ORIGINAL RESEARCH PAPER

ENT

STUDY OF INCREASED RISK OF SENSORI NEURAL HEARING LOSS DUE TO ATHEROSCLEROSIS.

KEY WORDS:

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INTRODUCTION: If some known risk factors for atherosclerosis like age, gender, obesity, diabetes ,blood pressure, dyslipidaemia, chronic kidney disease, high-sensitivity C-reactive protein (HSCRP), smoking and alcoholism are used as diagnostic tool to predict and access the nature and severity of SNHL atherosclerotic patients , significant morbidity and mortality can be averted by simple audiometric screening because atherosclerotic restriction of blood supply of peripheral and central auditory pathways can reflect itself in audiometry. The present study was designed to study the correlation of etiologies of atherosclerosis contributing SNHL and to study the magnitude and type of SNHL of common contributing factors for atherosclerosis.

METHOD: This prospective was done on three thousand five hundred and seventy six (3576) atherosclerotic patients (age group 20 – 55 years) attending the out-patient department with documented presence of positive risk factors. Age was limited to 55 years to exclude presbycusis. Atherosclerosis was measured from mean carotid intima-media thickness and the presence of carotid artery plaque. All patients had otoscopic examination and standard pure tone audiometry. Descriptive statistical analysis was done.

RESULT: Majority of the patients had combination of risk factors. 184(5.1%) patients had normal hearing. 1876 (52.4%) had mild SN loss, 954 (26.6%) had moderate SN loss and 546 (15.2%) had moderately severe SN loss. Only 11 patients(0.3%) had severe SN loss and 5 patients(0.1%) had profound SN hearing loss.

CONCLUSION: From best of our knowledge, this study is first to investigate the risk of hearing loss in patients with atherosclerosis. So dedicated research is required on larger samples.

INTRODUCTION

Atherosclerosis is a well-established risk factor for vascular occlusion of large arteries in coronary, cerebral, and peripheral circulation. Studies had conclusive evidence that it may play a similar role in the impairment of cochlear perfusion at terminal capillary beds[1]. Occlusive diseases of the vertebrobasilar system and carotid artery obstructive disease may reduce the blood flow through the labyrinth artery, thus leading to cochleovestibular manifestations such as sudden hearing loss and vertigo, which may be associated with symptoms relating to ischemia of the cerebral trunk[2] . The cochlea being an end organ is metabolically dependent on endarterial blood supply for nutrients and oxygen to maintain its normal physiological function which is very sensitive to alterations in blood circulation [3]. Cochlear ischaemia is considered to be one of the most important causes of idiopathic SNHL. Etiopathogenesis of the SNHL in atherosclerotic patients are probably due to microcirculatory failure, prothrombotic susceptibility, and inflammatory state of these high risk patients. Atherosclerosis of carotid artery is an well established important indicator of increased risk of stroke or myocardial infarction . Cochleovestibular symptoms due to low flow in the labyrinth artery. usually precede neurological manifestations leading to deafness along with vertigo. This most common clinical feature of cerebro basilar circulatory insufficiency due to atherosclerosis often goes undiagnosed and untreated. If some known risk factors for atherosclerosis like age, gender, obesity, diabetes ,blood pressure, dyslipidaemia, chronic kidney disease, high-sensitivity C-reactive protein (HSCRP), smoking and alcoholism are used as diagnostic tool to predict and access the nature and severity of SNHL atherosclerotic patients , significant morbidity and mortality can be averted by simple audiometric screening because atherosclerotic restriction of blood supply of peripheral and central auditory pathways can reflect itself in audiometry.

Rosen hypothesized low rates of cardiovascular disease (CVD), diabetes, and hypertension along with physically active lifestyles with low rates of smoking and noise exposure, and high fruit and fiber consumption may have contributed to the Mabaans' retaining good hearing sensitivity at older ages.[4] In a series of early ecologic studies, he found worse hearing in people living in areas with high rates of CVD compared to those living in areas with lower background rates of CVD.[5] It has been observed that women with ischemic heart disease were more likely than controls without atherosclerosis to have HI.[6] In the Framingham Heart Study, HI was associated with CVD events. Socioeconomic status, BMI and waist circumference, which are CVD risk factors, have been found to be associated with the incidence of hearing impairment in longitudinal studies.[7].

