age), Performance test (for children of 2 to 5 years age) and Pure Tone Audiometry (for children above 3 years age). The children were also examined for any features suggestive of syndromic deafness. Children with history of ear discharge, gross developmental delay and those with birth weight less than 1500g were excluded from the study. Once the child is confirmed to be having permanent hearing loss of above 40 dB by above tests, the parents of those children were asked in detail for any family history of permanent deafness in previous three generations. They were also asked for history of consanguinity in the parents of the affected child. The control group consisted of children of 6 months to 5 years age group who visited our Out Patient Department for complains other than hearing loss viz. upper respiratory tract infection, rhinitis, headache etc. All of them had normal hearing which was confirmed by above mentioned audiological tests. The parents of these children were similarly asked in detail for any family history of permanent deafness in previous three generations. They were also asked for history of consanguinity in the parents of the child. The data thus collected from both the groups was subjected for statistical analysis. Chi-square test was used for statistical analysis.

A written informed consent was taken from all the parents of the children whose family history was used in the study.

**RESULTS**

In the control group, none of the children’s parents had a positive family history of permanent deafness in their past three generations. While in the case group, 14 out of 50 (28%) children had a positive family history of permanent deafness in their previous three generations.

This is statistical highly significant (p=0.00005) (Table 1).

In the control group, 14 (28%) children had positive history for consanguinity of parents. Among them, second degree consanguinity was present in the parents of 5 (10%) children and third degree consanguinity was present in the parents of 9 (18%) children. In the case group, 24 (48%) children had positive history for consanguinity of parents. Among them, second degree consanguinity was present in the parents of 14 (28%) children and third degree consanguinity was present in the parents of 10 (20%) children. The finding is statistically significant (p=0.039) (Table 2). Thus, our study shows that there is a strong association between family history of deafness and consanguinity of parents and congenital hearing loss.

**Table 1: Association between family history and hearing loss.**

		Hearing level		Total
		Controls	Cases	
Family history	Positive	Count	0	14
		%	0.0%	28%
	Negative	Count	50	36
		%	100%	72%
		Count	50	50
			100%	100%
Chi-square= 16.28, df= 1, p=0.00005, significance= highly significant				

**Table 2: Association between consanguinity of parents and hearing loss.**

		Hearing level		Total
		Controls	Cases	
Consanguinity of parents	Positive: second degree consanguinity	Count	5	14
		%	10%	28%
	Positive: third degree consanguinity	Count	9	10
		%	18%	20%
	Negative	Count	36	26
		%	72%	52%
		Count	50	50
			100%	100%
Chi-square= 4.24, df=1, p=0.039, significance- significant				

**DISCUSSION**

Hearing loss in children may be due to genetic or non-genetic (environmental) causes. At times, it may be a combination of these two causes. For example, a particular kind of genetic change makes some people more prone for the damage caused by ototoxic drugs. Sometimes the cause of the hearing loss is unknown. Understanding the genetic nature of deafness has important benefits. This knowledge helps genetic

counsellors to inform families about their chances of having children with hearing loss. This knowledge also influences the way a person's deafness is treated. Sometimes, the deafness may be part of a syndrome. In such a scenario, knowing the genetics of hearing loss allows a doctor to be aware that there might be problems in other parts of the body.

Hereditary hearing loss may be inherited by autosomal dominant, autosomal recessive, X-linked or mitochondrial inheritance. It might be reasonable for us to suspect a genetic cause for the child's deafness if it runs in the family. Sometimes the genetic expressions run in families but none will be affected in the family. These may be recessive genotypes. Consanguinity of the parents predisposes to phenotypic expression of such recessive genotypes.<sup>4</sup>

Whilst many otologists and audiologists are concerned primarily with the management and rehabilitation of hearing loss, it is also important to discuss and investigate its aetiology for the following reasons:<sup>4</sup>

1. Parents may want to know the aetiology if they are thinking of having further children (recurrence risk) and to obtain any prognostic information about their child's hearing loss (e.g. progression).
2. Young adults with hearing loss may wish to have information about having deaf or hearing-impaired children themselves (offspring risk).
3. To exclude syndromic forms of deafness that may initially present as non-syndromic deafness (prognostic information, career planning).
4. To follow-up long-term outcomes (e.g. cochlear implant, other therapeutic interventions).

Once environmental factors have been excluded (as far as possible), a genetic etiology becomes more likely. Although hearing impairment can be inherited as an autosomal recessive, dominant, X-linked or matrilineal (mitochondrial) trait, recessive causes account for about 80% of all cases of genetic deafness. The implication of this is that most children with genetic deafness will be born to normally hearing parents and will have no family history of deafness, yet their parents have a 25% chance of having a subsequent child with a similar hearing impairment. The difficulty is that in many cases, a genetic cause cannot be excluded as not all genes can be tested (see below), so the geneticist may have to rely on empirical data in order to provide recurrence risks. It may be a surprising fact that for children born with a severe/profound hearing impairment in whom no definite aetiology can be ascribed, that about 1:8 of their parents will go on to have a further deaf child. This is presumably because the group of children with "unknown causes" will include both recessive cases (with a 1:4 recurrence risk) and those with an undiagnosed environmental cause with a lower recurrence risk.<sup>4</sup>

In our study, 14 out of 50 (28%) children in the control group had a positive family history of permanent deafness in their previous three generations. In a similar study by Nagapoorima, et al they found a positive family history in 25% of the babies in their study group.<sup>5</sup> In Netherland, Korver A M found in his study that 39% of permanent hearing loss is attributed to hereditary reasons.<sup>6</sup> A school based study in Mumbai found family history as a statistically significant risk factor for hearing impairment. Nearly, 30% of children with hearing impairment were having this risk factor, causing the highest association among the risk factors such as prematurity, low birth weight, infections etc., The risk estimate, when extracted appears to be 67.<sup>7</sup> In Kerala, 38% of children with hearing impairment were having a family history.<sup>8</sup> These data are highlighting the need of creating awareness on a preventable cause of hearing impairment in India.<sup>9</sup>

