

Review

Deaf mute or Deaf

Win Tin^{1*}, Zaw Lin², Swe³ and Nang Khin Mya⁴

¹Department of Surgical Based Department, Faculty of Medicine and Health Sciences, University Malaysia, Sabah

²Department of Pathobiology and Medical Diagnostics, Faculty of Medicine and Health Sciences, University Malaysia, Sabah

³Department of Community and Family Medicine, Faculty of Medicine and Health Sciences, University Malaysia, Sabah

⁴Department of Pathobiology and Medical Diagnostics, Faculty of Medicine and Health Sciences, University Malaysia, Sabah

*Corresponding author: Dr. Win Tin, Surgical Based Department, Faculty of Medicine and Health Sciences, University Malaysia Sabah, Jalan UMS, Kota Kinabalu, 88400, Sabah, Malaysia. Phone: 320000 Ext: 611315; E-mail: drwintin@ums.edu.my

Received: 23 February 2017/Accepted: 15 March 2017/ Published: 30 March 2017

Abstract: Hearing loss is a common disorder and can be conductive, sensorineural or mixed types. It can be congenital or acquired. In pediatric population more than 50% of deafness is genetic in origin. The patients may present as Deaf, mute or hard of hearing. Literature review was carried out on the pathophysiology including genetics, clinical presentation, etiology, diagnosis and various management, using internet Google, search PubMed. Additional information was obtained by cross referencing, using text and journals in the medical libraries.

Keywords: deaf mute; deaf; hard of hearing

1. Introduction

Deaf and dumb" or even "dumb" is an archaic term that is offensive, especially when referred to deaf people who do not speak. Many Deaf people do not use a spoken language, thus they are "mute". The word "dumb" means "mute". Deaf and Dumb Definition

(www.ncbi.nlm.nih.gov/glossary/dumb.htm).

Hearing loss is a very common congenital disorder with about 1.86 affected in every 1,000 newborns in US (Morton *et al.*, 2006), and affecting 4% of people aged younger than 45 years (Estivill *et al.*, 1998). In general, the type of hearing loss is classified as conductive, sensorineural, or mixed and either stable or progressive. In the pediatric population in US, more than 50% of patients with deafness have a genetic origin. (Morton *et al.*, 2006), with autosomal dominant, autosomal recessive, X-linked, or mitochondrial patterns of inheritance .In US less than 5% of deaf children have a deaf parent(Mitchell *et al.*, 2004). Etiologically it is classified into genetic (hereditary) or non-genetic (environmental) causes (Smith *et al.*, 2005). The time of onset in sensorineural hearing loss, is again classified as either congenital or acquired (or late-onset).

2. Deafness pathophysiology

Deafness can be from a mutation in a single gene or combination of mutations in different genes (Hildebrand *et al.*, 2008). Hereditary hearing loss and deafness may be conductive, sensorineural, or a combination of both, or syndromic or nonsyndromic. Syndromic with malformations of the external ear or other organs or, nonsyndromic which is not associated with abnormalities of the external ear or other medical problems. It can

be prelingual, where deafness occurs before language develops, ie congenital or begins before five years of age, or postlingual ie, after language develops (Hilgert *et al.*, 2009).

3. Historically

Deaf-mute is a term which was used to identify a person who is deaf using a sign language or both deaf and could not speak. These people communicate by using sign language. True communication occurs when ones message is understood by others, and they can respond in similar fashion (Padden *et al.*, 1988).

Muteness may result from two conditions: A person with problem in the throat or vocal chords and cannot produce sounds, ie physical muteness, and the deaf person who can make the sounds but not speak, as he cannot hear. Mute can also be due to genetics, drugs eg. aminoglycosides, cisplatin, and although not born mute, one out of about 1,000 school age children develop a condition called mutism, which is a psychological rather than a physical condition.

Historically , deaf-mute people were not possible to teach or communicate , thus they are considered as not moral, and therefore cannot own real estate, act as witnesses, or be punished for crimes(Griffith *et al.*, 2000; Creighton,2004) , But nowadays as methods for educating deaf people are known, they are not considered as before. Deaf with a lowercase "d" is usually noted as a person's hearing level through audiology. The uppercase D- Deaf, refers to a group of deaf people who uses American Sign Language (ASL), and a culture (Padden *et al.*, 1988). Deaf community today uses the term deaf and hard of hearing. In 1991, the World Federation of the Deaf voted to use the official terms deaf and hard of hearing (Creighton, 2004).

Perceptive deafness arising at birth, in infancy, or in early childhood, and needs a special education, is a heterogeneous condition. This condition has been known as deaf mutism. Since Aristotle and Hippocrates to recent times, mutism was considered a biological phenomenon, accompanying deafness. Children who failed to speak are not due to any pathological lesion of speech apparatus but because of lack of training. For the last 100 years due to the efforts by scholars, the term deaf-mutism now is replaced by profound childhood deafness (Fraser, 1965). They also noted that the proportion of deaf mute children born to deaf mute parents was many times greater than the proportion born to the people at large (Bell, 1969).

The term Hearing-impaired is no longer accepted by most in the community but was at one time preferred along with “visually,” “hearing,” and “mobility” impairment (Padden *et al.*, 1988).

