A COMPARATIVE STUDY OF METABOLIC DISORDERS IN VERTIGO

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ABSTRACT

BACKGROUND

Vertigo is a common medical condition, affecting around 1.8% of young adults to more than 30% in the elderly. Metabolic disorders commonly related to labyrinthine dysfunctions are glucose metabolism changes (diabetes, reactive hypoglycaemia and hyperinsulinaemia), thyroid hormones and lipid metabolism disorders.

The objective of this study is to compare the prevalence and association of metabolic disorders in vertigo cases to control under study.

MATERIALS AND METHODS

A case controlled study was done on patients presenting in ENT OPD, VIMSAR, Burla, with complaints of vertigo. 110 patients were chosen for the study between September 2015 and August 2017 and compared to age and gender matched controls (110). All patients and controls had the following blood investigations done: Fasting Blood Sugar (FBS), Oral Glucose Tolerance Test at 2 hrs. (OGTT2), thyroid profile (Free T3, Free T4, TSH) and Lipid Profile (Triglyceride (TG) and Low-Density Lipoprotein (LDL)). The metabolic disorders found were also compared to the ones found in the general population. The results were tabulated on excel sheets and statistical comparison and analysis was done with SPSS Version 16.0. Mann-Whitney U Test and chi-square test was applied for comparison. Statistical significance was set at $p < 0.05$.

RESULTS

The no. of vertigo patients with Type-2 diabetes mellitus were higher(1) in patients than controls.(2) Cases had more prevalence of thyroid disorders(3) than controls.(4) The incidence of abnormal lipid profile was higher in cases (35 cases with impaired TG, 27 cases with impaired LDL) than controls (17 each with impaired TG and LDL). The difference was significant in majority of parameters (FBS- $p < 0.015$; OGTT2- $p < 0.316$; T3- $p < 0.000$; T4- $p < 0.002$; TSH- $p < 0.000$; TG- $p < 0.003$; LDL- $p < 0.814$). The difference of diabetics and impaired glucose status in between cases of vertigo and controls are not statistically significant ($p=0.770$, $\chi^2=0.086$, chi-square test). The difference is highly significant in between cases and controls of thyroid disorder ($p=0.002$, $\chi^2= 14.66$) and lipid disorder ($p= 0.000$, $\chi^2= 12.53$, chi-square test).

CONCLUSION

Metabolic impairments in vertigo are substantial and hence cannot be ignored in management. FBS, TSH, T3, T4, TG and LDL values of cases were impaired more than controls and the difference was statistically significant for FBS, TSH, T3, T4, TSH and TG. Cases in our study had significantly higher prevalence of thyroid and lipid disorders than controls. This study could be applied in management of patients with chronic vertigo by dietary therapy or hormone replacement.

KEYWORDS

Vertigo, Metabolic Disorders, Diabetic Vestibulopathy, Hypothyroid Vestibulopathy, Lipid Disorders in Vestibulopathy.

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BACKGROUND

Vertigo is a medical condition where a person feels as if they or the objects around them are moving when they are not. Often it feels like a spinning or swaying movement. This may be associated with nausea, vomiting, sweating or difficulty walking. It is typically worsened when the head is moved. Dizziness is impairment in spatial perception and stability. In the community, the prevalence of dizziness ranges from 1.8% in young adults to more than 30% in the elderly.[5]

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Vertigo is associated with many metabolic disorders as accepted by many authors in the past. Metabolic disorders commonly related to labyrinthine dysfunctions are glucose metabolism changes (diabetes, reactive hypoglycaemia and hyperinsulinaemia),[6,7,8] thyroid hormones[9] and lipid metabolism disorders.[10,11]

Reports linking glucose metabolism with inner ear diseases date back in time, but it was not until 1960 glucose was recognised as one of the main elements responsible for maintaining of the inner ear functional activity.[12]

