Mutations in $GJB2$, $GJB6$ and mDNA 1555A>G variant explain only a minority of cases of nonsyndromic hearing loss in the Qatari population

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Hereditary hearing loss is a common genetic disorder accounting for at least 60% of prelingual deafness in children. Most cases (70%) are nonsyndromic and are not associated to other signs or symptoms, while the remaining 30% are syndromic. Nonsyndromic hereditary hearing loss has different patterns of inheritance. The most common one is autosomal recessive. This accounts for 75%-85% of the cases. Another 15%-25% of cases are inherited in an autosomal dominant (DNFA) pattern, while the remaining 1%-2% is inherited as X-linked disorder. Several mitochondrial mutations are also reported of which 1555A>G in the 12S rRNA gene is a common cause of mitochondrial-associated deafness in nonsyndromic progressive sensory neural hearing loss and its aminoglycoside induced state.

The two major genes for recessive forms are $GJB2$ and $GJB6$, which belong to the connexin family. $GJB2$ and $GJB6$ code for connexin 26 and connexin 30 proteins, respectively.

Here, we report for the first time results of a study in which a series of 120 patients affected by nonsyndromic hereditary hearing loss from 100 Qatari families were screened for mutations in $GJB2$ and $GJB6$ genes and the 1555A>G mitochondrial variant. 4 patients carried 35delG mutation, 5 patients the IVS1+1G<A, and 2 patients the Trp77Arg mutant alleles. None of the 120 patients were positive for $GJB6$ mutations or the 1555A>G variant.

These findings clearly demonstrate that $GJB2$, $GJB6$ and 1555A>G account for a minor proportion of nonsyndromic hereditary hearing loss in the Qatari population and further strengthen the need to search for causative genes in our population. Results presented here in combination with other molecular epidemiology data contribute to efforts for establishing preventive strategies and developing more targeted therapies.