2. REVIEW OF LITERATURE

2.1 Clinical &Audiological Profile:

Kaga and Starr et al., (1996) discerned and published a new type of bilateral hearing disorder. Although the pathophysiology of this disorder as reported by each author was essentially identical, Kaga used the term "auditory nerve disease" and Starr used the term "auditory neuropathy".

A clinical syndrome characterized by electrophysiological evidence of normal or near normal cochlear functions and absent or abnormal auditory pathwaycharacterized by preservation of outer hair cells function with normal otoacoustic emissions (OAEs), but with absent auditory brainstem responses (ABR).Perisynaptic synchronisation disorder is one of the possible pathogenesis underlying auditory neuropathy. Audiological findings shows normal outer hair cell function as measured by present otoacoustic emissions (OAEs) or the presence of a cochlear microphonic (CM) **(Starr, et. al., 1996).**When measuring CM, it is important to compare responses obtained with condensation stimuli to those obtained with rarefaction stimuli **(Berlin, et. al., 1998).** The OAEs may be present initially but disappear over time **(Zeng, et. al.,1999).**Abnormal auditory nerve response as observed by absent or markedly abnormal ABR. Acoustic reflexes are absent in most cases **(Kraus, et. al.,2000).** Clinical characteristics reported are pure tone thresholds ranging from normal to profound. Disproportionately poor speech recognition abilities for the degree of hearing loss.Difficulty hearing in noise. Impaired temporal processing **(Rance, et al., 2002).**Hearing fluctuation **(Rance, et al., 2004).**Some individuals with ANSD have little or no communication difficulties while others are functionally deaf **(Rance et. al., 2005)**. Not all individuals diagnosed with AN experience the same problems (**Zeng et. al., 2006)**.This disorder initially thought to be rare. Many published reports

since late 90's describing patients with similar audiologic test findings (absent ABR with present CM and/or OAEs). Estimates range from 7-10% of children diagnosed with permanent hearing loss **(Rance et. al., 2005).**

Auditory neuropathy/dys-synchrony disorder affects neural responses, either directly or indirectly. Patients may demonstrate good ability to detect sound, but have significant difficulty listening in noise. Clinical auditory physiologic measures should be used to characterize cochlear, eighth nerve, and brainstem function, and are needed to accurately identify this disorder. Cochlear implants provide benefit to many patients, and some patients derive benefit from amplification. This disorder can be identified and managed in infants, may have later onset, may be a part of a syndrome, and may include fluctuation in hearing ability **(Hood et. al., 2015).**

Madden et al. (2002) reported 22 ANSD patients from a pediatric otology clinic in a tertiary care pediatric hospital setting. Most of the children showed dominant audiological profile of ANSD that is present of OAE and absent or elevated ABR. He concluded that management of AN children requires serial clinical and audiometric evaluations, with a prominent role for behavioral testing. Prematurity, genetics, and hyperbilirubinemia appear to be significant factors in the development of AN. For those children not benefiting from amplification or FM systems, cochlear implantation remains a potentially successful method of habilitation.

Teresa et al. (2013) performed a longitudinal study and reported 47 children with ANSD. Main objective was to determine the influence of the presence of auditory neuropathy spectrum disorder (ANSD) on speech, language, and psycho-social development of children at three years of age. Result showed Sixty-four percent of children with ANSD have hearing sensitivity loss ranging from mild to severe degree, and the remaining have profound hearing loss. At three years, 27 children used

hearing aids, 19 used cochlear implants, and one child did not use any hearing device. Thirty percent of children have disabilities in addition to hearing loss. On average, there were no significant differences in performance level between children with and without ANSD. In addition, the variability of scores was not significantly different between the two groups.

Wurzburg et al. (2007) described the clinical presentation and audiological findings in pediatric auditory neuropathy and its management. They included 9 children with auditory neuropathy. An audiological evaluation was performed in all children including behavioural audiometry, measurement of the OAEs as well as electrocochleography (ECoG) and ABR recordings. Children who failed to get any benefit from conventional amplification received a cochlear implant. Prior to implantation, the responses to electrical stimuli were examined with the promontory test and with the electrically evoked ABR. One child showed auditory neuropathy only on one side with normal hearing thresholds on the contralateral ear. Another child had normal hearing thresholds after the follow up period. Four children received a hearing aid but variable hearing reactions were observed. Thus in three cases CI was planned. In three children cochlea implantation was done. Following implantation a remarkable improvement in hearing/speech capabilities with the CI compared to conventional hearing aids were observed in all three cases. Beside, these three children developed open set speech discrimination and were using oral language for communication.

