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SHORT REPORT

Genetic Non-Syndromic Hearing Loss in Turkey

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Hearing loss is the most common congenital disorder. A moderate to profound hearing loss is encountered in 1 to 4 per 1,000 live births, and there is a genetic etiology in 60%. Two hundred and sixty Turkish children with genetic non-syndromic profound hearing loss and 67 healthy controls were screened. The pattern of inheritance was DFNB in 87.5%, DFNA in 9.4%, x-linked in 3.1%, and mithochondrial in less that 1%.The GJB2 gene mutations caused hearing loss in 14.7 to 23.2% of children in Turkey. The 35delG was the most common GJB2 mutation both in sporadic and familial cases. The rate of consanguineous marriage was 12.6%. The overall hearing loss in rate in Turkish population is 0.41%. There are 300.000 people who suffer from hearing loss, and 180.000 of them have genetic hearing loss. There are 1 million GJB2 gene mutant allele carriers and 4 million people carrying a hearing loss allele. Every year 4.000 babies are born with hearing loss, and there is a genetic cause in 2.400 of them.

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Hearing loss is the most common congenital disorder. A moderate to profound hearing loss is encountered in 1 to 4 per 1,000 live births. There is a genetic etiology in 60% while 40% results from non-genetic factors. Although there are a variety of genetic disorders which can cause diseases, genetic hearing losses are usually caused by single gene mutations and rarely by mithochondrial gene mutations (Table 1). There are more than 100 genes responsible for genetic hearing losses. Almost 70% of genetic hearing losses are non-syndromic, and 30% are syndromic as there are more than 400 syndromes manifesting by hearing loss. The inheritance of a genetic non-syndromic hearing loss can be recessive (DFNB), dominant (DFNA), x-linked (DFN) or mitochondrial. The syndromic forms can also be inherited in autosomal dominant and recessive manner. In general 75-80% of genetic non-syndromic hearing losses segregates in DFNB form while 18% are DFNA, 3% are x-linked, and almost 1% is mitochondrial [1].

Table 1. Classification of genetic disorders

1- Chromosomal disorder
abnormality in the number of genes; chromosomal addition (trizomy) or deletion (monozomy)
2- Single gene disorder
Mendelian inheritance
> 4.000 diseases (dominant, recessive, x-linked)
3- Multifactorial diseases
interaction of multiple genes and environmental factors
congenital malformations like cleft palate or lip, congenital heart disease, diabetes mellitus, hypertension, etc
4- Mitochondrial diseases
mitochondrial DNA mutation
energy production is affected in the neurons and muscles
maternal inheritance
5- Somatic cell diseases
mutation in somatic cells (cancer)
mutation exist in only some of the somatic cells
not inherited to other generations

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In Turkey, we have screened totally 260 children with profound hearing loss (> 90 dB HL pure tone average at the frequencies 0.5 to 6 kHz) for genetic non-syndromic hearing loss as well as 67 healthy controls for carrier frequency. The pattern of inheritance is DFNB in 87.5%, DFNA in 9.4%, x-linked in 3.1%, and mithochondrial in less that 1%. The GJB2 gene mutations cause of genetic non-syndromic hearing loss in 14.7 to 23.2% of children in Turkey [2, 3]. The 35delG is the most common GJB2 mutation both in sporadic and familial cases (Figures 1 and 2). The rate of consanguineous marriage is estimated to be 12.6%. The 35delG is the most common GJB2 mutation, and the second most common mutation is IVS1+1 A → G in the presence of consanguinity.