Therefore, we designed this study to explore whether peripheral vascular inflammatory markers combined with metabolic or hemostatic parameters could predict incidence of SNHL in patients of atherosclerosis.

AIM OF THE STUDY
1. To study the correlation of etiologies of atherosclerosis contributing SNHL .
2. To study the magnitude and type of SNHL of common contributing factors for atherosclerosis.

STUDY DESIGN
Prospective, observational and analytical.

MATERIALS AND METHODS
Study area: Department of MEDICINE, Mursidabad Medical College, Berhampore. West Bengal. India.

Study period: December, 2014 – December, 2019.

Ethical clearance: Institutional ethics committee clearance was taken prior to the commencement of the study.

Study sample- Three thousand five hundred and seventy six (3576) patients (age group 20 – 55 years) attending the out-patient department with atherosclerosis with evident presence of positive risk factor like age, gender, obesity, diabetes ,blood pressure, dyslipidaemia, chronic kidney disease, high-sensitivity C-reactive protein (HSCRP),

smoking and alcoholism were evaluated. Particularly, age was limited to 55 years for purposes of excluding presence of presbycusis.

Atherosclerosis was measured as the mean carotid intima-media thickness and the presence of carotid artery plaque. They were further subdivided in multiple groups depending the duration of contributing risk factor.

INCLUSION CRITERIA
All patients with current confirmed presence of atherosclerosis in carotid Doppler aged between 20-55 years were included in the study.

EXCLUSION CRITERIA
Patients with history of the following were excluded from the study.
1) Acute inflammation, infection, autoimmune disorders.
2) Fluctuating cochlea-vestibular dysfunction suggestive of endolymphatic hydrops (history of vertigo with either fluctuating hearing loss, aural pressure or episodic tinnitus preceding the idiopathic sudden onset sensori neural hearing loss episode);
3) History of otological surgery;
4) Head and/or neck trauma or barotraumas
5) Otitis media;
6) Neurologic disorders that predispose a patient to deafness;
7) Recent use of ototoxic medications;
8) Neoplasm within the previous two years;
9) History of familial deafness.

STUDY METHOD
Informed consent was obtained from all participants prior to each examination.
1. Thorough history, physical examination and doppler exam of upper neck were done on an outpatient basis.
2. High resolution B-mode ultrasound was used to measure Carotid intima media thickness (IMT) and plaque were measured on the right and left sides using a modified Atherosclerosis Risk in Communities (ARIC) study protocol. Expert radiologists measured the IMT of the near and far walls within 1.0 cm segments of the common carotid, bifurcation, and internal carotid artery. The mean IMT was the average of the 12 wall measurements. Plaque was considered present if, with acoustic shadowing there was a change in the wall shape or texture or an IMT> 1.5mm, or without acoustic shadowing at least two of the previously mentioned changes were present. The number of sites with plaque (0 to 6) was scored.[7].
3. Complete history including smoking history by pack years unit were documented.
4. All patients obtained cardiology opinion and underwent a through physical examination including body mass index (BMI), waist circumference and blood pressure assessment. Body mass index was calculated as weight in kilograms divided by height in meters squared. Three BP measures were taken with the participant sitting quietly. The average of the 2nd and 3rd sets of systolic and diastolic pressures were used in these analyses. Hypertension defined by blood pressure more than 140/90 mmHg. An electrocardiogram (ECG) was also performed. Patients diagnosed with dysrhythmia, were subjected to Echocardiography and Halter examination for further assessment.
5. Venous blood samples were collected from patients and control subjects after at least 12 h of fasting for the evaluation of plasma lipids. Serum total cholesterol was measured in all patients .Serum HDL cholesterol , Non-HDL cholesterol , low-density lipoprotein (LDL), total cholesterol, triglycerides (TG)were measured .
6. Fating blood sugar (FBS) and post prandial blood sugar, glycosylated haemoglobin (Hb1Ac) were measured.

