ISSN: 2581 – 3633
PubMed - National Library of Medicine - ID: 101745081

International Journal of Medical Science and Advanced Clinical Research (IJMACR)

Available Online at:www.ijmacr.com

Volume – 6, Issue – 6, November - 2023, Page No. : 11 - 21

Serum Ferritin and Lipid indices in acute cerebrovascular accident

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How to citation this article: Dr. K. S. Meera, Dr. Krishnamurthy U, "Serum Ferritin and Lipid indices in acute cerebrovascular accident", IJMACR- November - 2023, Volume – 6, Issue - 6, P. No. 11– 21.

Type of Publication: Original Research Article

Conflicts of Interest: Nil

Abstract

Background: Cerebrovascular accident is an emergency medical condition characterized by an acute compromise of the cerebral perfusion or vasculature. The leading cause of cerebrovascular accident is due to atherothrombosis. There is paucity of information on the role of serum ferritin and lipid indices in prognosis and outcome of acute cerebrovascular accident.

Objectives: The study was undertaken to assess serum ferritin levels and lipid indices in patients of acute cerebrovascular accident.

Methods: The study population consisted of 45 healthy controls and 45 clinically diagnosed CVA cases of either gender between 25-75 years of age who presented within 48 hours of onset of symptoms of acute cerebrovascular accident. Serum Ferritin and lipid profiles including Total cholesterol, triglyceride, high density lipoprotein (HDL-cholesterol), and low-density lipoprotein (LDL-cholesterol) were estimated. The atherogenic index and lipid indices were calculated using established formulas.

Results: The study shows high BMI, high waist hip ratio, increased systolic blood pressure and diastolic pressure in CVA cases with p value less than 0.01 with Mann Whitney U test (two tailed). Significant increase in levels of serum ferritin, total cholesterol, triglyceride, low density lipoprotein, TC: HDL ratio, non HDL cholesterol and TG: HDL ratio in CVA cases in comparison to controls. However, there was significant decrease in HDL level in cases as compared to controls. There was significant correlation of TG, TC: HDL and non HDL-c with serum cholesterol level in cases with Spearman rank correlation, reassuring atherogenic nature of cholesterol. A significant ($p < 0.01$) association was found between acute cerebrovascular accident risk and serum ferritin level in cases with chi-square test of independence. This

study provided evidence on the association of ferritin, lipids and lipid ratios with cerebrovascular accident.

Conclusion: These lipid indices and serum ferritin levels appeared to be of important prognostic indicators for identifying high-risk participants predisposed to cerebrovascular accident in men and women and may serve as potential targets for cerebrovascular accident prevention. This study highlights the utility of a simple, easily available serum marker in prediction and prognosis of acute ischemic cerebrovascular accident.

Keywords: Atherogenesis, Atherogenic Indices, Cerebrovascular Accident, Dyslipidemia, Ferritin, Ischaemia.

Introduction

Cerebrovascular accident is a medical emergency characterized by an acute compromise of the cerebral perfusion or vasculature. It contributes to significant cause of morbidity and mortality worldwide. 70% of cerebrovascular accidents and 87% of both cerebrovascular accident-related deaths and disability-adjusted life years occur in lower and middle-income socio-economic status family [1]

The leading cause of cerebrovascular accident is due to atherothrombosis. Thrombotic occlusions causing cerebral infarctions are usually superimposed on atherosclerotic plaques. Major risk factors for cerebrovascular accident include age, diabetes mellitus, hypertension, smoking and others [2]. Modification of risk factors, early diagnosis and prompt management in cerebrovascular accident (CVA) can reduce its outcome. Some of the prognostic indicators, which have gained larger clinical interest in recent times includes blood pressure, serum cholesterol, lipid indices and acute phase reactants.

The role of inflammatory markers in predicting functional outcome in CVA, still remains controversial. Iron profile and ferritin are known to have a significant role in cardiovascular disease, malignancy, neurodegenerative disorder, etc [3] Serum ferritin, an acute phase reactant have been used along with other clinical parameters for monitoring inflammation in high-risk patients. Initially, considered as a stress response to cerebrovascular accident, serum ferritin is under evaluation as a prognostic marker of cerebrovascular accident. Adverse level of lipid indices are already well established risk factors or outcome for hypertension, cardiovascular events and diabetes mellitus [4]. Elevated plasma concentration of low-density lipoproteins (LDL-cholesterol) and low level of high-density lipoprotein (HDL-cholesterol) concentration are accompanied with augmented risk of atherosclerosis. Although, there are many studies relating high levels of serum total and LDL - cholesterol and low levels of HDL-cholesterol with coronary atherosclerosis, the relation between serum lipids, lipoproteins and cerebrovascular atherosclerosis is not very well reported. There is paucity of information on the role of serum ferritin and lipid indices in prognosis and outcome of acute cerebrovascular accident; hence, this study was undertaken to assess serum ferritin levels and lipid indices in patients of acute cerebrovascular accident.

