INTRODUCTION

Hearing impairment is said to be a hidden handicap. However, its consequences are not so. Congenital or early childhood hearing impairment has a profound effect on an individual due to its interference with the normal development of auditory behavior, speech and language. The causes of hearing impairment are many and several of them have been discovered over the last few decades. The interest in the awareness of these factors is in its prevention. These are also used as a means to identify the hearing impairment early in life as it may go unnoticed for a long time. Timely management can diminish the consequences of hearing impairment in a child’s life.

The study of distribution and determinants of hearing disorders in a population and application of the knowledge obtained in prevention and amelioration of hearing problems is called epidemiology of hearing impairment (Sancho, Hughes, Davis, & Haggard, 1988). Epidemiology provides information concerning the etiology of hearing impairment and the groups within the community who are most at risk, which can be used to develop guidelines for implementation of intervention programs. Such studies need to be carried out periodically to track the trend in association of risk factors with hearing impairment.

In neonates, hearing impairment is twenty times more prevalent than other disorders such as phenylketonuria and sickle cell anaemia that are routinely screened in a hospital (Oghalai, Chen, Brennan, Tonini, & Manolidis, 2002). It is very well documented (Yoshinaga-Itano, Sedey, Coulter, & Mehl, 1998) that if the sensory deficits
among babies remain undetected or untreated, it will lead to a significant handicap, ultimately affecting the quality of life. Hence, early identification and early intervention become the major justification factors for any screening program.

Screening for hearing impairment in newborns is no exception. Early detection of hearing loss can be accomplished through hearing screening at, or shortly after birth, facilitating initiation of appropriate intervention before one year of age which is critical for speech, language and cognitive development. Joint committee of infant hearing (1995, 2000, 2007) has given risk factors for hearing loss in newborns and infants. The condition/disorder which increases the chances of incidence of hearing loss is called high risk factors of hearing loss. High risk factors serve as red flags to clinicians to identify those infants for whom screening for hearing impairment may be considered mandatory (Cone-Wesson et al., 2000; Krishnan, Lafayette, & Donaldson, 2012; Vohr et al., 2000), especially in situations where time and manpower are limited due to high caseload and shortage of instrumentation.

1.1 Risk factors

Davidson, Hyde and Alberti (1989) have given a major etiological classification of hearing impairment. The categories are:

1. Genetic factors
2. Prenatal factors
3. Perinatal factors
4. Postnatal factors
5. Craniofacial anomalies

1) Genetic factors

At least half of all the permanent hearing impairment in childhood is reported to be associated with genetic risk factors (Morton & Nance, 2006). Genetic hearing impairment can be divided into autosomal dominant, autosomal recessive, X-linked and mitochondrial. The majority of genetic hearing impairment is inherited in an autosomal recessive way and is detectable at birth. Recessive inheritance occurs when both parents – who may not necessarily show the trait – carry a mutated gene that may cause a genetic syndrome. If both parents carry one normal copy of the gene and one mutated gene, there is a 25% chance of inheritance of both the mutated genes (one from each parent) and gets manifested as the disease. There is also a 50% chance that the child will inherit a mutated gene and become a carrier for that disease, but not manifesting the syndrome. Such disorders include Usher syndrome, Cockayne syndrome, Pendred syndrome, Jervell and Lange-Nielsen syndrome, Hurler syndrome and Alstrom syndrome (Kingston, 2002).

For dominant inheritance, only one mutated copy of the gene is needed for the hearing impairment to be manifested. Usually, one parent will have the manifestation, and there is at least a 50% chance of a child inheriting the gene and manifesting the disorder. If both parents exhibit the trait, there is a 75% chance of the child manifesting the disorder. Hearing impairment inherited in this way may be either congenital and progressive or late-onset. Examples of autosomal dominant syndromes include
Marshall-Stickler syndrome, Waardenburg syndrome and Treacher Collins syndrome (Keats, 2002).