Mittal et al. (2012) conducted study at tertiary care hospital at New Delhi, India. In her study, 487 pediatric cases were referred for hearing evaluation. 183 (37.6%) cases showed absent BERA and 26(5.3%) cases fulfilled the diagnostic criteria for ANSD. Repeat examination after 3months revealed presence of OAE's in 57.6% (15/26) cases

while cochlear microphonics were present in all the 26 cases. The prevalence of ANSD in study was 5.3% and in children diagnosed with severe to profound hearing loss is 14%.

Doyle et al. in (2009) conducted a retrospective review of audiologic findings in eight children with auditory neuropathy. Each subject was tested with pure tone and speech audiologic testing, auditory brainstem response, and click-evoked otoacoustic emissions. Pure tone audiological tests revealed five children with sloping sensorineural hearing loss, two with high frequency loss, and one with a mild, flat configuration. Six children demonstrated poor word discrimination scores, and the other two had fair to good word discrimination. All eight subjects had normal distortion product and transient otoacoustic emissions. All eight children demonstrated absent or marked abnormalities of brainstem auditory evoked potentials. These findings suggest that while cochlear outer hair cell function is normal, the lesion is located at the eighth nerve.

Harrison etal. (1998) described an animal model of auditory neuropathy in which subjects have extensive, scattered inner hair cell loss but with a relatively intact inner hair cell loss but relatively intact outer hair cell population. A pattern of cochlear hair cell damage can be produced in the chinchilla by treatment with the anticancer agent carboplatin. Result showed in these subjects were OAE and cochlear microphonics remain normal while ABR thresholds are significant elevated. However, in the same subjects, central auditory neurons (in the inferior colliculus) have response thresholds that are considerably lower (by up to 50 dB) than ABR thresholds. These findings parallel the characteristics of auditory neuropathy in humans, in which absent or abnormal ABRs were recorded in patients with only mild to moderate audiometric thresholds and preserved OAEs.

Berlin et al. (2010) summarized test results and management of 260 patients diagnoses with Auditory Neuropathy Spectrum Disorder (ANSD). Hearing aids were tried in 85 of these patients, and 49 patients tried cochlear implants. Approximately 15% reported some benefit from hearing aids for language learning, while improvement in speech comprehension and language acquisition reported in 85% of patients who were implanted. Approximately 5% (13/260) of the total population developed normal speech and language without intervention. Patients were diagnosed at our laboratory (n=66) or referred from other sites (n=194), and all showed absent/grossly abnormal auditory brainstem responses (ABR), often 'ringing' cochlear microphonics, and the presence or history of otoacoustic emissions. Etiologies and co-existing conditions included genetic (n=41), peripheral neuropathies (n=20), perinatal jaundice and/or anoxia and/or prematurity (n=74). These patients comprise 10% or more of hearing impaired patients; their language acquisition trajectories are generally unpredictable from their audiograms.

Buchman et al. (2006) showed retrospective review of nine children with cochlear nerve deficiency, five (56%) were affected unilaterally and four (44%) bilaterally. Eight of nine presented after failing a newborn infant hearing screening, whereas one presented at 3 yr of age. On diagnostic ABR testing, all 9 children (out of 18, 13affected ears; 69%) had evidence of a cochlear microphonic (CM) and absent neural responses in at least one ear. In the unilateral cases, AN characteristics were detected in all affected ears. In bilateral cases, at least one of the ears in each child demonstrated the AN phenotype, whereas the contralateral ear had no CM identified. Only one ear with cochlear nerve deficiency had present otoacoustic emissions as measured by distortion-product otoacoustic emissions.

Mahon and others (2008) stated that the physiological mechanisms underlying auditory neuropathy (AN) remain unclear and it is likely that the multiple disruptions were classified under the broadly defined term. To investigate the site-of-lesion in AN, frequency-specific round window electrocochleography (ECochG) was used to assess local hair cell, dendritic, and axonal currents generated within the cochlea in 14 subjects with AN and compared with responses from two normally hearing subjects. ECochG results were then compared with electrically evoked auditory brain stem response (EABR) measured after cochlear implantation. The results of this study demonstrate that two dominant patterns of ECochG waveforms (produced by a high-frequency alternating tone burst) can be identified in this population of AN subjects: (a) gross waveform showing a prolonged summating potential (SP) latency that, in most cases, is followed by a small compound action potential; and (b) gross waveform showing a normal latency SP waveform followed by a broad negative potential [assumed to reflect the dendritic potential (DP) identified in anaesthetized guinea-pigs]. This study demonstrates that in most subjects (n = 7) with a prolonged latency SP but no DP, normal morphology EABR waveforms were elicited for all electrode channels. On the other hand, all subjects (n = 7) who showed a normal latency SP followed by a broad negative DP, showed EABR waveforms that were absent or having poor wave V morphology.

