

Audiological Characteristics and Duration of the Disorder in Individuals with Auditory Neuropathy Spectrum Disorder (ANSD) – A Retrospective Study

Jijo¹ P. M. & Asha Yathiraj¹

Abstract

The study aimed to determine the relation between audiological characteristics seen in individuals with Auditory Neuropathy Spectrum Disorder (ANSD) with the duration of the condition. Additionally, the study aimed to compare the demographic data with that of earlier reported studies. Design and study sample: The retrospective study was carried out by reviewing the clinical records of 120 clients diagnosed as having ANSD. There was no relation between pure-tone thresholds and speech perception skills. However, better speech perception was found in clients who had peaked and rising audiometric configurations as compared to other patterns. A significant association was obtained between the duration of the disorder and audiometric configurations. However, no relation was found between the duration of the disorder and the degree of hearing loss and speech identification scores (SIS). The majority of the clients had a non-syndromic onset in the first two decades of life, unlike the reports of the Western population. The duration of the disorder had an impact on audiometric configuration, but not on the degree of hearing loss and SIS. A genetic condition could have led to the onset of the problem, as several clients either had a family history of hearing loss or consanguineous marriage.

Key words: Retrospective study, demographic data, pure-tone thresholds, speech identification scores, audiometric configuration.

Auditory Neuropathy Spectrum Disorder (ANSD) is a heterogeneous condition associated with a wide range of etiological factors, varying sites of lesion and diverse audiological characteristics. This hearing disorder has been identified in all ages from newborns to adults (Berlin et al., 2010; Kumar & Jayaram, 2006; Sininger & Oba, 2001; Starr, Sininger & Pratt, 2000). However, in literature it has been reported to occur predominantly in children below the age of 10 years. Sininger and Oba (2001) noted that in their 59 individuals with ANSD, 75% had an onset below 10 years of age. They also noted that within this group, 80% had the onset before the age of 2 years. Starr et al. (2000) observed that out of 67 clients with ANSD, 75% were children under the age of 10 years, whereas only 25% were older than 10 years at the time of onset of the symptom. Similar findings were observed in a retrospective study by Berlin et al. (2010), which comprised of 260 clients with ANSD evaluated over a period of 12 years. They found that 85.76% of the clients were below the age of 12 years and only some of them had an onset between puberty and adulthood.

In contrast, Shivashankar, Satishchandra, Shashikala, and Gore (2003) reported the onset of the problem to occur during the first and second decade of life in all the 24 patients they studied, except one

who had an onset at the age of 44 years. This clinical data was gathered over a period of 10 years from a tertiary referral institution in South India. Likewise, in another retrospective study carried out in South India, Kumar and Jayaram (2006) reported that 59% of their 61 patients with ANSD had an onset between 14 to 24 years of age.

The etiology of ANSD has been found to be different in paediatric and adult populations. The occurrence of ANSD in some children is not associated with any specific etiology (Berlin et al., 2010; Rance et al., 1999; Sininger & Oba, 2001; Starr et al., 2000), in which case it is termed as non-syndromic ANSD. In others, it is found to be linked with one or more risk factors and is termed as syndromic ANSD. Neonatal hyperbilirubinemia (Berlin et al., 2010; Rance et al., 1999), anoxia and premature birth (Berlin et al., 2010; Rance et al., 1999; Sininger & Oba, 2001) have been identified to be the most common risk factors in the paediatric population.

Among adults, the commonly reported etiologies leading to syndromic ANSD are conditions such as hereditary motor and sensory neuropathies (HMSN) and Friedreich's ataxia. Charcot-Marie-Tooth syndrome is the most common type of hereditary neuropathy (Jose & Onofre, 2003). Type I & II of this HMSN are commonly found etiologies for adult onset ANSD (Butinar et al., 1999; Leonardis et al., 2000; Sininger & Oba, 2001). Friedreich's ataxia,

¹, All India Institute of Speech and Hearing, Mysore.

another inherited condition, is also reported to result in ANSD (Merlini, Villanoa, & Sabtalli, 1998; Sininger & Oba, 2001). Genetic factors leading to ANSD in the above neurological disorders have been confirmed in studies carried out by Kalaydjieva et al. (2000) and Kovach, Lin, and Boyajiev (1999).

It is reported that 50% of the patients with ANSD are non-syndromic (Starr et al., 2000). The possibility of these individuals having an underlying genetic cause has been insisted in literature. Genetic studies have identified a number of gene mutations that lead to non-syndromic ANSD in children. Mutations in the otoferlin (OTOF) gene have been reported to be the cause of non-syndromic ANSD in children with congenital severe to profound hearing loss (Rodriguez et al., 2003, 2009; Varga et al., 2003, 2006). Pejvakin gene has also been identified as a cause of non-syndromic ANSD in children from certain Iranian families (Delmaghani et al., 2006). However, only a few investigations have been done regarding the genetic cause of non-syndromic ANSD in young adults. Wang, Gu, Han, and Yang (2003) analyzed the pattern of inheritance in 12 patients with ANSD from four Chinese families. In all their clients, the onset of the problem was during first and second decade of life. None of them had any clinical signs of peripheral neuropathy. The pedigree analysis revealed X-linked recessive inheritance in one family and autosomal recessive inheritance in the other three families. Similarly, Wang et al. (2010) noted mutational changes in OTOF gene in only 4 out of 73 Chinese Han patients with ANSD. All the clients had a non-syndromic form of ANSD with the age of onset prior to or during adolescence.

