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Serum Leptin in Cerebrovascular Stroke: A Case–Control Study with Implications for Pharmacotherapy and Risk Stratification

Syeda Asiya Fazilath*, N. Jaya

Department of Biochemistry, Osmania Medical College, Kaloji Narayana Rao (KNR) University of Health Sciences, Hyderabad, Telangana – 500001.

ABSTRACT

Leptin, an adipocyte-derived hormone with pro-inflammatory and atherogenic properties, has been implicated in vascular pathology, though its association with cerebrovascular stroke remains controversial. This hospital-based case–control study evaluated circulating serum leptin levels in 100 subjects, including 50 patients with cerebrovascular stroke (ischemic and hemorrhagic) and 50 age- and sex-matched healthy controls. Serum leptin levels were measured using ELISA, while fasting blood glucose and lipid profile parameters were assessed by standard enzymatic methods. Statistical analysis was performed using SPSS version 16, with $p < 0.05$ considered significant. Serum leptin levels were significantly higher in stroke patients compared to controls ($p < 0.001$), with mean values of 10.39 ± 4.25 ng/mL in ischemic stroke, 9.32 ± 3.45 ng/mL in hemorrhagic stroke, and 5.54 ± 0.85 ng/mL in controls. Leptin showed positive correlations with LDL cholesterol, body mass index, and blood pressure, and LDL and total cholesterol were significantly elevated in stroke patients ($p < 0.05$). These findings suggest that elevated leptin levels may serve as a biomarker of metabolic and vascular risk in cerebrovascular disease and may have clinical relevance in therapeutic risk stratification and drug safety monitoring. Integrative approaches, including nutraceuticals and lifestyle interventions targeting leptin modulation, may complement conventional therapy. Further prospective studies are required to clarify its predictive and clinical utility.

Keywords: Leptin; cerebrovascular stroke; biomarker; pharmacotherapy; metabolic risk.

1. INTRODUCTION

Cerebrovascular stroke is a leading cause of mortality and long-term disability worldwide. It is broadly classified into ischemic and hemorrhagic subtypes, with ischemic stroke accounting for approximately 85% of cases. Atherosclerosis, endothelial dysfunction, metabolic syndrome, diabetes mellitus, and dyslipidemia are well-established contributors to stroke pathogenesis.[1]

Leptin is a 16 kDa adipokine primarily secreted by adipocytes. Beyond its role in appetite regulation and energy homeostasis, leptin exhibits pro-inflammatory, pro-thrombotic, and angiogenic properties. Elevated circulating leptin levels have been associated with insulin resistance, dyslipidemia, hypertension, and obesity — all recognized vascular risk factors.[2]

Experimental evidence suggests that leptin may promote platelet aggregation, enhance monocyte chemoattractant protein-1 (MCP-1) expression, induce oxidative stress and contribute to endothelial dysfunction.[3]

Although several studies have explored the relationship between leptin and cardiovascular disease, data regarding its role in cerebrovascular stroke remain limited and somewhat inconsistent. Understanding the relationship between circulating leptin levels and stroke may provide valuable insight into the metabolic and inflammatory mechanisms underlying cerebrovascular disease.[4] Therefore, the present study was undertaken to evaluate circulating serum leptin levels in patients with

***Corresponding Author:** fsyedaasiya786@gmail.com

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ischemic and hemorrhagic stroke and to examine their association with metabolic risk parameters.

In addition to its role in vascular pathology, leptin may have potential relevance in therapeutic considerations and drug safety. Adipokines such as leptin may influence pharmacokinetic and pharmacodynamic processes,[5,6] particularly in individuals with metabolic disorders. Understanding leptin dynamics may provide insights into therapeutic optimization and identification of patients who may be at increased risk for adverse drug reactions.[6,7] However, these potential implications require further validation through prospective and interventional studies.