Hard of hearing. It is used by the deaf noting that a person still has some usable hearing and is more functional than audiologic. Although there is no agreed demarcation, people with severe or profound hearing loss are considered as deaf and those with mild or moderate hearing loss as hard of hearing (Gorlin *et al.*, 1995).

For normal speech to develop in a child, the hearing sensation should be good and intact. It was found that for postlingually deafened children, with multichannel cochlear implants, they will have better speech perception abilities than in postlingually deafened adults. It was also noted that children with prelingually acquired congenital deafness would not receive same benefits, as they have not developed a proper auditory memory (Gantz *et al.*, 1994). Thus the first three to five years of life is considered to be important for the development of speech. Loss of hearing due to any cause during this crucial period of development may cause the development of poor speech.

4. Causes of deafness

These can be classified into, pre-natal and post-natal.

Pre-Natal - A small percentage is due, to malformation of some portion of the auditory apparatus, while in others due to intermarriage of blood relations. Apart from inbreeding, some families have genetic background resulting in deafness. A chromosomal aberration can also produce deafness with or without a hereditary factor (Edwards, 1997).

9.7% of infants have bilateral hearing loss, especially in infants who survived despite very low birth weight which is less than or equal to 1500 gm (Bergman *et al.*, 1985).

In young children with autism, a delayed speech probably because of hearing loss, can be seen (Hilgert *et al.*, 2009).

Prenatal infections from "TORCH" organisms (i.e., toxoplasmosis, rubella, cytomegalovirus, and herpes), can also give rise to acquired hearing loss in children.

For postnatal infections, especially bacterial meningitis caused by *Neisseria meningitidis*, *Haemophilus influenzae*, or *Streptococcus pneumoniae*, and meningitis from other organisms, eg *Escherichia coli*, *Listeria monocytogenes*, *Streptococcus agalactiae*, and *Enterobacter cloacae*, can cause hearing loss, so as acoustic or cerebral trauma affecting the cochlea (Hildebrand *et al.*,2008).

In developed countries, serous otitis media is the most common cause of hearing loss in children, affecting up to two thirds of preschool children. In addition, 1.0–2.0/1000 children have bilateral SNHL of at least 50 dB. In developed countries, SNHL appears to occur almost twice as often, and mainly due to infection (Davidson *et al.*, 1989).

In underdeveloped countries, suppurative otitis media is common. Acquired hearing loss in adults is most often caused by environmental factors but mainly due to environmental-genetic interactions. Age-related and noise-induced hearing losses are the most frequent examples of complex ‘environmental-genetic’ hearing loss; but, up till now only a few genes have been associated with these complex traits (Konings *et al.*, 2009).

Aminoglycoside-induced hearing loss is more common in persons with an A-to-G transition at nucleotide position 1555 in the mitochondrial genome (mtDNA) (Nance, 2003). The aminoglycoside hypersensitivity is often maternally transmitted, and it suggests mitochondrial involvement (Hildebrand *et al.*, 2008).

Because of the recent reduction in above infections, due to various treatments, the most common causes of bilateral SNHL are unknown (37.7%), genetic non-syndromic (29.2%), prenatal (12%), perinatal (9.6%), postnatal (8.2%), and genetic syndromic (3.2%) (Morzaria *et al.*, 2004), and studies confirm that autosomal recessive genes are responsible for most cases of unknown etiology. Most of the non-syndromic recessive gene mutations produce congenital profound deafness, of more than 90 dB hearing loss.

5. The genetics of deafness

All genetic diseases are due to aberrations in the coding function or the processing of human DNA. Different patterns of inheritance may give a single gene disorder, but it depends on whether the gene is autosomal (chromosomal pair 1-22) or sex chromosomal (X & Y) in its location or whether the gene is dominant or recessive, and these patterns of inheritance are usually identifiable from the family tree.

Alleles are alternative forms of the gene and it may or may not interfere with the function of the gene. If both alleles of the pair are the same, at that gene locus, then the individual is called homozygous, and if two different allele forms of the gene exist within the pair, then the individual is heterozygous. When a gene is expressed (i.e. apparent in the phenotype) in the heterozygous state, that allele is known as dominant. If an allele undergoes a disease causing dominant mutation, the individual will show the disease even thou there is a normal allele present at the same locus on the paired chromosome.

Autosomal recessive disorder requires that, the individual must have disease causing mutations on both maternal and paternal alleles before the disease manifest clinically. The recurrence risk in these patients in future pregnancies is 25%, and more frequently seen in persons with high consanguinity.

Mygge (1879) reported 7.6% of pupils at Royal School for the deaf-mute had consanguineous parents and Lindenov (1945) reported 9.7%. According to Mendels law, recessive traits often manifest themselves in families where intermarriage has occurred, as the gene concerned is likely to be transmitted by both parents (Johnsen, 1952). If there is successive consanguinity, the disorder may appear in generations, and the phenomenon is known as pseudodominance.

There are a large number of genes that can cause deafness. More than half of all genetic cases in some of the populations are due to recessive mutations at a single locus, GJB2 (gene gap junction protein beta2) or Connexin 26. Especially in countries close to Mediterranean the most common mutation for sensorineural deafness, is in mutation of 35delG an allele of GJB2 (Estivill *et al.*, 1998; Cryns *et al.*, 2004) and about 4% carrier rates are seen in some ethnic groups (Griffith *et al.*, 2000).

