original article

The association between consanguineous marriage and offspring with congenital hearing loss

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BACKGROUND: Consanguinity is a commonly recognized practice among marriages in the Middle East and may lead to an increase in the prevalence of inherited disorders. Autosomal recessive deafness is the most common form of inherited congenital hearing loss (CHL).

OBJECTIVES: Determine the association of consanguineous marriages with congenital sensorineural hearing loss (SNHL) and auditory neuropathy.

DESIGN: Descriptive and analytical cross-sectional study.

SETTING: Ear specialist hospital.

PATIENTS AND METHODS: Children with severe-to-profound congenital SNHL, who had been referred to the specialist hospital for cochlear implant were analyzed. Patients were divided into subgroups based on degree of consanguinity.

MAIN OUTCOME MEASURE: The relative risk of having more than one child with SNHL in offspring of a consanguineous marriage.

SAMPLE SIZE: 189 parents and children with CHL.

RESULTS: The parents of 157 children (83.1%) were blood-related. Of those, 48 had more than one child with CHL (31.4%), while only two parents who were not blood-related had more than one child with CHL (6.25%; *P*=.005). Among the 189 children, 131 (69.3%) parents were direct cousins. Only 39 (20.6%) and 43 (22.8%) children had family histories of CHL on the paternal and maternal sides, respectively. There was no statistically significant difference in the prevalence of auditory neuropathy between the offspring of consanguineous and non-consanguineous marriages (*P*=.648).

CONCLUSION: The risk of having more than one child with SNHL in the offspring from a consanguineous marriage is 3.5 times higher than that of a non-consanguineous mating.

LIMITATION: The association of hearing loss degree with consanguinity was not studied.

CONFLICT OF INTEREST: None.

Congenital and genetic disorders account for a high prevalence of new-born mortality, morbidity, and disability in the Middle East.[1] Congenital hearing loss (CHL) is one of the most prevalent chronic conditions in children,[2] affecting 4.8 per 10 000 children in Saudi Arabia.[3] Moreover, it is well known that CHL can lead to a major delay in speech, language, and psychosocial development of the child.[2] Hereditary hearing impairment accounts for 50% of sensorineural hearing loss (SNHL),[4] and is classified into two types: syndromic and non-syndromic. Nonsyndromic deafness accounts for 70% of genetic hearing loss,[5] of which 60% to 80% is autosomal recessive[6] and usually congenital.[2,7]

Consanguineous marriage is defined as marriage of blood-related parents that have a recent common ancestor, second cousin, or closer relative.[8] The prevalence of consanguineous marriage varies globally, accounting for as much as 67.6% in the Middle East and as low as 0.5% in Europe.[9] According to El-Mouzan et al the overall prevalence of consanguinity in Saudi Arabia is 56%, of which 33.6% are first-cousin consanguineous marriages.[10] The high prevalence of consanguineous marriage is attributed to social customs involving the practice of arranged marriage within families and public unawareness of the adverse effects of such a practice.[4] It is important to note that by consanguinity we refer to first cousins (share a grandparent), second cousins (share a great-grandparent), and more distant cousin (share same tribe), as other forms of consanguineous marriage are religiously and legally prohibited.[11]

In addition to a high consanguinity rate, the Saudi Arabian population is also characterized by large families and individuals with advanced maternal or paternal age.[3,10] These factors increase the risk of congenital anomalies in their offspring with high consanguinity rate being the most important contributing factor.[12] However, a study in Saudi Arabia showed no significant association between first-cousin consanguinity and Down syndrome, sickle cell disease, glucose-6-phosphate dehydrogenase deficiency, type 1 diabetes mellitus, and major congenital malformations. The association with congenital heart disease was significant.[12] Meanwhile, consanguinity of parents was found in 80% of deaf children[13] and in 66% of patients with auditory neuropathy.[14] This study aimed to define the risk of developing hearing loss in offspring of consanguineous marriages in Saudi Arabia and to determine the relationship between consanguineous marriages and the number of children born with congenital sensorineural hearing loss SNHL and auditory neuropathy.

