Original Research Article

Analysis of GJB2 Gene Mutations in 1330 Deafness Cases of Major Ethnic Groups in Northwest China

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Panpan Bian, Master[1,*], Baicheng Xu, Doctor[1,*], Xiaoyun Zhao, Master[1], YiMing Zhu, Doctor[1], Chi Chen, Master[1], XingJian Chen, Master[1], Xiaowen Liu, Doctor[1], Yanli Wang, Master[1], and Yufen Guo, Doctor[1,2]

Abstract

Background: The *GJB2* gene is the most common deafness gene, and epidemic characteristics have obvious racial specificity. Our study aimed to investigate the prevalence and ethnic specificity of the *GJB2* gene in deafness in major ethnic groups in Northwest China, evaluate the value of molecular screening for deafness in minority populations, and explore the strategies and methods for genetic diagnosis. **Methods**: Ethics approval was obtained to collect 1330 cases of moderate to very severe nonsyndromic sensorineural deafness in northwestern China. The mutation characteristics of ethnic minorities were analyzed and compared with those of 464 patients with nonsyndromic sensorineural deafness among ethnic Han in the northwestern from research group by Sequence Scanner V25.0. Then, we analyzed the ethnic specificity of the mutations. **Results**: A total of 15 *GJB2* sequence changes were detected in 1330 minority patients. The study showed that the allele frequency in Tibetan patients was significantly lower than that in Hui and Dongxiang patients, that in Uygur patients was significantly lower than that in Han and Hui patients, and that in Kazak and Tibetan patients was significantly lower than that in Han patients, and the differences between other ethnic groups were not statistically significant. Each ethnic group has a unique *GJB2* gene mutation spectrum, and its hotspot mutation distribution has its own characteristics, with c.235delC, c.109 G > A, c.299-300delAT, and c.35delG being common. **Conclusions**: It has been confirmed that *GJB2* gene mutation has a high prevalence in patients with nonsyndromic sensorineural hearing loss in Northwest China. Each ethnic group has a unique mutation spectrum for the *GJB2* gene, which is related to its genetic background. It is necessary to develop a corresponding gene diagnosis strategy according to the hotspot mutations and mutation spectrum of each ethnic group.

Keywords

GJB2 gene, genetic epidemiology, ethnic specificity, Northwestern minorities, hotspot, deafness

[1]Department of Otolaryngology-Head and Neck Surgery, Lanzhou University Second Hospital, Lanzhou, China
[2]Health Commission of Gansu Province, Lanzhou, China

*These authors contributed equally to this work.

Corresponding Author:
Yu-F. Guo, Department of Otolaryngology Head and Neck Surgery, Second Hospital of Lanzhou University, No. 82, Cuiyingmen Street, Lanzhou 730030, Gansu, China.
Email: gyflhmm@163.com

What do we already know about this topic?
The *GJB2* gene is currently considered to be the most common deafness gene.
How does your research contribute to the field?
We find that the prevalence of the *GJB2* gene in the major minority ethnic groups in Northwest China is obviously different from that in people of Han nationality, which is of great significance for further expanding research on deafness genes and discover new deafness genes.
What are your research's implications toward theory, practice, or policy?
It will be beneficial to generate gene diagnosis strategies suitable for the northwest minorities.