7. High sensitivity C-reactive protein (HSCRP) was measured in patients with presence of more than 5 risk factors.
8. Pharmacological history of statins, antihypertensive therapy (including nitrates, angiotensin-converting enzyme inhibitors, betablockers, angiotensin receptor blockers, and calcium channel blockers).
9. All patients were subjected otoscopic examination and hearing assessment using standard pure tone audiometry at 250, 500, 1000, 2000, 3000, 6000, 7000, and 8000 Hz. Because bone conduction hearing testing is limited to 4000 Hz, measurements ≥4000 Hz were performed using air conduction testing alone. The sensorineural hearing at high frequencies (8000 Hz) tested by air conduction is unaffected by and independent of middle ear effusion. An average of the threshold levels of >26 db was considered as abnormal. A hearing loss of 26–40 db was classified as mild, 41–55 db as moderate, 56–70 as moderately severe, 71–90 as severe, and >90 db as profound hearing loss. Air and bone conduction thresholds were compared to identify the type and degree of hearing loss.

RESULT & ANALYSIS
Figure : 1 Patient Distribution In Major Categories
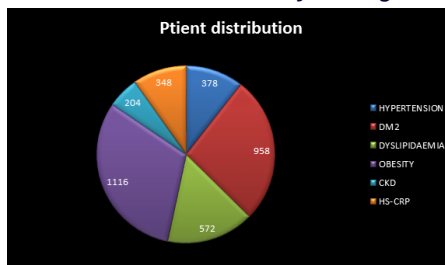
Out of 3576 patients , most of the patients ,1116,were obese. 958 patients were solely diabetic,204 patients had CKD,378 patients were hypertensive,572 patients solely had dyslipidaemia and 348 patients who had more than 5 risk factors, were positive for HS-CRP. Majority of the patients had combination of risk factors.

Diagram :2 Distribution Of Patients According To Presence Of Risk Factors Of Atherosclerosis Along With Duration
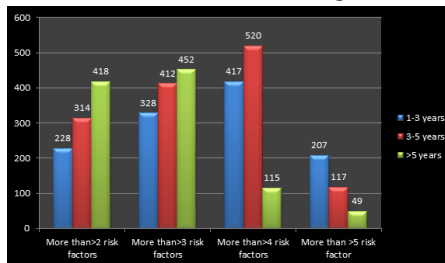

Diagram 2 shows distribution of patients according to presence of risk factors in respect to duration of atherosclerotic state.
• For 1-3 years duration, 228 patients had more than 2 risk factors,328 patients had more than 3 risk factors,417 patients had more than 4 risk factors and 207 patients had more than 5 risk factors.
• For 3-5 years duration, 314 patients had more than 2 risk factors,412 had more than 3 risk factors,520 had more than four risk factors and 117 patients had more than 5 risk factors.
• For 5 years duration, 418 patients had more than 2 risk factors,452 had more than 3 risk factors,115 patients had more than 4 risk factors and 49 patients had more than 5 risk factors.

So from this study it is evident that patients having more 4 and 5 risk factors have significantly poor life expectancy in comparison to those having fewer than 3 risk factors of

atherosclerosis at a time. High risk patients with poorly controlled status often succumbed to catastrophic conditions like cerebro vascular accident and myocardial infarction causing high morbidity and mortality.

CHART: 1 World Health Organization(WHO) classification of hearing loss

Mild	26-40
Moderate	41-55
Moderately severe	56-70
Severe	71-91
Profound	>91

Chart 1 shows WHO classification of hearing loss which was used to categorize patients of this present study.

Degree of hearing loss	dB hearing loss

Chart:2 Mean Frequency-specific Results In Pta (db) Of The Patients With Atherosclerosis