Diverse audiological findings have been reported in individuals with ANSD. Based on pure-tone audiograms, studies have revealed that their hearing levels range from normal to profound degrees (Berlin et al., 2010; Kraus et al., 2000; Rance et al., 1999; Starr et al., 2000). However, pure-tone thresholds were reported to be fluctuating (Kumar & Jayaram, 2006; Rance et al., 1999). Speech perception abilities were noted to range from no measurable speech identification scores (SIS) to 100% scores (Berlin et al., 2010; Kraus et al., 2000; Kumar & Jayaram, 2006).

Unlike what has been seen in individuals with sensorineural hearing loss (SNHL), the speech perception skills were not found to correlate with behavioural thresholds (Kumar & Jayaram, 2006; Starr et al., 2000; Zeng et al., 2001). However, a small percentage of subjects were reported to have speech perception skills similar to that of their sensorineural counterparts (Sininger & Oba, 2001; Starr et al., 1996). It was postulated that in those with speech perception abilities comparable to individuals

with SNHL, the advancement of the condition was less than those who had poorer speech perception (Rance, 2005). Better speech perception was also noted in individuals who had peaked audiograms than in any other audiometric configuration (Kumar & Jayaram, 2006).

Individuals with ANSD exhibit diverse audiological findings irrespective of the duration of the disorder. Shivashankar et al. (2003), who studied 24 clients, noted that the majority of those who had the condition for a lesser duration (less than 5 years) had mild degree of hearing loss. Further, losses ranging from moderately-severe to severe hearing loss were reported in those who had the problem for a longer duration (more than 5 years). However, among 7 clients who had the condition for a longer duration, 2 of them had only a mild degree of hearing loss. Speech perception testing has also shown a similar trend. Though better SIS was found in the majority of those who had a lesser duration, a few among them did not have any measurable SIS. Similarly, Starr et al. (1996) reported that among 10 clients with ANSD, the majority of those who had the condition for more than 5 years had moderate to severe degree of hearing loss, whereas two of them had only a mild degree of hearing loss.

Though studies have been done to determine the audiological findings in individuals with ANSD, the impact of duration of the disorder has not been given much importance. This information will be useful in predicting the possible changes in audiological characteristics as a function of duration of ANSD. It has also been reported in literature that there is a difference in demographic data across various ethnic groups. The limited studies done in India indicate that the age of onset of ANSD among Indians is different from that of other ethnic groups. Hence, this study aimed to investigate the impact of the duration of ANSD on audiological findings.

Method

Participants

This retrospective study was carried out by reviewing the clinical records of clients who visited the Department of Audiology, All India Institute of Speech and Hearing (AIISH), Mysore, India between October 2008 and October 2010. The diagnosis of all the clients had been carried out by experienced audiologists. During the period under review, a total of 120 clients who met the diagnostic criteria given by Starr et al. (2000) and Berlin et al. (2005) were identified. As per the above criteria, clients who had preserved cochlear amplification, impaired neural response (absent or abnormal brainstem responses

Table 1: Parameters used for Auditory Brainstem Response (ABR) and Cochlear Microphonics (CM) measurement.

	ABR	CM
Stimulus	Click	Click
Polarity	Alternating	Rarefaction/Condensation/ Alternating
Filter	30 Hz to 3000 Hz	0 Hz to 3000 Hz
Level	90 dB nHL	80 dB nHL
Montage	Cz-A1 and Cz-A2	A1-A2 and A2-A1
Transducer	ER3A Insert	Tiptrode
Time window	10 ms	5 ms
Number of sweeps	2000	1500

and middle ear reflexes), normal otological function and no space occupying lesion (identified based on clinical neurological examination) were included. Among the participants, 104 (87%) had otoacoustic emissions (OAE) present in the left ear while 100 (84%) had it present in the right ear. The remaining clients showed presence of cochlear microphonics. Auditory Brainstem Response (ABR) was absent for the majority, i.e. 114 (95%) in the right ear and 117 (98%) in the left ear at a repetition rate of 11.1/sec. Abnormal ABRs were noted in the remaining clients. In those with abnormal ABR, the fifth peak was present only at a lower repetition rate of 11.1/sec, but not at a higher repetition rate of 90.1/sec. During neurological examination, presence of any space occupying lesion was ruled out. All the clients were otologically normal. Acoustic reflexes were absent in both the ears for all the clients.

Procedure

All the investigations had been carried out in a sound treated two-room set-up (ANSI S3.1., 1999). Pure-tone thresholds had been obtained via the modified Hughson and Westlake procedure, using diagnostic audiometers which were calibrated regularly (Madsen-Orbiter OB-922 or GSI 61). Calibrated immittance instruments (GSI 33 or GSI-Tympstar) had been used to obtain tympanograms and acoustic reflex thresholds. SIS was obtained using live voice presentation of the phonemically balanced Kannada word test developed by Yathiraj and Vijayalakshmi (2005). Any one of the four equivalent lists of the test that contained 25 words was used. Transient Evoked Otoacoustic emissions were recorded using Otodynamics ILO 292 or Madsen Capella 1.3. Non-linear clicks were presented at 80 dB peak SPL. Responses having signal to noise ratio more than 6 dB and reproducibility above 80% were considered as responses. ABR and cochlear microphonics had

been recorded using two channel Auditory Evoked Potential (AEP) systems (Biologic Navigator or Intelligent Hearing Systems Smart EP version 2.12 C). The recording parameters are as given in Table I.

