ORIGINAL ARTICLE

The screening of hearing and the common deafness gene in the elderly in Iran

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ABSTRACT

Objective: To investigate the genetic characteristics of audiologic complication in the elderly population.
Methods: A total of 194 elderly cases were performed pure tone audiometry and middle ear analysis. And then five milliliter blood was extracted to detect the common deafness genes GJB2 and Mitochondrial DNA.
Results: From 194 of elderly cases that screened, 103 (53.1 %) people had normal hearing, and 91 (46.9 %) were detected hearing loss, including 32 cases mild deafness; 39 cases moderate hearing loss, 17 cases moderate to severe hearing loss, and 3 cases with severe hearing loss. The average hearing threshold in 60-70, 71-80 and more than 80-year -old cases were 43.8dB, 51.4dB and 58.1dB, respectively. 22 cases were detected heterozygous mutation of GJB2 gene. The mutation rate was 11.3% (22/194). Including heterozygous mutation of 109G>A, five cases were 233-.235delC heterozygous mutation, one case were detected 299 - 300delAT heterozygous. An unreported homozygous mutation 84T>C of GJB2 gene were detected in 2 cases. Mitochondrial DNA12SrRNA mutation was not found in loci 1494 and 1555.
Conclusion: Pay attention to the elderly population hearing loss, it is necessary to develop the elder population hearing screening accompany with the deafness gene screening at same time.
Key words: elderly people, deafness gene; screening

INTRODUCTION

Due to the increase in the elderly population in the world, it is very important to pay attention to the diseases of this population [1]. Presbycusis is a common disease in the elderly [2]. Presbycusis is defined by symptoms such as bilateral, progressive, dull, and hearing loss [3]. Presbycusis is classified as a multifactorial or hybrid disease and results from aging, genetic predisposition, environmental factors, underlying diseases, and ototoxicity drugs [4]. These external and internal underlying factors cause the death in the hair-sensory cells of the inner ear as well as spiral ganglion and striae vascular cells in Presbycusis [5].

Presbycusis has an inheritance of about 35-55% [6]. A Swedish study of twins aged 80-36 years showed that 47% of high-frequency hearing problems are due to genetics and 53% to environmental causes [7]. So far, more than 90 genes have been identified involved in the development of non-syndromic deafness [8].

Given the high prevalence of hearing loss mutations in gap-junction encoding genes, it is important to investigate the maturation in these encoding gene [9]. Gap junction beta-2 protein (GJB2) mutations have been found in a variety of populations [9]. Although several mutations have been discovered, only a few have a high prevalence in deaf people [10]. The aim of this study was to investigate the mutation of GJB2 in elderly in Iran.

MATERIALS AND METHODS

A total of 194 elderly people were selected to measure the pure tone hearing threshold with a pure tone audiometer, and the Madsen901 (Denmark) acoustic immittance tester was used to detect the tympanogram and the stapedius muscle reflex to understand the conduction status of the middle ear. Exclude the elderly who have communication barriers and decreased understanding. This study, which was carried out at Amir Alam hospital during 2019. The study was approved by the ethical committee and an informed consent form was signed.

According to the language frequency (0.5kHz, 1kHz , 2 kHz, 4 kHz) to judge the degree of hearing loss, refer to the World Health Organization (WHO) "International Classification of Handicap, Disability and Handicap" (1980) to classify the language frequency hearing loss as: mild deaf (hearing Loss 26-40dB), moderately deaf (hearing loss 41-55 dB), moderately severely deaf (hearing loss 56-70 dB), severely deaf (hearing loss 71-90 dB) and extremely severely deaf (>90 dB) and The standard of total deafness is used to diagnose.

Each elderly person collects 5 ml of venous blood and sends it to BGI for blood sample processing and DNA extraction, and then GJB2 and mitochondrial DNA 12SrRNA gene mutation detection. The GJB2 gene uses the Sanger sequencing method, and the sequencing results use Sequencher 4.8 software Perform analysis. The mitochondrial DNA 12SrRNA is mainly targeted at two common pathogenic mutation sites 1494 and 1555, using Sequenom matrix-assisted laser analysis and ionization time-of-flight mass spectrometry (MALDI-TOF) for mutation detection.