Ischaemic changes in the levels of glucose, glycogen, ATP and P-creatine are determined under "closed system" conditions in the organ of Corti, stria vascularis, ganglion spirale, cochlear nerve and vestibular sensory epithelia.[13] Immunohistochemistry approach has shown that the insulin receptor, insulin receptor substrate 1 (IRS1), protein kinase B (PKB) and insulin-sensitive glucose transporter (GLUT4) are expressed in the sensory epithelium of the human saccule,

which could explain link between diabetes and balance/hearing disorders.[14] Hence, the hair cells and the central vestibular system are sensitive to diabetes mellitus secondary changes, particularly small changes in blood glucose and insulin in plasma. This is further supported by clinical trial of IGF-1 treatment on human SSHL as well as in vivo animal experiments, which has confirmed its efficacy in hair cell injuries.[15] In a recent study, fractionated diet with glucose restriction was effective for the treatment of vestibular dysfunction associated with glucose metabolism disorders.[16] Disorders of glucose metabolism are considered the most common aetiology of metabolic labyrinthine disorders as per previous studies.

Talking about lipid metabolism, the increase of cholesterol blood level (LDL) and triglycerides are reported as aetiological agents of labyrinthine disorders.[11,4,17] While a greater prevalence of dyslipidaemia in sensorineural deafness patients is documented,[18,19] more recent studies disprove of any link.[20,21] One theory proposes that insulin and hyperinsulinaemia peripheral resistance would be responsible for increasing the production rate of triglycerides.[22] Chronic dyslipidaemia associated with elevated triglycerides may reduce auditory function, short-term dietary changes may not,[23] and lipid profile may not have a bearing on patients with idiopathic tinnitus.[24] Importance of dietary management of dyslipidaemia has been stressed for management of BPPV in elderly.[25]

Hypothyroidism may be responsible for elevated levels of circulating lipids. Thyroid disorders have affected both central and peripheral vestibular disorders in various experimental studies.[9,26] Thyroid hormone is suggested as a first transcriptional regulator of the motor protein prestin and as a direct or indirect modulator of subcellular prestin distribution[27] and autonomous functioning of TRα and TRβ in cochlear hair cells modulates active cochlear mechanics and inner hair cell output activity.[28] In hypothyroidism, vasopressin levels fall and increase in hypothyroid cases.[29] In contrast, aldosterone may be high in those who are hypothyroid due to the stimulating effect of TSH.[30] Vasopressin and Aldosterone ultimately cause electrolyte imbalance and hence induce vertigo.

Because of the importance of metabolic disorders in the field of labyrinthine dysfunction and a few discrepancies in literature, we decided to carry out an observation of patients with vertigo and prevalence of metabolic disorders in them in Indian patients.

Objective

To compare the prevalence and association of metabolic disorders in vertigo cases to controls under study.

MATERIALS AND METHODS

110 patients presenting in the Department of ENT and HN Surgery, VIMSAR, Burla with complaints of dizziness, between September 2016 and August 2017 were taken up for the study. Informed consent was taken from all patients. Patients with history of head trauma, taking neuropsychiatric medications and on oral contraceptive pills were excluded from the study. The 110 controls chosen were age and gender matched individuals.

Inclusion Criteria

1. Patients presenting with dizziness, 2. Age between 20 and 70 years, 3. Patients with informed consent for the study.

Exclusion Criteria

1. Patients with history of head trauma, 2. Intracranial tumours, 3. Patients on neuropsychiatric medications, 4. Patients on oral contraceptive pills, 5. Pregnancy.

In both groups, routine haematological investigations were carried out. Fasting blood sugar (FBS), Oral glucose tolerance test at 2 hours (OGTT2) with 75 mg of glucose, Thyroid profile (Free T3, Free T4, TSH) and Lipid profile (Triglyceride (TG) and LDL fraction of cholesterol (LDL)) were the parameters considered for the study. The normal values considered for the study were-

FBS

Less than 110 mg/dL; 111 - 125 (impaired fasting glucose); 126 or more- Frank diabetes mellitus.