2. MATERIAL & METHODS

2.1 Study Design

This hospital-based analytical case–control study was conducted in the Departments of Biochemistry and General Medicine in collaboration with the Neurology Unit of a tertiary care teaching hospital. The case–control design was chosen as it provides an appropriate and efficient approach for investigating potential biochemical markers associated with disease conditions in a clinical setting. The study was conducted over a period of 18 months. The primary objective of the study was to evaluate circulating serum leptin levels in patients with cerebrovascular stroke and to compare these levels with those of healthy control subjects. In addition, the study aimed to examine the relationship between serum leptin concentrations and selected metabolic parameters, including fasting blood glucose and lipid profile components.[8] The study also aimed to explore the potential clinical relevance of leptin as a biomarker for risk stratification, which may have implications for therapeutic monitoring in future studies.

2.2 Ethical Approval

The study protocol was reviewed and approved by the Institutional Ethics Committee prior to initiation of the study (ECR/300/Inst/AP/2013/RR-16). The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki (1975, revised 2000) and internationally accepted guidelines for biomedical research involving human subjects. Written informed consent was obtained from all participants or their legally authorized representatives before enrollment. Confidentiality and privacy of all participant information were strictly maintained throughout the study.

2.3 Study Population

A total of 100 subjects were included in the study and divided into two main groups:

Group I – Controls (n = 50)

Apparently healthy age- and sex-matched individuals with no history of:

- Stroke
- Coronary artery disease
- Diabetes mellitus
- Chronic kidney and inflammatory disorders

Group II – Cases (n = 50)

Patients diagnosed with cerebrovascular stroke based on:

- Clinical evaluation
- Neurological examination
- Neuroimaging (CT/MRI confirmation)

Cases were further classified into two subgroups:

- Ischemic Stroke
- Hemorrhagic Stroke

Classification was based on radiological findings.

2.3.1 Inclusion Criteria

- Age ≥ 18 years
- Newly diagnosed cerebrovascular stroke
- Radiologically confirmed ischemic or hemorrhagic stroke
- Willingness to participate and provide informed consent

2.3.2 Exclusion Criteria

Patients with the following conditions were excluded:

- Chronic kidney & liver disease
- Malignancy and autoimmune disorders
- Acute or chronic infections
- Endocrine disorders affecting leptin metabolism
- Patients receiving corticosteroids or hormonal therapy

These exclusions were applied to eliminate confounding factors that may independently influence serum leptin levels.[9,10]

2.4 Clinical and Anthropometric Assessment

For all participants, the following parameters were recorded:

- Age (years)
- Gender
- Body Mass Index (BMI)
- Systolic Blood Pressure (SBP)
- Diastolic Blood Pressure (DBP)

2.4.1 Body Mass Index (BMI)

BMI was calculated using the formula:

$$\text{BMI} = \frac{\text{Weight (kg)}}{\text{Height (m)}^2}$$

Participants were categorized according to standard WHO classification.

2.4.2 Blood Pressure Measurement

Blood pressure was measured using a calibrated mercury sphygmomanometer after 10 minutes of rest in a seated position. The average of two readings taken five minutes apart was recorded.

2.5 Sample Collection and Biochemical Analysis

All laboratory analyses were carried out under standardized laboratory conditions to ensure analytical accuracy and reproducibility. Following overnight fasting (8–12 hours), approximately 5 mL of venous blood was collected from the antecubital vein under aseptic precautions. The collected blood samples were divided into plain tubes for serum separation and fluoride tubes for glucose estimation. Serum was separated by centrifugation at 3000 rpm for 10 minutes and stored at −20°C until further analysis.

All biochemical estimations were performed in the central clinical biochemistry laboratory in accordance with standardized operating procedures, with both internal and external quality control measures implemented to maintain analytical reliability. Serum leptin concentration was quantified using a commercially available sandwich Enzyme-Linked Immunosorbent Assay (ELISA) kit (DRG International Inc., Springfield, NJ, USA) following the manufacturer's protocol. The assay is based on a two-site immuneenzymometric principle in which human leptin presents in the sample binds to monoclonal anti-leptin antibodies pre-coated on microtiter wells. A biotinylated secondary antibody and enzyme conjugate (horseradish peroxidase) were subsequently added, and color development was achieved using tetramethylbenzidine substrate. Optical density was measured at 450 nm using a microplate ELISA reader (Bio-Rad Laboratories Inc., Hercules, CA, USA). Concentrations were calculated from a standard calibration curve constructed using known leptin standards and expressed in ng/mL .[11]