5.1. Prevalence

The most common birth defect in developed countries is hearing loss especially the sensorineural (Hilgert *et al.*, 2009). One in 500 new borns has bilateral permanent sensorineural hearing loss ≥ 40 dB; and by adolescence, it becomes to 3.5 per 1000 (Morton *et al.*, 2006; Konings *et al.*, 2009). In US congenital SNHL occurs about three times more common than Down's syndrome (Gorlin *et al.*, 1995).

A small percentage of prelingual deafness is syndromic associated with other disorders, such as kidney, heart or vision abnormalities or may be nonsyndromic autosomal dominant.

More than 50% of prelingual deafness is genetic, autosomal recessive and nonsyndromic. And 50% of autosomal recessive nonsyndromic hearing loss can be due to the disorder DFNB1 (Arnos, 2003; Smith *et al.*, 2002) on chromosome 13 caused by mutation of GJB2 that encodes the protein connexin 26 and GJB6 that encodes the protein connexin 30 (Nance, 2003). Connexins are a class of membrane proteins that form hexameric connexions which form gap-junction channels with similar connexons of adjacent cells for exchange

of electrolytes and metabolites. The carrier rate in the general population for a recessive deafness causing *GJB2* variant is about 2.8 % (Kelley *et al.*, 1998).

5.2. Heritable causes. Single gene disorders

In syndromic hearing impairment it is in association with external ear or other organ malformations or with medical problems in other organs.

Nonsyndromic hearing impairment has normal external ears and no related medical problems, but, may be associated with middle and inner ear abnormalities (Smith *et al.*, 2002).

5.3. Syndromic hearing impairment

Of the more than 400 syndromes in which HL is a feature, with 30% having prelingual deafness (Smith *et al.*, 2002). the most common are, Usher syndrome, Pendred syndrome and Jervell and Lange-Nielsen syndrome (Hilgert *et al.*, 2009).

(1) Autosomal dominant syndromic hearing impairment, egs, are-Waardenburg syndrome (WS), Branchiootorenal syndrome (BOR), Neurofibromatosis 2.

(2) Autosomal recessive syndromic hearing impairment, egs, are - Usher syndrome ,Biotinidase deficiency, and Pendred syndrome which is the second most common type of autosomal recessive syndromic hearing loss , where mutations, with enlarged vestibular aqueduct (EVA), are the most common form of inner ear abnormality(Middleton *et al.*, 1998).

(3) For X-linked syndromic hearing impairment eg. Alport syndrome

(4) Mitochondrial syndromic hearing impairment, eg. Keane-Sayre syndrome, and in association with Diabetes mellitus, Parkinson, Alzheimers disease.

5.4. Non-syndromic hearing impairment

To date, 46 genes have been identified as causing nonsyndromic HL (Hilgert *et al.*, 2009).

The different gene loci for nonsyndromic deafness are designated DFN (for DeafNess), where Loci are named based on mode of inheritance as-

- DFNA: Autosomal dominant
- DFNB: Autosomal recessive
- DFNX: X-linked

Within the prelingual nonsyndromic hearing loss group, inheritance is 75%-80% autosomal recessive, 20%-25% autosomal dominant, and post lingual (Camp *et al.*, 1997) and 1%-1.5% X-linked Most autosomal recessive loci cause prelingual severe-to-profound hearing loss. An exception is DFNB8, in which there is postlingual hearing impairment and is progressive.

Most of the autosomal dominant loci cause postlingual hearing impairment, before the age of 20 years.

For X-linked nonsyndromic hearing loss it can be either pre- or postlingual.

(1)Autosomal dominant nonsyndromic hearing impairment

- For the majority of cases, autosomal dominant nonsyndromic hearing loss does not have an identifiable single gene which is responsible for deafness.(Smith *et al.*, 2014). Persons with DFNA3 is characterized by progressive, moderate-to-severe sensorineural impairment. It is less commonly caused by heterozygous pathogenic variants in GJB6 (Smith *et al.*, 2016). The affected persons in these families develop normal speech and retains partial hearing. Thus they seldom integrate into the deaf community and usually marry normal hearing person (Camp *et al.*, 1997).

Audioprofiling can be used for prognosis and measure the rate of hearing loss per year in individuals with nonsyndromic , autosomal dominant hearing loss of known cause (Hildebrand *et al.*, 2008).

As audioprofile can be distinctive, it can be used to evaluate molecular genetic testing (Hildebrand *et al.*, 2008).

(2) Autosomal recessive nonsyndromic hearing impairment (ARNSD) deafness

In the world, 50% of persons with autosomal recessive nonsyndromic hearing loss have deafness-causing variants in *GJB2* and mutations in the *GJB2* gene at the DFNB1 locus (Castillo *et al.*, 2002; Petersen *et al.*, 2006) .Thus it should facilitate diagnosis as well as counselling for the most common genetic form of deafness.

It is the most common cause of inherited hearing loss (Castillo *et al.*, 2002), and it is usually associated with retaining of low frequency tone, as degeneration starts from base and towards the apex later, where these low tone are felt.(Gorlin *et al.*, 1995)

- These mutations in *GJB2* cause severe or profound deafness (Smith *et al.*, 2016).