Material and methods

A prospective observational study was conducted on acute cerebrovascular accident cases admitted in the tertiary care hospital. The study population consisted of 45 clinically diagnosed CVA cases. Both male and female cases between 25-75 years of age who presented within 48 hours of onset of symptoms of acute cerebrovascular accident, diagnosed on the basis of clinical examination

and neuro-imaging (computed tomography/magnetic resonance imaging brain) indicative of cerebral infraction or intra-cerebral haemorrhage were enrolled for the study. The patients with underlying condition of liver disease, familial hypercholesterolemia and hypothyroidism, on drugs for dyslipidaemia, cerebral haemorrhage secondary to cerebral tumour or previous coagulation disorders were excluded from the study. The ethical clearance was obtained from the ethical review board of the institution. Control group included 45 healthy volunteers in same age group and had the same exclusion criteria as mentioned for cases. Consent was taken before collection of sample. After documenting demographic profile, relevant clinical history was taken. Clinical examination of the patients was performed and vitals were recorded. Following aseptic precautions, around 5 ml of venous blood sample was collected in BD vacutainer® gel tubes in healthy controls and within 48 hours of onset of manifestation in CVA cases. The collected samples were allowed to stand for 20 minutes. Serum was separated from samples after centrifugation at 3500 rpm for 15 minutes and stored till further processing. Lipid profile and serum ferritin were estimated in the samples at the earliest. Total cholesterol, triglyceride, high density lipoprotein (HDL-cholesterol), and low density lipoprotein (LDL- cholesterol) were estimated on cobas® 6000 analyser - Roche Diagnostics. Serum ferritin was estimated by ELISA. The atherogenic indices and lipid ratios were calculated. Atherogenic indices was calculated by using the formula: (TG/HDL-c). The other indices calculated includes TC/HDL-c and Non - HDL-c = Total Cholesterol - HDL-c

Statistical Analysis

Quantitative data summarized to test the difference in mean values obtained for Cases and Controls using Mann –Whitney U test. Further, two tailed Spearman Rank Correlation was used to correlate between the various parameters. Spearman's Rho (rs) was calculated to measure the strength and direction of the relationship between two variables. Significance is assessed at 5 % confidence interval. Statistical analysis was performed using SPSS 12.0 software.

Results

The study was conducted to do a comparative study of serum ferritin and lipid profile levels between controls and CVA cases. Table 1 shows difference in mean values from controls and cases using Mann Whitney U test. The table shows high BMI, high waist hip ratio, increased systolic blood pressure and diastolic pressure in CVA cases. An increase in serum ferritin level, total cholesterol, triglyceride, low density lipoprotein, TC: HDL ratio, non HDL cholesterol, TG: HDL ratio in CVA cases in comparison to controls. However, there was significant decrease in HDL level in cases as compared to controls. Table 2 shows Spearman’s rank correlation (two tailed) between demographic and quantitative profiles. BMI and WHR show significant correlation with weight in cases. There was significant correlation of TG, TC: HDL and non HDL-c with serum cholesterol level in cases, reassuring atherogenic nature of cholesterol Fig 1 shows significant correlation of ferritin with cholesterol, with p value of about 0.02 and rs=0.32. As in table 2, a significant correlation was observed between non HDL-c, TG:HDL-c, TC:HDL-c with TG levels in cases, with p value <0.01. There was statistically significant relation of LDL cholesterol with both systolic and diastolic blood pressure predisposing to greater atherosclerotic risk in these cases. The correlation between Non HDL cholesterol and ferritin, show rs value of 0.38 with p value of .003 (table 2, Fig 2). Similar correlation of non HDL cholesterol with WHR was observed (Fig 3). Serum TG

shows significant correlation with non HDL (Fig 4) and with HDL (table 2) at p value <0.01. Correlation of various profiles are represented in table 2. Table 3 represents chi-square test of independence of ferritin levels in cases. A significant association was found between acute cerebrovascular accident risk and serum ferritin level, with Ferritin χ^2 (2, N=90) = 67.9, p value<0.01. In the study, elevated serum ferritin was found to be independently related with risk factor for cerebrovascular accident along with other comorbid conditions.

Table 1: Mann–Whitney U test (two tailed)

	CONTROLS		CASES		Z Score	p value
	MEAN	SD	MEAN	SD		
Age(Yrs)	44.62	9.74	44.71	11.50	0.41559	0.67
Wt (kg)	67.02	7.70	74.67	8.62	-4.2608	< 0.01
Ht (m)	1.69	0.05	1.68	0.05	0.49225	0.62
BMI (kg/m^2)	23.60	2.60	26.34	2.31	-4.68043	< 0.01
Systolic BP mm Hg	132.18	5.67	151.29	10.74	-7.83164	< 0.01
Diastolic BP mmHg	80.93	6.17	91.96	6.01	-6.62119	< 0.01
WHR	0.96	0.04	1.04	0.04	-6.64943	< 0.01
TC (mg/dl)	152.87	6.45	173.99	36.41	-3.59102	< 0.01
TG (mg/dl)	121.53	13.33	172.16	57.81	-5.1404	< 0.01
HDL-c (mg/dl)	46.31	10.49	38.27	7.95	3.26016	< 0.01
LDL-c (mg/dl)	87.96	6.03	145.85	37.42	-6.79065	< 0.01
TC:HDL-c ratio	3.44	0.64	4.75	1.45	-4.51096	< 0.01
Non HDL-c (mg/dl)	106.56	12.16	135.72	37.10	-4.25677	< 0.01
TG:HDL-c ratio	2.73	0.59	4.76	2.10	-5.47529	< 0.01
Ferritin (ng/ml)	159.81	23.40	380.16	77.68	-8.15847	< 0.01