Emami et al. in (2015) conducted cross-sectional study, 100 children with bilateral severe-to-profound sensorineural hearing losses underwent audiologic tests and cervical vestibular-evoked myogenic potentials (cVEMPs). Eleven children with bilateral severe sensorineural hearing loss were given to unilateral AN/AD disorder (11 ears), and two children (4 ears) had bilateral AN/AD (total = 13 children). The ears with AN/AD took the form of unrepeatable or absent waves of ABR and

presence of OAEs. The statistical analysis of an independent t-test between AN/AD ears as compared to non-AN/AD ears of these 13 children showed that the mean latencies of p13 and the mean latencies of n23 and the mean peak-to-peak amplitude had significant differences.

2.2 Related Etiologies

The variation of characteristics among patients and the fact that several possible underlying mechanisms can result in normal OHC function and poor neural synchrony suggest that AN/AD is not a single entity with a single underlying etiology **(Starr, et. al., 2000).**

Since some of the possible mechanisms and etiologies may not be specifically neural in nature, believe that the term auditory dys-synchrony may provide a more comprehensive view of auditory neuropathy that connects logically to viable management options **Berlin, Hood and Rose (2001).**

Possible sites include the inner hair cells (IHC), the synaptic juncture between the IHC and auditory nerve, or the auditory nerve itself. Each of these could result in normal OAEs and a dys-synchronous ABR. Several sources of information support the possible involvement of IHC, including animal models **Deol and Kocher (1958), Bussoli, Kelly & Steel (2001)** and recent human histological data **(Amatuzzi, et. al., 2001).**

Some patients with AN/AD have demyelinating conditions such as hereditary motor sensory neuropathy, Charcot-Marie-Tooth disease or other neuralconditions. Some patients have risk factors related to hearing loss in their history, but there are also a significant number of patients with no risk factors. Factors observed in infants include hyperbilirubinemia, exchange transfusion, premature birth, and perinatal **asphyxia**

(Deltenre, et. al., 1997; Berlin, et. al., 1998; Rance, et. al., 1999; Simmons & Beauchene, 2000).

Auditory neuropathy spectrum disorder can be inherited or acquired **(Buchman et. al., 2014).** Notably, infants who spend a lot of time in the neonatal intensive care unit (NICU) were more frequently affected by ANSD, he added. About 50 percent of those with auditory neuropathy have spent time there. Whether this was directly related to being in the NICU, being premature, or a combination of both is not entirely clear. Most of the infants with ANSD have a specific medical risk factor for the condition. Transient neonatal insults, such as hypoxia or hyperbilirubinemia, are most common. Other causes, including infectious processes, such as mumps or meningitis; acoustic neuroma; inflammatory conditions, such as siderosis; autoimmune disorders, such as Guillain–Barré syndrome; and genetic mutations also have been reported in the literature. The most common genetic cause of ANSD related to mutation of the gene encoding otoferlin, which was not usually associated with lot of other health conditions. ANSD also can have a progressive onset, with auditory deficits often presenting in middle childhood or early adolescence, progressive ANSD is typically associated with a genetic neurodegenerative disease like Friedreich ataxia, Charcot–Marie–Tooth disease, Leber's hereditary optic neuropathy, where the auditory deficit may be part of a generalized pattern of neural deterioration. Interestingly, auditory symptoms often present first in these diseases. Genetic disorders are prominent in ANSD patients and generally can be identified at birth with appropriate screening.

Heredity is another possible underlying factor. Auditory neuropathy may accompany peripheral neuropathy in a variety of dominant syndromes such as Charcot-Marie-Tooth disease **(Satya-Murti et. al, 1979)** and has been observed in Friedreich ataxia

(Satya-Murti et. al, 1980). Auditory neuropathy unassociated with peripheral neuropathy most commonly occurs as a sporadic or recessive trait.