Fasting blood glucose was estimated by the hexokinase enzymatic method using commercially available reagent kits (Erba Mannheim, Mannheim, Germany). In this method, glucose is phosphorylated by hexokinase in the presence of ATP to form glucose-6-phosphate, which is subsequently oxidized by glucose-6-phosphate dehydrogenase with reduction of $NADP^+$ to NADPH. The increase in absorbance due to NADPH formation was measured at 340 nm using a semi-automated clinical chemistry analyzer (Erba Chem-5 Plus V2, Transasia Bio-Medicals Ltd., Mumbai, Maharashtra, India).[12]

Serum total cholesterol was measured by the enzymatic Cholesterol Oxidase–Peroxidase Aminophenazone (CHOD–PAP) method using reagent kits supplied by Transasia Bio-Medicals Ltd., Mumbai, Maharashtra, India. Cholesterol esters were hydrolyzed by cholesterol esterase and oxidized by cholesterol oxidase to produce hydrogen peroxide, which, in the presence of peroxidase, reacts with phenol and 4-aminoantipyrine to form a quinoneimine chromogen measured at 505 nm.[13]

Serum triglycerides were estimated using the Glycerol-3-Phosphate Oxidase–Peroxidase (GPO–Trinder) enzymatic method (Transasia Bio-Medicals Ltd., Mumbai, Maharashtra, India). Triglycerides were hydrolyzed to glycerol and fatty acids by lipase. Glycerol was phosphorylated and oxidized, producing hydrogen peroxide that reacts with chromogen to yield a measurable-colored complex at 505 nm.[14]

High-density lipoprotein (HDL) cholesterol was determined after precipitation of very low-density lipoproteins (VLDL) and low-density lipoproteins (LDL) using phosphotungstic acid and magnesium chloride reagent (Erba Mannheim, Mannheim, Germany), followed by enzymatic estimation of cholesterol in the supernatant using the CHOD–PAP method.[15] Low-density lipoprotein (LDL) cholesterol was calculated using Friedewald's formula:

LDL (mg/dL) = Total Cholesterol − [HDL + (Triglycerides/5)]

This calculation was applied only to samples with triglyceride levels below 400 mg/dL, as recommended.[16]

The analytical methods used in the present study were standardized clinical chemistry techniques commonly employed in biomedical research and diagnostic laboratories. All assays were performed in duplicate to minimize analytical variation. Calibration was carried out using manufacturer-provided calibrators, and two levels of internal quality control were analyzed daily to ensure analytical accuracy and precision.

2.6 Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) software version 16.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were expressed as mean ± standard deviation (SD), while categorical variables were presented as frequencies and percentages. The normality of distribution of continuous variables was assessed prior to inferential testing. Comparisons between stroke patients and control subjects were performed using the unpaired Student's *t*-test for normally distributed variables, and subgroup comparisons between ischemic and hemorrhagic stroke were analyzed similarly. The Chi-square test was used to compare categorical variables such as gender distribution. Pearson's correlation coefficient was applied to assess the strength and direction of association between serum leptin levels and metabolic parameters, including fasting blood glucose, lipid profile components, body mass index (BMI), and blood pressure. A two-tailed *P* value of <0.05 was considered statistically significant.

3. RESULTS

A total of 100 participants were included in the study comprising 50 patients diagnosed with cerebrovascular stroke (cases) and 50 healthy individuals (controls). Among the cases, patients were further categorized into ischemic stroke (n = 30) and hemorrhagic stroke (n = 20) based on clinical evaluation and radiological findings.

The biochemical and clinical parameters analyzed included serum leptin, total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), triglycerides (TG), fasting blood glucose (FBS), systolic blood pressure (SBP), diastolic blood pressure (DBP), body mass index (BMI) and age. The results were expressed as Mean ± Standard Deviation (SD) for continuous variables.