- Usually associated medical findings are absent (Smith *et al.*, 2016). Deafness is stable and non-progressive, but progression has been reported in some cases. Onset is nearly always pre-lingual (Castillo *et al.*, 2002; Pandya *et al.*, 2003) but may not be congenital, and hearing may be normal at birth but progress rapidly in the first few months of life (Smith *et al.*, 2016).

- Thus babies with mutations in *GJB2* may pass new-born hearing screening but found to be profoundly deaf during infancy (Smith *et al.*, 2016)

(3) X-linked nonsyndromic hearing impairment

- DFNX3* has a mixed conductive-sensorineural hearing loss, and is due to stapedial fixation (Camp *et al.*, 1997)

(4) Nonsyndromic hearing loss and deafness, mitochondrial

One variant in this gene, 1555G>A, is a frequent cause of maternally inherited nonsyndromic hearing loss (Camp *et al.*, 1997) and some individuals will have hearing loss which is caused by aminoglycosides. 1% of the children will have mitochondrial mutations with prelingual deafness, but may be more frequent at a later age (Green *et al.*, 1999; Hildebrand *et al.*, 2008).

A Person, whose family tree (pedigree) you make is called proband, and the sisters and brothers of this person are called sibships.

(1) Risk to family members-Autosomal dominant hereditary hearing loss.

- Most of the individuals diagnosed as having Autosomal dominant hereditary hearing loss will have a deaf parent, and the family history is rarely negative (Gorlin *et al.*, 1995; Smith *et al.*, 2014).
- A proband with autosomal dominant hereditary hearing loss may also have the disorder as the result of a de novo deafness-causing variant, but the number is usually small (Gorlin *et al.*, 1995).

Individuals diagnosed with autosomal dominant hereditary hearing loss will have a deaf parent, but the family history may not be there , due to failure to recognize hereditary hearing loss in family members, or late onset in a parent, reduced penetrance of the deafness-causing allele in an asymptomatic parent, or a *de novo* variant for hereditary hearing loss (Hilgert *et al.*, 2009).

- There is 50% chance of transmitting the mutated allele to each child in individuals with autosomal dominant hereditary hearing loss (Gorlin *et al.*, 1995). Usually both sexes are equally affected.and transmitted from generation to generation with no skip.
- The offspring of a deaf person and a hearing person have a 10% empiric risk of deafness.

(2) Risk to family members — Autosomal recessive hereditary hearing loss

- Both the parents are phenotypically normal but are heterozygous carriers with abnormal genes (Gorlin *et al.*, 1995) and therefore carry a single copy of a deafness-causing variant *GJB2*.
- Heterozygotes are asymptomatic (Smith *et al.*, 2016).
- At conception, each sib has a 25% chance of being deaf, a 50% chance of having normal hearing and becoming a carrier, and a 25% chance of having normal hearing but not being a carrier (Smith *et al.*, 2016).
- If at risk sib have normal hearing, the risk of his/her being a carrier is 2/3, like their parents with both sexes having equal chance of being affected (Gorlin *et al.*, 1995).

Offspring of a proband are obligate carriers.

Again, each of the parents' siblings is at 50% risk for being carrier (Smith *et al.*, 2002). When the hearing sibling who is a carrier of a *GJB2* deafness-causing mutation, marries a person with *GJB2*-related deafness, the chance of having a deaf child is about 50% (Smith *et al.*, 2002), and if both parents have *GJB2*-related deafness, the risk to their offspring is 100% (Smith *et al.*, 2002).

(3) X-linked hereditary hearing loss

For the offspring of a proband, males with X-linked hereditary hearing loss will pass the deafness-causing variant to all of their daughters and none of their sons (Gorlin *et al.*, 1995).

(4) Mitochondrial disorders with hearing loss

- All offspring of females with a mtDNA pathogenic variant are at risk of inheriting the variant (Hu *et al.*, 1991).
- But the offspring of males with a mtDNA pathogenic variant are not at risk (Gorlin *et al.*, 1995).
- Mutations in the mitochondrial genome are only inherited through the maternal line and are never transmitted by the father.
- Thus, mitochondrial inheritance can be considered in multigeneration families, and a history of exposure to aminoglycoside antibiotics.

6. Genetic counseling

Accurate genetic diagnosis can help in genetic counseling and risk assessment.

As it is also important for the families and individuals to make informed choices regarding the use of genetic testing, there should be genetic counselling by skilled geneticists (Arnos, 2003).

Genetic counseling will provide individuals and families with information on the nature, hereditary, and implications of genetic disorders so, to help them make informed medical and personal decisions, know genetic risk and make clear the genetic status for family members. Many deaf people are more interested in obtaining information about the cause of their own deafness, and information on medical, educational, and social services, rather than information on prevention, reproduction, or family planning (Smith *et al.*, 2016).

As in all genetic counseling, it is important for the counselor to acknowledge, identify, and respect the individual and family's concerns, and fears (Middleton *et al.*, 1998; Arnos, 2003). Just as a normal-hearing couple might wish to have a normal-hearing child, a deaf couple will also wish to have a deaf child (Smith *et al.*, 2002). The subsequent offspring of a hearing couple with one deaf child and an otherwise negative family history of deafness have an 18% (range, 15.0%-20.4%) empiric probability of deafness in future children (Green *et al.*, 1999).