Introduction

The molecular etiology of hereditary hearing loss has led to a new microscopic era in the understanding of hearing loss. With the expansion of molecular biology research techniques, more relationships between genetic hearing loss and genetic abnormalities have been revealed. It is now known that at least 120 genes are associated with nonsyndromic hearing loss (Hereditary Hearing Loss Homepage: http://hereditaryhearingloss.org). Autosomal recessive nonsyndromic hearing loss (ARNSHL) is the most common phenotype of hearing loss.[1] Current research suggests that such hearing loss may be a monogenic genetic disease related to specific mutations of a certain gene. The earliest associated gene was the *GJB2* gene, which encodes the Cx26 (Connexin 26) protein.[2] Mutation of this gene is associated with a variety of hearing loss phenotypes, the most common of which is autosomal recessive nonsyndromic hearing loss type 1 (DFNB1-A), which is characterized by extremely severe prelingual hearing loss.[3] Another phenotype associated with mutation of this gene, dominant hereditary nonsyndromic hearing loss type 3 (DFNA3), manifests as severe sensorineural hearing loss, mostly in puberty, is characterized by a significant decline in high-frequency hearing and develops to full-frequency hearing loss before middle age.[4] *GJB2* gene mutations are also associated with some rare hearing loss phenotypes, including KID (keratitis, ichthyosis, and deafness) syndrome,[5] Vohwinkel syndrome (expressed as destructive keratosis and moderate hearing loss),[6] and hyperkeratosis palmaris et plantaris.[7] Based on the high contribution rate of the *GJB2* gene to hearing loss, it is called the hearing loss susceptibility gene.

Due to the popularity, short coding sequence, and high mutation frequency of the *GJB2* gene, whole-genome screening has become the most common method for the molecular detection of deafness at home and abroad. One study found that the *GJB2* gene had a high mutation rate in deaf patients, and there was significant racial specificity in the distribution of mutant forms. In Caucasians, the most common hotspot mutation was c.35delG, accounting for 59.52%–80% of all mutations, while in East Asia, where the Mongolian ethnicity was distributed, the main hotspot mutation was c.235delC.[8] Among Jews, c.167delT was common,[4] and among Africans, the mutation frequency of c.427 C > T was higher.[9] Daipu and other researchers who performed studies on various ethnic groups in China also suggested that *GJB2* gene mutation had ethnicity specificity.[8,9]

China is one of the countries with the richest human genetic resources in the world. Minority genes are unique resources in the Chinese national gene bank and even the global human gene pool. The northwestern part of China is a concentrated area of ethnic minorities. A total of 23 ethnic minorities have been living in the region for a long time. Tibetan, Dongxiang, Hui, Kazak, and Uygur ethnic groups have large populations. The living environment, language, ethnic origin, and marriage customs of these peoples are unique. In this study, molecular epidemiological analysis of the *GJB2* gene in the above ethnic groups is performed to initially establish a genetic database for the northwestern minorities and shed light on the epidemic characteristics of *GJB2* mutations and their specificity to each ethnic group.

Materials and Methods

Research Objects

A total of 1330 patients with moderate or higher sensorineural hearing loss were enrolled in the study. The study was approved by the ethics committee of Lanzhou University Second Hospital (Approval Number: A2015-007). These patients were from independent ethnic minority families in the region. No other systemic conditions were found except for hearing and speech impairment. At the same time, 464 patients with nonsyndromic sensorineural hearing loss from the ethnic Han group were selected as controls in the northwestern region. Their age, sex, and regional distribution were similar to those of the minority groups. Clinical data collection, blood sample collection, and audiological examination (pure tone threshold, auditory brainstem response, and acoustic impedance) were performed for the patients by the Department of Otorhinolaryngology-Head and Neck Surgery, Second Hospital of Lanzhou University, Gansu Province. All patients with conductive hearing loss caused by abnormalities outside the middle ear and syndrome-type hearing loss were excluded. Informed consent was obtained from all patients or their families.

Table 1. Pathogenic Mutant Genotypes in Various Ethnic Groups.