OGTT2

Less than 140 mg/dL; 140 - 199 (impaired); 200 or more - frank diabetes.

Thyroid Profile

T3- (1.7-4.2) pg/mL; T4- (0.7-1.8) ng/ dL; TSH- (0.3-5.5) μIU/mL.

Lipid Profile

TG- less than or equal to 150 mg/dL; LDL- less than or equal to 130 mg/dL.

The data was tabulated on Excel Sheets and SPSS version 17 was used for statistical analysis. Mann-Whitney U test was used for comparison to see the statistical difference between variable parameters like FBS, OGTT2, TG, LDL etc. in vertigo cases with controls taken for the study. P value < 0.05 was taken as significant.

Chi-square test is used to see the association between metabolic disorders in vertigo cases with controls. P value <0.05 was taken to be significant.

RESULTS

Of the 110 patients and controls compared, 52 were males (47.27%) and 58 were females (52.73%) in cases and 50 were males (45.45%) and 60 were females (54.55%) in controls. The average age of the study group was 49.80 years and control group was 42.99 years.

The difference of FBS in case and controls were found to be significant (p= 0.015), but the difference in OGTT2 was not found to be significant (p= 0.316).

Of the cases 14 subjects (12.72%) had frank diabetes, while 7 (6.36%) individuals in controls had diabetes mellitus 2. The prevalence in general population is around 7.1% to 8.7% as per various studies.[31]

Impaired glucose tolerance was found in 25 cases (22.72%) and 15 controls (13.63%). The difference of levels of T3 (p= 0.00), T4 (p= 0.002) and TSH (p= 0.00) between cases and controls were found to be highly significant.

The difference of diabetics and impaired glucose status in between cases of vertigo and controls are not statistically significant (p= 0.770, ⍰= 0.086, chi-square test).

Thyroid disorders were found in 25 cases (22.72%) and 12 controls (10.90%). The incidence of thyroid disorders in Indian population is close to 11%.[32]

14 of the 25 cases (56%) and 7 of 12 controls (58.3%) were subclinical hypothyroid states. Subclinical hypothyroidism is the most prevalent thyroid disorder affecting 3% - 15% of the adult population.[33] Subclinical cases constituted 12.7% of sample size and 6.3% of controls, depicting similar levels to general population.

The difference of TG was significant in cases and controls (p= 0.003), whereas the difference was not significant in case of LDL (p= 0.81).

Lipid abnormalities with increased TG levels were seen in 35 cases (31.81%) and 17 controls (15.45%) and increased LDL were seen in 27 cases (24.54%) and 17 controls (15.45%).

The difference is highly significant in between cases and controls of thyroid disorder (p= 0.002, ⍰= 14.66) and lipid disorder (p= 0.000, ⍰= 12.53), chi-square test).

Recent reviews have reported that high cholesterol is present in 25% - 30% of urban and 15% - 20% of rural subjects.[34]

Combined TG and LDL increase was seen in 19 cases (17.27%) and 3 controls (2.72%).

Comparing the mean of individual parameters in cases and controls, we found a statistically significant difference in most.

Mean ± Standard Deviation of Individual Parameters of the Study							
	FBS	OGTT2	T3	T4	TSH	TG	LDL
Cases	99.091±	134.891±	2.4922±	1.1395±	5.1897±	137.0±	119.109±
	20.4103	27.3282	0.92	0.462	4.448	35.657	22.346
Controls	93.518±	134.927±	2.9141±	1.2710±	2.7562±	123.91±	115.836±
	17.6753	21.3858	0.984	0.374	2.646	25.667	20.824

Table 1. Table of Means of Individual Parameters in the Study, in Cases and Controls

From the above table, it is clear that the levels of FBS in cases was higher suggesting impaired carbohydrate metabolism in patients with dizziness. The levels of thyroid hormones were lower and TSH was higher in cases suggesting a higher prevalence of hypothyroid states in patients. TG and LDL levels were also higher in patients suggesting dyslipidaemia as a contributor to disease pathogenesis.

