Prevalence and physiological assessment of deafness in district Ghanche (Gilgit-Baltistan), Pakistan (An audiometry based study)

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ABSTRACT

Gilgit-Baltistan (GB) is located in Northern Mountain Regions of Pakistan. This study was conducted in Surmo village (Ghanche district) of GB during June 2005 to June 2006. Audiograms were obtained by using pure tone air conduction audiometry. 256 ears (both left and right) of deaf individuals from 16 targeted families belonging to same ethnic group i.e., Balti, and complicated consanguinity, maximizing the deafness gene concentration in small population, as there is high ratio of cousin marriages. Audiograms of both ears of 16 deaf were taken at eight different frequencies i.e. (16 deaf x 2 ears, left and right x 8 frequencies at 0.25 kHz, 0.5 kHz, 1 kHz, 2 kHz, 3 kHz, 4 kHz, 6 kHz and 8 kHz) total 256. One sample t-test of the mean of averages of all samples differs significantly from normal hearing i.e. 20 dB and even 40 dB. The two-tailed P value obtained is < 0.0001, considered extremely significant confirming that the differences are sampled from a Gaussian distribution (normal distribution). The Kolmogorov-Smirnov distance (KS) is 0.17 and The P value is >0.10 and the data passed the normality test with P>0.05. The significant finding are 53.91% profound (> 90dB = 138 ears), 32.81% severe (71 - 90dB = 84 ears), 3.13% moderately severe (56-70 dB=8 ears), 5.47% moderate (41-55dB=14 ears) and 4.69% mild (<40 dB=14 ears). Pedigrees of these 11 families showed there was no case of autosomal dominance inheritance. All were autosomal recessive. Four syndromic deafness were also recorded (2 mentally retarded, 1 goiter and 1 with balance problem).

Keywords: Gilgit-Baltistan, Audiogram, Deafness, Decibel

INTRODUCTION

Hearing is the process by which the ear transforms sound vibrations in the external environment into nerve impulses that are conveyed to the brain, where they are interpreted as sounds. Audiometry can be applied for the detection of severity of hearing loss in different age groups including children (Karanja et al., 2014). Sound is the physical phenomenon that stimulates the sense of hearing vibrations of frequencies from around 15 hertz to about 20,000 hertz, when reach the inner ear of human being (Redmond, 2008).

The human ear is an extremely complicated organ, which performs the dual function of balancing and perceiving sound. It is made up of three discrete parts, the outer, middle and inner ears, which function as a unit. The outer ear is composed of pinna and external auditory canal; forming the first distinct part of the ear. The middle ear is the cavity, which lies behind the ear drum; filled with air and with a lining of mucous membrane. It has a chain of three ossicles (bones). The malleus is the most lateral (toward the side of the head) of the three ear bones (ossicles) in the middle ear. The long process of the malleus (manubrium) is attached to the tympanic membrane. Tympanic membrane vibrates in response to sound, causing malleus to vibrate in concert. Attached to the malleus is a series of two ossicles, the incus and the stapes, which inturn is attached via a footplate to the oval window of the cochlea. The inner ear contains six mechno-receptive structures: three semicircular canals, utricle, saccule and the cochlea. It simultaneously regulates two sensory systems; the auditory system for hearing and the vestibular system for spatial orientation and equilibrium. The cochlea, specialized for detection of sounds, regulates the auditory system. The inner ear consists of two parts; the osseous or bony labyrinth and the membranous labyrinth. The osseous labyrinth is a series of cavities with the petrous portion. Information about the pathlogy of genetic deafness was based upon light microscopy so it could be explained by the degeneration of sensory hair cells (Steel & Brown, 1996).

