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Original Article

Hearing Loss Among Families with 2 and More Affected Members in Golestan Province, Iran: A Cross-Sectional Study of 320 Families

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BACKGROUND: Our study centers on various aspects of families who have 2 or more members with hearing loss (HL) and are living in Golestan province in Iran. We aimed to identify those families with the highest probability of hereditary HL and also to examine the impact of consanguinity among them.

METHODS: The families included in the study underwent a comprehensive screening process that involved their prenatal and postnatal histories as well as family medical histories. Additionally, each patient received a thorough clinical ear examination. The evaluation also took into account factors such as patterns of inheritance, consanguinity, a 3-generation pedigree, and physical examination. Following this initial assessment, patients were referred for a complete hearing evaluation, which included pure-tone audiometry, speech recognition threshold, otoacoustic emission, and auditory brainstem response tests.

RESULTS: We identified a total of 8553 individuals living in Golestan province who are hearing impaired. Among those, our records indicate that 320 families had at least 2 affected members. The rate of consanguinity marriage in non-syndromic families was 64.43%. Also, a significant number (88.12%, or n = 282) of the families exhibited hereditary HL, among which a substantial proportion (89.72%, or n = 253) presented with non-syndromic forms of HL. Furthermore, bilateral, stable, and prelingual HL were the most frequently observed types, and a majority of the patients were diagnosed with sensorineural and profound HL.

CONCLUSION: This study revealed a correlation between consanguinity and the incidence of familial HL, with more probability of bilateral, prelingual, sensorineural, and profound forms.

KEYWORDS: Hearing loss, hereditary, consanguinity, Golestan province, Iran

INTRODUCTION

Hearing loss (HL) is the most prevalent sensorineural disorder in humans. It can be caused by various factors, such as exposure to loud noise, aging, infections, and genetic predisposition. Hearing loss can be classified based on several criteria such as type (sensorineural, conductive, or mixed), etiology (acquired or inherited; the latter includes syndromic or non-syndromic causes), age of onset (before language acquisition: prelingual or after language acquisition; postlingual), severity (mild, moderate, severe, or profound), audiometric profile (characterized by different patterns of HL across frequencies such as sloping, low frequency, mid-frequency, etc.), and laterality (occurring in 1 ear, unilateral; or both ears, bilateral).[1] Understanding these classifications can assist healthcare providers in making proper diagnoses and developing customized treatment plans for individuals with HL. Hearing loss may cause lifetime challenges for those who do not receive prompt help and intervention, ranging from linguistic and social communication issues to obstacles in school and lifework.[2] Based on the global burden of disease 2019, HL affects more than 1.5 billion people (around 20% of the global population), of whom 62% are older than 50 years. Most severe HL cases are younger than 5 and older than 70 years old.[3] Sensorineural HL (SNHL) and conductive HL (CHL) are the 2 main types. Sensorineural hearing loss is when

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the auditory nerves in the cochlea are not able to transduce vibrations into neural electrochemical impulses. Conductive HL is the failure of sound transmission through the external or middle ear. Mixed HL is found in some children and is defined as the co-occurrence of SNHL and CHL.[4] Sensorineural hearing loss is a relatively common congenital disorder affecting 1-3 in 1000 individuals globally. Most hereditary HL cases are autosomal recessive non-syndromic hearing loss (ARNSHL). Like other autosomal recessive conditions, it frequently occurs due to consanguinity. High rates of consanguineous marriages are reported in developing countries like Iran. Saadat et al[5] calculated the rate to be 38.6% based on a sample of 300 000 couples. Hereditary HL and shared common ancestors are evidentially strongly associated.[6,7] Accordingly, the prevalence of SNHL in Iran is higher than elsewhere, as it affects up to 6 per 1000 newborns. In this paper, we aim to investigate the HL in Iranian families with 2 and more affected members in different populations (ethnicities) in Golestan province.[8]

MATERIAL AND METHODS

Study Design and Population

On a retrospective cross-sectional approach, we gathered data of hearing-impaired patients who reside in Golestan province, Iran, based on the number of affected in the families, consanguinity, population (ethnicity), and HL types and severity. About 1.9 million people from different populations (Turkmen, Fars, Sistani, etc.) live in the region. A total of 8553 patients with HL were evaluated in this study. They were under-covered and referred from the Welfare Organization of Golestan province. For a family to be included, they must have at least 2 hearing-impaired members.