Kim et al. (2004) described a multigenerational U.S. family of European descent segregating autosomal dominant auditory neuropathy. Hearing loss had an average age of onset of 18.6 years. Affected members were heterozygous except for 2 homozygous individuals whose parents were consanguineous. However, with the exception of an age of onset at the lower end of the range (8 and 9 years), there were no apparent clinical features differentiating their phenotype from that of the heterozygotes. **Kim et al. (2004**) predicted that the mutation in this family will be found to be noninactivating, e.g., a missense mutation rather than a null mutation resulting in haploinsufficiency. In the latter case, the complete lack of functional protein in the homozygotes would be expected to result in a more severe phenotype.

In a multigenerational US family of European descent segregating autosomal dominant auditory neuropathy, **Kim et al. (2004)** mapped the disorder to a locus on 13q14-q21 between markers D13S153 and D13S1317 (maximum 2-point lod score of 9.87 at theta = 0.019 for D13S153). **Schoen et al. (2010)** identified a heterozygous mutation (-172G-A; 614567.0001) in the 5-prime untranslated region of the DIAPH3 gene that resulted in increased mRNA and protein expression. Drosophila with constitutive overexpression of a mutant Diaph gene in the auditory organ had reduced sound-evoked potentials. The findings indicated that AUNA1 was caused by overexpression of the DIAPH3 gene due to a mutation in a transcriptional regulatory site, consistent with a gain of function.

Weng et al. (2003) described probands of the pedigrees, who had been diagnosed with auditory neuropathy, were evaluated and followed in the Department of Otolaryngology-Head and Neck Surgery, China. Patients with characteristics of

nonsyndromic hereditary auditory neuropathy identified in one large and three smaller Chinese families. Pedigree analysis suggested an X-linked, recessive hereditary pattern in one pedigree and autosomal recessive inheritances in the other three pedigrees. The phenotypes in the study were typical of auditory neuropathy; they were transmitted in different inheritance patterns, indicatingclinical and genetic heterogeneity of this disorder. The observed inheritance and clinical audiological findings are different from those previously described for nonsyndromic low-frequency sensorineural hearing loss. This information should facilitate future molecular linkage analyses and positional cloning for the relative genes contributing to auditory neuropathy.

Beutner et al. (2007) conducted a study; the aim of study was to describe risk factors in auditory neuropathy/auditory synaptopathy (AN/AS). Between 1997 and 2005, they diagnosed 37 children with AN/AS. They underwent a critical chart review for risk factors and etiological coincidences in this idiosyncratic disorder. Eighteen neonates had a history of prematurity and low birth weight. Hyperbilirubinaemia was present in 13 children. Three patients had evidence of infection during pregnancy, and AN/AS were associated with complex syndromal diseases in 2 cases. A congenital, familial pattern was seen in 2 siblings. Seven patients had idiopathic AN/AS. *Conclusion:* Rather than being a single etiological entity, AN/AS comprises a spectrum of risk factors and associated problems affecting the cochlea and the auditory pathway. This study shows that the majority of AN/AS in children is the result of perinatal problems and is not genetic in origin. Hyperbilirubinaemia is a common and etiologically significant finding in infants suffering from AN/AS.

Santarelli et al. (2015) suggested thatmutations in the OTOF gene encoding otoferlin result in a disrupted function of the ribbon synapses with impairment of the

multivesicular glutamate release. Most affected subjects present with congenital hearing loss and abnormal auditory brainstem potentials associated with preserved cochlear hair cell activities (otoacoustic emissions, cochlear microphonics [CMs]).

Foulon et al. (2015) conducted a study and his study has three main goals (1) to determine the hearing configuration in hearing-impaired children born with a congenital CMV (cCMV) infection, (2) to see whether auditory neuropathy spectrum disorder (ANSD) was present, and (3) to propose a flow chart for the follow-up of hearing in children with cCMV. Hearing configuration and the presence of ANSD in cCMV infected children was analysed. Selection criteria were hearing-impaired children with a regular audiometric follow-up for at least 36 months, no other major risk factors for hearing loss, a normal middle-ear status, and an appropriate behavioral response to the given pure-tone stimuli.Out of a cohort of 206 cCMV infected children, 18 hearing-impaired children were selected.Audiograms of all children showed a flat configuration of SNHL. The slope between octave bands was never greater than 10 decibels. None of the 18 children were found to have ANSD.