Results

Demographic data

The age of the participants ranged from 1 to 45 years, with the mean age being 18.6 and the SD being 10.8 years. In order to determine the age distribution of the participants, they were divided into nine different age groups in equal intervals of 5 years. It can be observed from Figure 1 that the majority of the individuals fell between the age range of 10 to 30 years. It is also noted that 72 (60%) of the 120 clients were females whereas only 48 (40%) of them were males.

It was found that 65 (54%) of the 120 clients/caregivers reported the age of onset of the disorder to be between 10;1 to 20 years. The age at which perceptual deficits was noticed by the clients was considered as the age of onset, though the actual onset could have occurred earlier. The mean age

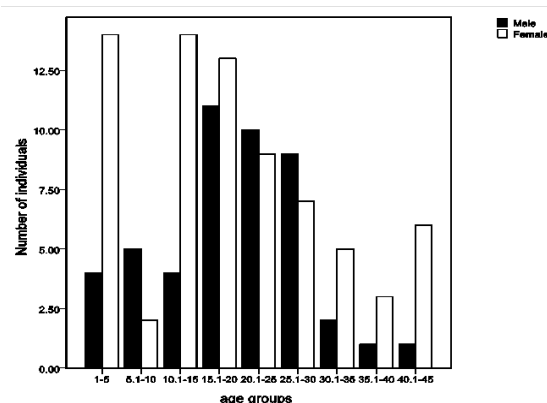


Fig. 1. Graph showing number of clients in different age groups.

Table 2. Age of onset of ANSD.

Age group	Number	Percent
0-5	23	19.1
5;1-10	5	4.1
10;1-15	29	24.1
15;1-20	36	30.0
20;1-25	16	13.3
25;1-30	3	2.5
Above 30	8	6.6

of onset was 14 years (Table 2). The duration of the disorder was determined by calculating the difference between the age of onset of the disorder and the age at which audiological evaluation was done. It was noted that in 75 (62%) of the 120 individuals, the duration of the disorder was less than 5 years. In 22 (18%) subjects, the duration was between 5 to 10 years. The remaining 23 (19%) clients had the condition for more than 10 years. The problem was reported to be progressive in 72 (60%) of the 120 clients.

In many adults, the disease condition was not associated with any specific etiology or associated problems. However, 2 adults had the condition associated with mumps, 2 had it following the onset of typhoid fever and 4 others had it associated with spinocerebellar ataxia. Family history of hearing loss and consanguineous marriage were reported in 30% and 25% of the clients respectively. In contrast, the entire paediatric group exhibited risk factors such as history of parental consanguinity (10), hyperbilirubinemia (6), anoxia (4) and premature delivery (4).

Audiological findings

The findings of pure-tone audiometry are described in terms of the degree of hearing loss and audiometric configuration. The results of speech audiometry and its relation with different audiological parameters are also illustrated.

Pure-tone audiometry

It was found that only 2 (1.6%) of the 120 individuals had unilateral ANSD with the problem occurring in their right ear. Among the 118 with bilateral hearing loss, 71 (60%) clients had symmetrical hearing loss (difference in pure-tone average between two ears < 10 dB HL) and 29 (26%) had asymmetrical hearing loss. The remaining 18 clients, who were less than 3 years of age, were reported to be uncooperative for testing under head phones and hence ear specific behavioural thresholds were not available from them.

Table 3. Degree of hearing loss in 100 clients with ANSD.

Degree of hearing loss	Number of clients	
	Right ear	Left ear
Normal	2	4
Minimal	12	14
Mild	34	35
Moderate	21	20
Moderately-Severe	10	9
Severe	8	8
Profound	13	10
Total	100	100

It can be noted from Table 3 that mild and moderate degree of hearing loss were the degrees that were commonly observed. Further, the behavioural thresholds were found to fluctuate in 30% of the clients, but these fluctuations did not lead to a change in the degree of hearing loss. Additionally, 72 (60%) clients reported that their hearing problem was progressive.

Based on the classification given by Schlauch and Nelson (2009), five different audiometric configurations were observed. It can be noted from Table 4 that peaked audiograms (peaking at a single frequency with deterioration of adjacent frequencies) were found in the majority of the clients, followed by flat (< 5 dB rise or fall per octave), rising (improvement of 5 dB or more per octave), sloping (5-12 dB threshold decline per octave) and trough (loss of 20 dB or more at the mid frequencies compared to the extremes) configurations.

Speech audiometry

Among the 100 clients whose data was analyzed, it was observed that their SIS was similar in the two ears. Only 54 had measurable SIS in the right ear.

Table 4. Audiometric configuration in 100 clients with ANSD.

Audiometric configuration	Number of clients	
	Right ear	Left ear
Peaked	37	40
Flat	27	32
Rising	26	19
Sloping	6	5
Trough	4	4
Total	100	100

Their SIS ranged from 4% to 80% with a mean score being 42.4%. The remaining 46 clients had 0% score in their right ear. Similarly, 56 clients had measurable SIS in their left ear, which ranges from 8% to 80% with the mean score being 43.7%. The remaining 44 clients had 0% score in their left ear.