Table 2: Spearman Rank Correlation (two tailed) of demographic and quantitative parameters

	Age	Wt	Height	BMI	SBP	DBP	WHR	TC	TG	HDL-c	LDL-c	TC:HDL	Non HDL	TG:HDL	Ferritin
Age		rs= -0.01 p= 0.91	rs= 0.10 p=0.48	rs= -0.04 p = 0.77	rs= 0.62 p<0.01	rs = 0.33 p= 0.02	rs = -0.07 p = 0.64	rs =0.06 p = 0.68	rs = 0.07 p = 0.62	rs = 0.01 p = 0.93	rs = -0.05 p = 0.71	rs = 0.02 p = 0.87	rs = .04 p = 0.75	rs = 0.01 p = 0.97	rs =-0.02 p = 0.88
Weight	rs=0.01 p= 0.91		rs=0.60 p <0.01	rs = 0.84 p < 0.01	rs = -0.06 p = 0.66	rs = 0.11 p = 0.43	rs = 0.50 p < 0.01	rs = 0.16 p = 0.27	rs = 0.08 p = 0.59	rs = 0.33 p = 0.02	rs = -0.09 p = 0.51	rs =-.14 p = 0.32	rs = .08 p = 0.57	rs = -0.13 p = 0.36	rs = -0.09 p = 0.52
Height	rs= 0.10 p=0.48	rs= 0.60 p= <0.01		rs = 0.14 p = 0.35	rs = 0.06 p = 0.67	rs = 0.04 p = 0.77	rs = 0.25 p = 0.09	rs = 0.14 p = 0.34	rs = 0.19 p = 0.20	rs = 0.19 p = 0.19	rs = -0.07 p = 0.63	rs = -0.10 p = 0.49	rs = .08 p = 0.59	rs = 0.00 p = 0.99	rs = -0.16 p = 0.27
BMI	rs= -0.04 p = 0.77	rs= 0.84 p < 0.01	rs=0.14 p = 0.35		rs = -0.07 p = 0.61	rs = 0.19 p = 0.20	rs = 0.42 p <0.01	rs = 0.11 p = 0.44	rs = -0.01 p = 0.91	rs = 0.24 p = 0.10	rs = -0.05 p = 0.71	rs = -0.07 p = 0.61	rs = 0.06 p = 0.65	rs = -0.13 p = 0.36	rs = 0.00 p = 0.97