METHODS

This cross-sectional study addresses the association between consanguineous marriages, CHL, and auditory neuropathy in offspring born to consanguineous marriages. The sample size was determined by the number of children available during the study period who met inclusion criteria. We included all children with severe to profound SNHL who were referred to King Abdullah Ear Specialist Centre (KAESC) for cochlear implant, at King Abdulaziz University Hospital (KAUH), during the time period of March 2016 to March 2018 participated in this study. Exclusion criteria consisted of patients with acquired hearing loss, unilateral SNHL, postlingual deafness, and adults (>14 years of age).

All participants voluntarily consented to be included in the project. Confidentiality of subjects was protected by ensuring privacy and de-identifying information in the data set used for the study. Ethical clearance (E19-4324) was obtained from Prince Naif Bin Abdulaziz Health Research Centre Ethical Committee and KAUH.

Data collection

Patient histories were collected by reviewing medical files and via telephone conversations with parents or direct guardians. Data retrieved from medical records included the demographics, onset, pre- and postnatal history, related ear/nose/throat (ENT) clinical examination including pure tone audiometry, tympanometry, auditory brainstem response, otoacoustic emissions, and computed tomography and magnetic resonance imaging (CT and MRI, respectively) findings. Patients' medical records were also reviewed for possible causes of SNHL. Patients with an acquired cause (such as prematurity, meningitis, hyperbilirubinemia, trauma, and/or exposure to ototoxic drugs) as well as documented congenital infections were excluded. Auditory neuropathy was diagnosed based on otoacoustic emission and auditory brainstem response, which is done routinely as a part of our center's protocol. After obtaining consent, parents were asked if they were blood relatives (first cousins who "shared the same grandparent," or second cousins who "shared the same great grandparent," or same tribe), family histories of hearing loss (paternal or maternal), number of children with congenital SNHL, education and socioeconomic status, and the awareness of the impact of consanguineous marriage on offspring hearing prior to their marriage.

Data analysis

Microsoft Excel was used for data entry; data was analyzed using IBM Corp. Released 2019 IBM SPSS

Statistics for Windows, version 26.0. Armonk, NY: IBM Corp. Descriptive statistics are presented as the median and interquartile range for the only continuous variable age, and as frequencies and percentages for the categorical variables. The two groups (consanguineous versus non-sanguineous) were compared with respect to several aspects: (1) the presence and degree of consanguinity, (2) number of children with congenital SNHL, (3) income, and (4) socioeconomic status. The degree of consanguinity was divided into three groups: 1) shared grandparent, 2) shared great grandparent, or 3) only a shared tribe. The relative risk was calculated to show the relationship between the consanguineous and unrelated groups. The chi-square test was used to compare categorical variables andthe Mann-Whitney U test for the continuous variable age. *P*<.05 was considered statistically significant.

RESULTS

Among 189 patients (45% females and 55% males), parents of 157 patients (83.1%) were blood-related (at least belonging to the same tribe), while only 32 (16.9%) were not. Among the whole sample, parents of 131 patients (69.3%) were direct cousins (shared the same grandparent), 13 (6.9%) shared the same great grandparent, 13 (6.9%) were only related by being from the same tribe, and 32 (16.9%) were not related before marriage (**Figure 1**) (Each set of parents had only one child in the study). Some (20.6% and 22.8%) of the families reported a family history of CHL from the paternal and maternal sides, respectively (**Table 1**). Regarding educational background, 52.9% and 50.8% of the fathers and mothers had college degrees or higher, respectively. The monthly income averaged 2500 and 4300 Saudi Riyals per family member in consanguineous and a non-consanguineous marriages, respectively (*P*=.002). Most parents (86.2%) were not aware of the adverse effects of consanguineous marriage on hearing.

Among the 157 blood-related parents, 48 had more than one child with CHL (31.4%), while only two out of 32 of the non-related parents (6.25%) had more than one child with CHL (*P*=.005) as shown in **Table 2**. Moreover, only two parents had two children with CHL in the non-blood related group, while in the blood-related group, 29 parents had two children with CHL, 17 parents had three children with CHL, and two parents had four children with CHL. A significant difference between groups (*P*=.023) was noted (**Table 3**). Moreover, we compared first cousin and second cousin marriages groups to those who were not blood related or distantly related (first cousin; *P*=.053 and second cousin; *P*=.001) and a significant difference was noted.