3.1 Comparison of Biochemical and Clinical Parameters

The mean values of biochemical and clinical parameters among ischemic stroke patients, hemorrhagic stroke patients, and healthy controls are presented in Table 1.

Serum leptin levels were markedly elevated in stroke patients compared to controls. The mean ± SD leptin levels were 10.39 ± 4.25 ng/mL in ischemic stroke patients and 9.32 ± 3.45 ng/mL in hemorrhagic stroke patients, whereas the control group demonstrated significantly lower levels (5.54 ± 0.85 ng/mL).

Similarly, higher mean values of total cholesterol, LDL cholesterol, fasting blood glucose, systolic blood pressure, diastolic blood pressure, and BMI were observed in stroke patients compared with controls. In subgroup analysis, the leptin, LDL, and BMI were higher in ischemic stroke patients while total cholesterol, fasting blood glucose, SBP, and DBP were higher in hemorrhagic stroke patients. Triglyceride and HDL levels did not show statistically significant differences between the groups.

The observed elevation in leptin levels along with increased LDL cholesterol, blood pressure, and BMI suggest that individuals with higher leptin concentrations may represent a higher-risk metabolic subgroup (Table 2). These findings may have potential implications for clinical risk stratification and could be explored in future studies evaluating therapeutic interventions and drug response.

Table 1: Comparison of biochemical & clinical parameters among ischemic, hemorrhagic, and control groups

Parameter	Ischemic Stroke	Hemorrhagic Stroke	Controls
Leptin (ng/mL)	10.39 ± 4.25	9.32 ± 3.45	5.54 ± 0.85
Cholesterol (mg/dL)	193.67 ± 57.15	210.64 ± 60.82	149.05 ± 26.32
Triglycerides (mg/dL)	123.97 ± 25.69	125.00 ± 25.28	120.64 ± 35.93
HDL (mg/dL)	42.73 ± 5.66	46.86 ± 7.14	45.79 ± 7.71
LDL (mg/dL)	135.33 ± 31.49	130.83 ± 45.78	94.36 ± 16.58
Glucose (mg/dL)	112.03 ± 11.12	125.30 ± 22.07	105.50 ± 12.79
SBP (mmHg)	141.17 ± 18.62	157.95 ± 18.87	115.18 ± 17.89
DBP (mmHg)	88.60 ± 11.11	92.95 ± 10.15	78.36 ± 12.90
BMI (kg/m^2)	27.06 ± 3.29	26.55 ± 2.52	22.19 ± 2.99
Age (years)	56.33 ± 9.05	56.85 ± 10.66	54.60 ± 9.66

Note: The values are expressed as mean ± SD (n=50). Unpaired Student's t-test was performed to assess the significance of differences between stroke patients and controls. Statistically significant differences were observed for serum leptin, total cholesterol, LDL cholesterol, fasting blood glucose, SBP, DBP, BMI (all p < 0.05). However, triglycerides and age did not show statistically significant differences between the groups.

3.2 Demographic Characteristics

The mean age of stroke patients was 56.54 ± 9.62 years, whereas the mean age of controls was 54.60 ± 9.66 years (Fig. 1). No statistically significant difference was observed between the groups (p = 0.32). Gender distribution among cases showed 31 males (62%) & 19 females (38%) whereas among controls, 24 males (48%) & 26 females (52%).

The difference in gender distribution between cases and controls was not statistically significant (Fig. 2) (p = 0.16). In contrast, BMI showed a statistically significant difference, with stroke patients having higher BMI (26.86 ± 2.99 kg/m^2) compared to controls (22.19±2.99 kg/m^2, P < 0.001).

3.3 Gender-wise Analysis of Serum Leptin

Gender-based analysis revealed that mean leptin levels were similar between males and females within stroke groups (Fig. 3). No statistically significant gender-based differences in leptin levels were observed (p > 0.05).