In X-linked recessive conditions, males are affected more because of their hemizygosity, a state of having unpaired genes since there will be only a single copy of genes in the X chromosome. However, the disease can be transmitted through supposedly normal females who are carriers. A female with a carrier gene of an X-linked recessive disorder will transfer the disease to half of her sons, and half of her daughters, who will be carriers. An unaffected male will not transmit the mutant gene. An affected male will transmit the defective gene to all his female children (because of his X chromosome), but to none of his sons (because of his Y chromosome). This lack of male to male transmission is a trademark of X-linked inheritance. Mitochondria have their individual DNA consisting of a double-stranded circular molecule. Disorders related to mitochondrial dysfunction may be controlled by nuclear gene mutation and trail Mendelian inheritance, or may result from mutations happening within the mitochondrial DNA (Kingston, 2002; NSW Health Department, 2012).

Consanguinity is a tradition which is followed in Asian, Arab, African and Latin American countries (Bittles, 2012). Genetic abnormalities caused due to consanguinity affects some pathway leading to congenital hearing loss. The growth of cochlea and hair cells is influenced by a genetic pathway named Planar Cell Polarity (PCP) pathway. This pathway is involved in the development of the polarized structure which in turn
forms the auditory sensory organ and determines a set pattern of embryonic development (Reddy, Rani, Reddy, & Bindu, 2006).

Kingston (2002) reported that the marriage between close relatives raises the chances of a recessive disorder as both parents have high probability to take the same mutant gene received from a common ancestor. The likelihood of occurrence of a disease in closely related parents is inversely proportional to frequency of its incidence. Risks are mainly increased for the offspring of first degree relatives in which 50% of gene sharing is present. Second degree consanguinity has a mild increase in risk with 25% of gene sharing and third degree relatives have 12.5% of gene sharing.

2) Prenatal factors

Infections are considered to be the main cause of prenatally acquired hearing impairment. When rubella infection occurs in the first eight weeks of pregnancy, there is 80-90% chance of neurological damage in surviving infants. The risk of hearing impairment can come down to 10-20% if the infection occurs between first 11 and 16 weeks of gestation. Risk of fetal hearing loss is rare over 16 weeks of gestation (Ganguly, 2013).

Sequelae of congenital rubella infection are learning disability, heart disease, cataracts, microcephaly, hepatomegaly, splenomegaly, bone lesions, purpura, glaucoma and hearing impairment (Davis, Davis, & Mencher, 2009). These features exist in congenital rubella syndrome (CRS). Hearing impairment is the most common permanent manifestation and affects 68 to 93% of children with congenital rubella
infection (Anvar, Mencher, & Keet, 1984). The hearing impairment is usually severe to profound sensorineural in nature and can be progressive (Roizen, 1999).

Congenital cytomegalovirus (CMV) is a ubiquitous herpes virus spread by close contact with saliva, blood, genital secretions, and urine or breast milk. It is the most common intrauterine infection, affecting between 0.4 and 2.3% of live born infants in the U.S. (Stagno, 1995). CMV belongs to the herpes virus family, not easily spreading from person to person. This can transfer itself via contact through saliva, blood, urine, breast milk, cervical secretions, or semen. As the age increases, people are more likely to be exposed to this infection. In the U.S. population, approximately 36% of children (6-11 years) were infected with CMV, with the seroprevalence increasing to 91% in persons who are 80 years and above. CMV is mostly asymptomatic when it is a primary infection; however, it can cause more devastating neuro-developmental sequelae in immune-compromised infants than other infections. The most frequently observed neuro-developmental sequel is hearing impairment (Swanson & Schleiss, 2013). For a long time, this infection may not have any effect on children and adults and they will be leading their normal life except for some rare mild mononucleosis-like illness (Ross & Fowler, 2008).

The virus will be in the dormant state at the outset. It is usually kept under the control of body’s immune system, so adults and children with adequate immune function rarely exhibit CMV-related disorders (Stagno, 1995). However, when CMV is infected in utero from the mother to the fetus, tissue insult may occur and the infant may have a
congenital or a late onset hearing impairment (Boppana, Rivera, Fowler, Mach, & Britt, 2001; Fowler, Stagno, & Pass, 2003).