SBP	rs= 0.62 p <0.01	rs= -0.06 p= 0.66	rs= 0.06 p= 0.67	rs = -0.07 p = 0.61		rs = 0.44 p < 0.01	rs = -0.28 p = 0.06	rs = 0.04 p = 0.79	rs = 0.13 p = 0.39	rs = -0.06 p = 0.66	rs = -0.29 p = 0.04	rs = 0.09 p = 0.54	rs = 0.05 p = 0.73	rs = 0.10 p = 0.50	rs = 0.01 p = 0.93
DBP	rs=0.33 p=0.02	rs= 0.11 p = 0.43	rs = 0.04 p = 0.77	rs = 0.19 p = 0.20	rs = 0.44 p < 0.01		rs = 0.13 p = 0.36	rs = -0.04 p = 0.78	rs = 0.05 p = 0.73	rs = 0.16 p = 0.28	rs = -0.33 p = 0.02	rs = -0.13 p = 0.36	rs = -0.09 p = 0.55	rs = -0.04 p = 0.76	rs = 0.32 p = 0.02
WHR	rs=-0.07 p =0.64	rs = 0.50 p < 0.01	rs= 0.25 p = 0.09	rs=0.42 p <0.01	rs = -0.28 p = 0.06	rs = 0.13 p = 0.36		rs = 0.38 p <0.01	rs = 0.13 p = 0.38	rs = 0.30 p = 0.04	rs = -0.01 p = 0.91	rs = 0.05 p = 0.69	rs = 0.32 p = 0.02	rs = -0.04 p = 0.78	rs = -0.14 p = 0.35
TC	rs= 0.06 p= 0.68	rs= 0.16 p= 0.27	rs= 0.14 p= 0.34	rs = 0.11 p = 0.44	rs = 0.04 p = 0.79	rs = -0.04 p = 0.78	rs = 0.38 p <0.01		rs = 0.39 p < 0.01	rs = -0.02 p = 0.89	rs = 0.01 p = 0.90	rs = 0.66 p <0.01	rs = 0.96 p <0.01	rs = 0.29 p = 0.05	rs = -0.32 p = 0.02
TG	rs = 0.07 p= 0.62	rs= 0.08 p= 0.59	rs= 0.19 p= 0.20	rs = -0.01 p = 0.91	rs = 0.13 p = 0.39	rs = 0.05 p = 0.73	rs = 0.13 p = 0.38	rs = 0.39 p < 0.01		rs = -0.13 p = 0.37	rs = 0.02 p = 0.88	rs = 0.29 p = 0.04	rs = 0.38 p <0.01	rs = 0.82 p <0.01	rs = -0.19 p = 0.19
HDL-c	rs= 0.01 p = 0.93	rs= 0.33 p = 0.02	rs= 0.19 p= 0.19	rs = 0.24 p = 0.10	rs = -0.06 p = 0.66	rs = 0.16 p = 0.28	rs = 0.30 p = 0.04	rs = -0.02 p = 0.89	rs = -0.13 p = 0.37		rs = -0.24 p = 0.11	rs = -0.72 p <0.01	rs = -0.22 p = 0.14	rs = -0.61 p <0.01	rs = -0.07 p = 0.63
LDL-c	rs = -0.05 p = 0.71	rs= -0.09 p= 0.51	rs= -0.07 p= 0.63	rs = -0.05 p = 0.71	rs = -0.29 p = 0.04	rs = -0.33 p = 0.02	rs = -0.01 p = 0.91	rs = 0.01 p = 0.90	rs = 0.02 p = 0.88	rs = -0.24 p = 0.11		rs = 0.20 p = 0.17	rs = 0.08 p = 0.56	rs = 0.11 p = 0.43	rs = -0.07 p = 0.61
TC:HDL	rs = 0.02 p = 0.87	rs = -0.14 p = 0.32	rs = -0.10 p = 0.49	rs = -0.07 p = 0.61	rs = 0.09 p = 0.54	rs = -0.13 p = 0.36	rs = 0.05 p = 0.69	rs = 0.66 p <0.01	rs = 0.29 p = 0.04	rs = -0.72 p <0.01	rs = 0.20 p = 0.17		rs = 0.81 p <0.01	rs = 0.61 p <0.01	rs = -0.19 p = 0.20
Non HDL	rs = 0.04 p = 0.75	rs = 0.08 p = 0.57	rs = 0.08 p = 0.59	rs = 0.06 p = 0.65	rs = 0.05 p = 0.73	rs = -0.09 p = 0.55	rs = 0.32 p = 0.02	rs = 0.96 p <0.01	rs = 0.38 p <0.01	rs = -0.22 p = 0.14	rs = 0.08 p = 0.56	rs = 0.81 p <0.01		rs = 0.39 p >0.01	rs = -0.31 p = 0.03
TG: HDL	rs = 0.01 p = 0.97	rs = -0.13 p = 0.36	rs = 0.00 p = 0.99	rs = -0.13 p = 0.36	rs = 0.10 p = 0.50	rs = -0.04 p = 0.76	rs = -0.04 p = 0.78	rs = 0.29 p = 0.05	rs = 0.82 p <0.01	rs = -0.61 p <0.01	rs = 0.11 p = 0.43	rs = 0.61 p <0.01	rs =0.39 p >0.01		rs = -0.10 p = 0.49
Ferritin	rs = -0.02 p = 0.88	rs = -0.09 p = 0.52	rs = -0.16 p = 0.27	rs = 0.00 p = 0.97	rs = 0.01 p = 0.93	rs = 0.32 p = 0.02	rs = -0.14 p = 0.35	rs = -0.32 p = 0.02	rs = -0.19 p = 0.19	rs = -0.07 p = 0.63	rs = -0.07 p = 0.61	rs = -0.19 p = 0.20	rs = -0.31 p = 0.03	rs = -0.10 p = 0.49	

Table 3: chi-square test of independence (Ferritin)

	Normal Ferritin ng/ml	High Ferritin ng/ml	Marginal Row Totals
Controls	44 (24) [16.67]	1 (21) [19.05]	45
Cases	4 (24) [16.67]	41 (21) [19.05]	45
Marginal Column Totals	48	42	90 (Grand Total)

A chi-square test of independence showed that there was significant association between acute cerebrovascular accident risk and Ferritin χ^2 (2, N = 90) = 67.9, p = < 0.01

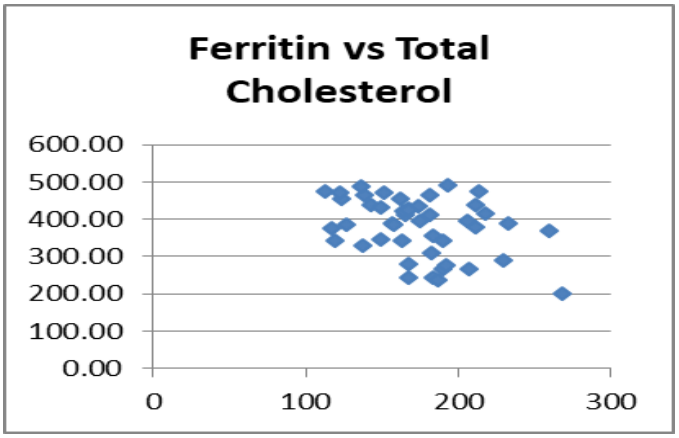

Fig 1: Correlation between Serum Ferritin and Serum Total Cholesterol in cases.