Pathogenic mutant genotypes	Hui	Uygur	Dongxiang	Kazakh	Tibetan	Han
109G>A/109G>A	**2**	**0**	**2**	**0**	**0**	**1**
235delC/235delC	**21**	**20**	**3**	**0**	**1**	**33**
257C>G/257C>G	**0**	**0**	**1**	**0**	**0**	**1**
299-300delAT/299-300delAT	**2**	**1**	**5**	**0**	**0**	**1**
35delG/35delG	**2**	**10**	**0**	**5**	**0**	**1**
235delC/109G>A	**1**	**1**	**0**	**0**	**0**	**2**
176-191del16/176-191del16	**0**	**0**	**0**	**0**	**0**	**2**
235delC/176-191del16	**6**	**0**	**0**	**0**	**0**	**0**
235delC/299-300delAT	**4**	**4**	**1**	**0**	**0**	**0**
235delC/35delG	**2**	**8**	**1**	**0**	**0**	**0**
235delC/439G>A	**1**	**0**	**0**	**0**	**0**	**0**
235delC/504insAACG	**0**	**0**	**0**	**0**	**1**	**0**
257C>G/368C>A	**0**	**0**	**0**	**0**	**1**	**0**
299-300delAT/257C>G	**0**	**0**	**0**	**0**	**1**	**0**
35delG/299-300delAT	**2**	**1**	**0**	**0**	**0**	**0**
109G>A/wt	**16**	**6**	**5**	**0**	**5**	**16**
176-191del16/wt	**2**	**2**	**0**	**0**	**0**	**3**
235delC/wt	**5**	**11**	**2**	**0**	**2**	**28**
299-300delAT/wt	**3**	**4**	**0**	**0**	**0**	**2**
35delG/wt	**1**	**10**	**0**	**2**	**0**	**3**
380G>A/wt	**0**	**7**	**2**	**0**	**0**	**0**
504insAACG/wt	**0**	**0**	**0**	**0**	**1**	**0**
571T>C/wt	**0**	**0**	**2**	**0**	**0**	**0**
368C>A/wt	**0**	**1**	**2**	**0**	**1**	**0**
Total	**70**	**86**	**26**	**7**	**13**	**93**

Note: The numbers in the table represent the number of patients.

General Procedures for DNA Isolation and Sequencing

Genomic DNA was extracted from leukocytes of peripheral venous blood by the salting out method,[10] PCR was performed on the coding region of the *GJB2* gene, and the amplified fragments were purified by a Millipore purification plate and then directly and reversely sequenced using an ABI 3730 DNA sequencer. Sequencing results were analyzed using Sequence Scanner V1.0 and DNAstar 7.0 software, and the normal control sequences were derived from the standard sequence available from the NCBI (NC-000013).

GJB2 *Mutation Screening*

The *GJB2* gene has 2 exons, and the coding region is located in exon 2. We chose exon 2 as the target. The primer pairs PCR and AGE were designed on the basis of a previous report by Guo et al.[11]

Statistical Analysis

Mutation comparisons among ethnic groups were performed by the chi-squared test via SPSS 25.0 software. $P < .05$ was considered statistically significant.

Results

Epidemiological Results

Of the 1330 patients with sensorineural hearing loss, 703 males and 627 females, aged from 3 months to 50 years, with a median age of 11 years. By region, 269 of the patients resided in Gansu, 154 in Ningxia, 165 in Qinghai, 1 in Shaanxi, and 741 in Xinjiang. By ethnic group, 107 of the patients were from the Tibetan group, 132 patients were from the Dongxiang group, 407 patients were from the Hui ethnic group, 72 patients were from the Kazakh group, and 612 patients were from the Uighur group. According to the degree of hearing loss, 57 patients had moderate hearing loss, 188 patients had severe hearing loss, and 1085 patients had very severe hearing loss. There were 265 patients who exhibited deafness before the age of 1 year, 918 between the ages of 1 and 3, and 147 after the age of 3. Thirty-eight patients had a clear family history of deafness, 56 were characterized by incest within three generations, 86 had a history of disease and medication during pregnancy, 186 had a history of premature birth or dystocia, 106 had a history of drug use, and the majority could not identify the cause of deafness.