Ethical Approval

Prior to inclusion in the study, informed written consent was obtained from patients or their legal guardians. Our study was approved by the Ethics Committee of Golestan University of Medical Sciences (Approval No: IR.GOUMS.REC.1397.343).

Measuring Tools

To collect the demographical and clinical status of all patients from families with at least 2 affected, questionnaires were filled out, and physical examination, familial medical history, pre- and post-natal records, and a 3-generation pedigree were evaluated. The last one was used to determine consanguinity and inheritance patterns. Moreover, pure-tone audiometry (PTA), the gold standard audiometry test, was conducted, and thresholds were obtained at 250, 500, 1000, 2000, 4000, and 8000 Hz frequencies with intensity of upto 120 dB. A tympanogram is a graph that represents the middle ear's pressure response to sound, based on the Jerger classification.[9] A graph that displays the middle ear's pressure reaction to sound is known as a tympanogram. There are 3 distinct types of tympanograms: type A, which indicates a normal curve; type B, which indicates an unusual curve; and type C, which indicates a negatively shifted curve. Individuals with air conduction thresholds exceeding 20 dB were identified as having hearing impairment. Assessing the hearing ability of young children can be challenging. To address this issue, we adopted the American Speech-Language-Hearing Association guidelines, which recommend specific testing approaches based on age. For infants under 6 months, we employed behavior observation audiometry, while visual reinforcement audiometry was used for those ranging from 6 to 24 months. For children between 2 and 5 years old, as well as adults, we utilized conditioned play audiometry.[10,11] We also set the following dB levels for each type of HL: normal (0-20), mild (26-40 dB), moderate (41-55 dB), moderate-to-severe (56-70 dB), severe (71-90 dB), and profound (>91 dB).[12]

Statistical Analysis

Data Analyses were carried out using Statistical Package for the Social Sciences version 29.0 (IBM SPSS Corp.; Armonk, NY, USA) and *P* values < .05 were considered statistically significant.

RESULTS

Baseline Data

According to our data, there are 8553 hearing-impaired patients living in Golestan province. The highest number of patients reside in Gorgan (1439, 16.82%), followed by Gonbad-e Kavus (1035, 12.1%) and Bandar-e Turkmen (900, 10.52%). The other cities with significant numbers of hearing-impaired patients include Gomishan (684, 8%), Kalaleh (749, 8.8%), Aq-Qala (712, 8.32%), Ali Abad (565, 6.6%), Kordkuy (436, 5.1%), Azad Shahr (415, 4.9%), Minudasht (399, 4.67%), Ramian (387, 4.52%), Maraveh Tapeh (306, 3.58%), Galikesh (267, 3.12%), and Bandar-e Gaz (258, 3.02%). In this population, we include families with 2 and more affected members. Therefore, a total of 649 hearing-impaired patients from 320 families with at least 2 affected members were recorded, considering 9 families with 3 affected members and 4 families with 4 affected members. In this cohort, 279 (42.99%) patients were female and 370 (57.01%) were male. The age variable ranged from 1 to 81 with a mean of 31.04 (SD = 13.673). As graphically illustrated by Figure 1, the data show that 88.12% of all patients had hereditary HL, of which 10.28% have been diagnosed with syndromic HL as follows: 7 patients had Usher syndrome, 9 had disability-associated HL syndromes, 5 had Waardenburg syndrome, and 6 had undefined syndromes. Two other patients had Treacher Collins syndrome and Crouzon syndrome. Moreover, non-syndromic HL accounted for 89.72% of all hereditary cases, with 81.81% autosomal recessive, 16.21% autosomal dominant, and 1.98% mitochondrial inheritance patterns. Acquired HL also accounted for 11.88% of all cases. Families affected by autosomal recessive HL had a higher average number of siblings compared to families affected by autosomal dominant HL. Specifically, in all autosomal recessive cases, the average number of siblings in families was 5, with a minimum of 4 and a maximum of 11. Meanwhile, in autosomal dominant cases, it was 4, with a minimum of 3 and a maximum of 8. Interestingly, they were all from 2 affected families as well. Of 253 non-syndromic families, 163 (64.43%) had consanguineous marriages, and 90 (35.57%) had non-consanguineous marriages. Furthermore, 74.40% (n = 154)