- If the deaf child does not have DFNB1 based on molecular genetic testing of GJB2 and GJB6, the recurrence risk is 14% for deafness unrelated to connexin 26 (Smith *et al.*, 2014).
- If the hearing couple is consanguineous, the subsequent offspring have close to a 25% probability of deafness because of the high likelihood of autosomal recessive inheritance (Smith *et al.*, 2014).
- The offspring of a deaf person and a hearing person have a 10% empiric risk of deafness (Green *et al.*, 1999; Smith *et al.*, 2014).

7. Family planning

- Testing before pregnancy is the optimal time for determination of genetic risk, clarification of carrier status, and discussion of the availability of prenatal testing (Smith *et al.*, 2016).
- Advances in genetics and genomics will give technologies for prenatal diagnosis and gene therapy for hearing loss as well as other communication disorders which are genetically based (Amos, 2008).
- It is also better to offer genetic counseling and risks to offspring and reproductive options, to young adults who are deaf.
- Thus, even before they are pregnant, genetics can provide knowledge to the deaf couples to know whether their children will be hearing or deaf (Nance, 2003).

8. Diagnosis

Congenital hearing loss can be identified by newborn hearing screening (NBHS) (Hilgert *et al.*, 2009).

For early detection of suspected hearing loss, it is the best method, and if the newborn hearing screening is not universal, more than 30% of permanent hearing loss can be missed (Jakubikova *et al.*, 2009).

Severe to profound hearing loss could reliably be detected by behavioral hearing screening of neonates and was detected in 17 of 17,000 infants. Two screening tests were used. Automated auditory brain stem response which measures average neural response to a large number of repeated sound signals, and measurement of spontaneous or sound induced otoacoustic emissions detects sound produced by movements of outer hair cells of cochlear (Morton *et al.*, 2006)

Screening of the GJB2 mutation can be done with high sensitivity and specificity for individuals with congenital deafness, by screening only for the 35delG mutation. A positive finding should make an etiologic diagnosis and affect genetic counselling (Green *et al.*, 1999).

PCR is also widely used as the initial DNA amplification step for genetic testing (Li *et al.*, 2008).

PCR-based sequence analysis has been shown to be an efficient method for identifying pathogenic mutations in this gene with non-syndromic deafness of uncertain etiology (Pandya *et al.*, 2003). A negative family history does not exclude GJB2 deafness (Pandya *et al.*, 2003). All PCR products should be sequenced on both strands, thus allowing to detect the normal and the mutated allele in the normal hearing parents and deaf children heterozygous for the 30delG mutation (Denoyelle *et al.*, 1997).

For possible future use, DNA banking, which is the storage of DNA extracted from white blood cells can be done.

Genetic forms of hearing loss must be distinguished from non-genetic (acquired) causes of hearing loss. The genetic forms of hearing loss are diagnosed by otologic, audiologic, and physical examination, family history, CT examination of the temporal bone, and molecular genetic testing. Molecular genetic testing, is possible for

many types of syndromic and nonsyndromic deafness, and for diagnosis and genetic counseling (Hilgert *et al.*, 2009).

Molecular genetic testing approaches can include a combination of gene-targeted testing (single-gene testing and a multi-gene panel) and genomic testing (comprehensive genomic sequencing) (Smith *et al.*, 2016; www.genetics.edu.au.2016).

Whole-exome sequencing (WES) and whole-genome sequencing (WGS) may be considered if the phenotype alone is insufficient to warrant gene-targeted testing. Both WES and WGS should be complemented with appropriate genetic counseling before and after testing to consider in interpretation of genomic test results (Smith *et al.*, 2016).

As serial gene sequencing approaches are expensive and time consuming some use comprehensive genetic diagnostic platform with massively parallel sequencing (Shearer *et al.*, 2010)

Mutations in GJB2 are the most common cause of nonsyndromic autosomal recessive hearing impairment, from mild to profound deafness, and mutation analysis of this gene is widely available as a genetic diagnostic test (Cryns *et al.*, 2004).

Once the GJB2 pathogenic variants have been identified in a family member with DFNB1, prenatal testing for a pregnancy at increased risk and preimplantation genetic diagnosis (Genetic Home Reference. <http://ghr.nlm.nih.gov/primer/testing/genetictesting>) are possible options, which can be done (Smith *et al.*, 2016).

Tests for mutations in GJB2, GJB3, SLC26A4 and mitochondrial 12S rRNA are now available on a research or clinical basis (Fu *et al.*, 2010). Screening the *GJB2* and *SLC26A4* genes should form the basis of any genetic testing programme for childhood deafness (Hutchin *et al.*, 2005). The high prevalence of mutations in GJB2 in some population provides the tools for molecular diagnosis, carrier detection and prenatal diagnosis of congenital hearing impairment (Rabionet *et al.*, 2000).

With hearing loss for mutations in GJB2 using an allele-specific polymerase chain reaction assay, single-strand conformation polymorphism analysis, and direct sequencing can also be used.

But as there are more than 80 genes and more than a thousand reported deafness-causing mutations. This extreme genetic heterogeneity makes genetic diagnosis for Non Syndromic Hearing Loss exceedingly difficult (Shearer *et al.*, 2015).

8.1. Establishing the diagnosis

Family history. A three-generation family history including relatives with hearing loss and associated findings should be obtained (Smith *et al.*, 2014). In simplex families (only one affected child) (Smith *et al.*, 2002), allele variants of many genes are known to cause hereditary deafness (Smith *et al.*, 2002). Children at risk for hereditary hearing loss should undergo molecular genetic testing, and also screening audiometry (Hilgert *et al.*, 2009).