Frequency group Ear	250 Hz		500Hz		1000Hz		2000Hz		4000Hz		8000Hz	
	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right	Left
DM2	15.2	14.3	22.7	22.3	24.3	23.7	28.6	27.3	36.6	35.7	43.2	41.5
Hypertension	10.6	9.1	12.5	11.7	16.2	15.8	19.7	19.1	25.4	24.8	29.5	28.8
Dyslipidaemia	15.4	14.8	23.5	23.1	25.6	25.1	31.3	30.2	38.5	38.2	47.2	46.1
Obesity	9.5	9.1	10.4	10.2	14.4	14.1	19.2	18.7	21.4	20.3	25.5	24.2
CKD	15.7	15.2	21.3	21.1	27.2	26.2	32.1	31.1	37.2	37.1	44.2	43.2
Smoking & Alcoholism	12.3	12.1	14.2	14.1	18.2	17.8	23.4	22.3	28.3	28.2	34.2	34.1
>2 risk factors present at a time	18.2	18.1	24.6	23.8	29.3	29.2	36.4	36.2	42.4	41.6	47.2	46.4
>3 risk factors present at a time	20.3	19.7	25.3	25.1	31.1	29.7	38.3	37.1	43.2	43.5	48.6	47.5
>4 risk factors present at a time	23.2	22.1	26.1	25.8	32.3	31.1	40.8	40.2	48.6	48.2	54.2	53.2
>5 risk factors present at a time	24.6	24.1	28.4	27.5	35.6	34.8	48.6	43.4	57.1	57.2	61.5	60.8

Chart 2 shows mean of each frequency of each ear of different types of patients of atherosclerosis .

All patients of atherosclerosis had high frequency hearing loss in variant grades. Patients of DM2 , dyslipidaemia and CKD had demonstrated some low frequency hearing loss along with high frequency hearing loss. It was evident that patients with higher combination of risk factors had higher degree of hearing loss. Patients with more than 5 risk factors were subjected higher degree of SN hearing loss. In our present study the mean frequency specific loss was even upto 60 Db.

Diagram:3 Degree of SN hearing loss of Atherosclerosis based on pure tone audiometry(PTA)
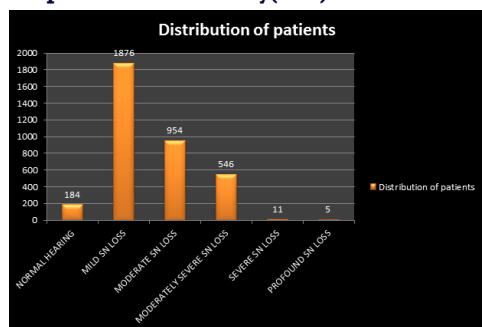
Distribution of patients

Out of 3576 patients, 1876 patients (52.4%) patients were noted to have mild SN hearing loss.954 patients (26.6%) had moderate SN loss and 546 (15.2%) patients had moderately severe SN loss. Only 11 patients(0.3%) were noted to have severe SN loss and 5 patients(0.1%) had profound SN hearing loss.184(5.1%) patients were noted to have normal hearing.

DISCUSSION

There are several traditional risk factors like diabetes mellitus, hypertension, smoking and dyslipidemia that usually cause atherosclerosis. Based on paraclinical data, HSCRP is a known predictor of atherosclerosis and acute coronary events. The intima media thickness (IMT) is also a helpful marker based on carotid intimal thickness to predict atherosclerotic changes throughout the body[21].The association between inner ear disorders and hemodynamic instability has been widely outlined and observed clinically in both children and adult patients. The pathophysiology of underlying hearing loss is mainly due to impaired blood perfusion to the inner ear which is particularly sensitive to circulatory alterations because of a lack of sufficient collateral circulation [8]. Previous studies have suggested that

thromboembolism due to atherosclerosis ultimately leading of ischemia changes the supply of blood to the inner ear and causes of hearing impairment[9]. Ischemia due to atherosclerotic thromboembolism of the anteroinferior cerebellar artery or megadolichobasilar artery devascularize the endarterial blood supply of cochlea. Cochleovestibular symptom occurs due to low flow in the labyrinth artery. In most studies, the clinical description was of sudden hearing loss and severe vertigo, thus demonstrating vestibular areflexia in 83% of the cases. Occipital headache, diplopia, cerebellar ataxia, hemiparesis, facial hypoesthesia, dysphasia and dysphonia may be associated symptoms.[10].