Among ischemic stroke patients, the mean serum leptin levels were 9.74 ± 4.72 ng/mL in females and 10.72 ± 4.09 ng/mL in males. In contrast, among hemorrhagic stroke patients, the mean leptin levels were 10.22 ± 3.00 ng/mL in females and 8.59 ± 3.74 ng/mL in males.

Table 2: Clinical and Therapeutic Implications of elevated leptin

Finding	Clinical Interpretation	Potential Therapeutic Implication
High Leptin	Metabolic dysregulation	May indicate need for closer monitoring
High leptin + LDL	Atherogenic risk	Could be explored in lipid-lowering strategies
High leptin + BP	Sympathetic activation	May influence antihypertensive response
High leptin + BMI	Obesity-related risk	May affect pharmacokinetics

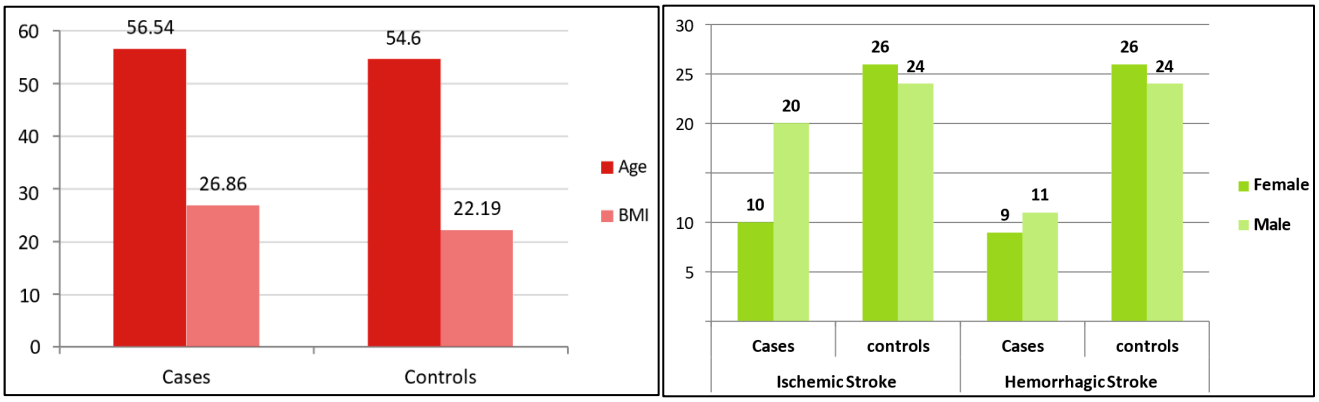

Fig. 1 & 2: The demographic & gender distribution characteristics of study participants

Note: Stroke patients demonstrated higher mean BMI compared with controls, whereas the difference in mean age between the two groups was not statistically significant. Males constituted 62% of stroke cases, whereas females constituted 38%. Among controls, females represented 52% and males 48%.

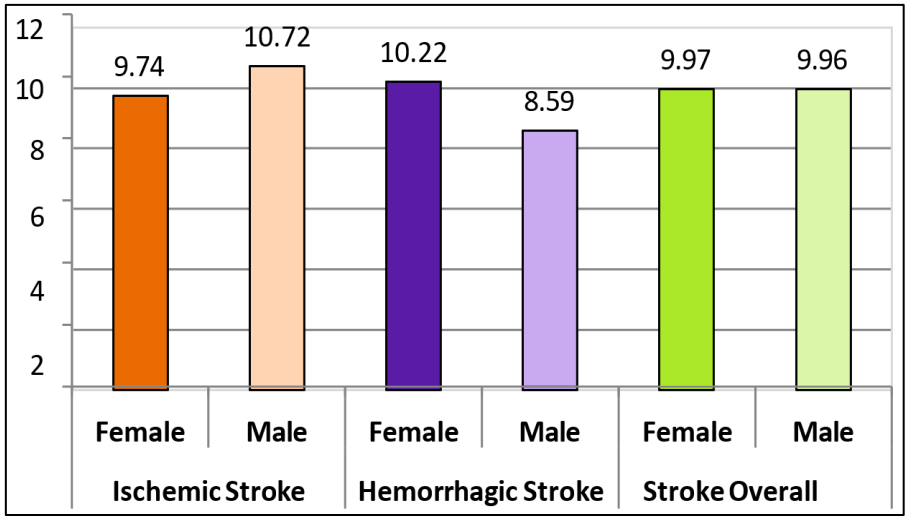

Fig. 3: Gender-wise comparison of serum leptin levels in ischemic and hemorrhagic stroke

Note: No statistically significant gender-based difference in leptin levels was observed among stroke patients.