MAIN POINTS

- Collecting data from a total of 8553 hearing-impaired individuals residing in Golestan province, Iran, with 578 individuals belonging to families with at least two affected members.
- Revealing correlations between familial hearing loss and consanguinity, as well as the incidence of hereditary non-syndromic hearing loss.
- Revealing correlation between familial hearing loss and sensorineural, profound, and pre-lingual types of hearing loss.

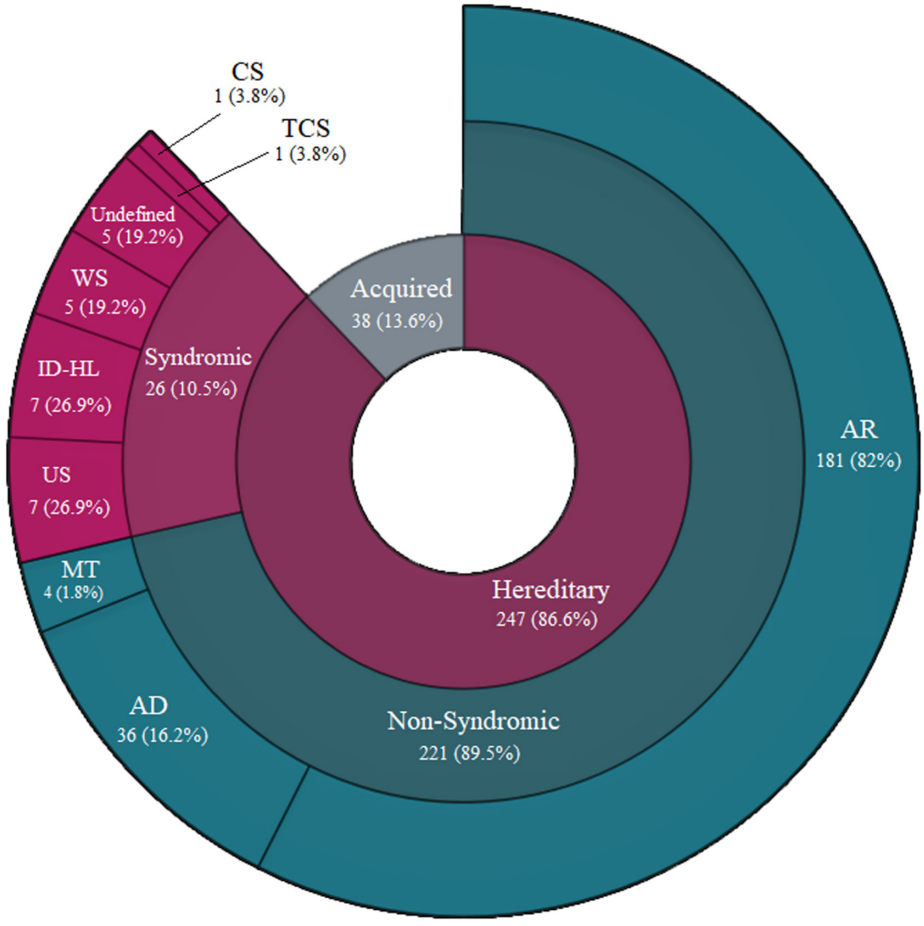

Figure 1. Classification of study sample based on etiology of HL. CS, Crouzon syndrome; ID-HL, intellectual disability-associated hearing loss; TSC, Treacher-Collins syndrome; US, Usher syndrome; WS, Waardenburg syndrome.

