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PROSPECTIVE EVALUATION OF SENSORINEURAL HEARING LOSS AS A COMPLICATION OF MENINGITIS AMONG PEDIATRIC PATIENTS ADMITTED IN A TERTIARY HOSPITAL

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ABSTRACT

Background Deafness or some degree of hearing loss is a frequent but unpredictable sequelae of meningitis with an obvious implication on the development and education of survivors.

Objectives To prospectively determine the incidence of hearing loss among children with meningitis, identify statistically significant risk factors for hearing loss, and quantify the percentage of children with transient or reversible hearing loss after meningitis.

Design Prospective analysis

Method All children (<18 years old) diagnosed with bacterial, tuberculous and viral meningitis who were admitted in wards 9 and 11 of Philippine General Hospital between June to September 2003 were recruited in this study. Subjects were required to have either a specific organism identified on microscopy or culture of cerebrospinal fluid, or to have a convincing clinical sign of meningism plus CSF pleocytosis or radiological evidence of meningitis (meningeal or basal enhancement on CT scan). Patients who were too unstable for transport to the Clinical Neurophysiology Laboratory and those who could not tolerate the procedure were excluded in this study. Clinical details were recorded. Complete physical and neurological examination were done. Brainstem Auditory Evoked Response (BAER) audiometry was performed initially on the first 5 days of illness and was repeated 3-4 weeks after receiving appropriate treatment.

Results Of the 31 children included in the study, 26 (83.9%) developed sensorineural hearing loss, bilateral in 24 (92.3%) and unilateral in 2(7.7%) Of those with bilateral hearing loss, impairment was asymmetric in 37.5%. There was no significant association between the types of meningitis and the occurrence of hearing loss. However, higher risk for deafness was associated with TB meningitis (OR=7.56). Of the variables examined using t-test, Fisher exact test and MannWhitney U test, only 2 parameters appeared to be significantly associated with the development of hearing loss: mean CSF glucose level of <2.9 mmol/L (p=0.04) and abnormal level of CSF protein (p=0.02). Repeat BAER audiometry after 3-4 weeks was performed only in 18 (58.1%) children. None persistence of these 18 children demonstrated hearing loss.

Conclusion In this study of children diagnosed as having meningitis, hearing loss developed in 26 (83.9%) of children. Low CSF glucose levels(<2.9 mmol/L) as well as abnormally high CSF protein levels were statistically significant risk factors for the development of future hearing loss. Transient or reversible hearing loss was not observed among the children included in this study.

INTRODUCTION

Hearing loss as a complication of meningitis exists, more often than not, as an invisible disability that remains undetected for long periods before eventual diagnosis.

A recent population study has shown that by the age of three years, the proportion of children with a known bilateral profound hearing impairment who have an acquired hearing loss is approximately 20%. Of these acquired impairments, 90% are probably due to meningitis.[1,2]

Sensorineural hearing loss as a complication of meningitis has been described by numerous investigators[1-6] with its incidence varying from 5% to 35%.[1,3,5,6] However, most of the studies reviewed were done in developed countries. There appears to have a paucity of similar studies in developing countries where the incidence and etiology for meningitis and hence, the incidence for postmeningitic hearing loss, may vary significantly from the industrialized ones.

Moreover, most developed nations s are currently implementing a policy on hearing testing of children surviving from meningitis. It was unfortunate however that in most developing countries, audiologic evaluation of children who had meningitis was not being routinely done. Hence, most children in third world countries with possible post-meningitic hearing loss remain undiagnosed and thus, untreated.

Therefore, the objective of this study is to determine the incidence of hearing loss among pediatric patients with meningitis.

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Specific objectives include the following:

1. To identify statistically significant risk factors for sensorineural hearing loss following meningitis
2. To quantify the percentage of children with transient or reversible postmeningitic hearing loss

MATERIALS AND METHODS

This is a preliminary prospective study among pediatric patients with meningitis who were admitted in a tertiary hospital.

A. Subjects

All children (<18 years old) diagnosed with bacterial, tuberculous and viral meningitis who were admitted in wards 9 and 11 of Philippine General Hospital between June to September 2003 were eligible for enrollment in this study. Criteria included in this study were the following: subjects were required to have either a specific organism identified on microscopy or culture of cerebrospinal fluid, or to have a convincing clinical sign of meningism plus CSF pleocytosis or radiological evidence of meningitis (meningeal or basal enhancement on CT scan). Patients who were too unstable for transport to the Clinical Neurophysiology Laboratory and those who could not tolerate the procedure were excluded in this study.