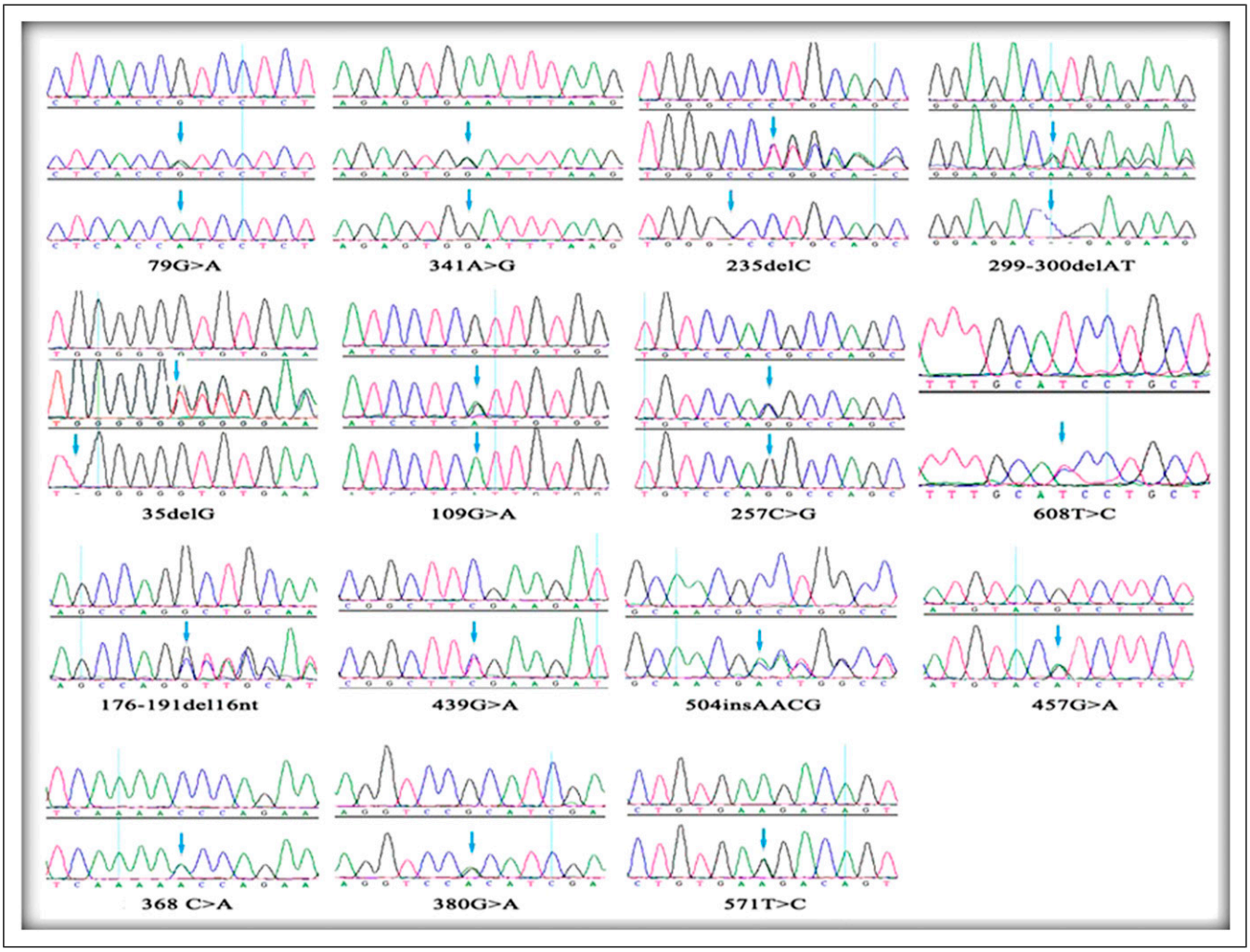

Figure 1. The sequence chromatograms of GJB2.

Gene Mutation Results (Shown in Table 1)

A total of 15 *GJB2* sequence changes were detected in 1330 minority patients (shown in Figure 1). Of the 1330 subjects, 110 were identified as having *GJB2* gene mutations (75 homozygous and 35 compound heterozygous), and 92 had heterozygous mutations. The frequency of pathogenic mutations was 8.27% (110/1330), the pathogenic mutation carrying rate was 15.19% (202/1330), and the pathogenic allele frequency was 11.73% (312/2660). Among the mutations, c.235delC and c.35delG had the highest allele frequencies, at 5.45% (145/2660) and 2.29% (61/2660), respectively, accounting for 66.03% (206/312) of all pathogenic alleles. These mutations were hotspot mutations in the main ethnic groups in the northwest.