Table 2 and 3. Median and IQR values of Cases and Controls

	MEDIAN	IQR
FBS	98	87-115.5
OGTT2	128	115.7-144.2
TG	134	109.7-158
LDL	114.5	104-128.5
T3	2.4	1.8-3.1
T4	1.19	.86-1.38
TSH	4.49	2.8-5.4

Table 2. For Cases

	MEDIAN	IQR
FBS	92	78.7-105.5
OGTT2	129	121.7-138
TG	119.5	105.7-135
LDL	119.5	107.7-122
T3	2.94	2.2-3.63
T4	1.32	1.15-1.46
TSH	1.84	0.96-3.31

Table 3. For Controls

The difference was significant in the following parameters

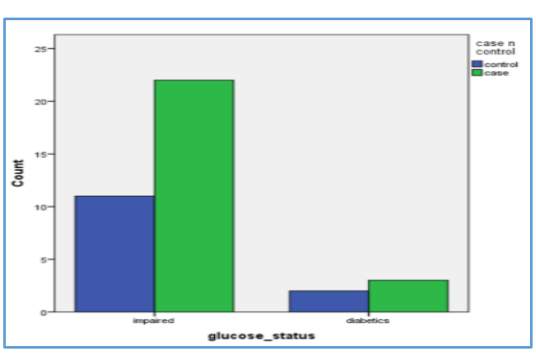

Figure 1. Graphical Representation comparing Diabetics and Impaired Glucose Status (More Prevalence in Cases than Controls)

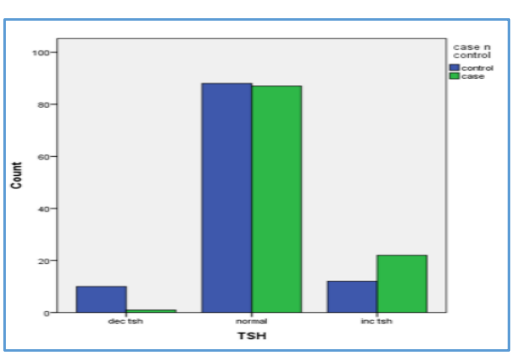

Figure 2. Graphical Representation comparing Hypothyroid, Hyperthyroid and Euthyroid States (In Terms of TSH) in Cases and Controls showing more Prevalence of Hypothyroid States in Cases

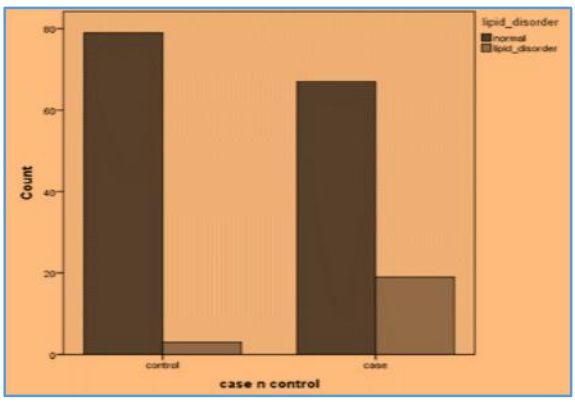

Figure 3. Graphical Representation comparing Prevalence of Lipid Disorders (More in Cases than Controls)

DISCUSSION

Inner ear, despite being considered a physiological masterpiece, is subject to influence and regulation by various metabolic mechanisms.

