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Research Article,

Measurement of Serum Ferritin among Sudanese Patients with Ischemic Stroke at Khartoum State, 2023

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Abstract:

Background:
Stroke is a non-traumatic, focal vascular injury of the nervous system and typically results in permanent damage in the form of cerebral infarction or intracerebral hemorrhage and/ or subarachnoid hemorrhage. This study was aimed to measure the ferritin Level among Sudanese patients with the ischemic stroke.

Material and method:
This was a case control hospital based study conducted at Ribat University Hospital at Khartoum state during the period of December 2022 to April 2023, It included all patients attending Ribat University Hospital and diagnosed with ischemic stroke during the aforementioned period as case group and compared to apparently healthy individuals with no history of thrombi or stroke as control group. Roche kits on the Hitachi 912 clinical analyzer were used for serum ferritin measurement.

Results:
Serum ferritin levels mean in the case group was (232.3± 36.3), in the control group was (114.1±11.7). Comparison between case and control in ferritin levels showed highly significant increase in the case group (p. v= 0.004) .Insignificant differences in ferritin levels between cases and controls in gender, past medical history and risk factors (p. v > 0.05) were shown. A negative correlation of ferritin levels was detected with age (p. v >0.05).

Conclusion: This study demonstrates the significant rise in serum ferritin in ischemic stroke Sudanese patients when compared with control, and the ferritin level had insignificant correlation with gender, age, past medical history and risk factors.

Keywords: ferritin, ischemic stroke, genetic factors, risk factors Hypertension, diabetes mellitus

Introduction:

Acute ischemic stroke (IS) is defined as a sudden loss of brain function resulting from severe interference in the flow of blood and oxygen in cerebral arteries. IS has a heterogeneous etiology caused by modifiable and non- modifiable risk factors. Genetic factors, age and gender are the non-modifiable risk factors while Hypertension, diabetes mellitus (T2DM), dyslipidemia, and smoking are modifiable risk factors. [1] Reports have demonstrated the increased burden of IS worldwide in the last 25 years, especially in developing countries. After acute myocardial infarction and malignancy, ischemic stroke is the third leading cause of death and disability. [1, 2]

Ferritin, a major iron storage protein, is essential to iron homeostasis and is involved in a wide range of physiologic and pathologic processes. Utilized as a serum marker of total body iron stores. In cases of iron deficiency and iron

overload, serum ferritin serves a critical role in both diagnosis and management. Elevated serum and tissue ferritin are linked to coronary artery disease, malignancy, sideroblastic anemias, neurodegenerative disorders, and hemophagocytic syndrome and poor outcomes following stem cell transplantation. Additionally, recent research describes novel functions of ferritin independent of iron storage.[3]

Serum ferritin has been used widely in clinical medicine chiefly as an indicator of body iron stores. It is an acute-phase reactant involved in cellular defense against oxidative stress and inflammation along with transferrin. Iron also plays a role in ischemic stroke by activating platelets via a protein kinase-C mechanism. Another proposed mechanism of ferritin in ischemic vascular disease, is through reperfusion injury. After the event of ischemic stroke, reperfusion causes marked increase in oxygen-radical production as well as a release of iron ions, causing further tissue damage and cellular death [4] Recent animal experiments have suggested that iron overload contributes to the vascular diseases development by promoting thrombosis after arterial injury.[5] High serum ferritin on admission of acute stroke patients (within 24 to 48 hours after stroke onset) had poor prognosis implicating that increase in body iron stores before stroke onset can aggravate the brain ischemia cytotoxicity. It also acts as a risk factor for ischemic episodes by enhancing atherogenesis.[6]

Material and methods:

This was a case-control hospital based study conducted at Ribat university hospital at Khartoum state during the period of December 2022 to April 2023, and aimed to measure ferritin level in the Sudanese patients with ischemic stroke. All patients attended to Ribat university hospital aged ≥18 years, presented within 48 hours of onset of symptoms of acute ischemic stroke, diagnosed on the basis of clinical examination and neuro-imaging (computed tomography/magnetic resonance imaging brain) were included in the study. In addition to that apparently healthy people with no history of thrombi or stroke were selected as control group. Patients presented after 48 hours of onset of symptoms of acute ischemic stroke, patients with recent infection, malignancy, anemia, or liver failure, patients received blood/blood component transfusion in the previous 7 days; and patients under anticoagulant therapy were excluded from the study. The data was collected using pre-designed structural questionnaire. The study was approved by the ethical committee of National University, faculty of medical laboratory, and the participants was fully informed about the advantages and disadvantages before participation in the research (verbal informed consent). From each participant 2.8 ml of blood samples was collected in trisodium citrate anticoagulant. Roche kits on the Hitachi 912 clinical analyzer was used for serum ferritin measurement.

