Research Article

Correlation of homocysteine and Vitamin B12 level as a surrogative marker for early detection of sensorineural hearing loss in children

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ABSTRACT

Background: Hearing impairment is the frequent sensory deficit which affects newborns, children, adults, and the elderly. **Objective:** This study was conducted to find out the correlation of homocysteine (Hcy) and Vitamin B_{12} level in children aged 2–12 years having sensorineural hearing loss (SNHL). **Materials and Methods:** Seventy subjects were taken in this cross-sectional study after taking approval from the Institutional Ethics Committee of KGMU, UP. (No.2096/ Ethics/R. Cell-17Dated-20/11/2017). Half (n = 35) had moderate-to-severe hearing loss, while remaining 35 had severe to profound hearing loss**.** The biochemical assessment of serum Hcy and Vitamin B_{12} level was done by chemiluminescent microparticle immunoassay method. The statistical analysis was done using Statistical Package for the Social Sciences (SPSS) Version 21.0 statistical Analysis Software. The values were represented in Number(%) and Mean±SD. **Results:** The mean Vitamin B_{12} level was significantly higher in children with moderate-to-severe hearing loss (241.06±75.25 pg/ml) as compared to those having severe to profound hearing loss (203.03±80.53 pg/ml) (P = 0.045). However, mean Hcy level was significantly higher in severe to profound hearing loss group (13.49±4.60 μmol/ml) in comparison to moderate-to-severe hearing loss group (11.14±4.57 μmol/ml) (P = 0.035). On evaluating the correlation between Vitamin B_{12} level and Hcy level, a strong inverse significant correlation was observed for overall cases (r=−0.691; P < 0.001) and strongly significant for moderate-to-severe hearing loss group (r=−0.779; P < 0.001). The correlation was moderate significant for severe to profound hearing loss group (r=−0.572; P < 0.001). **Conclusion:** This study concluded that increase Hcy level is inversely associated with decrease Vitamin B_{12} level in SNHL. This increase Hcy level may be used as a predictor for early detection of SNHL in children so that early therapeutic interventions can be started to improve the hearing in children.

KEY WORDS: Homocysteine; Vitamin B_{12}; Sensorineural Hearing Loss

INTRODUCTION

Hearing impairment is the frequent sensory deficit which affects newborns, children, adults, and the elderly.[1] The WHO has reported in 2015 that worldwide out of 360 million people, 32 million children are affected.[2] Diagnosis of sensorineural hearing loss (SNHL) is based on the reduced hearing acuity by auditory testing and WHO classified level of hearing loss, moderate-to-severe hearing loss 40–70 dB, and severe to profound hearing loss 71–90 dB.[3] There is significant risk for delayed speech, language, and subsequently poor academic and social development in children having hearing loss.[4-8]

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Homocysteine (Hcy) is an amino acid derived from the metabolic demethylation of dietary amino acid methionine

which is abundant in animal protein.[9] Vitamin B_{12} is required as a cofactor for remethylation of Hcy to methionine.[10] Hence, Vitamin B_{12} deficiency leads to impairment of remethylation, so increase quantity of Hcy is exported into the extracellular compartment and also in plasma.[11] Therefore, Hcy is a sensitive marker of intracellular Vitamin B_{12} level.[12]

High Hcy with low Vitamin B_{12} level may be the risk factors for cerebral, coronary, and peripheral vascular diseases and also affects the blood supply of the cochlea.[13] Therefore, we planned to investigate the Hcy and Vitamin B_{12} level for early detection of SNHL in children.

MATERIALS AND METHODS

This study has been carried out in the department of physiology along with collaboration of pathology and otorhinolaryngology of our institute from November 2017 to August 2018 after taking approval from Institutional Ethics Committee of our institute (No.2096/ Ethics/R.Cell-17Dated-20/11/2017). This is a cross-sectional descriptive study. The diagnosed cases of SNHL, aged 2–12 years of children, irrespective of sex were taken from department of otorhinolaryngology. Children <2 years or >12 years with conductive deafness, discharge, chronic suppurative otitis media ,and any other systemic and metabolic diseases were not included in this study. Seventy subjects were taken and categorized in two groups on the basis of severity of hearing loss, first group includes moderate to severe hearing loss, and second severe to profound hearing loss group. Informed consent was taken by parents for biochemical analysis.

Biochemical Analysis

All sterile and aseptic precautions were taken for the blood sample collection. Three milliliter venous blood sample was collected only once from the vein (preferably antecubital vein) in a plain vial. The serum Hcy and Vitamin B_{12} level were estimated by chemiluminescent microparticle (CMIA) immunoassay on ARCHITECT iSystem. Biochemical analysis has been carried out in the pathology department.

Hcy Estimation

The ARCHITECT Hcy assay is a one-step immunoassay. CMIA technology with flexible assay protocols is used for quantitative analysis of serum Hcy, referred as Chemiflex using Architect iSystem. The normal value of Hcy is 2.2–13.2 μmol/L.[14]

Estimation of Vitamin B_{12}

The ARCHITECT B_{12} assay is a two-step assay with an automated sample pretreatment. CMIA technology with flexible assay protocols was used to estimate serum Vitamin B_{12} level, referred as Chemiflex using Architect iSystem. Normal range was 187–883 pg/mL.[15]

Statistical Analysis

The statistical analysis was done using SPSS (Statistical Package for the Social Sciences) Version 21.0 statistical analysis software. Chi-square test, Student "*t*" test, and bivariate correlation analysis were applied. The ANOVA test was applied to compare within group and between group variances among the study groups. Analysis of variance of different study groups at a particular time interval revealed the differences amongst them. The Pearson's correlation analysis was applied to determine the correlation between Hcy and Vitamin B_{12} level. The data were expressed as mean±standard deviation (SD) and $P<0.05$ considered as statistically significant value.