4. DISCUSSION

Cerebrovascular stroke remains one of the leading causes of mortality and long-term disability worldwide. The pathogenesis of stroke is multifactorial and involves a complex interplay between metabolic, inflammatory, vascular, and hemodynamic factors. In recent years, increasing attention has been directed toward adipocyte-derived hormones, particularly leptin, as potential mediators linking metabolic dysfunction with vascular disease. The present study evaluated circulating serum leptin levels in patients with cerebrovascular stroke and compared them with healthy controls while examining their relationship with metabolic risk parameters.

The principal finding of the present study was that serum leptin levels were significantly elevated in patients with cerebrovascular stroke compared with controls, with mean leptin concentrations of 10.39 ± 4.25 ng/mL in ischemic stroke and 9.32 ± 3.45 ng/mL in hemorrhagic stroke, compared with 5.54 ± 0.85 ng/mL in healthy individuals. These findings suggest a significant association between hyperleptinemia and cerebrovascular stroke. In addition, the study demonstrated that stroke patients exhibited higher values of LDL cholesterol, fasting blood glucose, systolic blood pressure, diastolic blood pressure, and body mass index, further emphasizing the interrelationship between metabolic abnormalities and vascular pathology.

Leptin is a 16-kDa adipocyte-derived peptide hormone encoded by the *ob* gene, primarily involved in the regulation of appetite and energy expenditure through hypothalamic pathways. However, accumulating evidence indicates that leptin also plays an important role in vascular inflammation, endothelial dysfunction, oxidative stress, and thrombogenesis, which are key mechanisms in the development of atherosclerosis and stroke. Experimental studies have shown that leptin can stimulate endothelial cell proliferation, enhance oxidative stress through increased reactive oxygen species production, and promote vascular smooth muscle cell hypertrophy. Also, leptin increases platelet aggregation and contributes to the formation of atherosclerotic plaques, thus facilitating thrombotic events in cerebral circulation.[17]

The elevated leptin levels observed in the present study may therefore reflect a pathophysiological link between obesity-related metabolic disturbances and cerebrovascular injury. Adipose tissue is increasingly recognized as an active endocrine organ that secretes numerous cytokines and adipokines that influence vascular homeostasis. Among these mediators, leptin has been shown to promote the expression of monocyte chemoattractant protein-1 (MCP-1) and other proinflammatory cytokines that initiate endothelial dysfunction and vascular inflammation, thereby accelerating atherogenesis.[18]

In the current study, ischemic stroke patients demonstrated slightly higher leptin levels than hemorrhagic stroke patients, suggesting a possible association between leptin and atherosclerotic mechanisms underlying ischemic cerebrovascular events. This observation is consistent with previous epidemiological and experimental findings indicating that leptin contributes to the development of atherosclerotic plaque formation and arterial thrombosis. Soderberg and colleagues conducted a prospective population-based study demonstrating that elevated plasma leptin levels were independently associated with an increased risk of both ischemic and hemorrhagic stroke.[19] Similarly, Wannamethee et al. reported that higher circulating leptin concentrations were associated with grew incidence of stroke in older men, independent of traditional cardiovascular risk factors.[20]

The association between leptin and stroke risk may also be mediated through its interaction with other metabolic risk factors. In the present study, stroke patients exhibited significantly higher body mass index (BMI) compared with controls, and correlation analysis revealed a positive association between leptin levels and BMI. This finding is consistent with previous studies demonstrating that leptin concentrations are strongly correlated with adiposity and visceral fat accumulation. Obesity is an established risk factor for atherosclerosis, hypertension, and insulin resistance, all of which contribute to cerebrovascular disease.[21]