Of the 407 patients with deafness of Hui nationality, 43 exhibited *GJB2* gene mutations (27 homozygous and 16 compound heterozygous), and 27 had heterozygous mutations. The frequency of pathogenic mutations was 10.57% (43/407), the pathogenic mutation carrying rate was 17.20% (70/407), and the pathogenic allele frequency was 13.88% (113/814). Among the mutations, c.235delC and c.109 G>A had the highest allele frequencies, at 7.49% (61/814) and 2.58% (21/814), respectively, accounting for 72.57% (82/113) of all pathogenic alleles. These mutations were hotspot mutations in the Hui group.

Of the 612 Uygur patients with deafness, 45 were confirmed to have *GJB2* gene mutations (31 homozygous and 14 compound heterozygous), and 41 had heterozygous mutations. The frequency of pathogenic mutations was 7.35% (45/612), the pathogenic mutation carrying rate was 14.05% (86/612), and the pathogenic allele frequency was 10.70% (131/1224). Among the mutations, c.235delC and c.35delG had the highest allele frequencies, at 5.23% (64/1224) and 3.19% (39/1224), respectively, accounting for 78.63% (103/131) of all pathogenic alleles. These mutations were hotspot mutations in the Uygur group. The allele frequency of c.235delC was significantly lower than that in patients of Han nationality by 10.34% (96/928); the allele frequency of c.35delG was significantly higher than that in patients of Han nationality by .54% (5/928).

Table 2. Statistical Results of Pathogenic Mutation Rates.

Ethnic groups	Hui	Uygur	Dongxiang	Kazakh	Tibetan
Hui					
Uygur	.03				
Dongxiang	.718	**.059**			
Kazakh	.068	**.379**	**.06**		
Tibetan	.02	**.22**	**.021**	**.895**	
Han	.739	**.009**	**.892**	**.047**	**.011**

Note: The numbers in the table represent the *P* values.

Thirteen of the 132 patients with deafness of Dongxiang nationality were identified as carrying *GJB2* gene mutations (11 homozygous and 2 compound heterozygous), and 13 had heterozygous mutations. The frequency of pathogenic mutations was 9.85% (13/132), the pathogenic mutation carrying rate was 19.70% (26/132), and the pathogenic allele frequency was 14.77% (39/264). Among the mutations, c.299_300delAT and c.235delC had the highest allele frequencies, at 4.17% (11/264) and 3.79% (10/264), respectively, accounting for 56.41% (22/39) of all pathogenic alleles. These mutations were hotspot mutations in the Dongxiang group. The allele frequency of c.299_300delAT was significantly higher than that in patients of Han ethnicity by .43% (4/928); the allele frequency of c.235delC was significantly lower than that in patients of Han ethnicity by 10.34% (96/928).

Of the 72 Kazakh patients with deafness, 5 were confirmed to have *GJB2* gene mutations (both homozygous mutations), and 2 had heterozygous mutations. The frequency of pathogenic mutations was 6.94% (5/72), the pathogenic mutation carrying rate was 9.72% (7/72), and the pathogenic allele frequency was 8.33% (12/144). c.35delG was the only pathogenic mutation detected. The frequency of allele mutations was 8.33% (12/144), which was significantly higher than that in patients of Han ethnicity by .54% (5/928)). This mutation was the hotspot mutation in Kazakh patients.

Of the 107 Tibetan patients with deafness, 4 were confirmed to have *GJB2* gene mutations (1 homozygous and 3 compound heterozygous), and 9 had heterozygous mutations. The frequency of pathogenic mutations was 3.74% (4/107), the pathogenic mutation carrying rate was 12.15% (13/107), and the pathogenic allele frequency was 7.94% (17/214). Among the mutations, c.235delC and c.109 G > A had the highest allele frequencies, at 2.34% (5/214), accounting for 58.82% (10/17) of all pathogenic alleles. This mutation was the hotspot mutation in Tibetans. The allele frequency of c.235delC was significantly lower than that in patients of Han ethnicity by 10.34% (96/928).