Genetic testing is a family, rather than an individual, matter and that family involvement in the decision making process should be strongly encouraged in order to help families adjust (Sobel *et al.*, 2000).

Clinical examination. All persons with hearing loss of unknown cause should be evaluated for signs and symptoms of syndromic deafness. Important features include branchial cleft pits, cysts or fistulae, high myopia, white forelock, pigmentary retinopathy, telecanthus, preauricular pits, heterochromia iridis, pigmentary anomalies, goiter, and craniofacial anomalies. Serologic tests for toxoplasma (IgM, CMV IgM, Rubella IgM, HSV1 IgM), CT scan, and ophthalmologic evaluation can also be done (Morzaria *et al.*, 2004).

Physiologic tests like auditory brain stem response testing (ABR/ BAER). Auditory steady-state response testing (ASSR), Evoked oto-acoustic emissions (EOAEs), Immittance testing tympanometry, acoustic reflex decay, acoustic reflex thresholds, Audiometry, Behavioral testing, and Audioprofile should be done by persons who specialise in these subjects.

9. Management

Heredity hearing loss should be managed by a team with otolaryngologist, audiologist, pediatrician, clinical geneticist, and a neurologist, with educator of the Deaf, and a pediatric ophthalmologist (Hilgert *et al.*, 2009). Early auditory intervention by amplification, otologic surgery, or cochlear implantation is important and necessary for optimal cognitive development in children with prelingual deafness (Hilgert *et al.*, 2009).

During the past three to four decades, the incidence of acquired sensorineural hearing loss (SNHL) in children living in more developed countries has reduced, because of the immunisation programmes. Though there is overall decrease there is increase again in the inherited forms of SNHL (Gorlin *et al.*, 1995; Smith *et al.*, 2005; Marazita *et al.*, 1993).

Some mute patients, to overcome their disability use machines that vibrate their vocal cords, allowing them to speak. Oesophageal speech also gives speaking ability and others learn sign language as communication (<https://en.wikipedia.org/wiki/Deaf-mute>).

Computers, smart phones and the Internet facilitate communication. Many communication devices help people to communicate, and these includes "text-to-speech" devices and software, which turns typed text into electronic vocalizations, enabling the mute and the speech-impaired to "speak".

Other techniques of communication include:

- notes, books with letters, helper pages, words, iconic and Bliss symbols and pictures, lip-reading vocalization speech recording and replaying
- Rehabilitation of the deaf includes hearing aids, vibrotactile devices, and cochlear implantation. Cochlear implantation can be considered in children between 12 months ,and 2 years, and it shows better speech perception and language abilities, when compare with those done after that age (Kirk *et al.*, 2000; Svirsky *et al.*, 2004) in severe-to-profound hearing loss.
- In 2012 researches detected growth of cochlear nerve cells with hearing improvements in gerbils, by using human embryonic stem cells (Rojahn , 2012). In 2013 there was also a report, saying there could be regrowth of hair cells in deaf adult mice, using a drug resulting in hearing improvement. A potential cure for permanent deafness has been found by scientists using a drug that stimulates the inner ear, in a study by Harvard Medical School. The drug, codenamed LY411575, can trigger and regenerate the sensory hair cells (www.dailymail.co.uk)
- To restore hearing, the Hearing Health Foundation in US had started a project called Hearing Restoration Project and in UK Action on Hearing loss were done.
- Genetically deaf mice which were treated with TMC1 gene therapy can recover some of their hearing (Askew *et al.*, 2015) was also reported in 2015.

With these numerous research, in the world, there is future and hope for sensorineural hearing loss and deaf mute or deaf people.

10. Conclusions

It should be noted that there should be a concerted effort in identifying the patients and looking for the itiology, managing, counselling these people early, so as to make and help these people in their life.

Acknowledgements

I would like to thank Professor Dr. Zainal Arifin Mustapha, Dean, Faculty of Medicine and Health Sciences, University Malaysia Sabah, Deputy Deans, all lectures and staff of University Malaysia Sabah, library staff and not the least, my wife Dr Khin who all help and encourage me to bring out this paper.

Conflict of interest

None to declare.

References

- Arnos KS, 2003. The implications of genetic testing for deafness. *Ear Hearing*, 24: 324–331.
- Amos KS, 2008. Ethical and social implications of genetic testing for communication disorders. *J. Commun. Disord.*, 41: 444-457.
- Askew C, C Rochat, B Pan, Y Asai, H Ahmed, E Child, BL Schneider, P Aebscher and J R Holt, 2015. Tmc gene therapy restores auditory function in deaf mice. *SciTransl Med.*, 7: 295ra108.
- Bell AG, 1969. Memoir upon the formation of a deaf variety of the human race. – ERIC
- Bergman I, RP Hirsch, TJ Fria , SM Shapiro, I Holzman and MJ Painter, 1985. Cause of hearing loss in the high-risk premature infant. *J. Pediatr.*, 106: 95-101.
- Camp GV, PJ Willems and Smith RJ, 1997. Nonsyndromic hearing impairment:unparalleled heterogeneity. *Am. J. Hum. Genet.*, 60: 758-764.
- Castillo I del, M Villamar, M A. Moreno-Pelayo, F J. del Castillo, A Álvarez, D Tellería, I Menéndez, and F Moreno, 2002. A deletion involving the connexin 30 gene in nonsyndromic hearing impairment. *N. Engl. J. Med.*, 346: 243-249.
- Creighton N, 2004. What is wrong with the use of the terms: 'deaf-mute', 'deaf and dumb', or 'hearing impaired'? National Association of the Deaf. www.eamo.org/assets/spdeafterminology.pdf.

