SERUM FERRITIN LEVELS AS A PROGNOSTIC INDICATOR IN ACUTE ISCHEMIC STROKE: A COMPREHENSIVE CLINICAL STUDY

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Received: 04 August 2023, Revised and Accepted: 20 September 2023

ABSTRACT

Objective: This clinical study investigates the potential of serum ferritin levels as a prognostic indicator in acute ischemic stroke.

Methods: This cross-section study included 75 patients enrolled in our outpatient clinic. General Medicine Department, and SMS Medical College. The study enrolled all patients who had a new onset focal neurological deficit due to a stroke. A total of 75 patients (25 in each group (mild/moderate/severe) as per the National Institute of Health Stroke Scale scoring) of >14 years old, presenting in the general medicine wards were enrolled for the study. The study assesses the correlation between serum ferritin levels and various clinical parameters, including stroke severity, consciousness status, and disability outcomes.

Results: Severe group had the highest average blood ferritin level (408.48 with a standard deviation (SD) of 68.63). A significant relationship was observed between ferritin levels and loss of consciousness. In addition, the mean ferritin residue ratio (MRS) also correlated with ferritin levels, with MRS correlating to ferritin levels. A significant association between elevated serum ferritin levels and severe stroke, as well as unfavorable outcomes.

Conclusion: The findings suggest that serum ferritin could serve as a promising prognostic index in acute ischemic stroke, aiding in patient risk stratification and clinical decision-making.

Keywords: Serum ferritin, Acute ischemic stroke, Prognostic indicator, Stroke severity, Consciousness status, Disability outcomes.

INTRODUCTION

Stroke, according to the WHO, is defined as “a rapidly progressing clinical manifestation of focal (and in some cases global) brain dysfunction that lasts more than 24 h, or without apparent signs leading to death.” Clinical syndrome: stroke has now overtaken heart disease, cancer, and diabetes as the most common, potentially fatal, preventable neurodegenerative disease. According to the Indian Council of Medical Research, diabetes and stroke caused $46 billion economic losses in India from 2006 to 2015 [1]. In medical practice, stroke and cerebral accidents (CVAs) can be categorized as follows: Ischemic strokes: Strokes that are ischemia and hemorrhage-free but do not involve bleeding around the brain. About 80% of CVA cases are caused by a lack of blood flow to the brain. The remaining 20% are caused by brain hemorrhage. When something blocks a blood vessel in the brain, a stroke is an ischemia.

Vascular inflammation and coagulation are both thought to be involved in the formation of the blood clot. These theories suggest that coagulopathy and vascular abnormalities may be associated with an increase in the likelihood of either a hematologic or ischemic stroke, as a result of interactions between these risk factors [3,4] and other risk factors [5]. Evidence from acute stroke (a condition in which prognostic factors are poor) [6] supports this hypothesis.

It is generally thought that the brain is more susceptible to hypoxic injury than other organs in the body. This is largely due to the high concentration of glutamate (a neurotransmitter) in the brain, as well as the relatively high level of metabolic activity. Hypoxic injury can also be caused by an occlusive cerebral artery, such as an embolism or an intracerebral thrombus [7,8].

Lipid peroxidation, to which iron contributes, results in the activation of membrane-binding enzyme complexes, reduced membrane fluidity, cell membrane breakdown, and ultimately cell death. Therefore, tissue iron content and lipid peroxidation are thought to be related [9,10]. Ferritin is the positive acute phase iron storage protein. It is the primary protein responsible for storing iron within cells [11,12]. The main control of cellular ferritin level is the level of free iron intracellularly. Thus, ferritin provides a method to safely store the metal within the cells. Although ferritin occurs in blood in very small amounts, its function is as yet unknown. Serum ferritin has been used extensively in clinical practice, mainly as a measure of body iron stores [13-15].

Even with extensive research on the topic of stroke, predicting an acute attack may be challenging. Future prognostic biomarkers are currently being studied, such as stroke hyperglycemia, stroke infection, stroke TNFα, or interleukin, among others. Serum ferritin is one of the predictive biomarkers that have recently gained considerable clinical attention. Serum fibrillation was initially thought of as a stress-related response to stroke but is now being studied as a prognostic marker [16-18].

Serum ferritin testing helps identify high-risk individuals due to the close relationship between the early neurological decline in stroke patients and serum ferritin levels.

METHODS

This cross-section study included 75 patients enrolled in our outpatient clinic, General Medicine Department, SMS Medical College, and its associated network of hospitals. All patients provided written informed consent before enrollment in this study. This hospital-based comparative observational study is scheduled to commence in May 2020 with a full year of follow-up. A randomized, stratified sample of 25 patients (mild, moderate/severe) was selected based on their National Institute of Health Stroke Scale (NIHSS) scores.
The study enrolled all patients who had a new onset focal neurological deficit due to a stroke. Patients who arrived within 48 h after the onset of the stroke were excluded from the study. Patients with bleeding-related characteristics, such as recent surgery or trauma, tumors in the central nervous system, cancer, transient ischemic attacks, reversible ischemic neurological impairment (RIND), or CVA were also excluded from the study.

Blood samples were taken to measure serum ferritin levels. Baseline clinical data were collected based on demographics, medications, and biochemistry. Each registered patient had their personal and family medical records as well as a complete medical history. The Institution’s Ethics Committee gave permission to conduct the study.

**Statistical analysis**

The data were analyzed and statistical analysis was performed using SPSS -PC-20 (SPSS Version 20) software (SPSS, Inc., Chicago, IL, USA). The data were presented as a mean and SD for continuous variables (normal distribution) and as a frequency for the categorical variables (range). The means were compared between the two samples using the Student’s t-test (Student’s t) for the continuous variables and χ² analysis (χ²) for the categorical variable. The level of significance was p<0.05 for all statistical analysis.