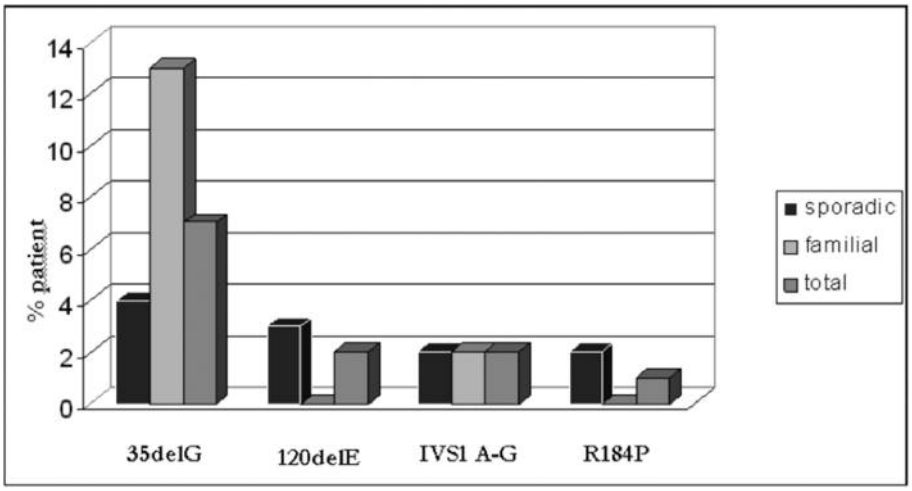

Figure 1- GJB2 mutations in children with profound hearing loss in Turkey.

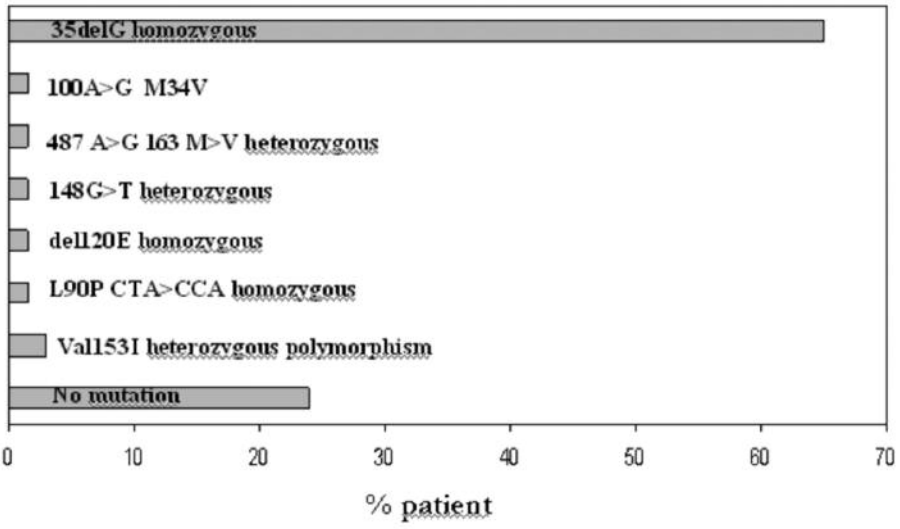

Figure 2- GJB2 mutations in children who had cochlear implantation.

The population of Turkey is around 73 millions; 50.3% males and 49.7% females. The annual live birth rate is 14.5 per 1.000. Almost 0.32% of the people with hearing loss live in urban areas while 0.45% lives in rural areas. The overall hearing loss in rate in Turkish population is 0.41% (Figures 3 and 4) (Table 2). There are 6,155,321 children aged between 0-4 years. Of these children, 4,607,804 live in cities and towns, and 1,547,517 live in villages (Table 3) [4]. Every year 1 million (73 million x 14.5 per 1.000) babies are born. As the rate of congenital hearing loss is 4:1.000, the annual congenital hearing loss rate is around 4.000 (1 million x 4/1.000) (Table 4).

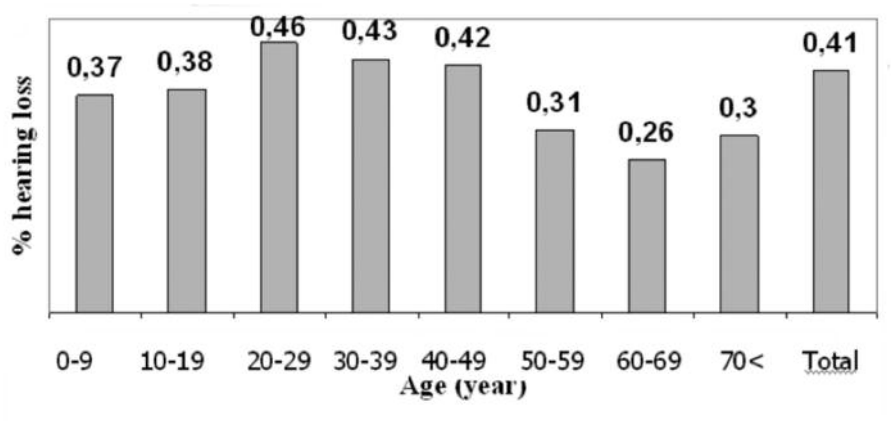

Figure 3- Hearing loss versus population rate; distribution according to age in Turkey