Results:

In the present study total of sixty participants were included, thirty as a case group and thirty as control group, their mean of age was (48.9±5.5). In the case group 53% were female and 47% were male, their mean of ages was (64.9±11. 9), for the past medical history: 20% had history of thrombi, 20% had high lipid level, 13.3% had one of heart illnesses, 63.3% were hypertensive (HT) and 36.7% were diabetic (D.M). Regarding the risk factors: 40% were overweight, 13.3 % practicing exercise and only 3.3% were smoker. (table1) (figure1, 2)

Hematological Result:

In the present study the results revealed that; the mean of ferritin levels in the case group was (232.3± 36.3), in the control group was (114.1±11.7) (Figure3). Comparison between case and control in ferritin levels showed highly significant increase in the case group (p. v= 0.004) (Table 2). However, there were insignificant differences in ferritin levels between cases and controls in gender, past medical history and risk factors (p. v > 0.05). Furthermore, a negative correlation of ferritin levels was detected with age (p. v >0.05). (Table 3, 4, 5).

Table (1): Distribution of past medical history:

Variables	Yes		No	
	Frequency	Percent	Frequency	Percent
HT	19	63.3	11	36.7
D.M	11	36.7	19	63.3
History of previous thrombi	6	20.0	24	80.0
High lipid level	6	20.0	24	80.0
Heart conditions	4	13.3	26	86.7
Alcohol taker	0	0.0	30	100.0
Smoker	1	3.3	29	96.7
Practice exercise	4	13.3	26	86.7
Overweight	12	40.0	18	60.0
Family history of thrombi	12	40.0	18	60.0