RESULTS

There were 194 elderly volunteers including 115 males and 79 females. Age 60-86 years old, with a median age of 66 years old. 109 people aged 60-70 (65 males, 44 females), 71-80 years old: 79 people (47 males, 32 females); 5 males over 80 years old (2 people, 3 females). 3 people with chronic otitis media, 4 people with a history of head trauma or ear trauma, 5 people with a family history of deafness, 5 people working in a noisy environment, suffering from

cardiovascular and cerebrovascular diseases, diabetes, high blood pressure and other diseases 72 people.

All the elderly were tested, 53.1% (103/194) of the elderly with normal hearing, 46.9% (91/194) of the elderly with hearing loss, including 32 cases of mild deafness and 39 cases of moderate hearing loss. Cases, 17 cases of moderate to severe hearing loss, 3 cases of severe hearing loss. According to age, 41 people with hearing loss between 60 and 70 years old have an average hearing threshold of 43.8dB; accounting for 33.9% (37/109) of this age group, and an average hearing threshold of 51.4dB from 71 to 80 years old, accounting for 25.8% (50/194), Accounting for 63.3% (50/79) of this age group, the average hearing threshold over 80 years old is 58.1dB, and hearing loss accounts for 80% (4/5) of this age group.

22 cases of heterozygous mutations in the pathogenic gene were detected, of which 16 cases were heterozygous for 109G>A (Figure 1), 5 cases were heterozygous for 233-.235delC, 1 case was heterozygous for 299-300delAT, and mutations of the pathogenic gene were carried the rate was 11.3% (22/194).