Auditory neuropathy was detected in 15 patients. However, its prevalence was not significantly different between consanguineous and non-consanguineous (12 and three patients, respectively) marriages (*P*=.648) (**Table 4**). The relative risk of having more than one child with SNHL was 3.5 times higher in consanguineous marriages, while the odds ratio was 4.8 (**Table 5**). Even after excluding marriages between second and third cousins, the relative risk of developing CHL in the offspring of first cousins remains significantly high when compared to that of non-related parents (RR: 1.4, OR:1.6) (**Table 6**).

DISCUSSION

This study addresses the risk of developing hearing loss in the offspring of consanguineous parents in Saudi Arabia. In this study, the majority of children with CHL had blood-related parents (83.1%), most of whom were first cousins (69.3%). In comparison, consanguinity accounts for 56% of the total population in Saudi Arabia.[12]

The association between consanguinity and autosomal recessive disorders has been highlighted in previous studies,[15] which can explain the high prevalence of congenital deafness in any community with high consanguinity rates.[3,8] Consanguineous parents are more likely to be homozygous for the same trait, and therefore, increase the chance of having a child affected by congenital deafness.[16]

This study demonstrated a significant relationship between how closely the parents were related and the

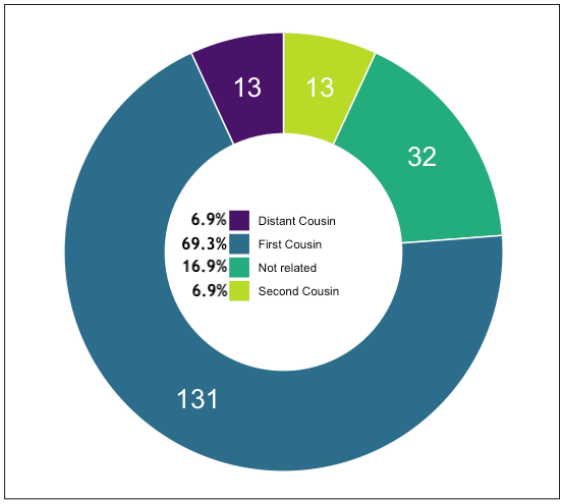

Figure 1. Degree of consanguinity of the parents of the 189 children in the study.

risk of being born with CHL for subsequent siblings (*P*=.001). This finding is consistent with previous studies by Zakzouk et al[4] and Khabori et al,[17] both of which also showed a significantly higher prevalence of hearing impairment in children whose parents were first cousins or relatives as opposed to those with unrelated parents. Parents having more than two children with CHL were typically blood-related and were mostly first cousins. The risk of having more than one child with SNHL was 3.5 times higher in consanguineous marriages. Even after excluding marriages between second and third cousins, the relative risk of developing CHL in the offspring of first cousins remains significantly high when compared to that of non-related parents (RR: 1.4). This evidence is supported by Zakzouk et al[8] (RR: 1.6; 95% CI: 1.18–2.27) and Sanyelbhaa et al[9] (RR: 1.76; 95% CI 1.57–1.97) with *P*<.001 for both studies.

Although many environmental and genetic etiologies of auditory neuropathy have been identified, several factors remain unexplained and further research is needed.[18] Lepcha et al[14] found auditory neuropathy to be present in 65.7% of patients born to consanguineous parents. In addition, Delmaghani et al[19] reported a cluster of 12 auditory neuropathy patients in two consanguineous Iranian families. However, the prevalence of auditory neuropathy in our study did not differ significantly between the offspring of consanguineous and non-consanguineous parents (*P*=.648). Due to the small number of positive cases with auditory neuropathy, this could be type 2 error.

The last study discussing the topic in Saudi Arabia was in 1995.[4] Since then, it would be assumed that marriage outside the family would be more socially acceptable. In addition, we would assume increased public awareness of the adverse effects of consanguinity and approachable pre-marital counselling. However, consanguinity remains an issue, as our study shows a prevalence of 83.1% of consanguinity among parents of congenitally-deaf children. Since prevention is a

Table 1. Demographic and clinical characteristics of the child patients (n=189).

	n (%)
Gender	
Female	85 (45)
Male	104 (55)
Family history of hearing loss	
Paternal side	39/189 (20.6)
Maternal side	43/189 (22.8)
Sibling	50 (26.5)
Number of siblings	
0-2	99 (52.4)
3-5	62 (32.8)
>5	28 (14.8)
Age at diagnosis (months)	36.0 (21.0, 53.5) (17.2)
Intelligence quotient (IQ) score	90.0 (12.6)

Data are n (%) except for age (median, first and third quartile) and IQ (mean, standard deviation).