- Cryns K, E Orzan, A Murga, PLM Huygen, F Moreno, Id Castillo, GP Chamberlin, H Azaiez, S Prasad, RA Cucci, E Leonardi, RL Snoeckx, PJ Govaerts, PH Van de Heyning, CM Van de Heyning, RJH Smith and G Van Camp , 2004. A genotype-phenotype correlation for GJB2(connexin 26) deafness. *J. Med. Genet.*, 41: 147-154.
- Davidson J, ML Hyde and PW Alberti, 1989. Epidemiologic patterns in childhood hearing loss: a review *International Journal of Pediatric Otorhinolaryngology*, 17: 239-266.
- Deaf-mute - Wikipedia
<https://en.wikipedia.org/wiki/Deaf-mute>
- Denoyelle F, D Weil, M A. Maw, S A. Wilcox, N J. Lench, D R. Allen-Powell, A H. Osborn, H-H M. Dahl, A Middleton, M J. Houseman, C Dodé, S Marlin, A Boulila-ElGaïed, M Grati, H Ayadi, S B Arab, P Bitoun, G Lina-Granade, J Godet, M Mustapha, J Loiselet, É El-Zir, A Aubois, A Joannard, J Levilliers, É N Garabédian, R F. Mueller, R. J. M Gardner and C Petit, 1997. Prelingual deafness: high prevalence of a 30delG mutation in the connexin 26 gene. *Human Molecular Genetics*, 6: 2173-2177.
- Drug could reverse ‘permanent’ deafness by regenerating hair cells in inner ear. 2013. www.dailymail.co.uk/health/article.
- Edwards ML, 1997. Deaf and Dumb in Ancient Greece; The disability studies reader. books.google.com. 29-49.
- Estivill X, P Fortina , S Surrey , R Rabionet , S Melchionda , L D'Agruma , E Mansfield , E Rappaport , N Govea , M Mila , L Zelante and P Gasparini , 1998. Connexin-26 mutations in sporadic and inherited sensorineural deafness. *Lancet*, 351:394-398.
- Fraser GR , 1965. Sex-linked recessive congenital deafness and the excess of males in profound childhood deafness. *Annals of Human Genetics*, 29: 171-196
- Fu S, J Dong, C Wang and G Chen, 2010. Parental attitudes toward genetic testing for prelingual deafness in China. *International Journal of Pediatric Otorhinolaryngology*, 74: 1122-1125.
- Gantz BJ, RS Tyler , GG Woodworth, TM Nancy and FB Holly,1994. Results of multichannel cochlear implants in congenital and acquired prelingual deafness in children: Five-year follow-up. *American Journal of Otology*, 15: 1-27
- Genetic Home Reference. US National Library of Medicine. <https://ghr.nlm.nih.gov/primer/testing/genetictesting>.
- Gorlin RJ, HV Toriello and MM Cohen, 1995. Hereditary hearing loss and its syndromes. –9-20. books.google.com.
- Green GE, DA Scott , JM McDonald , GG Woodworth , VC Sheffield and RJ Smith , 1999. Carrier rates in the midwestern United States for GJB2 mutations causing inherited deafness. *JAMA*, 281: 2211-2216.
- Griffith AJ, AA Chowdhry, K Kurima, LJ Hood, B Keats, CI Berlin, RJ Morell, and TB Friedman, 2000. Autosomal Recessive Non-syndromic Neurosensory Deafness at *DFNB1* Not Associated with the Compound-Heterozygous *GJB2* (Connexin 26) Genotype M34T/167delT. *Am. J. Hum. Genet.*, 67: 745-749.
- Hildebrand MS, D Tack , SJ McMordie, ADe Luca , IA Hur, C Nishimura , P Huygen, TL Casavant and RJ Smith , 2008. Audioprofile-directed screening identifies novel mutations in KCNQ4 causing hearing loss at the DFNA2 locus. *Genet. Med.*, 10: 797-804.
- Hilgert N, RJH Smith and GV Camp, 2009. Forty-six genes causing nonsyndromic hearing impairment: Which ones should be analyzed in DNA diagnostics? *Mutation Research/Reviews in Mutation Research*, 681: 189-196.
- Hu DN, WQ Qui, BT Wu, LZ Fang, F Zhou, YP Gu, QH Zhang, JH Yan, YQ Ding and H Wong, 1991. Genetic aspects of antibiotic induced deafness: mitochondrial inheritance. *J. Med. Genet.*, 28:79-83.
- Hutchin T, NN Coy, H Conlon, E Telford, K Bromelow, D Blayton, G Taylor, E Coghill, S Brown, R Trembath, XZ Liu, M Bitner-Glindzicz and R Mueller, 2005. Assessment of genetic causes of recessive childhood non-syndromic deafness in the UK-implications for genetic testing. *Clinical Genetics*, 68: 506-512.
- Jakubikova J, Z Kabatova, G Pavlovcinova and M Profani, 2009. Newborn hearing screening and strategy for early detection of hearing loss in infants. *International Journal of Pediatric Otorhinolaryngology*, 73: 607-612
- Johnsen S, 1952. The heredity of perceptive deafness. *Journal Acta Oto-Laryngologica*, 42: 539-552, Published online 2009.
- Kelley PM, DJ Harris, BC Comer, JW Askew, T Fowler, SD Smith, and WJ Kimberling, 1998. Novel mutations in the connexin 26 gene (GJB2) that cause autosomal recessive (DFNB1) hearing loss. *Am. J. Hum. Genet.*, 62:792-799.
- Kirk KI, RT Miyamoto, EA Ying, AE Perdew and H Zuganelis, 2000. Cochlear implantation in young children: effects of age at implantation and communication mode. *Volta Review*, 102: 127-144.