3) Perinatal factors

Perinatal factors that may predispose to permanent hearing impairment (PHI) include prematurity, low birth weight, low Apgar score and hyperbilirubinemia. Any baby born before 37 weeks of gestation is generally termed as premature baby (Aruchamy, 2010). Both gestational age and birth weight are the important determinants of baby’s general condition (Hayes & Northern, 1996). Certain physical and neuromuscular characteristics of the fetal development can objectively estimate the gestational age. This estimate can be compared to birth weight to determine if the baby is small for gestational age (SGA), appropriate for gestational age (AGA), or large for gestational age (LGA) (Hayes & Northern, 1996).

In 1953, Dr. Virginia Apgar, an anesthesiologist developed a tool for assessing infants’ condition in delivery room which is reported as Apgar score (Hayes & Northern, 1996). It is performed at 1 min and 5 minutes. Five important observations are made viz. heart rate, respiratory effort, reflex irritability, muscle tone and color and a rating of 0-2 is assigned to each observation. Maximum Apgar score obtainable is 10. Infants with the score of < 3 need ventilator assistance and intensive care (Hayes & Northern, 1996). Several studies have linked this score with the permanent hearing impairment (Ari-Even Roth et al., 2006; Chu et al., 2003; Coenraad, Goedegebure, van Goudoever, & Hoeve, 2010). Because of its simplicity, this tool is administered in almost all hospitals
Bilirubin is a byproduct of breakdown of red blood cells. When it exceeds a specific range in the circulating blood, it has potential to damage the CNS. Hyperbilirubinemia (Jaundice) results in yellow coloration of skin and sclera of eye. Clinically significant jaundice occurs mostly in premature babies and infants with fetal blood group incompatibility and infections (Aruchamy, 2010).

Some perinatal problems that were known to cause neurological damage have diminished in the modern maternity hospitals. For example, the introduction of photosynthetic lights to reduce jaundice (hyperbilirubinemia) to non-toxic levels and rhesus inoculation to prevent rhesus incompatibility in future pregnancies. On the other hand, medical advances have ensured that more premature, anoxic and low-birth-weight (LBW) babies survive, leading to more babies graduating from NICU with a hearing impairment (Davis et al., 2009).

4) Postnatal factors

The majority of postnatal causes of hearing impairment are infections and genetic related disorders (Davidson et al., 1989). The infections can affect middle ear and inner ear. Otitis media should be included since permanent hearing impairment (PHI) secondary to this infection is not uncommon in the developing world. Several studies in developing countries have shown that otitis media could be a cause for permanent hearing impairment because of ignorance and inadequate medical care.
Systemic and neurological infections that have been linked with congenital PHI are bacterial meningitis, measles, and mumps.

McPherson and Holborow (1985) in a 2-year (1981–1983) fieldwork undertaken throughout Gambia observed 41.3% congenital causes of severe to profound sensorineural hearing loss among 259 children aged 2–10 years. Of the acquired causes, meningitis and meningitic symptoms (31.7%), febrile illness, (21.2%), measles (1.9%), and rubella (1.5%) were the main factors. However, things have improved to a much better state in the present days. Thanks to successful vaccination programme and better general health, new-onset measles and mumps-related hearing loss is now rare except in a few underdeveloped countries like Nigeria and Egypt (Dunmade, Segun-Busari, Olajide, & Ologe, 2007; Taha et al., 2010).

Bacterial meningitis is a serious infectious disease in the neonatal period and throughout childhood. It can be caused by a variety of pathogens, including Haemophilus influenzae type b (Hib), Streptococcus pneumoniae (pneumococcus) and Mycobacterium tuberculosis (TB). For children who survive meningitis, there are often sequelae, which include learning disabilities, hydrocephalus, motor abnormalities, vestibular deficits, psychosis, hyperactivity and visual and sensorineural hearing impairment. Reports have indicated that acquired hearing impairment represents 9.5% of total PCHI, with 6.5% of these cases being caused by meningitis (Davis, Wood, Healy, Webb, & Rowe, 1995).
Meningitis-induced hearing impairment is often bilateral, severe or profound and rapid in onset. Clinical and experimental studies have shown that the loss results from direct damage to the cochlea by the infection, but it may be exacerbated by additional cochlear damage resulting from any ototoxic drugs used to treat the disease (François, Laccourreye, Huy, & Narcy, 1997).