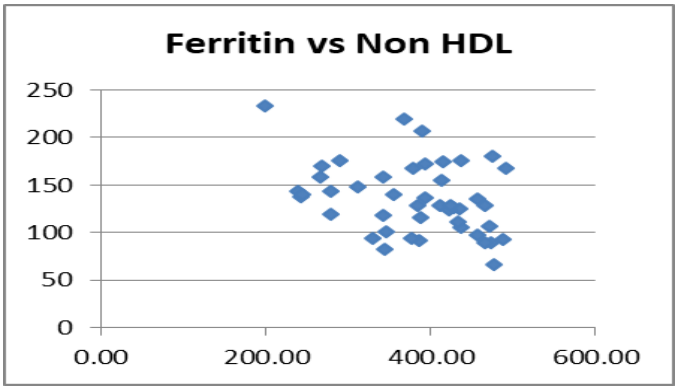

Fig 2: Correlation between Serum Ferritin and Serum non HDL cholesterol in cases

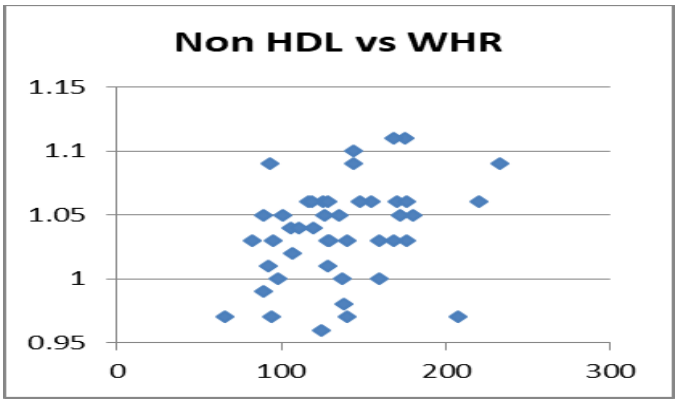

Fig 3: Correlation between non HDL cholesterol and Waist hip ratio in cases

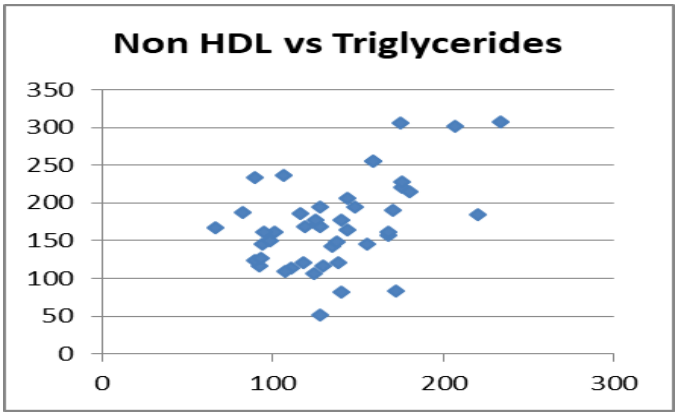

Fig 4: Correlation between non HDL cholesterol and Serum Triglyceride in cases.

Discussion

Cerebrovascular accident is a nontraumatic, focal vascular injury of the nervous system and results in permanent damage due to cerebral infarction or intracerebral hemorrhage and/ or subarachnoid

hemorrhage. It is one of the common preventable life-threatening neurological problem, worldwide and leading cause of death after heart diseases and cancer [5]. There are several etiologies and risk factors which are associated with predisposition to cerebrovascular accident. The present study was undertaken to find association of serum ferritin and lipid indices in acute cerebrovascular accident. Ferritin is present in most of the body cells in the form of cytosolic proteins. Ferritin makes iron available for critical cellular processes while protecting lipids, DNA, and proteins from the potentially toxic effects of iron. Alterations in ferritin are seen commonly in clinical practice, often reflecting perturbations in iron homeostasis or metabolism. CVA cause an increase in superoxide free radicals due to oxidant injury. The presence of superoxide oxygen radicals increases the amount of iron in the cytosol by releasing iron from ferritin. The amount of iron ions in the cytosol increases during oxidative stress. Free iron in the cell or the so-called labile iron pool (LIP) becomes a sensor for homeostatic iron in the cell [6]. When the iron in LIP increases, it acts as a source of iron for the Fenton reaction. The brain's oxygen demand increases when hypoxia occurs, resulting in an increase in the need for iron transport and its use in certain areas.