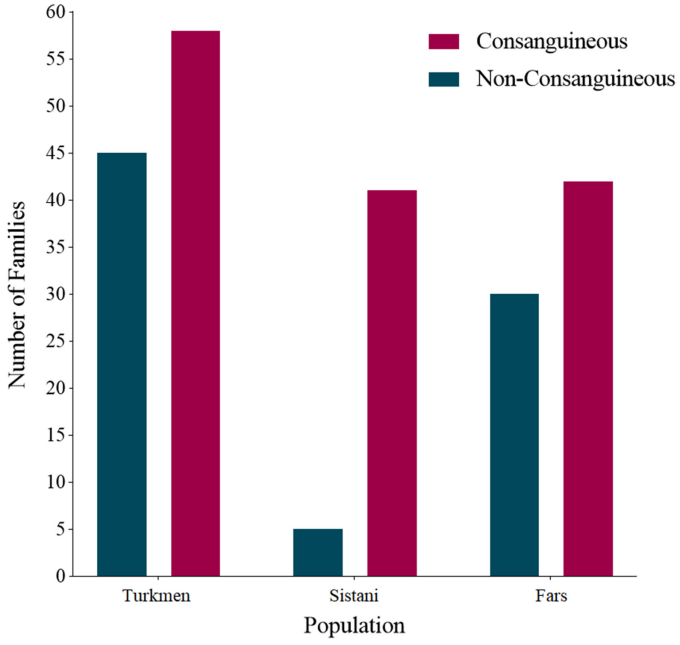

Figure 2. Type of marriages in the 3 ethnic groups. For Turkmen, 67 consanguineous and 50 non-consanguineous marriages; 46 consanguineous and 5 non-consanguineous marriages in Sistani; and 50 consanguineous and 35 non-consanguineous marriages in Fars were documented.

of families with a non-syndromic autosomal recessive inheritance pattern had consanguineous marriage, while this rate among non-syndromic autosomal dominant cases was 9.76% (n = 5), and no consanguinity was observed among mitochondrial cases. Figure 2 shows the difference of consanguinity rate in ethnic groups of this study. Demographical data are presented in Figure 3. The cities Gorgan, Gonbad-e Kavus, and Kalaleh had the most number of patients. Also, 322 individuals were from rural areas, and 327 lived in urban areas.

Clinical Characteristics

Based on our results, which are summarized in Table 1, most of the patients suffered from bilateral (99.4%) and stable (94.14%) HL and were diagnosed prelingually (85.82%). In like manner, the majority of patients (n = 608, 93.68%) were diagnosed with SNHL, while conductive and mixed types accounted for less than 7% combined. Of all ears (1298) in this cohort, 774 (59.63%) had profound HL, 230 (17.72%) had severe HL, 171 (13.17%) had moderate to severe, 95 (7.32%) had moderate, 25 (1.93%) had mild, and only 3 (0.23%) had normal hearing. Figure 4 shows the severity of HL in relation to the age and gender of patients. A PTA test of all patients showed that, except for 4 ears, all others had type A tracing. (Table 2)

DISCUSSION

This study was conducted to investigate demographical and clinical aspects of hearing-impaired subjects in families with 2, 3, and 4