Vandana et al. (2015) reported audiological manifestations in a four-year-old child with Infantile Refsum disease. He was born to non-consanguineous parents and had normal birth history and mildly delayed milestones. Clinical features were characterized by neuroregression, retinitis pigmentosa, hearing loss, peripheral neuropathy and white matter signal changes on magnetic resonance imaging. Biochemical evaluation showed elevated serum levels of long chain fatty acid and phytanic acid confirming the diagnosis. The audiological profile was characterized by absent auditory brainstem responses with robust otocoustic emissions, which indicated auditory neuropathy as the possible cause of hearing loss.

Lepecha et al. (2015) conducted a study and aim of study was to find out the prevalence and types of neurological abnormalities associated with auditory neuropathy spectrum disorder. Study showed the frequency of auditory neuropathy spectrum disorder was 1.12%. Sixty percent were found to have neurological involvement. This included cerebral palsy in children, peripheral neuropathy (PN), spinocerebellar ataxia, hereditary motor-sensory neuropathy, spastic paresis, and ponto-bulbar palsy. Neurological lesions did not present simultaneously with hearing loss in most patients. Sixty-six percent of patients with auditory neuropathy spectrum disorder were born of consanguineous marriages.

Chandran et al. (2015) reported Brown-Vialetto-Van Laere syndrome characterised by pontobulbar palsy and sensorineural hearing loss. Audiological investigations revealed normal otoacoustic emissions with absent auditory brainstem responses and middle-ear reflexes in sensorineural hearing loss, suggestive of auditory neuropathy spectrum disorder.Unal et al (2015) conducted a study on fifteen patients with AN/AD. Possible etiology of AN/AD was neonatal hyperbilirubinemia in three patients, family history of hearing loss in three patients, consanguineous marriage in two patients, head trauma in two patients, mental motor retardation in one patient, cerebrovascular disease in one patient, and there was no apparent cause in three patients.

Manchaiah et al. (2011) suggested that the aetiology of auditory neuropathy is vast, which may include prematurity, hyperbilirubinaemia, anoxia, hypoxia, congenital brain anomalies, ototoxic drug exposure, and genetic factors. It was estimated that approximately 40% of cases have an underlying genetic basis, which can be inherited in both syndromic and non-syndromic conditions. He also reported that the largest proportion of auditory neuropathy spectrum disorders (ANSDs) is due to genetic

factors, which can be syndromic, non-syndromic, or mitochondrial related. The inheritance pattern can include all the four main types of inheritances such as autosomal dominant, autosomal recessive, X-linked and mitochondrial.

Bielecki et al. (2012) conducted a study on 9419 infants whose hearing ability was uncertain or who had risk factors for hearing loss. Aim was to determine the prevalence of Auditory Neuropathy Spectrum Disorder (ANSD) among infants with sensorineural hearing loss (SNHL) and discuss the risk factors. In the ANSD group, prematurity and low birth weight (<1500 g) were observed in 5 cases; ototoxical medication in 8 cases; mechanical ventilation in excess of 5 days in 5 cases. Hyperbilirubinemia was observed in 7 cases, but severe hyperbilirubinemia requiring an exchange transfusion was not observed; 4 patients had no risk factors, 6 patients had only one risk factor, and the 8 remaining had two or more risk factors.

Analysis of electrophysiologic measures and medical record reviews of the first 22 months of the universal newborn hearing–screening program was conducted by **(Abbey et. al, 2005).** Association of the AN/AD profile was evaluated with the following factors: gender, gestational age, ototoxic drug regimen, low birth weight, hyperbilirubinemia, hydrocephalus, low Apgar score, anoxia, respiratory distress syndrome, pulmonary hypertension, intraventricular hemorrhage, multiple birth, seizure activity, and family history. They reported that One hundred fifteen (24.1%) of the 477 infants failed the ABR in 1 or both ears and passed OAEs bilaterally. Comparisons of infants fitting the AN/AD profile with those not fitting the AN/AD profile were negative with 3 exceptions those with hyperbilirubinemia and those who were administered vancomycin or furosemide. A logistic-regression analysis model failed to predict which infants would be at risk for the AN/AD profile either unilaterally or bilaterally.