Four types of hearing loss may be described. The first, conductive hearing loss is caused by diseases or obstruction in the outer or middle ear and usually is not severe. A person with a conductive hearing loss generally can be helped by a hearing aid. Often conductive hearing losses can also be corrected through surgical or medical treatment. The second kind of deafness, sensorineural hearing loss, results from damage to the sensory hair cells or the nerves of the inner ear and can range in severity from mild to profound deafness. Such loss occurs in certain sound frequencies more than in others, resulting in...
distorted sound perceptions even when the sound level is amplified. A hearing aid may not help a person with a sensorineural loss. The third kind, mixed hearing loss, is caused by problems in both the outer or middle ear and the inner ear. Finally, central hearing loss is the result of damage to or impairment of the nerves. Deafness in general can be caused by illness or accident, or it may be inherited. Continuous or frequent exposure to noise levels above 85 dB can cause a progressive and eventually severe sensorineural hearing loss (Redmond, 2008).

![Illustration of Noise Intensities of Common Sounds](Hearing Disability Assessment, Nov. 1997, Department. of Health and Children, Ireland)

The temporal bone and membranous labyrinth is a series of communicating sacs and ducts, which lie within the bony labyrinth (Hudspeth, 1989). In the brain, sound is processed in cerebral cortex of the opposite temporal bone. The cells are thought to recover from the stimulus by pumping out the potassium through gap junctions and voltage gated potassium channels (Petit, 1996). Hearing impairment can result if any pathway in this chain is disturbed, either by birth or later on in life, due to some injury or drug usage. High proportions of hearing loss cases are due to outer hair cell abnormalities (Kossal, 1997). Hearing impairment may be partial or total inability to hear. It has long been known that deafness is the most common and perhaps one of the most distressing disorders affecting humanity. Family history (pedigree) is the earliest way to diagnose either the deafness is genetic or not (Smith & Robin, 2002) because genetic diseases proliferate by Mandalian inheritance pattern (Burchard, 2003). Mutations in one gene, connexin 26 (CX26GJB2), are responsible for most cases of recessive non-syndromic deafness, accounting for 30–40% of all childhood genetic deafness in some populations (Tekin et al., 2001).

The main aim of the study is to extract some result by comparing the global prelingual deafness cases (1/1000) (Morton, 1991) with the special case in Surmo (1/100).

**MATERIALS AND METHODS**

This study was conducted during June 2005 and June 2006 in Surmo, a populous village in Ghangche district of Gilgit-Baltistan (GB), Pakistan. Its geographical coordinates are 35° 10' 0" North, 76° 25' 0" East (Google Earth, 2014). Shiyok River runs in the north of Surmo. On the other side of the
river, Mashabrum Peak and Siachen Glacier are located. Haldi is also situated in this side. Khaplu and Youchung are situated in the west. In the east, Lunkha, Dawa and Frano are present. South is covered by mountain ranges.

**Audiometry:** An earphone, connected to an electronic oscillator capable of emitting pure tones ranging from low frequencies to high frequencies was used. The instrument was calibrated so that the zero intensity level of sound at each frequency was the loudness that can barely be heard by the normal person, based on previous studies of normal persons. However, a calibrated volume control was used to increase or decrease the loudness of each tone above or below the zero level.

The lowest intensity heard by the patient was recorded e.g. at 1000Hz the patient responds to 20dB but not 15dB so 20dB at 1000Hz is recorded. Generally, if a person can hear as low as 25 dB at the test frequencies, his/her hearing was considered acceptable. Pure-tone audiometry (air and bone conduction) involves determination of the lowest intensity at which an individual “hears” a pure tone, as a function of frequency (or pitch). In performing a hearing test using an audiometer, one tests approximately 6-8 frequencies (250, 500, 1000, 2000, 3000, 4000, 6000, 8000) covering the auditory spectrum and hearing loss is determined for each of these frequencies. Hearing is measured in decibels (dB). These values were drawn on a graph paper showing the frequencies in Hz on horizontal axis and intensity in dB on vertical axis using Free Hand Software. This graph is known as an audiogram. These audiograms may be from one individual at different times, but more frequently they are from different members of the same family segregating deafness usually in an autosomal dominant fashion. Severity includes Mild (26-40 dB), Moderate (41-55 dB), moderately severe (56-70 dB), Severe (71-90 dB) and Profound (>90dB) while frequencies of hearing loss is designated as: Low (<500 Hz), Middle (501-2000 Hz) and High (>2000 Hz). GraphPad, DataPilot and PAST softwares (Hammer et al, 2001) were used for statistical data analysis.