During hypoxia and oxidative stress, the synthesis of ferritin is increased in brain in response to the accumulation of reactive oxygen species as a part of neuroprotection, to quench reactive oxygen species [7]. Ferritin catalyzes the conversion of superoxide and hydrogen peroxide into highly reactive hydroxyl radical, during a state of cerebral hypoperfusion. Several studies have reported serum ferritin, to be an independent predictor of long-term functional outcomes in critically ill patients [8]. Higher serum ferritin levels can also be considered an indirect indicator of body iron store and subsequently reflected on the iron stores in the brain. When brain ischemia occurs during CVA, more iron will be released from the injured brain cells due to larger iron stores present in them. Consequently, there is enhanced oxidative stress in the local environment of the injured tissue, generating free radicals, especially hydroxyl radical resulting in aggravation of tissue injury during ischemia. During reperfusion, this tissue insult is further augmented because of reperfusion injury that causes even more iron release and even higher oxidative stress [9].

Release of free iron from intracellular stores such as ferritin as a result of cerebral ischemia, particularly during reperfusion, catalyses the generation of hydroxyl radical which destroys cellular and micro vascular integrity [10]. Due to increase in ferritin level there can be larger infarct volume, greater reactive oxygen species (ROS) generation in brain and peripheral vasculature and inflammatory response after thrombotic cerebrovascular accident [11]. These findings suggest that generation of ROS during reperfusion, increased excitotoxic damage, inflammation and blood brain barrier disruption might be potential mechanisms of increase in brain and endothelial injury in ischemic cerebrovascular accident patients with iron overload who are treated with t-PA. High serum ferritin levels are reported to be associated with poor functional outcome, haemorrhagic transformation and severe brain oedema in patients treated with tissue plasminogen activator (t-PA) after ischemic cerebrovascular accident [12].

Of the cerebrovascular disease, the most common is stroke, focal disruption of blood supply to some part of the brain. Other causes include transient impairment of blood flow to the entire brain, global ischemia, as occurs during cardiac arrest. When brain hypoxia or ischemia

occurs, tissue energy demands cannot be met, so ATP levels fall. Loss of ATP results in decreased function of active ion pumps, such as the Na^+- K^+ ATPase, the most important transporter for maintaining cation concentrations. Alteration of ion pump function leading to membrane depolarization, the opening of voltage-sensitive ion channels and a cascade of events which can be restricted to selectively vulnerable neuronal populations or may involve all cells resulting in tissue infarction. Hypoxia-ischemic state induces expression of ferritin in oligodendrocytes and microglia [13]. Elevated serum ferritin at admission has been reported to predict a poor prognosis in acute cerebrovascular accident patients, implicating potential increase in body iron stores before cerebrovascular accident onset can aggravate the cytotoxicity of brain ischemia. Sultana, et.al. have reported high serum ferritin influences the prognosis of ischemic cerebrovascular accident and also acts as a risk factor for ischemic episodes by enhancing atherogenesis [14]. The exact source and form of iron ions released during cerebral hypoxia have not yet been identified. There are several forms of iron imbalance in the brain after cerebrovascular accident, including interruption in transferrin, ferritin or transitional iron ions. It can be released from its binding with storage proteins in the brain in the event of hypoxic conditions. These free iron ions can oxidize lipids in the cell membrane and provoke an inflammatory response [15].

Although derangements in the lipid profile have been suggested as a risk factor for the development of cerebrovascular accident, studies show inconsistent results on the association between lipid profile and cerebrovascular accident. 91% of cerebrovascular accident patients had alterations in one or more lipid parameters considering values as per ATP III guidelines [16, 17]. All the parameters of lipid profile with exception to HDL-c, were significantly higher in cases when compared to controls. Our findings were inconsistent with studies by Bowman, et al. which reported the lack of association between lipids and cerebrovascular accident [18]. Lipid profile changes are thought to be a risk factor in the occurrence of CVA. On the other hand, CVA itself is also associated with changes in the lipid levels probably because of the accompanying stress and catecholamine overproduction that occurs during an acute cases [19].

Dyslipidaemia is also one of the major risk factors noted in patients of CVA without diabetes mellitus. It has been reported aggressive treatment of dyslipidaemia decreases the risk of cerebrovascular accident. The simultaneous use of lipid profile in ratio is more useful than individual lipid values as it more closely reflects the complex interactions of lipoprotein metabolism. The ratio of total cholesterol to HDL- c and to a lesser extent, the ratio of LDL- c to HDL-c have been shown to be better predictors of risk factors than lipid alone [20]. The possible differences in the effects of cholesterol at different vascular sites, could be the reason of complex association between serum cholesterol levels and CVA [21]. Some studies have proclaimed lipid ratio indicates the proportion of atherogenic to anti-atherogenic lipoproteins. Individuals with a high TC/HDL-c ratio have greater cerebrovascular accident risk undoubtedly owing to the imbalance between the cholesterol carried by atherogenic and protective lipoproteins.