- Konings A , LV Laer , S Michel , M Pawelczyk , PI Carlsson , ML Bondeson, E Rajkowska, A Dudarewicz, A Vandevelde, E Fransen, J Huyghe, E Borg, MS Kowalska and GV Camp, 2009 .Variations in HSP70 genes associated with noise-induced hearing loss in two independent populations. European Journal of Human Genetics, 17: 329–335.
- Li J, LWang, H Mamon, MH Kulke, R Berbeco and GM Makrigiorgos, 2008. Replacing PRC with COLD-PRC enriches variant DNA sequences and redefines the sensitivity of genetic testing. Nature Medicine, 14: 579-584.
- Marazita ML, LM Ploughman, B Rawlings, E Reminton, KS Arnos, and WE Nance, 1993.Genetic Epidemiological Studies of Early -Onset Deafness in the US School –Age Population. Am. J. Med. Gen., 46:486-491.
- Middleton A, J Hewison, and RF Mueller, 1998. Attitudes of deaf adults toward genetic testing for hereditary deafness. Am. J. Hum. Genet., 63: 1175–1180.
- Mitchell RE and MA Karchmer, 2004. Chasing the mythical ten percent. Parental hearing status of deaf and heard of hearing students in the United States. Sign Language Studies, 4: 138-163.
- Morton CC and WE Nance, 2006. Newborn hearing screening-a silent revolution. N. Engl. J. Med., 354: 2151-2164.
- Morzaria S, BD Westerberg and FK Kozak, 2004. Systematic review of the etiology of bilateral sensorineural hearing loss in children. International Journal of Pediatric Otorhinolaryngology, 68: 1193–1198.
- Nance WE, 2003. The genetics of deafness. Ment Retard Dev Disabil Res Rev., 9: 109-119
- Padden C and T Humphries, 1988. *Deaf in America: Voices from a Culture* National Association of Deaf.
- Pandya A, KS Arnos, XJ Xia, KO Welch, SH Blanton, TB Friedman, GG Sanchez, XZ Liu, R Morell and WE Nance, 2003. Frequency and distribution of GJB2 (connexin 26) and GJB6 (connexin 30) mutations in a large North American repository of deaf probands. Genet. Med., 5: 295–303
- Petersen MB and PJ Willems, 2006. Non-syndromic, autosomal-recessive deafness. Clin. Genet., 69: 371-392.
- Rabionet R, P Gasparini and X Estivill, 2000. Molecular genetics of hearing impairment due to mutations in gap junction genes encoding beta connexins. Hum.Mut., 16: 190-202.
- RojahnSY, 2012. Researchers Use Human Embryonic Stem Cells to Restore Hearing. MIT Technology Review.
- Shearer AE, AP DeLuca, MS Hildebrand, KR Taylor, J Gurrola, S Scherer, TE Scheetz and RJH Smith, 2010. Comprehensive genetic testing for hereditary hearing loss using massively parallel sequencing. Proceedings of the National Academy of Sciences of the United States of America., 107: 21104-21109.
- Smith RJH and NH Robin, 2002. Genetic testing for deafness-GJB2 and SLC26A4 as causes of deafness. Journal of Communication Disorders, 35: 367–377.
- Smith RJH, JF Bale Jr and KR White, 2005. Sensorineural hearing loss in children. The Lancet, 365: 879–890.
- Smith RJH, AE Shearer, MS Hildebrand and GV Camp, 2014. Deafness and Hereditary Hearing loss Overview. Gene Reviews (Internet).
- Shearer AE and RJH Smith, 2015. Massively Parallel Sequencing for Genetic Diagnosis of Hearing Loss. The New Standard of Care. Otolaryngol Head Neck Surgery, 153: 175-182.
- Smith RJH, and M K N Jones, 2016. Nonsyndromic Hearing Loss and Deafness, DFNB1Synonym: GJB2-Related DFNB 1 Nonsyndromic Hearing Loss and Deafness. GeneReviews® [Internet].
- Sobel SK and B Cowan, 2000. Impact of genetic testing for Huntington disease on the family system. American Journal of Medical Genetics, 90: 49-59.
- Svirsky MA, SW Teoh, and H Neuburger, 2004. Development of language and speech perception in congenitally, profound deaf children as a function of age at cochlear implantation. Audio Neurotol., 9: 224-233.
- Understanding Genetic testing-Centre for Genetics Education. www.genetics.edu, au.2016. www.ncbi.nlm.nih.gov/dumb.htm.