B. Data Collection

Complete clinical details were obtained from all the subjects recruited. Physical and neurological examinations were done. Ears were examined by otoscopy.

Specifically, the following variables were noted:

1. patient' s characteristics: age, sex, nutritional status
2. disease characteristics: fever, number of days before treatment, CSF WBC, CSF glucose, CSF protein, opening pressure on lumbar tap, specific pathogen identified, and other neurologic sequelae (seizures, hydrocephalus, subdural effusion, cranial nerve deficits, coma, hemiplegia, infact)
3. treatment variables: use of steroids, partial antibiotic therapy and use of aminoglycosides.

C. Hearing Testing

After a verbal consent was obtained, Brainstem Auditory Evoked Response audiometry was performed initially during the first 5 days of admission and again 3 to 4 weeks after receiving appropriate treatment for meningitis.

Children were evaluated in their natural state of somnolence due to meningitis or under sedation if necessary. One certified audiologist in the Clinical Neurophysiology Laboratory of Philippine General Hospital performed the procedure.

Brainstem Auditory Evoked Responses were elicited by monoaural click stimulations using varying stimulus intensities (40, 60, 80, 90 decibels) over both ears. Single channel recording from each ear was obtained for each stimulus intensity and recorded at the ipsilateral mastoid area referred to a vertex electrode. Averages were recorded after 2000 stimulations presented at 10 Hz. The results were interpreted by 2 neurophysiology consultants.

D. Analysis

Data were analyzed using the software SPSS (Statistical Package for Social Sciences) and EPIINFO (Epidemiologic Information), significance placed at 95% confidence interval.

RESULTS

During the 4-month study period, 38 patients were recruited in this study. Of these, 5 patients expired prior to the scheduled hearing testing while 2 patients were too unstable to be transported to the Neurophysiology laboratory. Hence, only 31 patients were included in the study. The mean age of the children was 4.25 years. 20 (64.5%) were males, 11 (35.5%) were females.

Eleven children (35.5%) were given a diagnosis of bacterial meningitis.18 subjects (58%) had tuberculous meningitis and 2 (6.5%) were diagnosed with viral meningitis. (Figure 1) Of those with bacterial meningitis, Hemophilus influenzae was isolated in 2 (6.5%) of children while 9 (29%) had no growth on culture of the cerebrospinal fluid.

Of the 31 children examined, sensorineural hearing loss was identified in 26 children (83.9%). (Table 1) 17 (94%) of those with tuberculous meningitis developed hearing loss. On the other hand, 8(73%) out of the 11 children with bacterial meningitis and 1 (50%) out of the 2 children with viral meningitis had hearing impairment. (Table 2)

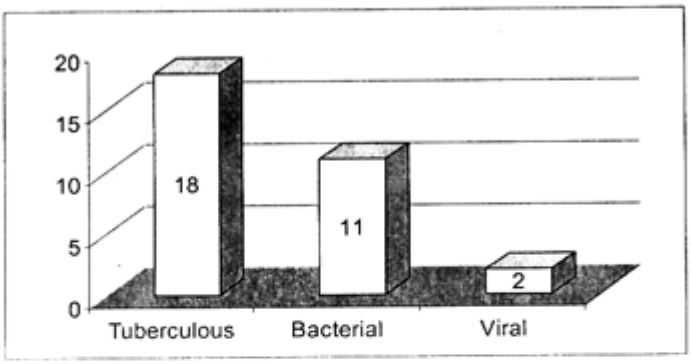

Figure 1. Distribution of patients according to types of meningitis

Table 1. Distribution of patients according to hearing loss based on the initial hearing test

Hearing Loss	Frequency(n=31)	Percentage
(+)	26	83.9%
(-)	5	16.1%

There was no significant association between the types of meningitis and the occurrence of hearing loss. However, higher risk for deafness was associated with TB meningitis (OR=7.56). **(Table2)**

Table 2. Association of the types of meningitis with hearing loss

Meningitis	(+) Hearing Loss	(-) Hearing Loss	P value	OR (95% CI)
TB	17	1	0.13	7.56 (0.61-207.73)
Bacterial	8	3	0.32	0.3 (0.03-2.87)
Viral	1	1	0.30	0.16 (0-7.42)

Hearing loss was bilateral in 24 (92.3%) and unilateral in 2 patients (7.7%). Of those with bilateral hearing loss, deafness was asymmetric or more severe in one ear in 9 children (37.5%).