Table 2. Prevalence of more than one child with congenital hearing loss with different degrees of consanguinity.

Degree of consanguinity	Number of children with congenital hearing loss	Total	
		1	>1
First cousin	93 (71.0)	38 (29.0)	131 (69.3)
Second cousin	5 (38.5)	8 (61.5)	13 (6.9)
Distant cousin	11 (84.6)	2 (15.4)	13 (6.9)
Not blood-related	30 (93.8)	2 (6.3)	32 (16.9)
Total	139 (73.5)	50 (26.5)	189

Data are n (%). The difference between subgroups regarding the prevalence of having more than one child with congenital hearing loss was statistically significant (*P*=.006).

Table 3. Relationship between the degree of consanguinity and number of children with congenital hearing loss.

Degree of consanguinity	Number of children with congenital hearing loss (%)				Total
	1	2	3	4	
First cousin	93 (71.0)	23 (17.6)	13 (9.9)	2 (1.5)	131
Second cousin	5 (38.5)	6 (46.1)	2 (15.4)	0	13
Distant cousin	11 (84.6)	0	2 (15.4)	0	13
Not blood-related	30 (93.75)	2 (6.25)	0	0	32
Total	139 (73.5)	31 (16.4)	17 (9.0)	2 (1.1)	189

Data are n (%). Statistically significant differences between subgroups for degree of consanguinity and number of subsequent siblings congenital hearing loss (chi-square test, *P*=.001).

Table 4. Prevalence of auditory neuropathy among consanguineous and non-consanguineous marriages.

Type of marriage	Auditory Neuropathy		Total
	N	Y	
Non-consanguineous	27 (90)	3 (10)	30
Consanguineous	147 (92)	12 (8)	159
Total	174 (92)	15 (8)	189

Data are n (%). Chi-square test revealed no significant difference in the prevalence of auditory neuropathy between consanguineous and non-consanguineous marriage (*P*=.648).

Table 5. The relative risk (RR) of having >1 child with congenital hearing loss in consanguineous parents.

Degree of consanguinity	Number of children with congenital hearing loss		Total
	>1	1	
First and second-degree cousins	46	98	144
Non-related[a]	4	41	45
Total	50	139	189

RR = (46/144)/(4/45) = 3.5; [a]Non-related include those who are remotely related from the same tribe.

Table 6. The relative risk (RR) of having >1 child with congenital hearing loss in first cousins parents.

Degree of consanguinity	Number of children with congenital hearing loss		Total
	>1	1	
First cousins	38	93	131
Non-first cousins	12	46	58
Total	50	139	189

RR=(38/131)/(12/58)=1.4

way to reduce the prevalence of genetic hearing loss, early identification of deafness and its cause is highly desirable for preventing this disability. The results of our study emphasize the importance of addressing this social health issue and implementing preventive measures, including genetic counseling, early screening, and increasing public awareness regarding the risk of hearing impairment in consanguineous families. Granting ready access to genetic premarital counselling and reproductive risk assessments for high-risk families is crucial for decreasing the prevalence of CHL. Counseling is especially beneficial for consanguineous parents who are planning to have another child as it can impact their decision or guide them through preventive measures. A neonatal hearing-screening program has been in effect for all newborns in Saudi Arabia since 2016. Affected children require a comprehensive medical history, physical examinations, and audiometric tests. In addition, early intervention in the form of fitting of hearing aids, auditory and speech rehabilitation, and support for patients and their families during pre- and early-school periods are of great value. Needless to say, it is also important to increase the awareness in the youth and unmarried population regarding the potential risks of consanguineous marriage, especially in those who have a genetic predisposition to such hereditary disorder.

This study has a few limitations. It involved patients with severe to profound SNHL; therefore, the association of the degree of hearing loss to consanguinity was not studied. In addition, not all patients in this study underwent genetic testing during the diagnosis to establish the aetiology of hereditary SNHL. Another limitation was the design of this study, which would have been stronger as a case-control instead of cross-sectional design.

Future research is needed to examine public awareness about the association of consanguinity with genetic disorders and highlight the role of public health professionals and campaigns in raising awareness. Consanguineous marriage is a common practice in Saudi Arabia and is associated with a higher prevalence of producing offspring with impaired hearing. The risk of having more than one child with SNHL in consanguineous marriage is 3.5 times higher than that of non-consanguineous mating. Therefore, preventive strategies, including public awareness and genetic counseling in addition to early screening and intervention are highly recommended.