In order to study the relation between pure-tone average (PTA) and SIS, Pearson product-moment correlation was performed. This was calculated only in clients who had measurable SIS. There was a significant but low negative correlation between these two variables in the right ($r = -0.304, p = 0.027$) and the left ($r = -0.368, p = 0.020$) ears. It is evident in the scatter plot (Figure 2) that, regardless of the degree of hearing loss a large number of clients had SIS ranging from 0% to 60%.

Speech identification scores for each ear were compared with the scores reported to be found in individuals with SNHL (Yellin, Jerger & Fifer, 1989). It was found in the right ear that only 29% of the clients had SIS similar to that of individuals having equivalent degree of SNHL. Likewise, 26% had similar scores in the left ear. The comparison between audiometric configuration and SIS shown in Figure 3 revealed that, highest SIS was obtained for the peaked configuration followed by the rising pattern. Those with a flat and sloping configuration had similar but low SIS.

Effect of duration of the disorder on audiological findings

The effect of duration of the disorder on PTA and SIS was analyzed using Pearson product moment

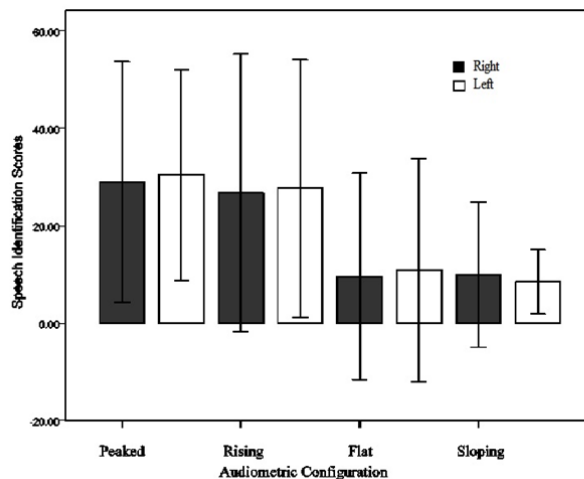


Fig. 3. The graph compares audiometric configuration and mean speech identification scores.

correlation. It was found that a significant but low positive correlation was found between the duration of the disorder and degree of hearing loss in the right ear ($r = 0.273, p = 0.006$) and the left ear ($r = 0.319, p = 0.001$). The scatter plot (Figure 4) revealed that a majority of the individuals who had the condition for a lesser duration (less than 5 years) had mild to moderate degree of hearing loss. However, such degrees were also seen in those who had the condition for a longer duration (more than 5 years).

Similarly, the relation between duration of the disorder and SIS was analyzed using Pearson product moment correlation. A significant but low negative correlation was obtained between the two in the right ear ($r = -0.227, p = 0.023$) and the left ear ($r = -0.227, p = 0.023$)

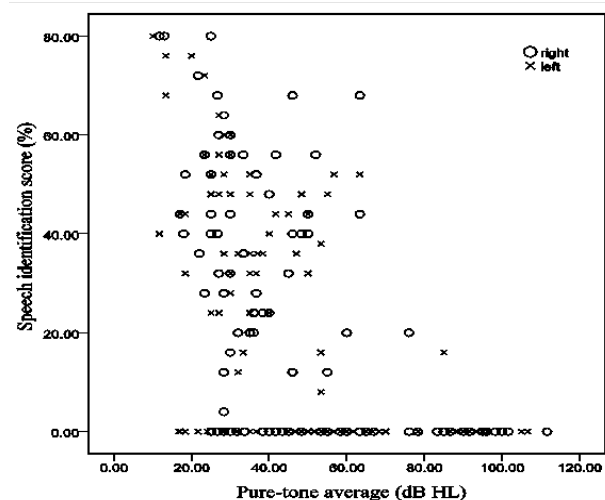


Fig. 2. The scatter plot shows no relation between pure-tone average and speech identification scores in the 200 ears with ANSD.

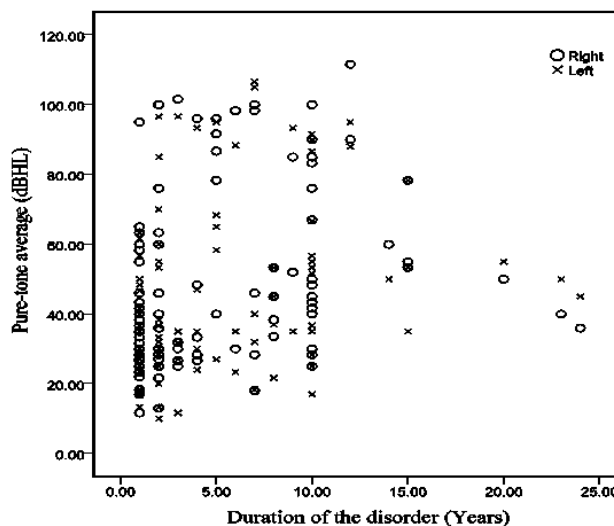


Fig. 4. The scatter plot shows no relation between the duration of the disorder and the degree of hearing loss in the 200 ears with ANSD.