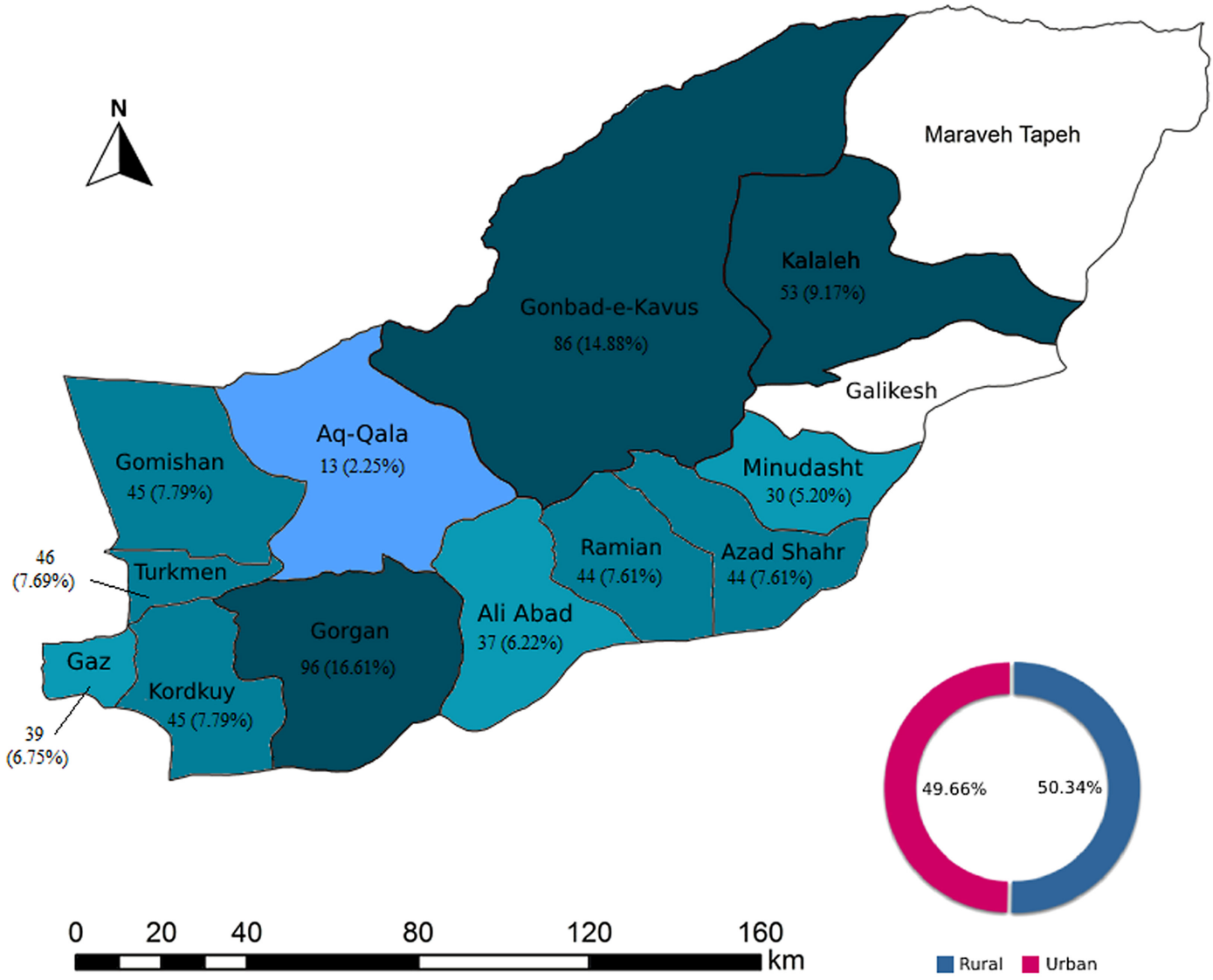

Figure 3. Geographical distribution of hearing loss patients from families with at least 2 affected members in Golestan province in the north of Iran.