Of the 31 children who initially underwent hearing testing, 5 (16.1%) expired, while 8 (25.8%) where lost to follow-up. Hence, only 18 (58.1%) patients, all of which had abnormal initial hearing test, had repeat BAER 3-4 weeks after they had received appropriate treatment. All of these 18 children (100%) demonstrated persistence of sensorineural hearing loss on repeat examination.

Potential risk factors for hearing loss were evaluated in this study. Each possible risk factor was individually analyzed to evaluate its association with hearing loss. Variables such as age, sex, nutritional status, delay before treatment, csf wbc count, opening pressure, presence of seizure, hydrocephalus, cranial nerve deficits, infarcts, change in sensorium, partial antibiotic and aminoglycoside use were not significantly associated with hearing loss. This can be proven by all p values >0.05. There was nosignificant difference in the above mentioned characteristics between children with or without hearing loss.

However, there was a significant difference in the mean CSF glucose of patients with or without hearing loss (p=0.04). (Table 3)Children with CSF glucose of <2.9mmol/L were at higher risk for developing hearing loss (relative risk 1.49; 95%CI 0.94-2.36). In contrast, there was no statistically significant difference in the mean CSF protein of those with or without hearing loss but the mere presence of abnormal CSF protein values were found to be significantly associated with postmeningitic hearing impairment (p=0.02). The relative risk of sensorineural hearing loss for those with abnormal CSF protein was 1.72 (95% CI 0.95-3.1) (Table 4) Children who developed hearing loss had a relatively higher CSF protein level.

Table 3. Association between CSF glucose and hearing loss

CSF Glucose (mmol/L)	Sensorineural Hearing Loss		Total	P value
	Present (n=26)	**Absent (n=5)**		
<2.9	19	1	20	0.04
≥2.9	7	4	11	
Total	26	5	31	

Table 4. Variables with significant association with hearing loss

Variable	Sensorineural Hearing Loss		Relative Risk (95% CI)
	Present (n=26)	Absent (n=5)	
CSF Glucose (<2.9mmol/L)	19 (73%)	1(20%)	1.49(0.94-2.36)
CSF Protein (abnormal)	21 (81%)	1(20%)	1.72 (0.95-3.1)
Steroid Use	15 (58%)	0	1.45 (1.05-2.02)

In this study, 15 children were given steroids (dexamethasone) as part of their treatment. All of these 15 children were diagnosed with TB meningitis stage II-III. The steroids were given concurrently with the anti-TB drugs. Steroid use in this study did not appear to affect positively the audiological outcome. Children treated with steroids in this non-randomized study actually had a higher incidence of hearing loss($p=0.04$) and did not regain normal hearing on repeat hearing test.

DISCUSSION

Acquired hearing loss in children could either be conductive or sensorineural. The type of hearing loss associated with infection such as meningitis is the sensorineural type. This form of hearing loss results from defects in the inner ear and in the transmission of electrical signals from the hair cells.

Deafness or some degree of hearing impairment is seen in about 5%-35% of children surviving from meningitis.[1,3,5,6] However, not all of these children suffer permanent sensorineural hearing loss. In a recent meta-analysis of studies done in developed countries, about 10.5% of survivors of meningitis were left with permanent sensorineural form of deafness.[7] Other children experience only a partial and transient loss of hearing[1,3,8,9] which may go undetected even in careful follow-up. In this study however, none of the children with evidence of hearing loss upon admission regained normal hearing on repeat BAER done 3-4 weeks after treatment. The timing of the performance of repeat hearing test in this study was based on previous investigations which showed that the crucial phase of possible recovery or worsening of postmeningitic hearing loss occur during the first two weeks of illness; there were no delayed deafness nor late recovery.[9,10]

The persistence of hearing loss in all of the subjects who had repeat hearing test may be explained by the mechanism involved in the development of deafness following meningitis. It is the effect of suppurative labyrinthitis, due to direct spread of the infection from the subarachnoid space through the cochlear aqueduct.[1,5,10] This will lead to destruction of sensory structures and thus, no recovery of hearing.