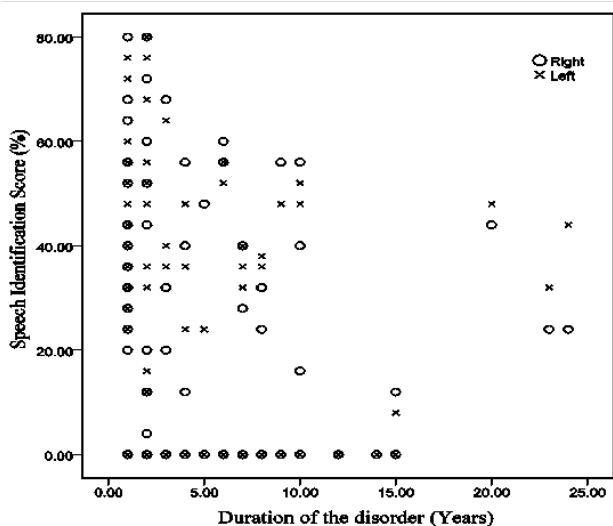


Fig 5. The scatter plot shows no relation between the duration of the disorder and speech identification scores.

= -0.209, p = 0.037). It can be observed in the scatter plot (Figure 5) that, some individuals who had the problem for a relatively shorter duration (less than 5 years) had scores ranging from 0% to 80%. Similarly, those who had the problem for a longer duration (more than 5 years) also had variable SIS.

The audiological configuration as a function of the duration of the disorder is shown in Table 5. Chi square test was performed to analyze the association between the two. Sloping and trough configurations were eliminated as their number was not adequate for Chi square analysis. The three other configurations (peaked, flat and rising) which were common among individuals with ANSD were analyzed. It was found that there was a significant difference in the audiometric configuration between the three groups ($\chi^2 = 28.44$, $df = 4$, $p = 0.00$).

Discussion

Demographic data

It was found that a large number of affected individuals (50%) were in the first two decades of their life. Many of them (54%) reported that the age of

onset of the problem was between 10-20 years. Only 23% of the clients had onset of the problem below 10 years of age. Similarly, other studies done in India reported that the problem occurred more frequently during the first and second decade of life (Kumar & Jayaram, 2006; Shivashankar et al., 2003). Kumar and Jayaram (2006) also found that only 20% of their participants were below 10 years of age. This confirms that the age of onset of the condition is uniform across various studies done in India, though the studies were done in different cities or periods of time.

Unlike the findings of the present study, Berlin et al. (2010), Sininger and Oba (2001) and Starr et al. (2000) observed that ANSD was primarily seen in the paediatric population, with only 25% of their clients being adults. The authors attributed this finding to the mandatory OAE and ABR hearing screening procedure that was carried out. They also reported that fewer adults had been recognized due to the loss of OAEs over time and cochlear microphonics evaluation not being included in the diagnostic criteria. The lack of widespread use of OAE and ABR in hearing screening in India might have resulted in fewer paediatric clients being identified. However, age-wise statistics of clients evaluated at the Department of Audiology of AIISH during this period shows that the majority of clients who sought services were children below the age of 5 years (AIISH Annual Report, 2010-11). It has been observed that audiological services were sought primarily due to the delay in development of speech and language in these children. This indicates that, despite the universal hearing screening procedure not being used currently in India, children with hearing impairment are still being identified based on deficits in their speech and language development. However, this did not happen with the paediatric ANSD group, indicating that ANSD is more predominantly seen in adolescents or young adults. If the condition had occurred predominantly in the paediatric group, it would have been identified due to a delay in speech and language, as seen in children with other sensorineural hearing losses

The gender distribution seen in the present study is in agreement with earlier studies in India (Kumar & Jayaram, 2006; Shivashankar et al., 2003) which

Table 5: Number of ears having different audiometric configuration and duration of the disorder.

Duration (years)	Audiometric configuration				
	Peaked	Flat	Rising	Sloping	Trough
Less than 5	56	16	24	11	3
5-10	12	20	10	0	2
Above 10	9	23	11	0	3

reported that the condition was seen more in females than in males. As per the Annual Report of AIISH (2010-11), among the clients seeking audiological services at AIISH, more males (59%) were evaluated compared to females (41%). Thus, it is evident that gender distribution of clients with ANSD differs from that seen in general hearing loss. Contrary to these findings, no such gender difference was reported by Berlin et al. (2010) and Sininger and Oba (2001) who found the distribution across the two genders to be almost similar. The greater number of female ANSD clients and the occurrence of the onset of the disorder during puberty imply a possible hormonal influence on ANSD which needs to be explored further.

From the etiology reported by the clients/caregivers, it was observed that all the paediatric clients with ANSD had one or more associated risk factors. Of the 18 children reviewed, 6 had two risk-factors, while the remaining had only one risk-factor. However, many of the young adults had a sudden onset of the problem without any specific etiology. None of these young adults had any associated neurological impairment as per their neurological report, except four who had cerebellospinal ataxia. However, 30% of the young adults reported a family history of hearing loss, the nature of which was not known. Yet another factor observed was parental consanguinity, which was noted in 25% of the clients. The presence of family history and consanguinity indicate a possible genetic cause underlying the problem in the group studied. Similarly, Sininger and Oba (2001) reported the presence of a family history of hearing disorder in 46% of individuals with ANSD. Berlin et al. (2010) noted that 16% of patients with ANSD had a family history of the same condition. Some of these patients were confirmed to have a mutation in the OTOF gene (Varga et al., 2003). OTOF gene mutations have been reported to be the common cause of non syndromic ANSD in the Western population (Rodriguez et al., 2003, 2009; Varga et al., 2003, 2006). In contrast, Wang et al. (2010) found that only 4 out of 73 Chinese Han patients with ANSD had OTOF mutation. The authors attributed this to the lesser genetic load of this particular gene in the Chinese population. Similar findings have been found in literature indicating the possibility of different gene mutation in different ethnic populations (Choi et al., 2009; Ramanos et al., 2009). This highlights the need for genetic studies in the Indian population, a unique ethnic group which is noted to have multiple genetic isolates by Bittles (2002).