The relationship between leptin and dyslipidemia observed in this study further supports the role of leptin in vascular pathology. Stroke patients showed significantly higher total cholesterol and LDL cholesterol levels compared with controls. Elevated LDL cholesterol is a well-recognized contributor to atherosclerotic plaque formation and arterial stenosis. Leptin has been shown to enhance lipid oxidation and macrophage infiltration within the vascular wall, thereby accelerating the progression of atherosclerosis. Previous studies have also demonstrated that leptin can promote endothelial oxidative stress and impair nitric oxide-mediated vasodilation, leading to vascular stiffness and reduced cerebral perfusion.[22]

Another important observation in this study was the significant association between leptin levels and blood pressure parameters. Both systolic and diastolic blood pressure were significantly higher in stroke patients compared with controls, and correlation analysis indicated a positive relationship between leptin and blood pressure values. Hypertension is the most significant modifiable risk factor for stroke, and several experimental studies have suggested that leptin may contribute to the development of hypertension through activation of the sympathetic nervous system.[23] Chronic hyperleptinemia has been shown to increase sympathetic nerve activity, particularly in renal and cardiovascular tissues, leading to vasoconstriction and elevated blood pressure.[24]

Hyperglycemia and insulin resistance represent additional mechanisms linking leptin with vascular disease. The present study demonstrated elevated fasting blood glucose levels among stroke patients compared with controls. Hyperglycemia has been shown to exacerbate ischemic brain injury through mechanisms involving oxidative stress, lactic acidosis, and inflammatory cytokine activation.[25] Diabetes mellitus and insulin resistance are strongly associated with dyslipidemia and endothelial dysfunction, which further contribute to cerebrovascular pathology. Interestingly, leptin secretion is partially regulated by insulin, and several studies have demonstrated a close association between circulating leptin levels and insulin resistance.[26]

Despite the strong associations observed between leptin and several vascular risk factors, the precise role of leptin in stroke pathogenesis remains complex and may vary depending on underlying metabolic conditions. Some investigators have suggested that elevated leptin levels may reflect leptin resistance, a condition characterized by impaired hypothalamic signaling despite high circulating leptin concentrations. In such circumstances, hyperleptinemia may serve as a marker of metabolic dysfunction rather than a direct causal factor in vascular disease.[27] Nevertheless, evidence from experimental models indicates that peripheral vascular tissues may remain sensitive to leptin even when central leptin resistance develops, thereby allowing leptin to exert pro-atherogenic and pro-thrombotic effects within the vasculature.[28]

Gender-specific differences in leptin levels have been reported in several epidemiological studies; however, the present study did not demonstrate a statistically significant association between serum leptin levels and gender among stroke patients. In the present study, gender-wise analysis showed that mean serum leptin levels were 9.74 ± 4.72 ng/mL in females and 10.72 ± 4.09 ng/mL in males among ischemic stroke patients, whereas in hemorrhagic stroke patients, levels were 10.22 ± 3.00 ng/mL in females and 8.59 ± 3.74 ng/mL in males. Although minor variations were observed, these differences were not statistically significant, supporting the absence of a clear gender-based association in this study population. This observation is consistent with certain previous investigations that failed to identify a significant gender-based difference in leptin-associated stroke risk.[29] However, other studies have suggested that leptin may play a more prominent role in vascular disease among women, possibly due to differences in body fat distribution and hormonal regulation.[30,31]

In addition to its pathophysiological relevance, these findings may also have potential clinical implications. Elevated leptin levels may be associated with alterations in pharmacological response, particularly in therapies targeting metabolic and cardiovascular disorders. Leptin has been shown to influence endothelial function, inflammatory pathways, and sympathetic nervous system activity, which may indirectly affect the efficacy and safety profiles of commonly used medications such as statins, antihypertensive agents, and antidiabetic drugs. Hyperleptinemia may also reflect underlying metabolic disturbances that could contribute to variability in drug response. In addition, such metabolic alterations may potentially increase susceptibility to adverse drug reactions, including drug-induced dyslipidemia and insulin resistance. Therefore, leptin may be explored as a potential biomarker for identifying individuals who may require closer monitoring during pharmacological treatment. However, these associations require further validation in prospective studies.