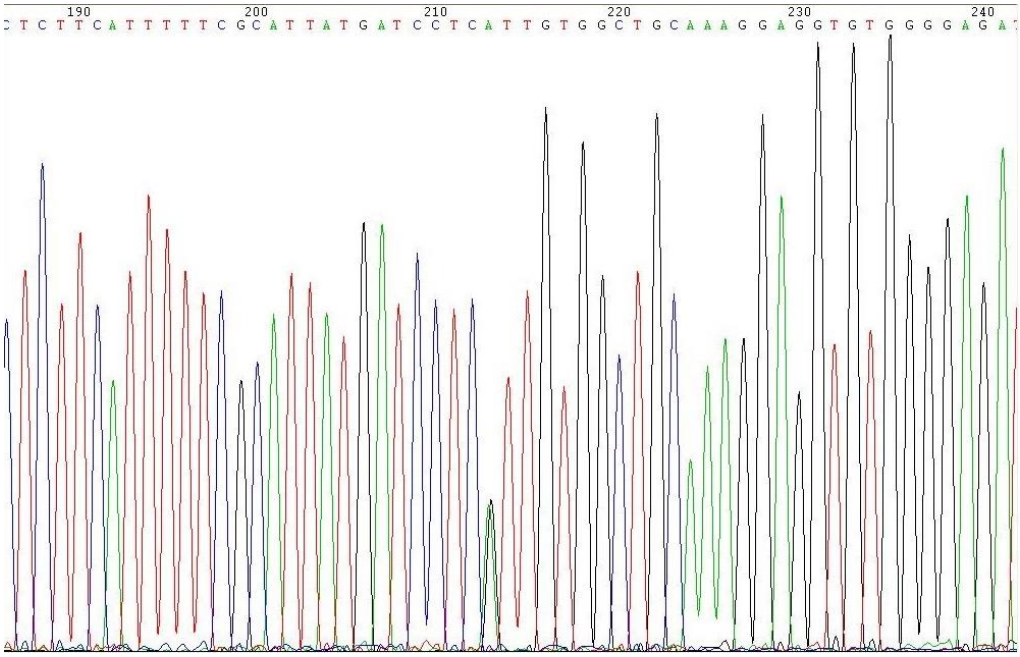

Figure 1. 109 heterozygous mutation

An unreported gene mutation site 84T>C homozygous mutation was detected in 2 cases; benign polymorphisms detected include: 11G>A heterozygous 1 case, 22G>T heterozygous 1 case, 56C>T homozygous mutation 1 case , 3 cases were heterozygous; 29 cases were 79G>A homozygous, 102 cases were heterozygous, 18 cases were 341A>G homozygous mutations, 80 cases were heterozygous mutations, 368C>A heterozygous 3 cases, 385G>A heterozygous 1 case, 457G>A heterozygous 1 case, 495G>A heterozygous 2 cases, 608T>C heterozygous 12 cases.

No mutations were found at positions 1494 and 1555 of 12SrRNA in mitochondrial DNA. (Fig 2-3)