Contrary to positive association between TG and cerebrovascular accident in some studies, others found no association [22, 23]. In the present study, high TG levels were found in acute cerebrovascular accident cases. Elevated level of TG indicates the presence of increased level of atherogenic remnant lipoproteins like LDL and small dense LDLs, consequently entry of large amounts

of cholesterol into the arterial intima predisposes to atherosclerosis and subsequently to cerebrovascular accident [24]. Some studies indicated no association between TG and cerebrovascular accident, and a systematic review showed a weak detrimental effect of higher triglyceride levels on cerebrovascular accident risk. The Copenhagen Male Study showed triglycerides on their own to be another strong risk factor, but it found that stratifying triglyceride levels by HDL-c levels led to more accurate detection of increased risk of coronary disease [25]. The ratio TG/HDL-c was originally proposed by Gaziano et al. [26]. It is an atherogenic index that has proved to be a highly significant independent predictor of myocardial infarction, even stronger than TC/HDL-c. The atherogenic link between high triglycerides and HDL-c is due to the higher plasma concentration of triglyceride-rich, very low-density lipoprotein that generates small, dense LDL during lipid exchange and lipolysis. These LDL-c particles accumulate in the circulation and form small, dense HDL-c particles, which undergo accelerated catabolism, therefore continuity of atherogenic circle. Thus this ratio can be considered a better, non-invasive profile for predicting the presence atherosclerosis. Evidently, findings of the study presented that a pattern of "high-TG and low-HDL cholesterol" pattern may be harmful. This "atherogenic dyslipidemia" has been considered as a surrogate marker of harmful small/dense LDL particles that could contribute to cerebrovascular diseases. Second, the hypertriglyceridemia itself could have harmful effects on cerebrovascular diseases, which is in line with several studies [27, 28].

Ferritin, being an acute-phase protein, should be estimated within 72 hours of symptom onset to exclude any possible elevations in an acute phase reaction. Serum ferritin levels were analysed within 48 hours of admission in the study and there is positive correlation between serum ferritin and non HDL cholesterol. The present study shows that monitoring of serum ferritin and several lipid indices levels during follow-up can offer significant benefit in prognosis of patients with CVA.

Strength of the study

Very few studies from India have focused on the role of serum ferritin along with lipid indices as a prognostic marker in acute cerebrovascular accident. Role of serum ferritin in prediction of cerebrovascular accident in high-risk cases is also supported by the observations in this study.

Limitation of the study

This was a single-centre study with a small sample size. Hence association cannot be significantly correlated. There is absence of data on lipid indices and serum ferritin levels before the onset of CVA. Hence it is not known for certain whether serum ferritin levels in these patients increased, were equal, or even decreased during the event of a CVA. Long term follow-up of the cerebrovascular accident patients need to be done to assess the precise severity and prognosis.

Conclusion

Cerebrovascular accident is a cause of significant morbidity and mortality in both developed and developing nations. This study provides evidence on the association of ferritin, lipids and lipid ratios with cerebrovascular accident. These lipid indices and serum ferritin levels appeared to be of important prognostic indicators for identifying high-risk participants predisposed to cerebrovascular accident in men and women and may serve as potential targets for cerebrovascular accident prevention. This study highlights the utility of a simple, easily available serum

marker in prediction and prognosis of acute ischemic cerebrovascular accident.

References

1. Feigin VL, Stark BA, Johnson CO, Roth GA, Bisignano C, Abady GG, Abbasifard M, Abbasi-Kangevari M, Abd-Allah F, Abedi V, Abualhasan A. Global, regional, and national burden of stroke and its risk factors, 1990–2019: a systematic analysis for the Global Burden of Disease Study 2019. The Lancet Neurology. 2021; 20(10):795-820.
2. Alharbi AS, Alhayan MS, Alnami SK, Traad RS, Aldawsari MA, Alharbi SA, Sharif AO, Alboqami ST, Alshammari SA, Alzeer MK, Alshammari MA. Epidemiology and Risk Factors of Stroke. Archives of Pharmacy Practice. 2019;10(4):60-66.
3. Knovich MA, Storey JA, Coffman LG, Torti SV, Torti FM. Ferritin for the clinician. Blood Rev. 2009;23(3):95-104
4. Omran F, Kyrou I, Osman F, Lim VG, Randeva HS, Chatha K. Cardiovascular biomarkers: lessons of the past and prospects for the future. International Journal of Molecular Sciences. 2022;23(10):1-42
5. Hering D, Lachowska K, Schlaich M. Role of the sympathetic nervous system in stress-mediated cardiovascular disease. Current hypertension reports. 2015; 17:1-9.
6. Bresgen N, Eckl PM. Oxidative stress and the homeodynamics of iron metabolism. Biomolecules. 2015;5(2):808-847.
7. Pisoschi AM, Pop A, Iordache F, Stanca L, Predoi G, Serban AI. Oxidative stress mitigation by antioxidants-an overview on their chemistry and influences on health status. European Journal of Medicinal Chemistry. 2021; 209:112891.
8. Xie L, Peng Y, Huang K, Wu Y, Wang S. Predictive value of iron parameters in neurocritically ill patients. Brain and Behavior. 2018;8(12):1-7.
9. Sinning C, Westermann D, Clemmensen P. Oxidative stress in ischemia and reperfusion: current concepts, novel ideas and future perspectives. Biomarkers in Medicine. 2017; 11(11):11031-11040.
10. Tardy AL, Pouteau E, Marquez D, Yilmaz C, Scholey A. Vitamins and minerals for energy, fatigue and cognition: a narrative review of the biochemical and clinical evidence. Nutrients. 2020;12(1):228.
11. Rodrigo R, Fernandez-Gajardo R, Gutierrez R, Manuel Matamala J, Carrasco R, Miranda-Merchak A, Feuerhake W. Oxidative stress and pathophysiology of ischemic stroke: novel therapeutic opportunities. CNS & Neurological Disorders-Drug Targets (Formerly Current Drug Targets-CNS & Neurological Disorders). 2013;12(5):698-714.
12. Thomas SE, Plumber N, Venkatapathappa P, Gorantla V. A review of risk factors and predictors for hemorrhagic transformation in patients with acute ischemic stroke. International Journal of Vascular Medicine. 2021; 4244267.
13. Merelli A, Repetto M, Lazarowski A, Auzmendi J. Hypoxia, oxidative stress, and inflammation: three faces of neurodegenerative diseases. Journal of Alzheimer's disease. 2021; 82(s1): S109-126.
14. Sultana J, Sharma DJ. Evaluation of Serum Ferritin as a Prognostic Marker in Acute Ischemic Stroke Patients-A Prospective Cohort Study. The Journal of the Association of Physicians of India. 2022;70(4):11-12.
15. Stoyanovsky DA, Tyurina YY, Shrivastava I, Bahar I, Tyurin VA, Protchenko O, Jadhav S, Bolevich SB,