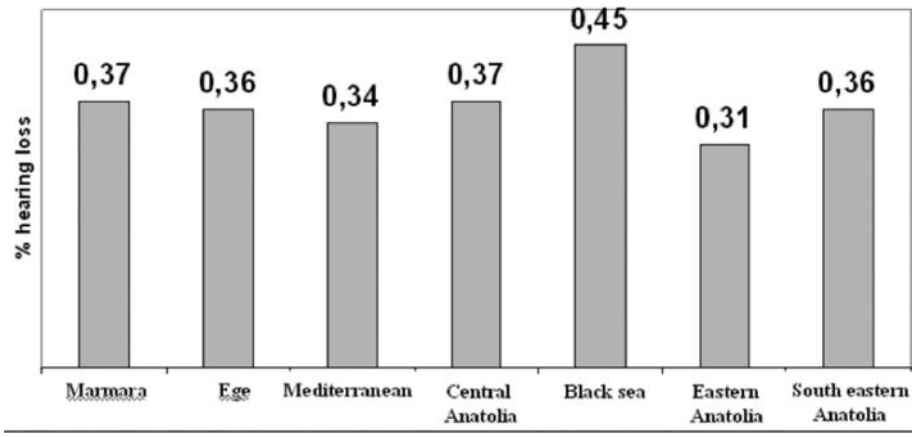

Figure 4- Hearing loss rates in different regions of Turkey

Table 2. People with hearing loss in Turkey

Hearing loss rate is 0.41%
73 million x 0.41% = 299.300 people with hearing loss already exist.
299.300 x 60% = 179.580 people with genetic hearing loss
179.580 x 70% =125.706 people with non-syndromic hearing loss
179.580 x 30% = 53.874 people with syndromic hearing loss
125.706 x 80% = 100.565 segregating with DFNB
125.706 x 18% = 22.627 segregating with DFNA
125.706 x 3% = 3.772 segregating with DFN
125.706 x 1% = 126 mitochondrial

Table 3. Hearing loss between 0-4 years of age in Turkey

6 million x 4:1.000 = 24.000 children with hearing loss already exist.
24.000 x 60% = 14.400 children with genetic hearing loss
14.400 x 30% = 4.320 children with syndromic hearing loss
14.400 x 70% = 10.080 children with non-syndromic hearing loss
10.080 x 80% = 8.064 segregating with DFNB
10.080 x 18% = 1.814 segregating with DFNA
10.080 x 3% = 302 segregating with DFN
10.080 x 1% = 144 mitochondrial

Table 4. Annual hearing loss in Turkey

4 000 x 60%= 2.400 babies born with genetic hearing loss every year.
2.400 x 30% = 720 babies born with syndromic hearing loss
2.400 x 70% = 1.680 born with non-syndromic hearing loss
1.680 x 80% = 1.344 newborns segregating with DFNB
1.680 x 18% = 302 newborns segregating with DFNA
1.680 x 3% = 50 newborns segregating with DFN
1.680 x 1% =17 newborns with mitochondrial hearing loss

The carrier rate of GJB2 gene mutations is estimated to be 1.4%, and 35delG is the most common mutant allele encountered in the carriers [5]. Then the number of people carrying the mutant allele of GJB2 gene is 1 million (73 million x 1.4%). As the GJB2 gene mutations are responsible for almost 25% of all genetic non-syndromic hearing losses, the number of healthy people carrying a mutant allele for genetic hearing loss should approach to 4 million. Since every year 1 million babies are born, this means 14.000 (1 million x 1.4/100) newborns are added as the carriers for 35delG mutation, and 56.000 as the carriers for GJB2 mutation.

In conclusion, there are 300.000 people who suffer from hearing loss, and 180.000 of them have genetic hearing loss. There are 1 million GJB2 gene mutant allele carriers and 4 million people carrying a hearing loss allele. Every year 4.000 babies are born with hearing loss, and there is a genetic cause in 2.400 of them.

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