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REFERNCES

1. Al-Gazali L, Hamamy H, Al-Arrayad S. Genetic disorders in the Arab world. BMJ. 2006 Oct 21;333(37573): 831-34.
2. Korver AMH, Smith RJH, Van Camp G, Schleiss MR, Bitner-Glindzicz MAK, Lustig LR, et al. Congenital hearing loss. Nat Rev Dis Prim. 2017 Jan 12;3:16094.
3. Al Salloum A, El Mouzan MI, Al Herbish A, Al Omer A, Qurashi M. Prevalence of selected congenital anomalies in Saudi children: A community-based study. Ann Saudi Med. 2015 MAr-Apr; 35(2): 107-10.
4. Zakzouk S. Consanguinity and hearing impairment in developing countries: A custom to be discouraged. J Laryngol Otol. 2002 Oct; 116(10):811-16.
5. Bussoli TJ, Steel KP. The molecular genetics of inherited deafness – current and future applications. J Laryngol Otol. 1998 Jun;112(6): 523-30.
6. Zakzouk SM, Fadle KA, Al Anazy FH. Familial hereditary progressive sensorineural hearing loss among Saudi population. Int J Pediatr Otorhinolaryngol. 1995 Jul; 32(3): 247-55.
7. Smith RJH, Bale JF, White KR. Sensorineural hearing loss in children. In: Lancet. 2005 Mar 5-11;365(9462): 879-90.
8. Zakzouk S, El-Sayed Y, Bafaqeeh SA. Consanguinity and hereditary hearing impairment among Saudi population. Ann Saudi Med. 1993 Sept 13; 13(5): 447-50.
9. Sanyelbhaa H, Kabel A, Abo El-Naga HAER, Sanyelbhaa A, Salem H. The risk ratio for development of hereditary sensorineural hearing loss in consanguineous marriage offspring. Int J Pediatr Otorhinolaryngol. 2017 Jul 18; 101:7-10.
10. El-Mouzan MI, Al-Salloum AA, Al-Herbish AS, Qurachi MM, Al-Omar AA. Regional variations in the prevalence of consanguinity in Saudi Arabia. Saudi Med J. 2007 Dec;28(12): 1881-84.
11. Warsy AS, Al-Jaser MH, Albdass A, Al-Daihan S, Alanazi M. Is consanguinity prevalence decreasing in Saudis?: A study in two generations. Afr Health Sci. 2014 Jun; 14(2): 314-21.
12. El Mouzan MI, Al Salloum AA, Al Herbish AS, Qurachi MM, Al Omar AA. Consanguinity and major genetic disorders in Saudi children: A community-based cross-sectional study. Ann Saudi Med. 2008 May-Jun; 28(3): 169-73.
13. Zakzouk SM, Fadle KA, Anazy FH Al. Familial hereditary progressive sensorineural hearing loss among Saudi population. 1995;32:247-55.
14. Lepcha A, Chandran RK, Alexander M, Agustine AM, Thenmozhi K, Balraj A. Neurological associations in auditory neuropathy spectrum disorder : Results from a tertiary hospital in South India. 2015;18(2): 171-80.
15. Bayoumi RA, Yardumian A. Genetic disease in the Arab world. BMJ. 2006 Mar-Apr; 35(2): 107-10.
16. Bergstrom L, Hemenway WG, Downs MP. A high risk registry to find congenital deafness. Otolaryngol Clinics North America. 1971 June; 4(2):369-99.
17. Khabori M Al, Patton MA. Consanguinity and deafness in Omani children. Int J Audiol. 2008; 47(1): 30-33.
18. Marlin S, Jonard L, Loundon N, Bonnet C, Leboulanger N, Van Maldergem L, et al. Genetic Update on Auditory Neuropathy. Audiol Neurotol Extra. 2011;1(1): 20-29.
19. Delmaghani S, Del Castillo FJ, Michel V, Leibovici M, Aghaie A, Ron U, et al. Mutations in the gene encoding pejvakin, a newly identified protein of the afferent auditory pathway, cause DFNB59 auditory neuropathy. Nat Genet. 2006 Jul; 38(7): 770-78.