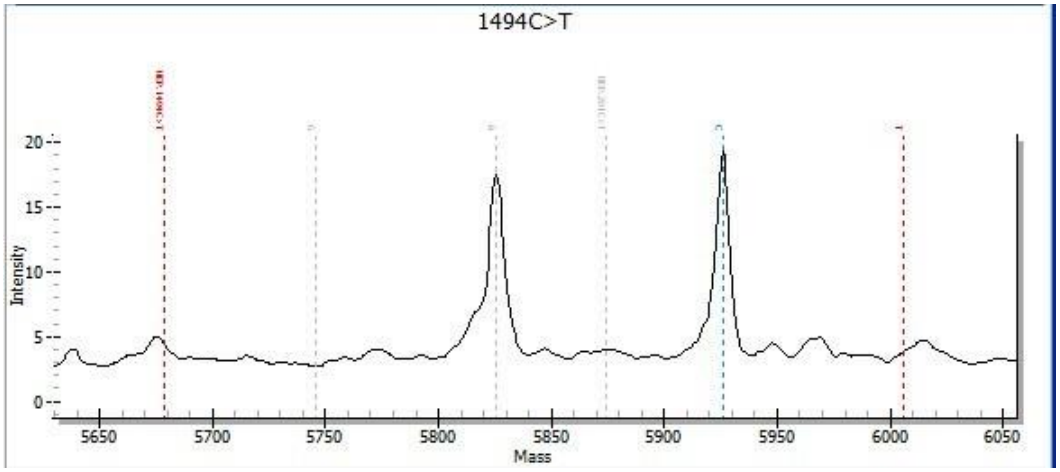

Figure 2. No mutations detected in 1494

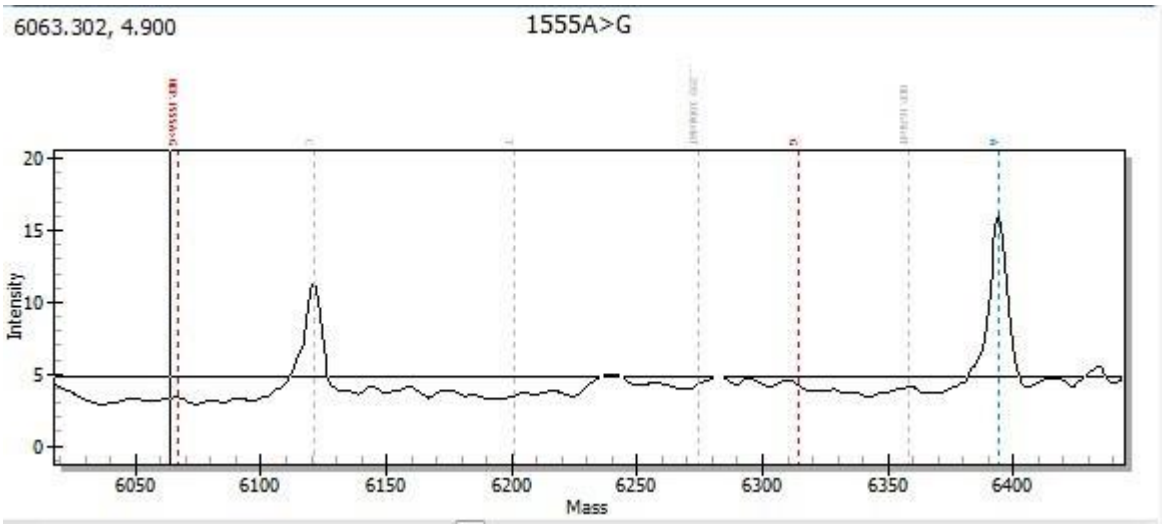

Figure 3. No mutations detected in 1555

DISCUSSION

At present, there is no effective treatment and prevention for the hearing problems of the elderly. With the increase of age, the incidence of deafness gradually increases [11]. Cooper et al. investigated the risk factors for hearing loss in the elderly include cochlear aging, environmental factors (including occupational and noise exposure), genetics (including gender, race, genetics, etc.) [12]. Therefore, the diagnosis of hearing loss in the elderly must consider the reasons for the deterioration of hearing function, and at the same time, make a diagnosis based on their medical history, past hearing conditions, work and living environment, living habits, genetic background, and other comprehensive factors.

At present, there is no method to predict or prevent presbycusis, and there are no effective drugs for intervention and treatment. The early hearing loss of the elderly mostly occurs in the high-frequency area, which is difficult to detect by themselves and others, and the disease gradually progresses when the language frequency is affected. There are 24 elderly people in this group who have never had a hearing test, and 7 of the elderly with mild hearing loss think that they have no hearing problems. Hearing monitoring for the elderly is beneficial to early detection of hearing loss. The medical perspective helps the elderly to pay more attention to their own diseases, promptly remind the elderly to use drugs in a standardized and reasonable manner, as well as the use of disease prevention and control and the popularization of medical care.

increasingly research show that the interaction between genetics and environment is an important factor in the onset of presbycusis [13]. GJB2 is the most common deaf gene. In our study, 11.3% of elderly people with pathogenic mutations (22/ 194), 60% (3/5) of the elderly with a genetic family history of deafness, the proportion of 109G>A mutations is significantly higher than that of mutations at other sites. Mitochondrial DNA12SrRNA gene is also the most common deaf gene. Mutations in mitochondrial DNA are currently considered to be one of the most important factors in all genetic studies of presbycusis. It plays an important role in cochlear aging and age-related hearing loss [14]. The cumulative effect of oxidative stress may lead to mitochondrial DNA damage, resulting in mitochondrial DNA mutation or deletion, and decline in mitochondrial function, thereby inducing the process of cochlear cell apoptosis, leading to an increase in hearing threshold and a decrease in speech recognition ability [15]. Prior research carried out mitochondrial DNA12SrRNA gene screening on patients with presbycusis and believed that mitochondrial DNA12SrRNA mutations and genetic polymorphisms are related to age, which may increase the susceptibility to presbycusis [16]. This group only detects common pathogenic mutation sites 1494 and 1555, and further research is needed. This study is only a preliminary screening of a small sample of common deaf genes. It is not yet possible to determine the frequency spectrum characteristics of common deafness gene mutations in the elderly population in this region. However, researchers should pay attention to the genetics and genetics research of the elderly population. It is of great significance to study the ancestor mutations of deafness genes, hereditary modes, and the influencing factors of presbycusis and even the prevention of deafness.

At present, community health services provide the elderly with a convenient and fast medical treatment model and have formed a relatively complete model for the prevention and health care, disease management and even emergency treatment of common diseases such as hypertension and heart disease. Therefore, it is jointly developed with the community. Hearing monitoring and deafness genetic testing can learn from the model of community health services, not only can effectively solve the problem of inconvenience for the elderly, but also can detect hearing loss in time, provide timely treatment, and early intervention to improve the quality of life of the elderly.

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