In our study, in the control group, 14 (28%) children had positive history for consanguinity of parents. Among them, second degree consanguinity was present in the parents of 5 (10%) children and third degree consanguinity was present in the parents of 9 (18%) children. In the case group, 24 (48%) children had positive history for consanguinity of parents. Among them, second degree consanguinity was present in the parents of 14 (28%) children and third degree consanguinity was present in the parents of 10 (20%) children. The incidence of consanguineous marriages is more in developing countries than in developed countries. This increases the probabilities of incidence of hearing impairment.<sup>9</sup> In a Saudi Arabian population survey, between 45% and 47% had consanguineous marriage in first and second survey. In that same population between 66% and 37% had hereditary sensorineural hearing impairment.<sup>10</sup> In a large-scale national study of Oman, 70% of deaf children had consanguineous parents.<sup>11</sup> In a recent study in Iran, 61.4% of consanguinity was found in hearing impaired population.<sup>12</sup> Prevalence of consanguinity seems to be slightly less in Indian population. A similar study in Chennai by Selvarajan HG showed an incidence of 28% consanguinity in the parents of hearing loss affected children.<sup>9</sup> Second degree and third degree consanguinity can cause 25% and 12.5% chances of gene sharing in the off-spring.<sup>13</sup> Therefore, there are proportionate chances of incidence of hearing impairment in the family. Earlier literature shows there is 30-50% of consanguinity in south India.<sup>14</sup> In the present study, 38% had consanguineous marriage. This is in the lower range of earlier prevalence literature.

More than 50% of prelingual deafness is genetic, most often autosomal recessive and nonsyndromic. Approximately 50% of autosomal recessive nonsyndromic hearing loss can be attributed to the disorder DFNB1, caused by mutation of GJB2 (which encodes the protein connexin 26) and GJB6 (which encodes the protein connexin 30). The carrier rate in the

general population for a recessive deafness-causing GJB2 variant is approximately one in 33.<sup>15</sup>

Nonsyndromic hearing impairment has no associated visible abnormalities of the external ear or any related medical problems; however, it can be associated with abnormalities of the middle ear and/or inner ear. More than 400 genetic syndromes that include hearing loss have been described.<sup>16</sup> Syndromic hearing impairment may account for up to 30% of prelingual deafness, but its relative contribution to all deafness is much smaller, reflecting the occurrence and diagnosis of post lingual hearing loss.<sup>15</sup>

More than 70% of hereditary hearing loss is nonsyndromic. The different gene loci for nonsyndromic deafness are designated DFN (for Deafness). Loci are named based on mode of inheritance:

- DFNA: Autosomal dominant
- DFNB: Autosomal recessive
- DFNX: X-linked

The number following the above designations reflects the order of gene mapping and/or discovery.<sup>17</sup>

The subsequent offspring of a hearing couple with one deaf child and an otherwise negative family history of deafness have an 18% empiric probability of deafness in future children. The offspring of a deaf person and a hearing person have a 10% empiric risk of deafness. The child of a non-consanguineous deaf couple in whom autosomal dominant deafness has been excluded has an approximately 15% empiric risk for deafness. The child of a hearing sib of a deaf proband (presumed to have autosomal recessive nonsyndromic deafness) and a deaf person has a 1/200 (0.5%) empiric risk for deafness, or five times the general population risk.<sup>18</sup>

Family history and consanguinity are strongly associated with congenital permanent hearing impairment. According to Selvarajan HG, et al a child with family history has six times more chances of having permanent hearing impairment. Family history is still continuing to be an important risk factor as in the past in the southern part of India. A child with consanguineous parents has three times more chances for developing permanent hearing impairment. The second degree consanguinity is having three times chances, and third degree is having two times chances of occurrence of hearing impairment.<sup>9</sup>

Also, all persons with hearing loss of unknown cause should be evaluated for features associated with syndromic deafness. Important features include branchial cleft pits, cysts or fistulae; preauricular pits; telecanthus; heterochromia iridis; white forelock; pigmentary anomalies; high myopia; pigmentary retinopathy; goitre; and craniofacial anomalies. Because the autosomal dominant forms of syndromic deafness tend to have variable expressivity, correct diagnosis may depend on

careful physical examination of the proband as well as other family members.<sup>9</sup>

The optimal time for determination of genetic risk, clarification of carrier status, and discussion of the availability of prenatal testing is before pregnancy. It is appropriate to offer genetic counselling (including discussion of potential risks to offspring and reproductive options) to young adults who are deaf.<sup>9</sup> Regardless of its etiology, uncorrected hearing loss has consistent sequelae. Auditory deprivation through age two years is associated with poor reading performance, poor communication skills, and poor speech production. Educational intervention is insufficient to completely remediate these deficiencies. In contrast, early auditory intervention, whether through amplification, otologic surgery, or cochlear implantation, is effective.<sup>19</sup>

## CONCLUSION

Our study shows that there is a strong association between family history of deafness and consanguinity of parents and congenital hearing loss. A child with family history has more chances of having permanent hearing impairment. A child with consanguineous parents has more chances for developing permanent hearing impairment. It is appropriate to offer genetic counselling (including discussion of potential risks to offspring and reproductive options) to young adults who are deaf. Also a strong message must be conveyed to the society against the practice of consanguineous marriages. Also, universal neonatal hearing screening must be made a mandatory part of National Health Mission which shall include points like family history of deafness and consanguinity.

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