Roche et al. (2010) conducted a study, objective of the study was to identify and define the imaging characteristics of children with auditory neuropathy spectrum disorder (ANSD). Retrospective review and analysis of both temporal bone computed tomography (CT) and magnetic resonance images (MRI) was done. Result showed Sixty-eight (64%) MRIs revealed at least one imaging abnormality while selective use of CT identified 23 (55%) with anomalies. The most prevalent MRI findings included cochlear nerve deficiency (n=51; 28% of 183 nerves), brain abnormalities (n=42; 40% of 106 brains) and prominent temporal horns (n=33, 16% of 212 temporal lobes). The most prevalent CT finding from selective use of CT was cochlear dysplasia (n=13; 31%).

A prospective clinical study was conducted by **(Anjali et. al, 2015)**. All patients diagnosed with auditory neuropathy spectrum disorder during a 17-month period. In their study they reported, Sixty percent were found to have neurological involvement. This included cerebral palsy in children, peripheral neuropathy (PN), spinocerebellar ataxia, hereditary motor-sensory neuropathy, spastic paresis, and ponto-bulbar palsy. Neurological lesions did not present simultaneously with hearing loss in most patients. Sixty-six percent of patients with auditory

2.3 Prevalence Rate:

The available information on the prevalence of auditory neuropathy is poor & limited. About 1 in 10 children with permanent hearing loss where PHL = average loss ≥ 40 dBHL from 0.5-4kHz bilaterally **(Sininger, 2002).** Estimates vary between studies. True prevalence in children with hearing loss not determined. Most ANSD cases occur in special care/NICU babies, but significant number may occur in well babies **(Sininger, et. al, 2002).**However, if oto-acoustic emission screening was used in the first stage of a neonatal hearing screening program, children with auditory neuropathy

are missed. The cost-effectiveness of population-based screening using auditory brainstem response should be studied **(Korver et. al, 2012).** Prevalence is likely to be changing with immunization, neo-natal detection, improved diagnostic acumen & facilities, advances in genetics, family size limitation, population demographic & treatment. **(Wiley et. al, 2009).**

Xoinis et al. (2007) conducted study on low birth weight infants. Objectiveof the study was to establish a prevalence rate and characterize risk factors for NICU graduates who demonstrate the AN electrophysiologic profile. They reported thatwith a SNHL prevalence of 16.7/1000, the rate for AN was 5.6/1000 NICU infants. Compared to infants with SNHL, infants with AN were significantly younger (GA 28.3±4.8 AN vs 32.9±5.2 weeks SNHL, $P<0.0001$) and smaller (BW 1318±894 AN vs 1968±1006 g SNHL). Nearly two-thirds of the AN infants were ELBW and had significantly longer hospital stays compared to SNHL infants of the same birth weight group. Exposure to furosemide, aminoglycosides, vancomycin or dexamethasone was associated with increased AN but not SNHL. Peak bilirubin level correlated with SNHL but not AN. They also suggested that Low birth weight NICU infants are at significant risk for AN. ELBW infants are at significantly higher risk for both AN and SNHL.

Bielecki et al. (2012) conducted a study on 9419 infantswhose hearing ability was uncertain or who had risk factors for hearing loss. Aim was to determine the prevalence of Auditory Neuropathy Spectrum Disorder (ANSD) among infants with sensorineural hearing loss (SNHL) and discuss the risk factors. From this population, 352 were diagnosed with SNHL. Of these 352 children, 18 (5.1%) were diagnosed with ANSD.

Mittal et al. (2012) conducted a study to determine prevalence and audiological characteristics the ANSD in an Indian tertiary care hospital. They prospectively enrolled all the pediatric cases less than 12years of age. A total of 487pediatric cases were referred for hearing evaluation. 183 (37.6%) cases showed absent BERA and 26(5.3%) cases fulfilled the diagnostic criteria for ANSD. Repeat examination after 3months revealed presence of OAE's in 57.6% (15/26) cases while cochlear microphonics were present in all the 26 cases. They reported 5.3% of ANSD prevalence rate.Similar study was conducted by (Penido, et. al, 2013). This retrospective study was carried out between 2010 and 2012 and included 2,292 individuals with SNHL. Study showed 1.2% of prevalence rate.

Talaat et al. (2009) conducted a study on 112 infants and young children with age ranged 6-32 months.15 patients were found to have auditory neuropathy according to criteria for diagnosis.The prevalence of ANSD in the study group was 13.4%.

Lotfi et al. (2007) reported prevalence of auditory neuropathy among the students with hearing impairment. They conducted study from 2002 through 2003, 841 hearing impaired students, aged 2 - 20 years, underwent a complete history taking, clinical examination, and audiometry. They found 13 students with auditory neuropathy who comprised 1.55% (CI 95%: 0.71 - 2.38%) of the students with hearing impairment.