RESULTS

Age of subjects ranged from 2 to 10 years with a mean age of 4.67 ± 2.15 years. Majority were male (65.7%) and 24 (34.3%) were female. Half (n = 35; 50%) had moderate-to-severe hearing loss while remaining half (n = 35; 50%) had severe to profound hearing loss. Vitamin B_{12} level of study population ranged from 120 to 396 pg/ml with a mean of 222.04 ± 79.70 pg/ml. Hcy level of the study population ranged from 4.1 to 23.58 μmol/ml with a mean of 12.31 ± 4.70 μmol/ml [Table 1].

In Table 2, mean Vitamin B_{12} level w significantly higher among those with moderate-to-severe hearing loss (241.06 ± 75.25 pg/ml) as compared to those having severe to profound hearing loss (203.03 ± 80.53 pg/ml) (P = 0.045). On the other hand, mean Hcy level was significantly higher among those having severe to profound hearing loss (13.49 ± 4.60 μmol/ml) as compared to those having moderate-to-severe hearing loss (11.14 ± 4.57 μmol/ml) (P = 0.035).

Table 1: General profile and clinical characteristics of subjects (n=70)

Characteristic	Statistic
Mean age±SD (Range) in years	4.67±2.15 (2-10)
Sex	
Male	46 (65.7%)
Female	24 (34.3%)
Type of hearing impairment	
Moderate to severe	35 (50.0%)
Severe to profound	35 (50.0%)
Mean Vitamin B_{12} level±SD (Range) (pg/ml)	222.04±79.70 (120–396)
Mean homocysteine level±SD (Range) (μmol/ml)	12.31±4.70 (4.1–23.58)

Table 2: Comparison of general and clinical profile between different types of hearing impairment

Characteristic	Moderate to severe impairment (*n*=35)	Severe to profound impairment (*n*=35)	Statistical significance
Mean age±SD in years	4.57±2.21	4.77±2.12	"t"=0.386; *P*=0.700 (NS)
Sex			
Male	22 (62.9%)	24 (68.6%)	χ^2=0.254; *P*=0.615
Female	13 (37.1%)	11 (31.4%)	
Mean Vitamin B_{12} Level±SD (pg/ml)	241.06±75.25	203.03 ±80.53	"t"=2.041; *P*=0.045
Mean homocysteine level±SD (Range) (μmol/ml)	11.14±4.57	13.49±4.60	"t"=2.146; *P*=0.035

Table 3: Correlation between Vitamin B_{12} and homocysteine level

Comparison	Correlation	Significance
Vitamin B_{12} versus homocysteine (Overall) (*n*=70)	−0.691	<0.001
Moderate-to-severe hearing loss (*n*=35)	−0.779	<0.001
Severe to profound hearing loss (*n*=35)	−0.572	<0.001

In [Table 3] on evaluating the correlation between Vitamin B_{12} level and Hcy level, a strong inverse significant correlation was observed for overall cases (r=−0.691; $P < 0.001$) and strongly significant for moderate-to-severe hearing loss group (r=−0.779; $P < 0.001$). The correlation was moderate significant for severe to profound hearing loss group (r=−0.572; $P < 0.001$).

DISCUSSION

In the present study, mean Vitamin B_{12} level was compared between two groups of hearing loss moderate to severe hearing loss and severe to profound hearing loss which showed that Vitamin B_{12} level is inversely related to degree of severity of hearing impairment and mean Hcy level was significantly higher among those having severe to profound hearing loss as compared to those having moderate-to-severe hearing loss. Increase in serum Hcy level is proportional to degree of hearing impairment.

The another study of Taha *et al*. also showed that median Vit. B_{12} level was significantly higher in the control group than in the severe to profound and moderate-to-severe SNHL group ($P < 0.001$).[16] Another hypothesis was given by Houston *et al*. that impairment of myelination of neurons may be due to Vitamin B_{12} deficiency in the cochlear nerve; thus, hearing is affected.[17] This may be explained by Vitamin .B_{12} deficiency leads to delay development of brain through demyelination, inflammation, and simulating an autoimmune process that blocks intrinsic factor for Vitamin B_{12} absorption. Gocer *et al*. also found that correlation analysis between the mean level of Hcy and Vitamin B_{12} level of the hearing impaired and control group yielded statistically significant differences. They concluded that high Hcy with low Vitamin B_{12} level may be cause for hearing loss.[18] Many changes in microvessel flow, permeability, cochlear blood flow, and stria vascularis atrophy may be due to elevated Hcy level in hearing loss. Increased Hcy and low Vitamin B_{12} level has been shown to be risk factors for cerebral, coronary, and peripheral vascular diseases.[13] This may be risk factor for blood supply of cochlea, leading to SNHL. Hyperhomocysteinaemia may be involved in SNHL. This has been investigated by some authors with divergent results.[19]

A study should be conducted with larger sample size from different cross-section of society and demographic profile for the normal value of Hcy and Vitamin B_{12} level. Further, larger sample is required to conclude on the definite inference on the correlation between Hcy and Vitamin B_{12} level for diagnostic marker to diagnose early cases of SNHL in children.

CONCLUSION

In this study, we found that increase Hcy level is inversely related with decrease Vitamin B_{12} level. This affects the circulation of cochlea and may be reason of SNHL. Thus, increase Hcy level may be used as a predictor for early detection of SNHL so that early therapeutic interventions can be started to improve the hearing in children.

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