Table 1. Data on Type, Laterality, Stability, and Age of Onset of Cohort of This Study

Type of Hearing Loss	n (%)
Conductive	12 (1.85%)
Sensorineural	608 (93.68%)
Mixed	29 (4.47%)
Laterality	
Unilateral	4 (0.6%)
Bilateral	645 (99.4%)
Stability	
Progressive	38 (5.86%)
Stable	611 (94.14%)
Age of onset	
Pre-lingual	557 (85.82%)
Post-lingual	92 (14.18%)

occurrences of HL among Sistani, Turkmen, and Fars ethnic groups. Our results showed 88.12% hereditary forms of HL in the study sample, with 89.72% exhibiting NSHL. Autosomal recessive non-syndromic hearing loss was the most frequent type of HL. These data are consistent with our previous study on the Turkmen population of Iran.[13] Consanguineous marriage is particularly prevalent among Asian, Latin American, and North African societies. It can be as high as 70% or as low as 10% in some regions. We calculated a 64.43% consanguineous marriage rate in families with at least 2 NSHL-affected members (90.2%, 58.82%, and 57.26% for Sistani, Fars, and Turkmen ethnicities, respectively). Similarly, our previous report on consanguinity among HL patients of the Turkmen population in Iran showed a rate of 65%.[13] Moreover, Abtahi et al[14] evaluated 618 Iranian SNHL patients and reported that 61.4% of them were from consanguineous marriages. Ajallouyan et al[15] also found that 65% of the parents of 310 Iranian deaf children had consanguineous marriages.[15] It is clear that the high rate of consanguinity in Iranian populations has a direct correlation with the prevalence of HL. While there are other factors that can contribute to HL, these studies highlight the need to consider consanguinity's potential to increase the risk of hearing