Evidence suggests that the stria is the site of intense metabolic activity in the labyrinth.[35,36] A study revealed vestibular caloric stimulation (CS) inhibited noradrenergic (NA) neurons of the locus coeruleus (LC) in rats and hence speculating that LC-NA inhibition participates in the development of sensory mismatch during vertigo and motion sickness.[37] In diabetes mellitus, the observed changes are microangiopathy and peripheral neuropathy with consequent terminal blood flow problems and irregular supply of glucose.[10,2] Some authors also reported minimal cellular changes and central vestibular system functional impairment as a complication of early diabetes mellitus, even without neuropathy or microangiopathy.[8,38,39] There are no tissue reserves of energy in the labyrinth and its ongoing activity makes it sensitive to variations of glucose supply during hypoglycaemia or in the presence of high insulin levels.[7,40] In a study subjecting cases to a 5-hour glucose tolerance test with simultaneous titration of insulin, it was found that 82% of the patients presented abnormal glucose and/or insulin values responding well to diet on followup.[41,42] Also, hyperglycaemia and thyroid disorders (discussed later) are much more frequent in patients with sudden deafness than in the general population and should be considered as important associated risk factors.[18] Of the cases in our study 14 subjects (12.72%) had frank diabetes, while 7 (6.36%) individuals in controls had diabetes mellitus 2, agreeing with previous studies.[43] Prevalence of diabetes in cases was also lower than general population. Impaired glucose tolerance was found in 25 cases (22.72%) and 15 controls (13.63%) coinciding with results of previous studies.[44] A study of biopsies of jejunal mucosa revealed abnormal enzyme activity or deficiencies in transport mechanisms of glucose, which further lays importance on close follow-up and dietary management options in managing vertigo in patients with impaired glucose tolerance.[45]

Variations in blood viscosity can compromise terminal flow into the cochlea, hampering oxygen supply required for Na/K system operation and maintenance of end cochlear potential.[11,4] Besides this effect, the metabolism of lipids is directly associated with that of insulin[46,1,47] and the association between lipid and carbohydrate disorders in patients with vertigo is related to increased risk of atherosclerosis or myocardial infarction.[11,4] Serum cholesterol and hyperlipidaemia as an aetiology of the atherosclerosis of all blood vessels also have a role in vestibule-cochlear vessels and usually above the age of 40 yrs.[3] Chronic hypercholesterolaemia with alterations in both the stria vascularis and outer hair cells metabolically stresses inner ear tissue increasing susceptibility to ototraumatic agents.[48] Our study found lipid abnormalities with increased TG levels were seen in 31.81% cases vs. 15.45% controls, and increased LDL were seen in 24.54% cases and 15.45% controls. This was more than the prevalence in general population. Combined TG and LDL increase was seen in 17.27% cases vs. 2.72% controls. The difference was significant for triglycerides in contrast to other studies, which found out higher rates of LDL disorders with normal triglyceride levels[49] or lower than population levels.[50] Thus, the role of triglycerides is still unclear and needs to be investigated further.

Studies assessing thyroid dysfunctions and the inner ear are still rare.[51] However, it was experimentally demonstrated that presence of the alpha and beta specific receptors for the thyroid hormone in the ear of mice are essential for its maturation.[52] Thyroid hormones are responsible for the performance of prestin protein directly linked to the outer hair cells activity as seen in rats. Absence of thyroid hormone stimulation impairs neural stimulus conduction in the central vestibular system.[53] Our study found out thyroid disorders based on TSH levels, which were found in 22.72% cases and 10.90% controls. Thyroid disorders in Indian population exhibit lesser prevalence than our cases. Studies have shown subjective improvement of all symptoms in Meniere's disease with hypothyroidism after 12 weeks of treatment.[54] Thyroid and lipid disorders showed statistically significant difference in our study, but diabetes and impaired glucose status were not significantly higher in cases in our study.

CONCLUSION

Metabolic impairments in vertigo are substantial and hence cannot be ignored in management. FBS, TSH, T3, T4, TG and LDL values of cases were impaired, more than controls and the difference was statistically significant for FBS, TSH, T3, T4, TSH and TG. Cases in our study had significantly higher prevalence of thyroid and lipid disorders than controls. This study could be applied in management of patients with chronic vertigo by dietary therapy or hormone replacement.

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