Ototoxic medication is known to cause hearing impairment for long. Cisplatin, carboplatin and aminoglycosides are some of the examples. The hearing loss initially affects the high frequencies and is more disabling in children who are still developing language than in adults (Bellman, 1996; Brock & Bellman, 1991). Children with aminoglycoside induced hearing loss and particularly those of Asian origin should be screened for the A0444G mitochondrial mutation which increases the susceptibility to aminoglycoside ototoxicity (Usami et al., 1997). A mitochondrial involvement in aminoglycoside toxicity is well established through intrinsic pathways of cell death (Huth, Ricci, & Cheng, 2011; Op de Beeck, Schacht, & VanCamp, 2011). The effect is more pronounced in outer hair cells at the basal turn of the cochlea, the region most sensitive to aminoglycosides (Jensen-Smith, Hallworth, & Nichols, 2012).

5) Craniofacial anomaly

Craniofacial anomaly associated with ear malformations is syndromic and non-syndromic. These malformations may be aural atresia or aural stenosis. The syndromes include Goldenhar syndrome which involves defective aural/oral and mandibular development, Treacher Collins syndrome involving ear canal, middle ear, eyelids,
maxilla and mandible, branchio-oto-renal syndrome involving malformation of middle ear ossicles, inner ear and maxilla. Some of the other examples are Crouzon syndrome, Noonan syndrome, Fetal alcohol syndrome and CHARGE association (Levi & Grundfast, 2012).

External auditory canal (EAC) malformations occur when canalization of epithelial plug that originates from the first branchial cleft at 26-28 weeks does not occur (Northern & Downs, 2002). Several factors including intra uterine toxin exposure and infection, low birth weight and intra uterine trauma have been cited as causes of this malformation (Cressman & Pensak, 1994). Ossicular and middle ear anomalies are commonly associated with aural atresia and microtia. In isolated conditions, ossicular malformations are generally classified as minor deformity. Audiometric manifestation of these anomalies is usually moderate to severe hearing loss (Levi & Grundfast, 2012).

Aural stenosis is defined as an EAC size of 4 mm with the appearance of hour glass type of configuration. This criterion is not applicable for Down’s syndrome and Cornelia de lange syndrome because hypoplasia of the external ears causes the typical uniformly narrowed ear canals (Levi & Grundfast, 2012). Congenital stenosis occurs when there is incomplete canalization of the canal epithelial plug at 28 to 30 weeks of gestation (Northern & Downs, 2002). As this is a late event in the fetal development, the facial nerve will be in the normal position providing a reduced risk for surgical repair (Sataloff, 1990).
Numerous studies have attempted to estimate the significance of above mentioned risk factors in causing hearing impairment in infants. The importance of these risk factors varies with different geographical locations. For example in Netherlands, hereditary reasons, craniofacial anomaly and low Apgar score were shown to have highest association with hearing impairment (Coenraad et al., 2010; Korver et al., 2011); In Iran, ototoxicity and prematurity had the highest association (Fakhim et al., 2010). In USA, ototoxicity, very low and low birth weight and craniofacial anomaly were having highest association (Chu et al., 2003; Vohr et al., 2000). In India, no systematic risk factor association studies were reported in infants till now. However, a school based study (age not mentioned) before 20 years (D’ Mello, 1995), revealed that rashes with fever during pregnancy, family history of hearing loss and birth asphyxia were having highest association with hearing impairment. High-risk registers for childhood hearing impairment had been listed by few authors (Ashok kumar, 1981; D’Mello, 1995) in the past based on high prevalence among children with hearing impairment. In an attempt to curb the causal factors and to detect hearing impairment early, a National program of prevention of deafness has been implemented through All India Institute of Speech and Hearing, Mysore in Karnataka (Yathiraj, Sameer, & Jayaram, 2002).

Any program on prevention is based on up-to-date data on risk factor association with hearing loss. The medical facilities for neonatal and infant care (Photo therapy, Mechanical ventilation, etc.) and prevalence of risk factor changes over time and place. Though some preliminary studies have been done in India earlier in enlisting the risk factors, there is no focused study on prioritizing them. Hence, there is a dire need to
study the strength of association of individual and combined (multiple) risk factors in our country, both hereditary and acquired.