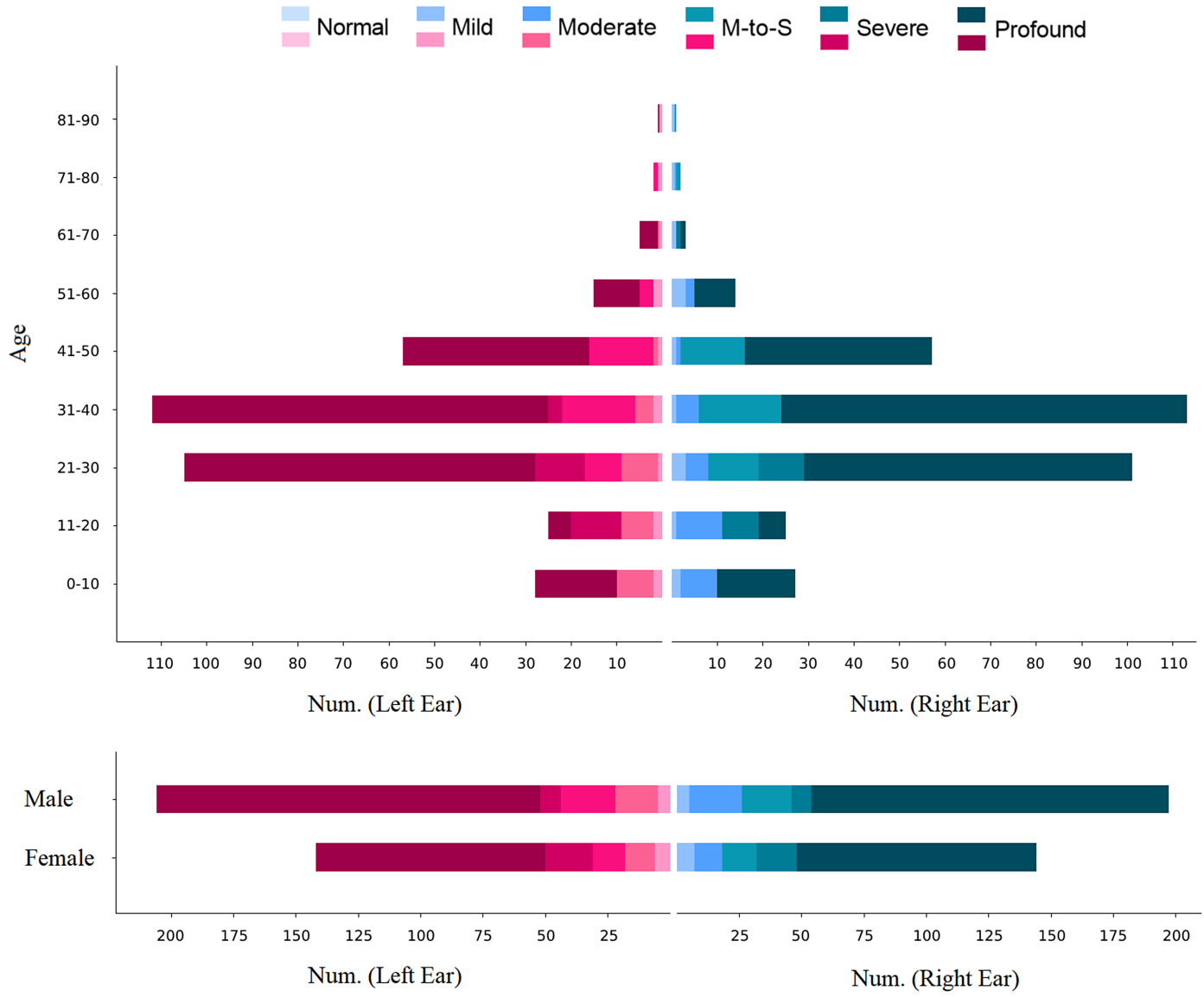

Figure 4. Hearing loss severity of left and right ears of patients from families with 2 and more affected members, based on gender and age.

impairment. The same results have been reported in other Middle-Eastern populations like Oman,[16] Qatar,[17] and Palestine.[18] However, a 2020 study in Saudi Arabia did not find any significant data between consanguineous and non-consanguineous marriages.[19] Based on our results, the severity of HL substantially increases in familial cases, as 77.35% of patients had severe and profound HL, and the share of mild cases was only about 2%.

Limitations and Future Direction

This study mainly focuses on families with 2 affected members. According to the latest announcement, there is a large number of hearing-impaired patients under-covered by the Golestan province welfare organization (8553 individuals). The patients in this study were not genetically evaluated. We previously calculated the frequency of the c.35delG mutation in the GJB2 gene, the most frequent variant in ARNSHL, among 128 families with HL in this province.[20] Therefore, future studies are suggested to work on other GJB2 variants and other HL-related genes like GJB6 and GIPC3. Such attempts would expand our understanding of HL epidemiology. Our study was limited to the Golestan province region. Elevated rates of consanguineous marriage were also recorded in other provinces, particularly Sistan and Baluchestan. As a result, these regions are regarded as an ideal sample to conduct studies on HL.

Table 2. Tympanometry Results. Number of Recorded Tympanograms for Left and Right Ears

Type of Tympanogram	Right Ear (n = 578)	Left Ear (n = 578)
Type A	644 (99.23%)	647 (99.69%)
Type B	3 (0.46%)	2 (0.31%)
Type C	2 (0.31%)	0 (0%)

Ethics Committee Approval: This study was approved by Ethics Committee of Golestan University of Medical Sciences (Approval No: IR.GOUMS.REC.1397.343).

Informed Consent: Informed consent was obtained from the patients or their legal guardians who agreed to take part in the study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – M.O.; Design – M.O.; Supervision – M.O.; Resources – M.O.; Materials – Z.A., T.K.; Data Collection and/or Processing – Z.A., T.K.; Analysis and/or Interpretation – Z.A., T.K.; Literature Search – Z.A.; Writing – Z.A., T.K.; Critical Review – M.O., Z.A.

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Declaration of Interests: The authors have no conflict of interest to declare.