Statistical Analysis Results

(1) The frequency of pathogenic mutations in ethnic minorities was not different from that in patients of Han nationality (P =.706); the pathogenic mutation carrying rate (P = .015) and the frequency of pathogenic alleles (P = .031) were significantly lower than those in patients of Han nationality. The mutation rate of 235delC was significantly lower than that in patients of Han nationality (P = .000); the mutation rates of c.35delG (P = .001) and c.299_300delAT (P = .021) were significantly higher than those in patients of Han nationality.

(2) The frequencies of pathogenic mutations among ethnic groups were not significantly different, except between the Tibetan and Hui ethnic groups (P = .029). The rates of pathogenic mutation between each ethnic group and the Han group were not different, except for the Uygur (P = .009) and Kazakh (P = .036) ethnic groups, and there were no differences between the ethnic groups. The frequencies of pathogenic alleles were significantly different between the Tibetan and Hui, Uygur and Hui, Uygur and Han, Kazakh and Han, Tibetan and Dongxiang, and Tibetan and Han populations (the statistical results are shown in Table 2).

(3) The allele frequencies of the hotspot mutation c.235delC in the Hui (P = .038), Uygur (P < .001), Dongxiang (P = .001), and Tibetan (P < .001) ethnic groups were significantly lower than that in the Han ethnic group. The allele frequencies of the hotspot mutation c.35delG in the Kazakh (P < .001) and Uygur (P < .001) groups were significantly higher than that in patients of Han nationality, and that in the Kazakh group was significantly higher than that in the Uygur group (P = .002). The allele frequency of c.299_300delAT was significantly different between the Dongxiang and Han ethnic groups (P =.038). There were no significant differences in the allele frequency of c.109 G > A among the Hui, Tibetan, and Han ethnic groups.

Discussion

In this study, 1330 major ethnic minority patients in Northwest China were studied for common deafness genes, and it was found that the pathogenic mutation carrying rate of 15.19% (202/1330) and pathogenic allele frequency of 11.73% (312/2660) were both significantly lower than those in the Han group. In a large-sample study conducted by Daipu et al, 2063 patients with nonsyndromic sensorineural hearing loss (NSHL) were found to have a pathogenic allele frequency of the *GJB2* gene of 17.9% (739/4126),[12] which was closer to the 14.44% (134/928) observed in the Han group in this study. This further verified that the mutation rate of the *GJB2* gene in the major ethnic groups in Northwest China was lower than that in the Han group. Previous studies suggested that *GJB2*, SLC26A4, and mtDNA12SrRNA were the most common molecular causes of deafness, but the mutation frequency and hotspot mutations were different among groups, mainly because of the ethnic origins and environmental factors of the

groups.[8,9,13,14] Based on the above views, we reviewed the Yearbook of Chinese Minorities on the origin of major ethnic minorities in Northwest China and found that the Hui ethnic group was mainly composed of Middle Eastern Arab and Persian ethnic groups and compatible with the Mongolian, Han, Uygur, and Tibetan ethnic groups (the integration of Mongolians and Caucasians). The Uyghur people are a multiethnic group with 2 major origins: the Huihe people from the Mongolian grassland and the indigenous people in the oasis of southern Xinjiang (the fusion of Caucasians and Mongolians). The Dongxiang ethnic group mainly includes the Mongolian ethnic group and some Caucasian ethnic groups. The Kazak people belong to the Europa-Turan race (Caucasians). The Tibetan people are a branch of the Xiqiang people of the Han Dynasty (the fusion of Caucasians and Mongolians). The Han people are Mongolians. It can be seen that the major ethnic minorities in Northwest China have more introgressed Caucasian genes than the Han people. Considering that the Han people in the control group all come from Northwest China, we believe that the low mutation frequency of the *GJB2* gene in ethnic minorities may be related to introgression from Caucasians. In addition, the pathogenic mutation frequencies of the *GJB2* gene in the Uygur, Kazak, and Tibetan ethnic groups, mainly Caucasians, were significantly lower than that in the Han group, while the pathogenic mutation frequencies of the *GJB2* gene in the Hui and Dongxiang ethnic groups, mainly Mongolians, were not different from that in the Han group, which further verified the above views. On the other hand, the major ethnic minorities in Northwest China may have a low mutation rate of the *GJB2* gene and a high incidence of mutations in other deafness genes or even a new deafness gene. Therefore, further study is needed to yield valuable results.