The influence of consanguinity on congenital hearing impairment has been well documented (Reddy, Bindu, Reddy, & Rani, 2006; Zakzouk, 2002). However, not much has been studied regarding

adult-onset hearing impairment and consanguinity. It is well known that consanguineous marriages are extremely common in South India whereas it is rare in Western countries (Bittles, 2002; Krishnamoorthy & Audinarayana, 2001). Hence, genetic analysis in individuals with ANSD having a background of consanguinity might shed light on adult-onset ANSD, a predominant group in the Indian scenario.

Audiological findings

The pure-tone audiometric results revealed that nearly 97% of the clients had hearing loss ranging from minimal to profound degree. Of these individuals, 68% had hearing loss up to a moderate degree. Hearing loss, rather than any neurological deficit was their major complaint. Similarly, Starr et al. (1996) also reported that hearing loss was the primary complaint in 80% of clients with ANSD. It is also reported that the presence of normal OAEs with corner audiograms may be associated with complete loss of inner hair cells (Amatuzzi et al., 2001; Varga et al., 2003, 2006) or absence of auditory nerves (Buchman et al., 2006). In contrast, mild to moderate degree of hearing loss is noted to be an indication of compromised neural functioning in the presence of preserved inner hair cell functioning to some extent (Starr et al., 1996). This highlights the possibility of neuronal impairment in majority of the clients with ANSD in the current study as they had lower degrees of hearing impairment.

From the history of the clients, it was noted that 60% of them reported of progressive hearing loss. It was found that only 4 clients had associated neurological problems that have been reported in literature to be associated with progressive hearing loss (Starr et al., 1996). The remaining clients did not have any associated neurological problem as per the neurological screening. Though 60% of the clients reported of a progressive hearing loss, from the data analysed in the present retrospective study, inference regarding the progressive nature of the condition cannot be made. A longitudinal study would be required to conclude regarding the progressive nature of the ANSD.

Among the clients seen in the present study, it was found that over 50% had no measurable SIS in both the ears. It was also noted that almost 1/3rd of the clients had SIS similar to individuals with equivalent degrees of SNHL, as reported by Yellin et al. (1989). Very poor speech perception abilities in individuals with ANSD have been well documented in the past (Kumar & Jayaram, 2006; Sininger & Oba, 2001; Starr et al., 1996). However, it is reported that a few clients with ANSD exhibit SIS similar to individuals with equivalent degrees of SNHL (Sininger & Oba,

2001; Starr et al., 1996). Rance (2005) hypothesized that among such individuals with ANSD, the disease process may be less advanced. Hence, it is probable that the condition was less advanced in 1/3rd of the clients seen in the present study who exhibited such findings.

Effect of duration of the disorder on audiological findings

It was found that there was a significant but low positive correlation between the duration of the disorder and the degree of hearing loss. It was noted that the majority of the clients who had the condition for a lesser duration (less than 5 years) had a mild degree of hearing loss, though a few of them who had it for a longer duration (more than 5 years) also exhibited similar degrees. Analogous findings have been noted in client with and without associated neurological problem (Shivashankar et al., 2003; Starr et al., 1996). This highlights that ANSD is a heterogeneous condition and that its nature varies across individuals. Such individual variability has been reported even in the presence of similar pathophysiology (Spoendlin, 1974).

It was found that though the duration of the disorder had a low negative correlation with the SIS obtained, this was found to be significant. It was also noted that among the 1/3rd of the clients who had SIS similar to those with equivalent degrees of SNHL, 80% had the problem for less than 5 years. However, in a few clients who also had the problem for a shorter duration, no measurable SIS was found. It has been hypothesized that SIS in individuals with ANSD is an indication of the advancement of the condition (Rance, 2005). In the present study, it was found that some clients had no measurable SIS despite a shorter duration (indicating a faster advancement of the condition) while others might have had a slower advancement which spared their speech perception abilities. Hence, it is inferred that the advancement of condition cannot always be predicted based on the duration of the disorder.

It was observed in the present study that there was a significant association between the duration of the disorder and the audiometric configuration. Peaked and rising audiometric configurations were often found in clients who had the condition for less than 5 years. Among the clients who had the problem for more than 10 years, flat configuration was seen more commonly than any other type. However, such a trend was not seen in all the clients. The occurrence of low frequency hearing loss in the early stages of a disorder is attributed to the longer course of low frequency fibers (Arnesen & Osen, 1978) which make them more susceptible to neuronal pathologies than

the short fibers, which corresponds to the mid and high frequencies. Hence, it is possible that during the initial stages the longer fibers which mediate the low frequencies are affected, leading to a peaked or rising configuration. Later the audiometric configuration may become flat as the short fibers are also affected. Changes in audiometric configuration along course of the disease require further longitudinal investigations.