**RESULTS**

In total, 75 patients were enrolled (25 patients in each group based on NIHSS score (mild, moderate/severe). Table 1 shows the age and gender distribution of patients in the study population. Maximum patients (40%) were observed in all three study groups. Mean ages observed in the mild, moderate, and severe groups were 51.96/18.79/17.89/49.24/20.13 years. Maximum patients (72/68/68) in the mild, medium, and severe study groups were 72/68/68 males, suggesting a male-to-male predominance. Chi-square statistical analyses revealed an insignificant (p<0.05) age-to-gender association between the three study groups (Table 1).

Table 2 shows the study population by serum ferritin level, with the severe group having the highest average blood ferritin level (408.48 with SD of 68.63). An analysis of variance (ANOVA) statistical analysis revealed a statistically significant relationship between ferritin levels and loss of consciousness (p=0.05). In addition, the mean ferritin concentration ratio (MRS) was also correlated with ferritin levels, with MRS correlating to ferritin levels using a single sample t-test statistical analysis (Table 5).

**Discussion**

The results of a stroke may vary depending on the location and extent of brain damage. The degree of RIA after a stroke can be evaluated through the use of scales such as the Glasgow coma scale, the NIHSS, and the Canadian stroke scale [19].

While the reliability of risk variables such as blood pressure, smoking, diabetes, and dyslipidemia is not yet fully established, there is still considerable debate and research into the adequacy of prognostic indicators and the ability to predict the occurrence of strokes. Recently, there has been an increase in interest in strokes. Some studies suggest that ferritin may affect the prognosis of ischemic stroke and contribute to ischemia. In this study, the majority of patients (100%) in the mild group had moderate/severe score, the majority (70%) in the moderate group had intermediate (5–15) score and the majority (80%) in the severe group had severe (>15) score mic episodes due to increasing atherogenesis [16].

Patients in this study ranged in age from 41 to 50 years old, with a maximum patient prevalence of 18.67%. The mean age of the mild and moderate groups was 51.96 and 51.79 years, respectively, while the mean age of the severe and severe groups was 51.4 and 49.13 years, respectively, with a maximum of 40% of patients in each group. About

**Table 1: Distribution of study population according to age group**

<table>
<thead>
<tr>
<th>Age group</th>
<th>Group mild</th>
<th>Group moderate</th>
<th>Group severe</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>%</td>
<td>Frequency</td>
<td>%</td>
<td>Frequency</td>
</tr>
<tr>
<td>&lt;20</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>20–30</td>
<td>2</td>
<td>8</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>31–40</td>
<td>3</td>
<td>12</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>41–50</td>
<td>5</td>
<td>20</td>
<td>5</td>
<td>20</td>
</tr>
<tr>
<td>51–60</td>
<td>3</td>
<td>12</td>
<td>4</td>
<td>16</td>
</tr>
<tr>
<td>&gt;60</td>
<td>10</td>
<td>40</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td>Total</td>
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<td>25</td>
<td>100.0</td>
</tr>
<tr>
<td>Mean</td>
<td>51.9600</td>
<td>18.79379</td>
<td>51.4000</td>
<td>17.89786</td>
</tr>
<tr>
<td>Gender</td>
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</tr>
<tr>
<td>Female</td>
<td>7</td>
<td>28.0</td>
<td>8</td>
<td>32.0</td>
</tr>
<tr>
<td>Male</td>
<td>18</td>
<td>72.0</td>
<td>17</td>
<td>68.0</td>
</tr>
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</table>

**Table 2: According to serum ferritin level**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Group mild</th>
<th>Group moderate</th>
<th>Group severe</th>
<th>Analysis of variance statistical analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
</tr>
<tr>
<td>Serum Ferritin</td>
<td>155.2</td>
<td>102.17</td>
<td>305.84</td>
<td>66.08</td>
</tr>
</tbody>
</table>

SD: Standard deviation, *p<0.05 is significant
Mean ferritin and consciousness levels are statistically related (p<0.05). Furthermore, based on the findings of Thamicalachalam et al. [21], there is a significant positive relationship between the levels of ferritin in the blood and the degree of acute ischemic stroke severity at admission. As a result, ferritin may serve as a prognostic factor in acute ischemic strokes.

The correlation between serum ferritin levels and NIHSS scores was statistically significant (p<0.0001) in a study by Gupta et al., published in the Journal of Neuropsychopharmacology [23]. In other words, the degree of stroke at admission is correlated to serum ferritin concentration on the day of admission.

One possible explanation is that high levels of ferritin in the serum indicate higher levels of iron storage in the brain. Cerebrovascular ischemia causes more iron to be discharged from injured brain cells during a CVA. More iron leads to more oxidative stress. When more iron is discharged into the area surrounding the damaged tissue, more free hydroxy radicals are produced. This increases the risk of further tissue damage during cerebral ischemia. Another possible explanation is that damaged brain cells released more glutamate during ischemia, which further damages the tissue. Both of these mechanisms lead to further tissue injury during ischemia [24,25].

CONCLUSION

According to our analysis, men predominate. The severe group had the highest mean blood ferritin levels, which were strongly related to all three research groups. According to the research, serum ferritin may be a useful prognostic indicator for acute ischemic stroke patients, helping with patient risk classification and clinical judgment.

ACKNOWLEDGMENT

We would like to express our gratitude to SMS Medical College for supporting us during this project.

AUTHORS' CONTRIBUTION

All the authors have contributed equally.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

AUTHOR'S FUNDING

By signing this statement, the authors affirm that they received no financial support for their research, writing, or publication of this paper.
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