The mutation rates of the *GJB2* gene of all ethnic minorities were relatively high. According to the statistical analysis of mutation rates, we found that the pathogenic mutation rate in only patients of Tibetan nationality was significantly lower than that in patients of Hui nationality. The pathogenic mutation carrying rates in the Uygur and Kazak groups were significantly lower than that in patients of Han nationality. The pathogenic allele mutation rate in patients of Tibetan nationality was significantly lower than those in the Hui and Dongxiang ethnic groups; those in patients of Uygur, Kazakh, and Tibetan nationalities were significantly lower than that in the Han group; and that in the Uygur group was significantly lower than that in the Hui group. According to the statistics for the 3 different rates, the allele mutation rate was the most sensitive and thus could reveal more subtle differences and significant differences than the pathogenic mutation frequency and pathogenic mutation carrying rate, making it conducive to comparative data analysis. Therefore, we recommend the allele mutation rate when statistically analyzing the gene mutation rate.

In this study, hotspot mutations differed among ethnic groups: those in patients of Hui nationality were c.235delC and c.109 G>A; those in patients of Uygur nationality were c.235delC and c.35delG; those in the Dongxiang group were c.299-300delAT and c.235delC; that in Kazakh patients was c.35delG; and those in Tibetan patients were c.235delC and c.109 G>A. In previous studies, the hotspot mutations in Mongolian people were identified as c.235delC and c.299-300delAT, while the hotspot mutation in Caucasian people was c.35delG.[1,12,15] Therefore, the hotspot mutations in various ethnic groups are generally consistent with ethnic origin: Kazakhs show typical Caucasian characteristics, and the Uygur ethnic group shows obvious background characteristics consistent with the integration of Caucasians and Mongolians.

c.235delC was previously detected in a large proportion of the Asian population and considered to be an ancestral mutation in Mongolian people.[12,16,17] Our study revealed that all ethnic groups incorporating Mongolian populations, except Kazakhs of Caucasian origin, contained the c.235delC mutation at a high frequency. This indicates that c.235delC is a hotspot mutation of the *GJB2* gene in Northwest China and supports the view that c.235delC is an original mutation in Mongolians.

Multiple studies on the Caucasian ethnic background have shown that c.35delG is a hotspot mutation in this group, representing an ancestral mutation in Caucasians.[15,18-20] In our study, all ethnic groups were found to harbor c.35delG, the mutation rate of c.35delG in Kazakh deaf patients with a Caucasian majority was significantly higher than that in Uygur patients with Caucasian and Mongolian integration ($P < .001$), and the mutation rate in patients of Uygur nationality was significantly higher than that in patients of Han nationality with a Mongolian majority ($P < .001$). This also verifies that c.35delG is a founder mutation in Caucasians and shows that all ethnic groups have a Caucasian background.

In this study, c.109 G > A had a higher mutation frequency in Tibetan, Dongxiang, Hui and Han deaf populations, especially in the Hui and Han populations with a Mongolian majority, where the allele frequencies were 2.58% and 2.16%, respectively, indicating that the alleles were the second most common in each nationality. In contrast, the mutation rates of c.109 G > A in Uygur and Kazakhs, who were predominantly Caucasian, were only .57% and .00%, respectively. Thus, c.109 G > A tends to occur in the Mongolian ethnic group, which is consistent with the results of previous domestic and foreign research.[21,22] However, the c.109 G > A mutation rate was still very high in the Tibetan group with the integration of Caucasians and Mongolians, and there were no significant differences between Tibetans and the Hui and Han ethnic groups. We believe that this may be caused by the genetic dominance of Mongolian ethnic groups due to the long-term intermarriage between Tibetan and Han ethnic groups, and further studies are needed to verify this.