On the other hand, a toxic or serous labyrinthitis is thought to be the mechanism responsible for partial or reversible losses.[1,5] None of the children in this study demonstrated reversible hearing loss. Other possible mechanisms include direct nerve fiber damage[9] and secondary ischemic damage.[1,9,10]

In this study, 83.9% of children developed sensorineural hearing loss following meningitis. This incidence is markedly higher than those cited in literature. This higher incidence may be attributed to the small sample size but we could not disregard the possibility that this could be due to other factors such as the severity of illness and the presence of other neurologic complications in most of the subjects. 58% of the subjects had communicating hydrocephalus severe enough to require ventriculoperitoneal shunting. Although this study was not able to demonstrate statistically significant correlation between hydrocephalus and hearing loss, a retrospective study by Nadol et al showed that the presence of other neurologic complications makes a child at higher risk for eventual hearing loss.[5] This is further supported by Wooley et al who demonstrated statistically significant correlation between CT scan evidence of increased intracranial pressure and hearing loss (odds ratio 2.3).[6]

Futhermore, more than half of the subjects (58%) included in this study had TB meningitis as their diagnosis. Since most of the studies reviewed were done in developed countries, where the incidence of TB meningitis is markedly lower (1%), [5] the actual correlation between tuberculous meningitis and hearing loss had not really been studied. The usual organisms significantly associated with postmeningitic deafness are Hemophilus influenzae,[3,14] *Streptococcus pneumoniae,*[6] and *Neiserria meningitidis.*[5] No previous investigation had correlated hearing loss with TB meningitis. An interesting finding in this study was the higher risk for deafness associated with tuberculous menngitis (OR=7.56).

Interestingly, unilateral hearing loss was seen in 2(7.7%) children included in this study. Unilateral hearing loss must likewise be identified with minimal delay because these children may also suffer auditory and linguistic disabilities that are only subtly symptomatic.[1,3,8,9] Even unilateral deafness has now been associated with poor school performance, increased likelihood of repeating a grade and behavioral problems.[11]

This study was also able to show statistically significant correlation between the mean CSF glucose level and sensorineural hearing loss. This finding was consistent with that of Kaplan,[4] Vienny,[9] and Wooley.[6] A low CSF glucose level appears to be a reflection of the number of organisms present in the CSF which then reflects the severity of infection. Hence, hearing loss is directly proportional to the severity of the illness.

An abnormal CSF protein level was likewise noted to be significantly associated with hearing loss. Most of the literature reviewed did not identify increased CSF

protein as a statistically significant risk factor. Again, this may be explained by having TB as the most common etiology of meningitis in this study. Elevated protein is a prominent feature of the CSF of patients with TB meningitis. High CSF protein levels correlate proportionately with the load of tubercle bacilli in the CSF, hence likewise reflecting severity of infection. Dexamethasone has been shown to significantly reduce the incidence of deafness in some studies.[15] However, in this study, all the children given dexamethasone developed sensorineural hearing loss(p=0.04).

This study provides further evidence that hearing impairment develops early in the course of meningitis. Although the relationship between the duration of illness and complications of meningitis remains controversial, hearing loss, according to Richardson, commences during the first 2 days of illness. In his prospective study done in 124 children, hearing loss was noted to be three times more common in children who had been ill for more than 24 hours.[8] However, it is important to emphasize that is usually difficult to tell exactly when meningitis begins. Hence, this study looked at the number of days of illness before admission and found no statistically significant correlation with hearing loss.

CONCLUSION

In this study of children diagnosed as having meningitis, hearing loss developed in 26 (83.9%) of children. Low mean CSF glucose levels (<2.9mmol/L) as well as abnormally high CSF protein levels are statistically significant risk factors for the development of future hearing loss. Transient or reversible hearing loss was not observed among the children included in this study.

RECOMMENDATION

Further studies involving larger number of patients are needed to confirm these findings. Hearing screening should be done in all children who developed meningitis so that early intervention may be possible. Moreover, careful follow-up is warranted for these children in order to detect learning disablities and eventually ensure that they receive appropriate educational assistance that may help to compensate for these difficulties. Emphasis must also be placed upon prevention of meningitis if hearing loss caused by this disease is to be eliminated.

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