Conclusion

There was a change in audiometric configuration as a function of duration of the disorder indicating a sign of advancement of the condition. However, the duration of the disorder had no relation with other audiological findings such as pure-tone thresholds and SIS. This indicates the heterogeneous nature of the disorder. Thus, longitudinal studies need to be conducted for further understanding of this relation. Additionally, there was a discrepancy in the age of onset of ANSD between Indian and Western population. It was found that in the Indian population, adult-onset non-syndromic ANSD was predominantly seen. This could have probably resulted from genetic factors indicated by the presence of family history of hearing loss and consanguineous marriage, the latter being a common tradition in South India. A study exploring these genetic influences has to be carried out to confirm this.

Acknowledgements : The authors would like to thank the Director, All India Institute of Speech and Hearing for granting permission to carry out the study. Thanks to Dr. Gowamma for her valuable suggestions. We express our sincere thanks to fellow audiologists, Dept of Audiology, who had evaluated our clients. Truthful thanks to the reviewers for their valuable comments.

Address for Correspondance : Mr. Jijo P. M., Junior Research fellow, Department of Audiology, All India Speech and Hearing, Manasagangothri, Mysore - 570006. Email: jijoaudio@gmail.com

References

- Amatuzzi, M. G., Northrop, C., Liberman, M. C., Thornton, A., Halpin, C., Herrmann, B., et al. (2001). Selective inner hair cell loss in premature infants and cochlea pathological patterns from neonatal intensive care unit autopsies. *Archives of Otolaryngology Head and Neck Surgery*, 127, 629-636.
- AllSH Annual Report. 2010-2011. Edited and published by Dr. Savithri S.R. All India Institute of Speech and Hearing, Mysore.

- ANSI: American National Standard Institute. 1999. American national standard: *Maximum permissible ambient noise for audiometric rooms*. ANSI S3.1-1999. New-York, ANSI.
- Arnesen, A. R., & Osen, K. K. (1978). The cochlear nerve in the cat: topography, cochleotopy and fiber spectrum. *Journal of Comparative Neurology*, 178, 661-678.
- Berlin, C. I., Hood, L. J., Morlet, T., Wilensky, D., St John, P., Montgomery, E., et al. (2005). Absent or elevated middle ear muscle reflexes in the presence of normal otoacoustic emissions: a universal finding in 136 cases of auditory neuropathy/ dys-synchrony. *Journal of the American Academy of Audiology*, 16, 546-553.
- Berlin, C. I., Hood, L. J., Morlet, T., Wilensky, D., Li, L., Mattingly, K. R., et al. (2010). Multi-site diagnosis and management of 260 patients with Auditory Neuropathy/ Dys-synchrony (Auditory Neuropathy Spectrum Disorder). *International Journal of Audiology*, 49, 30-43.
- Bittles, A. H. (2002). Endogamy, consanguinity, and community genetics. *J Genet*, 81, 91-98.
- Buchman, C. A., Roush, P. A., Teagle, H. F. B., Brown, C. J., Zdanski, C. J., & Grose, J. H. (2006). Auditory neuropathy characteristics in children with cochlear nerve deficiency. *Ear and Hearing*, 27, 399– 408.
- Butinar, D., Zidar, J., Leonardis, L., Popovic, M., Kalaydjieva, L., Angelicheva, D., et al. (1999). Hereditary auditory, vestibular and motor neuropathy in Slovenian Roma (Gypsy) kindred. *Annals of Neurology*, 46, 36-44.
- Choi, B. Y., Ahmed, Z. M., Riazuddin, S., Bhinder, M. A., Shahzad, M., Husnain, T., et al. (2009). Identities and frequencies of mutations of the otoferlin gene (OTOF) causing DFNB9 deafness in Pakistan. *Clinical Genetics*, 75, 237-243.
- Delmaghani, S., del Castillo, F. J., Michel, V., Leibovici, M., Aghaie, A., Ron, U., et al. (2006). Mutation in the gene encoding pejkakin, a newly identified protein of the afferent auditory pathway, cause DFNB59 auditory neuropathy. *Nature Genetics*, 38, 770-778.
- Jose, B., & Onofre, C. (2003). Hereditary neuropathies. *Current Opinion in Neurology*, 16, 613-622.
- Kalaydjieva, L., Gresham, D., Gooding, R., Heather, L., Bass, F., de Jonge, R., et al. (2000). N-myc downstream-regulated gene 1 is muted in hereditary motor and sensory neuropathy- Lom. *American Journal of Human Genetics*, 67, 47-58.
- Kovach, M. J., Lin J., Boyadjiev, S., Campbell, K., Mazzeo, L., Herman, K., et al. (1999). A unique point mutation in the PMP22 gene is associated with Charcot-Marie-Tooth disease and deafness. *American Journal of Human Genetics*, 64, 1580-1593.
- Kraus, N., Bradlow, M. A., Cunningham, C. J., King, C. D., Koch, D. B., Nicol, T. G., et al. (2000). Consequences of neural synchrony: a case of auditory neuropathy. *Journal of the Association for Research in Otolaryngology*, 1, 33-45.
- Krishnamoorthy, S., & Audinarayan, N. (2001). Trends in consanguinity in south India. *Journal of Biosocial Science* 33, 185-197.
- Kumar, A. U., & Jayaram, M. (2006). Prevalence and audiological characteristics in individuals with auditory neuropathy/auditory dys-synchrony. *International Journal of Audiology*, 45, 360-366.
- Leonardis, L., Zidar, J., Popovic, M., Timmerman, V., Lofgren, A., Broeckhoven, C., et al. (2000). Hereditary motor and sensory neuropathy associated with auditory neuropathy in a Gypsy family. *European Journal Physiology*, 439, 208-210.
- Merlini, L., Villanoa, M., & Sabtalli, P. (1998). Hereditary motor and sensory neuropathy Lom type in an Italian Gypsy family. *Neuromuscular Disorders*, 8, 182-185.
- Romanos, J., Kimura, L., Favero, M. L., Izarra, F.A., de Mello Auricchio, M. T., Batissoco, A. C., et al. (2009). Novel OTOF mutation in Brazilian patients with auditory neuropathy. *Journal of Human Genetics*, 54, 382-385.
- Rance, G., Beer, D. E., Cone-Wesson, B., Shepherd, R. K., Dowell, R. C., King, A. M., et al. (1999). Clinical findings for a group of infants and young children with auditory neuropathy. *Ear and Hearing*, 20, 238-252.
- Rance, G. (2005). Auditory neuropathy/Dys-synchrony and its perceptual consequences. *Trends in Amplification*, 9, 1-43.
- Reddy, M. V. V., Bindu, L. H., Reddy, P. P., & Rani, P. U. (2006). Role of consanguinity in congenital neurosensory deafness. *International Journal of Human Genetics*, 6, 357-358.