In this study, c.299-300delAT was the most common mutation in patients of Dongxiang nationality, with a mutation rate of 4.17%, and the Dongxiang nationality had the

highest mutation rate among all nationalities. c.299-300delAT mutation rates were significantly higher in patients of Dongxiang nationality ($P < .001$) and major minority nationality ($P = .021$) than in those of Han nationality. A pure ethnic origin cannot explain the high mutation rate of c.299-300delAT in the Dongxiang group. We know that the Dongxiang nationality mainly evolved from the migration of Turkic people, Mongolians, and other minorities. Therefore, we think that the significantly higher mutation rate of c.299-300delAT in patients of Dongxiang nationality than in those of other nationalities may be due to the gathering of people with this mutation during the migration and evolution of the Dongxiang nationality and the custom of intermarriage. Of course, it may also be related to the regional environment, genetic variation, and other factors, which need further study.

The mutation frequency of the *GJB2* gene is high in deaf patients in ethnic minority groups in Northwest China, so the diagnosis of *GJB2* gene mutations in ethnic minorities has significant social value. The hotspot mutations differ between these minorities and patients of Han nationality. On the one hand, we need to consider the mutation spectrums of different nationalities in the design of gene diagnosis strategies. According to the results of our study, in the design process involving basic loci such as c.235delC, c.109 G > A, c.299-300delAT, and c.176-191del16, we have to pay attention to c.35delG and c.257 C > G, which are rare mutations in the Han population. Doing so could provide a more comprehensive exploration of the molecular etiology of deafness. On the other hand, it is necessary to carry out extended gene research in minority deaf patients, which would be beneficial to finding new genes and new loci and thereby enriching the database of deafness genes.

Conclusions

The *GJB2* gene is currently considered to be the most common deafness gene, and the mutation rate of this gene is generally high in the major minority groups in Northwest China. In the statistical analysis of *GJB2* gene mutation frequency, we found that allele frequency was more sensitive than the pathogenic mutation rate and pathogenic mutation carrying rate. Therefore, we recommend the use of allele frequency in the analysis of the deafness mutation rate. The mutation rate of the *GJB2* gene in minority ethnic groups was lower than that in patients of Han nationality, which may be related to the integration of more Caucasian people. The mutation rates of the *GJB2* gene in Kazakh, Tibetan, and Uygur ethnic groups with Caucasian ethnic backgrounds were also lower than the rate in patients of Han nationality. Therefore, it is speculated that the mutation rate of the *GJB2* gene in Caucasian people is lower than that in Mongolian people. The hotspot mutations and mutation frequencies of the minority nationalities in Northwest China were not the same, which is mainly related to the origins of the ethnic groups, and some of the differences may also be related to ethnic group migration, the regional environment, and genetic variation. In conclusion, we believe that the prevalence of the *GJB2* gene in the major minority ethnic groups in Northwest China is obviously different from that in people of Han nationality, which is of great significance for further expanding research on deafness genes. It will be beneficial to generate gene diagnosis strategies suitable for the northwest minorities and discover new deafness genes.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethical Approval

Ethical approval to report this case was obtained from the ethics committee of Lanzhou University Second Hospital (Approval Number: A2015-007).

Statement of Human and Animal Rights

All procedures in this study were conducted in accordance with the ethics committee of Lanzhou University Second Hospital (Approval Number: A2015-007) approved protocols.

Informed Consent

Verbal informed consent was obtained from the patients for their anonymized information to be published in this article.

ORCID iDs

Panpan Bian https://orcid.org/0000-0003-4520-4106
Chi Chen https://orcid.org/0000-0003-0285-9292

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