In addition to conventional pharmacotherapy, integrative and alternative therapeutic approaches may play a role in modulating leptin levels and improving metabolic health. Nutraceuticals such as omega-3 fatty acids, curcumin, and resveratrol have been reported to modulate leptin levels and reduce inflammatory activity. Phytomedicinal agents and plant-derived bioactive compounds may also influence adipokine signaling pathways. Lifestyle interventions, including dietary modification, physical activity, and yoga-based practices, have been associated with improved leptin sensitivity and

metabolic regulation. These approaches may complement conventional therapies and could be explored as part of a comprehensive and patient-centered management strategy for reducing cerebrovascular risk.

From a clinical perspective, measurement of serum leptin may have potential utility in risk stratification and identification of patients with increased metabolic risk. Individuals with elevated leptin levels may require closer clinical monitoring and early intervention targeting modifiable risk factors. However, the incorporation of leptin into routine clinical practice requires further validation through large-scale prospective studies.

Despite these limitations, the present study provides important evidence supporting the association between hyperleptinemia and cerebrovascular stroke. The findings reinforce the concept that adipose tissue–derived mediators play a critical role in the pathophysiology of vascular disease and highlight the potential clinical value of leptin as a biomarker for stroke risk stratification. Future large-scale prospective studies incorporating longitudinal measurements of leptin and other adipokines will be necessary to determine whether leptin has a causal role in stroke development or primarily reflects underlying metabolic dysregulation.

5. LIMITATIONS OF THE STUDY

While the present study provides important findings, certain limitations should be considered when interpreting the results. The study involved a relatively small sample size from a single institution, which may limit the generalizability of the findings to broader populations. In addition, the case–control design of the study limits the ability to establish a causal relationship between leptin levels and cerebrovascular stroke. Serum leptin concentrations were measured after the occurrence of stroke; therefore, it is difficult to determine whether elevated leptin levels preceded the cerebrovascular event or resulted from the acute inflammatory response associated with stroke. The study also evaluated a limited number of metabolic parameters, and other adipokines and inflammatory biomarkers such as adiponectin, insulin, and C-reactive protein were not assessed. Furthermore, leptin measurements were obtained at a single time point, and potential influences of circadian variation or acute physiological stress could not be evaluated. The study did not evaluate therapeutic interventions or drug response outcomes; therefore, any implications related to pharmacotherapy and drug safety remain exploratory and require confirmation in prospective and interventional studies. Future large-scale prospective and longitudinal studies incorporating additional metabolic and inflammatory biomarkers are warranted to further clarify the role of leptin in cerebrovascular stroke pathophysiology and risk prediction.

6. CONCLUSION

The findings of the present study indicate that circulating serum leptin levels are significantly elevated in patients with cerebrovascular stroke compared with healthy controls, suggesting an association between hyperleptinemia and cerebrovascular disease. Stroke patients also exhibited higher levels of LDL cholesterol, fasting blood glucose, blood pressure, and body mass index, reflecting the presence of multiple cardiometabolic risk factors. The observed associations between leptin and these parameters suggest that leptin may be linked to vascular dysfunction through mechanisms involving inflammation, endothelial impairment, and atherosclerotic processes. These findings support the potential role of leptin as a biomarker of metabolic dysregulation and vascular risk in cerebrovascular disease. Measurement of leptin may have clinical relevance in risk stratification and identification of individuals with increased metabolic risk. Further large-scale prospective and interventional studies are required to clarify whether leptin plays a causal role in stroke pathogenesis or primarily reflects the underlying metabolic environment associated with cerebrovascular disease.

Conflict of Interest: The authors declare that they have no conflicts of interest related to this study or its publication.

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