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REFERENCES

1. Zahnert T. The differential diagnosis of hearing loss. *Dtsch Ärztebl Int*. 2011;108(25):433-43; quiz 444. [CrossRef]
2. Shukla A, Harper M, Pedersen E, et al. Hearing loss, loneliness, and social isolation: a systematic review. *Otolaryngol Head Neck Surg*. 2020;162(5):622-633. [CrossRef]
3. Haile LM, Kamenov K, Briant PS. Hearing loss prevalence and years lived with disability, 1990-2019: findings from the Global Burden of Disease Study 2019. *Lancet*. 2021;397(10278):996-1009. [CrossRef]
4. Wroblewska-Seniuk K, Dabrowski P, Greczka G, et al. Sensorineural and conductive hearing loss in infants diagnosed in the program of universal newborn hearing screening. *Int J Pediatr Orl*. 2018;105:181-186. [CrossRef]
5. Saadat M, Ansari-Lari M, Farhud DD. Consanguineous marriage in Iran. *Ann Hum Biol*. 2004;31(2):263-269. [CrossRef]
6. Sanyelbhaa H, Kabel A, Abo El-Naga HAE, Sanyelbhaa A, Salem H. The risk ratio for development of hereditary sensorineural hearing loss in consanguineous marriage offspring. *Int J Pediatr Orl*. 2017;101:7-10. [CrossRef]
7. Mahdieh N, Rabbani B, Shirkavand A, et al. Impact of consanguineous marriages in GJB2-related hearing loss in the Iranian population: a report of a novel variant. *Genet Test Mol Biomarkers*. 2011;15(7-8):489-493. [CrossRef]
8. Oladnabi M, Hasheminasabgorji E, Mohammadi M, et al. Hereditary and non-hereditary pattern of deafness in Golestan Province, Iran. *J Mazandaran Univ Med Sci*. 2021;31(199):174-178.
9. Jerger J. Clinical experience with impedance audiometry. *Arch Otolaryngol*. 1970;92(4):311-324. [CrossRef]
10. Katz J, Chasin M, English KM, Hood LJ, Tillery KL. *Handbook of Clinical Audiology*; vol 7. Wolters Kluwer Health Philadelphia, PA; 2015.
11. Northern JL, Downs MP. *Hearing in Children*. Lippincott Williams & Wilkins; Philadelphia; 2002.
12. Stach BA, Ramachandran V. *Clinical Audiology: an Introduction*. Plural Publishing; 2021.
13. Hajilari M, Oladnabi M, Kianmehr A, Taziki MH, Abdollahi F. Hereditary hearing loss and consanguinity in Turkmen population of Iran: a retrospective study. *Int J Pediatr*. 2019;7:10323-10334.
14. Abtahi SH, Ebrahimi Z, Sepehrnejad M, Nilforoush M-H. The relationship between consanguineous marriage and hearing loss in patients referring to Isfahan cochlear implant center, Iran. *J Isfahan Med Sch*. 2019;37(529):587-592.
15. Ajallouyan M, Radfar S, Nouhi S, et al. Consanguinity among parents of Iranian deaf children. *Iran Red Crescent Med J*. 2016;18(11):e22038. [CrossRef]
16. Al Khabori MA, Patton MA. Consanguinity and deafness in Omani children. *Int J Audiol*. 2008;47(1):30-33. [CrossRef]
17. Girotto G, Mezzavilla M, Abdulhadi K, et al. Consanguinity and hereditary hearing loss in Qatar. *Hum Hered*. 2014;77(1-4):175-182. [CrossRef]
18. Abu Rayyan A, Kamal L, Casadei S, et al. Genomic analysis of inherited hearing loss in the Palestinian population. *Proc Natl Acad Sci U S A*. 2020;117(33):20070-20076. [CrossRef]
19. Almazroua AM, Alsughayer L, Ababtain R, Al-Shawi Y, Hagr AA. The association between consanguineous marriage and offspring with congenital hearing loss. *Ann Saudi Med*. 2020;40(6):456-461. [CrossRef]
20. Hajilari M, Sharifinya A, Khosravi T, et al. Frequency of c. 35delG mutation in GJB2 gene in patients with autosomal recessive non-syndromic hearing loss of five ethnic groups in Golestan, Iran. *Int J Pediatr*. 2023;11(1):17286-17298.