Kozlov AV, Vladimirov YA, Shvedova AA. Iron catalysis of lipid peroxidation in ferroptosis: Regulated enzymatic or random free radical reaction? Free Radical Biology and Medicine. 2019; 133:153-161.

16. Sengupta D, Bardhan J, Mahapatra AB, Banerjee J, Rout JK. Correlation between lipid profile and carotid intima-media thickness in cerebral ischemia. Indian J Physiol Pharmacol. 2014;58(4):354-64.
17. Balachandiran M, Selvakumar C, Sridhar MG. Platelet aggregation, fibrinogen and lipid profile in cerebrovascular accidents. Int J Pharma Bio Sci. 2012;3(2):115-121.
18. Bowman TS, Sesso HD, Ma J, Kurth T, Kase CS, Stampfer MJ, Gaziano JM. Cholesterol and the risk of ischemic stroke. Stroke. 2003; 34(12):2930-2934.
19. Sawka MN, Leon LR, Montain SJ, Sonna LA. Integrated physiological mechanisms of exercise performance, adaptation, and maladaptation to heat stress. Compr Physiol. 2011;1(4):1883-1928.
20. Hadjiphilippou S, Ray KK. Lipids and lipoproteins in risk prediction. Cardiology Clinics. 2018;36(2):213-220.
21. Tirschwell DL, Smith NL, Heckbert SR, Lemaitre RN, Longstreth WT, Psaty BM. Association of cholesterol with stroke risk varies in stroke subtypes and patient subgroups. Neurology. 2004;63(10):1868-1875.
22. Varghese NS, Varghese GM, Reddy MG, Bakam A, Radhakrishnan V, Chandrababu S. Association between lipoprotein (a) levels and risk factors for cerebrovascular accidents, coronary artery disease, and dyslipidaemia. Latin American Journal of Pharmacy. 2023;42(5):27-34.
23. Lee SY, Koo BK, Moon MK. Non-fasting triglyceride levels in the Korean population with and without ischemic heart disease and cerebrovascular disease. The Korean journal of internal medicine. 2019;34(2):353-364.
24. Wadström BN, Wulff AB, Pedersen KM, Jensen GB, Nordestgaard BG. Elevated remnant cholesterol increases the risk of peripheral artery disease, myocardial infarction, and ischaemic stroke: a cohort-based study. European heart journal. 2022;43(34):3258-3269.
25. Sandesara PB, Virani SS, Fazio S, Shapiro MD. The forgotten lipids: triglycerides, remnant cholesterol, and atherosclerotic cardiovascular disease risk. Endocrine reviews. 2019;40(2):537-557.
26. Gaziano JM, Hennekens CH, O'Donnell CJ, Breslow JL, Buring JE. Fasting triglycerides high-density lipoprotein and risk of myocardial infarction. Circulation 1997;96(8):2520-2525.
27. Lechner K, McKenzie AL, Kränkel N, Von Schacky C, Worm N, Nixdorff U, Lechner B, Scherr J, Weingärtner O, Krauss RM. High-risk atherosclerosis and metabolic phenotype: the roles of ectopic adiposity, atherogenic dyslipidemia, and inflammation. Metabolic syndrome and related disorders. 2020;18(4):176-185.
28. Han SH, Nicholls SJ, Sakuma I, Zhao D, Koh KK. Hypertriglyceridemia and cardiovascular diseases: revisited. Korean circulation journal. 2016;46(2):135-144.