- Rodriguez- Ballesteros, M., del Castillo, F. J., Martin, Y., Moreno-Pelayo, M. A., Morera, C., et al. (2003). Auditory neuropathy in patients carrying mutations in the otoferlin gene (OTOF). *Human Mutations*, 22, 451-456.
- Rodriguez Ballesteros, M., Reynoso, R., Olarte, M., Villamar, M., Morera, C., Prieto, F., et al. (2009). A multicenter study on the prevalence and spectrum of mutations in the otoferlin gene (OTOF) in subjects with non syndromic hearing impairment and auditory neuropathy. *Journal of Human Genetics*, 54, 382-385.
- Schlauch, R. S., & Nelson, P. (2009). Pure tone evaluation. In J. Katz, L. Medwetsky, R. Burkard & L.Hood (eds) *Handbook of Clinical Audiology*. Lippincott Williams & Wilkins, pp. 41.
- Shivashankar, N., Satishchandra, P., Shashikala, H. R., & Gore, M. (2003). Primary auditory neuropathy-an enigma. *Acta Neurologica Scandinavica*, 108, 130-135.
- Sininger, Y. S., & Oba, S. (2001). Patients with auditory neuropathy: Who are they and what they can hear? In Sininger Y.S & Starr .A (eds.) *Auditory Neuropathy: A New Perspective on Hearing Disorders*. Sandiago: Singular-Thomson Learning, pp. 15-35.
- Spoendlin, H. (1974). Optic and cochleovestibular degenerations in hereditary ataxias. *Brain*, 97, 41-48.
- Starr, A., Picton, T., Sininger, Y.S., Hood, L. J., & Berlin, C. I. (1996). Auditory Neuropathy. *Brain*, 119, 741-753.
- Starr, A., Sininger, Y. S., & Pratt, H. (2000). The varieties of auditory neuropathy. *Journal of Basic and Clinical Physiology and Pharmacology*, 11, 215– 230.
- Varga, R., Kelley, P. M., Keats, B. J., Starr, A., Leal, S. M., Cohn, E., et al. (2003). Non- syndromic recessive auditory neuropathy is the result of mutations in the otoferlin (OTOF) gene. *Journal of Medical Genetics*, 40, 45-50.
- Varga, R., Avenarius, M. R., Kelley, P. M., Keats, B. J., Berlin, C. I., Hood, L. J., et al. (2006). OTOF mutations revealed by genetic analysis of hearing loss families including a potential temperature sensitive auditory neuropathy allele. *Journal of Medical Genetics* 43, 576-581.
- Wang, Q., Gu, R., Han, D., & Yang, W. (2003). Familial auditory neuropathy. *Laryngoscope*, 113, 1623-1629.
- Wang, D. Y., Wang, Y. C., Weil, D., Zhao, Y. L., Rao, S. Q., Zong, L., et al. (2010). Screening mutations in Chinese patients with auditory neuropathy, including a familial case of temperature- sensitive auditory neuropathy. *BMC Medical Genetics*, 11, 79.
- Yathiraj, A., & Vijayalakshmi, C. S. (2006). Phonemically balanced wordlist in Kannada. A test developed at the department of Audiology, AIISH, Mysore.
- Yellin, M. W., Jerger, J., & Fifer, R. C. (1989). Norms for disproportionate loss in speech intelligibility. *Ear and Hearing*, 10, 231-234.
- Zadro, C., Coirba, A., Fabris, A., Morgutti, M., Trevisi, P., Gasparini, P., et.al. (2010). Five new OTOF gene mutations and auditory neuropathy. *International Journal of Pediatric Otorhinolaryngology*, 74, 494-498.
- Zakzouk, S. (2002). Consanguinity and hearing impairment in developing countries: a custom to be discouraged. *The Journal of Laryngology and Otology*, 116, 811-816.
- Zeng, F.G., Oba, S., Grade, S., Sininger, Y., & Starr, A. (2001). Psychoacoustics and speech perception in auditory neuropathy. In Y. Sininger & A. Starr (eds.) *Auditory Neuropathy: A New Perspective on Hearing Disorders*. San Diego: Singular-Thomson Learning, pp. 141-164.