Duman et al. (2008) conducted a study on deaf school children. The ages of the children were between 6 and 17 (mean age 11.9) and 32 (42.9%) of them were girls and 43 (57.1%) were boys. Three cases (4%) were diagnosed as AN, however, no risk factors were determined in two of them. A history of hearing loss following a vaccination was found in only one patient.Khiari et al (2009) reported three cases of auditory neuropathy, out of 211 children with sensorineural hearing loss from April 1,

1999 to December 31, 2003. Two patients did not have a risk factor for hearing impairment.

Korver et al. (2012) conducted a study on low-risk population. They collected and reported all available published evidence on the prevalence of auditory neuropathy in the well-baby population and calculate the contribution of this to the false negative rate of oto-acoustic emission based newborn hearing screening programs. PubMed and EMBASE were searched for relevant articles published between 1996 and 2010. Included were original studies, which focused on well babies and reported the prevalence of auditory neuropathy. Of 519 citations, 4 articles met the inclusion criteria. The population based prevalence of auditory neuropathy in children in population hearing screening was found to vary between 0.006% (SD 0.006) and 0.03% (SD 0.02). The false negative rate, caused by missed children with auditory neuropathy, is between 4 and 17%.

Ching et al. (2013) conducted a study and determined the influence of the presence of auditory neuropathy spectrum disorder (ANSD) on speech, language, and psycho-social development of children at three years of age. Study sample consists of 47 children with ANSD. Sixty-four percent of children with ANSD have hearing sensitivity loss ranging from mild to severe degree, and the remaining has profound hearing loss. For three years, 27 children used hearing aids, 19 used cochlear implants, and one child did not use any hearing device. Thirty percent of children have disabilities in addition to hearing loss. On average, there were no significant differences in performance level between children with and without ANSD. In addition, the variability of scores was not significantly different between the two groups.

Anjali et al. (2015) conducted a clinical study**.** All patients diagnosed with auditory neuropathy spectrum disorder during a 17-month period. In their results, frequency of auditory neuropathy spectrum disorder was 1.12%. Rance et al (1999) reported One in 433 (0.23%) of the children had evidence of auditory neuropathy. The results suggest that auditory neuropathy is more common in the infant population than previously suspected.

Caldas et al. (2012) conductedanalytical, prospective study on 15 participants (30 ears) aged 10-12 years, with bilateral sensorineural hearing loss, from the total sample (30 ears), 8 ears (26.7%) presented absent responses in the Auditory Evoked response with the presence of cochlear microphonism. Within the selected eight ears, six (75%) showed presence of otoacoustic emissions test in isolated frequencies and two (25%) ears had otoacoustic emissions test even in the presence of the isolated frequencies. It was found that 26.7% of the ears tested presented results that are compatible with Auditory Neuropathy Spectrum Disorder.

Forest et al. (2006) conducted a study from 1997 until 2004, 5190 children, aged 1–15 years, whose hearing ability was uncertain or who had risk factors for hearing impairment were investigated with subjective and objective hearing tests. Three thousand four hundred and fifteen from these children were screened for AN/AS using pure-tone audiometry, impedance measurement, transient evoked otoacoustic emissions (TEOAE) and click-evoked auditory brainstem responses (ABR). Result showed from 3415 patients who participated in an ABR and TEOAE assessment, 379 children showed absent or elevated (≥80 dB nHL) ABR thresholds. Within the group we found 32 cases with evidence of AN/AS via visible TEOAE and/or cochlear microphonics (CM) coupled with absent ABR. In the remaining 3036 children, AN/AS, could be ruled out by means of detectable ABR-thresholds and coherent

findings in pure-tone audiometry and TEOAE assessment. This results in a prevalence of AN/AS of 0.94% within the group at risk for hearing loss, compared to 8.44% among profoundly hearing impaired children.

Similar study was conducted by **(kumar, et. al, 2006)** between January 2000 and December 2003. Results showed that the prevalence of auditory dys-synchrony was around 1 in 183 in individuals with sensory neural hearing loss. Behavioural thresholds and speech identification scores were variable. Around 60% of the individuals had no measurable speech identification scores. There was no relation between the hearing thresholds and speech identification scores or between otoacoustic emissions and speech identification scores. These results indicate that auditory dys-synchrony is not an extremely rare disorder.