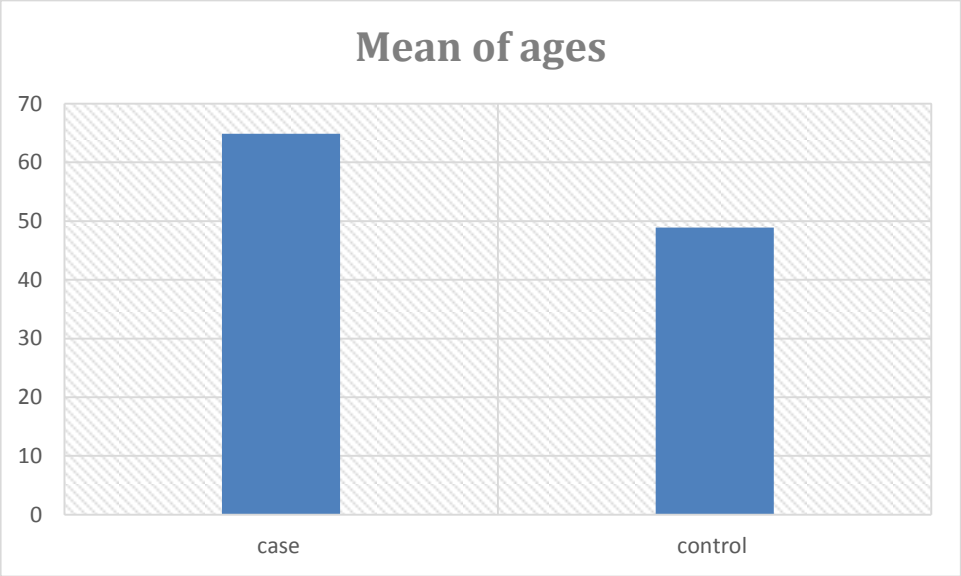

Figure (1): Mean of ages in the case and control group

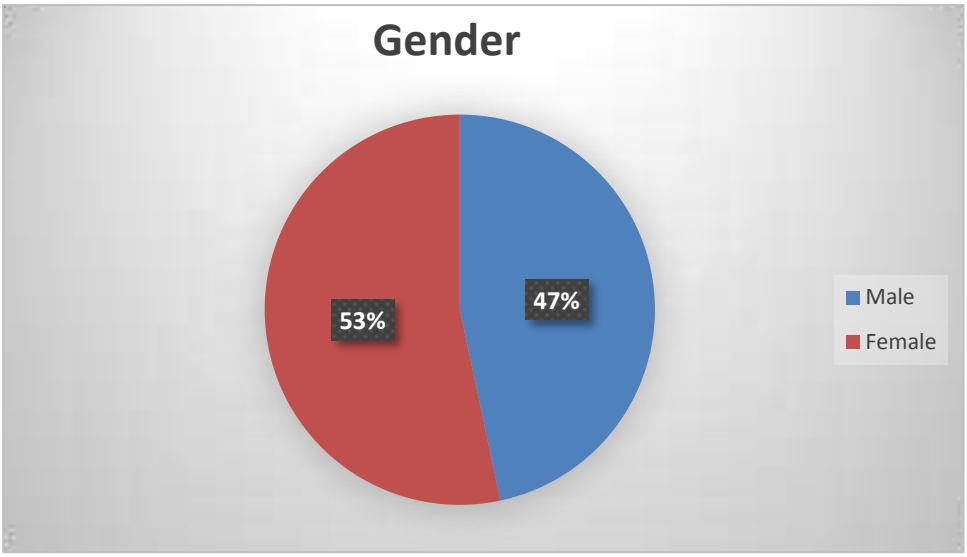

Figure (2): Distribution of gender

Table (2): Comparison of ferritin between case and control

Parameters	Study population		P. value
	Case	Control	
Ferritin	232.3 ± 36.3	114.1 ± 11.7	0.004*

Table (3): Comparison of ferritin according to gender

Parameters	Gender		P. value
	Male (n=14)	Female (n=16)	
Ferritin	237.5 ± 45.4	227.8 ± 56.6	0.896

Table (4): Comparison of ferritin according to past medical history

Past medical history		N	Ferritin		P. value
			Mean	Std. Deviation	
B. P	Yes	19	177.9	24.4	0.119
	No	11	326.2	84.6	
D.M	Yes	11	201.0	31.1	0.512
	No	19	250.4	54.6	
History of previous thrombi	Yes	6	153.5	37.3	0.285
	No	24	252.0	43.7	
High lipid level	Yes	6	174.2	39.0	0.432
	No	24	246.8	44.1	
Heart conditions	Yes	4	169.0	40.3	0.503
	No	26	242.0	41.2	
Practice exercise	Yes	4	187.8	46.2	0.638
	No	26	239.2	41.3	
Overweight	Yes	12	195.2	29.5	0.413
	No	18	257.1	57.2	
Family history of thrombi	Yes	12	187.8	32.7	0.325
	No	18	261.9	56.1	

Table (5): Correlations of age with ferritin

	Age	
	Pearson Correlation	P. value
Ferritin	.259	.167

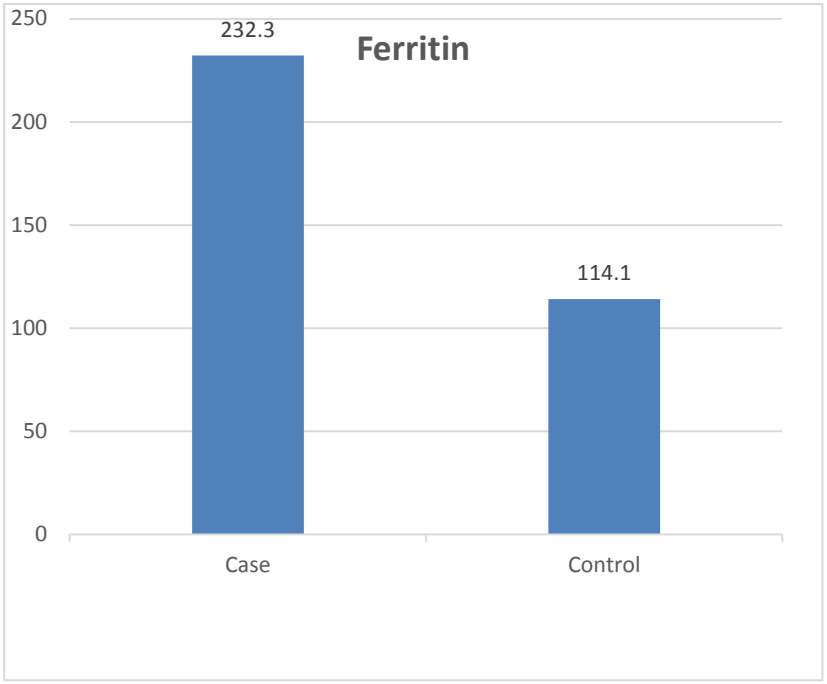

Figure (3): Mean of ferritin in case and control

Discussion:

Stroke is a non-traumatic, focal vascular injury of the nervous system and typically results in permanent damage in the form of cerebral infarction or intracerebral hemorrhage and/ or subarachnoid hemorrhage. An ischemic stroke occurs due to cessation of blood flow due to extra cranial or intracranial thrombosis, embolism, and hypo perfusion. [7] This was a case control hospital based study conducted at Ribat University Hospital at Khartoum state during the period of December 2022 to April 2023, and aimed to measure the Ferritin level among Sudanese patients with the ischemic stroke, the results revealed that; In the case group 53% were male and 47% were female, their mean of ages was (64.9±11. 9), 20% history of thrombi, 20% had high lipid level, 13.3% had heart condition, 63.3% were hypertensive and 36.7% were diabetic. Regarding the risk factors: 40% were overweight, 13.3 % practicing exercise and only 3.3% were smoker. These findings are consisting with the Dania Mohyeldin *et al* finding who reported; in the ischemic stroke Sudanese patients the most affected age group was between (56-60), the frequency of males is greater than the females, 94% with hypertension, 20 % of case are diabetic, 19% smoker and 16 % of case group with familial history of thrombi. [8] Yousufuddin *et al* reported; Aging is the most robust non-modifiable risk factor for ischemic stroke, which doubles every 10 years after age 55 years. Approximately three-quarters of all strokes occur in persons aged ≥65 years. [9] Moreover Gibson *et al* mentioned; men have been found to experience more ischemic stroke whereas women tend to have more infarctions involving the anterior circulation and experience more subarachnoid hemorrhages. On the other hand in terms of stroke onset, women tend to be, on average, approximately 4 years older than men at the age of ischemic stroke onset. [10] In addition Fahimfar *et al* said: the risk factors for ischemic stroke include aging, hypertension, diabetes, smoking, history of cardiovascular diseases (CVD), atrial fibrillation, and left ventricular hypertrophy. [11] In the present study when compared the ferritin mean between the case and control group there was highly significant increase with (p. v= 0.004). While the ferritin level had insignificant differences with gender, past medical history and risk factors. Also has negative correlation with the age. These results agreed with Garg *et al* results who revealed : Serum ferritin has a significant positive correlation with the severity of acute ischemic stroke ($P < 0.001$), and the levels correlate with

the outcome of the disease ($P < 0.001$) , patients with higher serum ferritin at admission tend to deteriorate more as compared to those with lower levels. Thus, serum ferritin can be used as a prognostic marker in acute ischemic stroke. [12] It also consists with Hrishikesh *et al* study which concluded to that serum Ferritin level had a positive correlation with the severity of ischemic stroke indicating that serum Ferritin levels can also be used as an adjuvant tool for assessing the severity of stroke along with other tools and facilitate adequate and timely management of the patients. [13] A study by Van der DL *et al.* in postmenopausal women between 49 and 70 years of age observed that higher serum ferritin concentrations in those postmenopausal women were associated with an increased risk of ischemic stroke. [14] Egovindarajulu *et al*. in their study also noted that there was no significant difference in the serum ferritin levels between the two age groups (≤50 years and >50 years) taken in their study ($P = 0.918$). [15]

In one study there was no significant correlation between serum ferritin and age, sex, smoking, cholesterol level, but there was significant correlation between serum ferritin and diabetes, hypertension and cardiovascular risk factors. [16] Finally, Previous studies had suggested that iron overload contributes to the development of vascular disease by promoting thrombosis after arterial injury. High serum ferritin at admission was reported to predict a poor prognosis in acute stroke patients (within 24–48 h after stroke onset), implicating that increase in the body iron stores before stroke onset can aggravate the cytotoxicity of brain ischemia. Thus, it has been suggested that high serum ferritin influences the prognosis of ischemic stroke and also acts as a risk factor for ischemic episodes by enhancing atherogenesis. [17]

Conclusion:

This study demonstrates the significant rise in serum ferritin in ischemic stroke Sudanese patients, and the ferritin level had insignificant corelation with gender, age, past medical history and risk factors.

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