Intima-media thickness and plaque count in the carotid artery may be used as markers of generalized vascular disease causing microvascular compromise of stria vascularis in the lateral wall of the cochlea. This stria vascularis is actually the electrochemical pump involved in the endolymphatic potential which performs the amplification function of the cochlea.[11] Animal models have demonstrated age-related degeneration of the stria vascularis[12] probablydue to microvasculature changes such as reductions in capillary densities and vessel diameters[13,14]A relationship between strial atrophy and age has also been found in a study using human temporal bones[15].A reduction in blood flow to the stria vascularis may thus contribute to a loss in the endolymphatic potential resulting in diminishment of cochlear amplification. Blood flow reduction may also be associated with the histopathological changes observed with age in the organ of Corti, such as the loss of hair cells[16]. Another possible mechanism for the involvement of atherosclerosis with SN hearing loss is because of its association with oxidative stress which has been found to be related to hearing loss[17].

Unlike other animal species, the regeneration ability of vestibular and cochlear hair cells of mammals is completely limited after birth [18], and many reasons such as diseases, noise and drugs can result in the degeneration and necrosis of the inner hair cells, leading to the SNhearing loss in mammals at last. Research has proved that the envelope protein is contributed to the function of hair cells in the inner ear as an important material base, in which the prestin is one of most important envelope proteins, and is mainly adjusted by cholesterol [19]. In addition, the activity of hair cells was reduced when they were cultured *in vitro* with high cholesterol medium, which could be caused by the significant amount of cholesterol aggregated in the hair cell membrane. In the contrary, the activity of hair cells increased after the

cholesterol was washed from the cell membrane [20].

To the best of our knowledge, this is the first study to investigate the risk of hearing loss in patients with atherosclerosis. The duration of the study was sufficient enough to observe the magnitude of SN loss due to common etiologies of atherosclerosis. It was evident that patients with higher number of combination of risk factors had higher degree of hearing loss. Patients with more than 5 risk factors were subjected higher degree of SN hearing loss. In our present study the mean frequency specific loss was even upto 60 Db. It is hypothesized from this current study that systemic stress-related chronic inflammation would impair endothelial function and then produce atherosclerosis. Atherosclerosis is known to predispose clot formation, which may get free and circulate into the terminal labyrinthine artery or its branches; this can lead to ischemic changes in microvascular structures of cochlea which finally causes SN hearing loss. Out of 3576 patients, 1876 patients (52.4%) patients were noted to have mild SN hearing loss.954 patients (26.6%) had moderate SN loss and 546 (15.2%) patients had moderately severe SN loss. Only 11 patients(0.3%) were noted to have severe SN loss and 5 patients(0.1%) had profound SN hearing loss.184(5.1%) patients were noted to have normal hearing. So it was evident that hearing loss is a part of the spectrum of atherosclerosis-related disorders. The major strength of the present study is that it was a prospective study design in which hearing sensitivity was measured by standard audiometric methods, thus providing an excellent opportunity to evaluate the relationship between atherosclerosis and the 5-year risk of hearing impairment.

CONCLUSION
Atherosclerosis is a whole-body phenomenon, changes of as little as 0.1 mm in small vessels such as the labyrinthine artery (which is only 0.5 mm in diameter) can deleteriously influence the blood flow in cochlea ultimately affecting the perception of hearing. The present prospective study of atherosclerotic patients showed the magnitude of SN hearing loss in different categories of patients. Still dedicated future studies are required on larger samples to predict burden hearing loss in patients of vascular , metabolic and systemic disorders.

ABBREVIATIONS
1. SNHL - Sensorineural hearing loss
2. CKD - Chronic kidney disease
3. HS-CRP - High selective C reactive protein
4. CVD - Cardiovascular disease
5. HI - Hearing Impairment
6. CAD - Coronary artery disease
7. CVA - Cerebrovascular accident
8. BMI - Body mass index
9. DM2 - Diabetes Mellitus
10. IMT - Intima media thickness
11. ARIC - Atherosclerosis Risk in Communities
12. BP - Blood pressure
13. ECG - Electrocardiogram
14. HDL - High density lipoprotein
15. LDL - Low density lipoprotein
16. TG - Triglyceride
17. FBS - Fasting blood sugar
18. PPBS - Postprandial blood sugar
19. Hz - Hertz
20. WHO - World Health Organization
21. PTA - Pure tone audiometry
22 dB - Decibel

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