**RESULTS**

16 deaf belonging to 16 families with 256 ears (16x2x8) were applied audiometry and constructed audiograms for analysis using Free Hand software for physiological study. The prevalence of the deafness in the targeted district (Ghangche) was found to be very high (1/100) as compared to the global deafness birth rate (1/1000). Air conduction audiometry of sixteen deaf individuals from targeted families of Gilgit-Baltistan (Pakistan) selected for this study. Audiograms of both ears of 16 deaf at 8 different frequencies (total 256 ears i.e. 16x2x8) indicated that the ratio of hearing loss are: 53.91% profound (>90dB=138 ears), 32.81% severe (71-90dB=84 ears), 3.13% moderately severe (56-70dB=8 ears), 5.47% moderate (41-55dB=14 ears) and 4.69% mild (<40dB=12 ears) as shown in fig., 2.

**Statistical Analysis**

One sample t-test was applied to check either the mean of averages of all samples differ significantly from normal i.e. 20 dB. The two-tailed P value obtained is < 0.0001, considered extremely significant. (t = 159.67 with 7 degrees of freedom. 95% Confidence interval)

**One sample t test (Current cases vz normal ears i.e., 20 dB)**

Mean difference = 69.043 (Mean of Averages of all samples minus 20 dB)

The 95% confidence interval of the difference: 68.020 to 70.066

**Assumption test:** Are the data sampled from a Gaussian distribution (Normal distribution)?

The one sample t test assumes that the differences are sampled from a Gaussian distribution.

This assumption is tested using the method of Kolmogorov and Smirnov:

The Kolmogorov-Smirnov distance (KS) is 0.17

The P value is >0.10 The data passed the normality test with P>0.05.
Table 1: The levels of HL at different frequencies using air conduction audiometry

<table>
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<tr>
<th>Sr No.</th>
<th>Family Code</th>
<th>Ears (Left/Right)</th>
<th>Frequencies (in Hz)</th>
<th>Severity of Hearing Loss (in dB)</th>
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</table>

Keys: * All 100 dB values are assumed because of failure of responding at 90 dB, dB=Decibel (the unit of hearing loss), GBDF=Deaf from Gilgit Baltistan, Hz=Hertz
PREVALENCE AND PHYSIOLOGICAL ASSESSMENT OF DEAFNESS

Fig. 2: Comparison of deafness levels (ML=Mild <40dB, MO=Moderate 41-55dB, MS=Moderately Severe 56-70dB, SE=Severe 71-90dB and PR=Profound >90dB).

One sample t test (Current cases vz partial deafness i.e. 40 dB)
Does the mean of averages of all samples differ significantly from 40 dB?
P value
The two-tailed P value is < 0.0001, considered extremely significant.
t = 113.42 with 7 degrees of freedom.
95% Confidence interval
Mean difference = 49.043 (Mean of Averages of all samples minus 40 dB)
The 95% confidence interval of the difference: 48.020 to 50.066
Assumption test: Are the data sampled from a Gaussian distribution (Normal distribution)?
The one sample t test assumes that the differences are sampled from a Gaussian distribution.
This assumption is tested using the method of Kolmogorov and Smirnov:
The Kolmogorov-Smirnov distance (KS) is 0.17
The P value is >0.10
The data passed the normality test with P>0.05.

Summary of Data:
Cum. Mean: 89.043,
No of points: 8,
Std deviation: 1.223,
Std error: 0.4324,
Minimum: 87.500,
Maximum: 90.938,
Median: 88.828,
Lower 95% CI: 88.020,
Upper 95% CI: 90.066

DISCUSSION

Hearing impairment is presented as a major health problem universally. Cases with recessive mode of inheritance for congenital deafness are more prevalent in Pakistan due to consanguineous marriages. Cousin marriages decrease the proportion of shared genes in families with increase in degree of consanguinity, making them an excellent resource material for conventional linkage analysis and hence are suitable for identification of new loci, genes and mutations. In a study of consanguinity, caste and deaf-mutism in Punjab in 1921, it was resulted that similar levels of inter-caste differences in disease frequency currently exist due to overwhelming majority of Hindu marriages continue to be within-caste. It was also inferred that the lower level of inter-biraderi variation among Muslims is probably indicative of the dissolution of pre-existing caste boundaries and the resultant gene pool mixing that followed the large-scale conversion of Hindus to Islam during Muslim rule in North India from the 13th to the 19th centuries (Bittles et al., 2004). Average deafness in dB and...
degree of deafness in percentage (%) are 50-53 dB (20%), 61-66 dB (40%) and 96-105 dB (90%) at common audible frequencies i.e. 1, 2 and 3 kHz (Social Welfare, 1983). High degree of deafness in this case is due to complicated consanguinity as there are so many cousin marriages in the same family in district Ghanche, due to which most of the ears shown high concentration of genes causing 54% profound deafness. For a cousin couple before marriages, it is recommended strongly to screen at least three generations from both sides to avoid any possible deafness gene. The hearing levels 53.91% profound (>90dB=138 ears), 32.81% severe (71-90dB=84 ears), 3.13% moderately severe (56-70dB=8 ears), 5.47% moderate (41-55dB=14 ears) and 4.69% mild (<40dB=12 ears) predicts that most of the deaf person in district Ghanche suffer from profound hearing loss. Generally, if a person can hear as low as 25 dB at the test frequencies, his/her hearing was considered acceptable. The threshold or 0 dB mark for each frequency refers to the level at which normal young adults perceive a tone burst 50% of the time. Pedigrees of these 16 families having same ethnic group and high ratio of consanguineous marriages showed that there was no case of autosomal dominance inheritance. All cases were autosomal recessive. Abnormal translation of connexin 26 protein from gap junction protein beta 2 (GJB2) gene, was the first gene to be implicated in nonsyndromic hearing loss, and mutations in this gene are associated nonsyndromic hearing loss e.g. one is DFNB1, the most common form of nonsyndromic autosomal recessive hearing loss (Willems, 2000).

Gap junction is a region of intimate cell contact that enables passage of small molecules (%1 kDa) between cells (e.g. ions, metabolites and second messengers). Gap junction channels form by the docking of two hemichannels, the connexons, present on two neighbouring cells. Connexons are hexamers of connexins (Petit, 2006). About 90 GJB2 mutations leading to abnormal Cx26
(mutation) expression have been reported and linked to deafness (Apps et al, 2007). The negative aspect of autosomal recessive is that it is most difficult to investigate because the large number of genes known to produce a similar phenotype (Brown & Steel, 1994). The recorded 4 syndromic deafness (2 mentally retarded, 1 goiter and 1 with balance problem) may increase the genetic concentration of deafness genes in district Ghanche, if the people were not avoided from cousin marriages. A pleasant aspect in deafness gene therapy is the recent advances in therapies for hearing loss have resulted in more specific and less traumatic strategies aimed at functional restoration of the auditory system (Hildebrand et al, 2007).

**CONCLUSIONS**

Frequent cousin marriages causing profound deafness which run in generations in district Ghanche, so need to be discourage in affected families. Awareness regarding genetic diseases is significant in remote areas, so role of NGOs may be fruitful in such matters. A few chances of presence of hidden radioactive Uranium and other elements in mountains may also contribute in deafness mutations, are still the blind aspect of research, and need to be explored.

**REFERENCES**


