Zagazig University Medical Journal
www.zumj.journals.ekb.eg
Volume 29, Issue 1, January 2023 https://dx.doi.org/10.21608/zumj.2022.138123.2567
ORGINAL ARTICLE
Manuscript ID ZUMJ-2205-2567 (R2)
DOI 10.21608/zumj.2022.138123.2567

The Role of Serum Leptin as a Prognostic Biomarker for Short-Term Outcome in Acute Ischemic Stroke

Hala Ahmad Fathy[1], El Hady Ahmed Abd El Gwaad[1], Karam Selim Amin[1], Sally Mahmoud Said[2], Ghada Abd El Wahab Khalil Ibrahim[1]

[1]Neurology Department, Faculty of Medicine, Zagazig University, Egypt.

[2]Biochemistry Department, Faculty of Medicine, Zagazig University, Egypt.

*Corresponding author:
Ghada Abd El Wahab Khalil Ibrahim.
Department of Neurology, Faculty of Medicine, Zagazig University, Egypt.
E-mail address: dr.g.abdelwahab@gmail.com

Submit Date 2022-05-24 22:33:59
Revise Date 2022-07-21 20:38:13
Accept Date 2022-07-30 02:20:49

ABSTRACT

Background: Stroke is a multifactorial disease that affects people all over the world. Elevated plasma leptin levels have been found to be independently related to ischemic stroke; additionally, high serum leptin levels serve as an independent biomarker of poor outcome after ischemic stroke. The current study sought to investigate the role of serum leptin levels as a predictor of short-term outcome in acute ischemic stroke.

Methods: This prospective cohort study included sixty patients with their first acute ischemic stroke (19 males and 41 females). All patients underwent a full clinical evaluation as well as a thorough general and neurological examination. The NIHSS was used to assess stroke severity on admission, and the mRS was used to assess functional outcome 30 days later. Serum leptin levels and routine laboratory tests were also evaluated. All patients had neuroimaging, including CT and/or MRI brain scans.

Results: from the analysis it was found a statistically significant link between serum leptin levels and diabetes, hypertension, cardiac disease, and obesity. A statistically significant positive correlation was found between serum leptin levels and infarction size. There was also a statistically significant relationship between serum leptin level and stroke severity as measured by NIHSS score on admission. AIS patients with poor functional outcome as measured by mRS after 30 days of admission had highly statistically significant serum leptin levels. After adjusting for other confounding variables, a binary logistic regression analysis of neurological outcome with associated risk factors revealed that diabetes mellitus, elevated serum leptin levels, NIHSS, and mRS scores were the most significant risk factors for predicting deterioration and short-term outcome after ischemic stroke.

Conclusions: Elevated serum leptin levels were associated with vascular risk factors, infarct size, and severity of acute ischemic stroke, supporting the hypothesis that serum leptin can be used as a significant and reliable biomarker of poor outcome after ischemic stroke, independent of other baseline variables. **Keywords:** Ischemic stroke; Serum leptin; Functional outcome.

INTRODUCTION

Stroke is a multifactorial disease that affects people all over the world. It is regarded as the leading cause of disability and death worldwide. Stroke is a serious neurological disease that is the leading cause of disability in the world. It is the second leading cause of death worldwide, and the third leading cause in more developed countries [1].

Stroke is caused primarily by thrombosis, embolism, and focal hypoperfusion, all of which can result in a decrease or interruption in cerebral blood flow (CBF), affecting neurological function. Because the brain receives 20% of cardiac output at rest it is extremely sensitive to ischemia, and even brief ischemic periods to neurons can set off a complex chain of events that can result in permanent cerebral damage [2].

The metabolic syndrome is a group of vascular risk factors and metabolic abnormalities that include: 1-centrally distributed obesity; 2-atherogenic dyslipidemia, which is characterized by elevated triglycerides and decreased high-density lipoproteins; 3-high blood pressure; and 4-hyperglycemia [3]. This group of interconnected factors appears to increase an individual's risk of vascular disease by promoting the development of

atherosclerotic vascular disease and type II diabetes [4].

Leptin is a hormone that is primarily produced by adipose cells in adipose tissue and is increased in response to various stimuli (insulin, glucose, tumor necrosis factor alpha (TNF)-a, interleukin one (IL-1) Glucocorticoids and estrogens) and in renal failure. Leptin and adipokines act as ligands that connect risk factors and molecular mechanisms of ischemic stroke. In healthy conditions, the multivalent activities of these two factors are normally balanced, but any change in their levels can disrupt homeostasis [5].

Furthermore, [4] hypothesized that the change in their levels could be gender and/or age related, although leptin was discovered to be a risk biomarker for first-ever hemorrhagic stroke, [6] demonstrated in their study that elevated plasma leptin levels have been found to be independently associated with ischemic and hemorrhagic stroke in men.

A recent prospective study carried out on white Europeans (>99%) and British aged men without a history of stroke, followed-up to 9 years, revealed that higher Lept [7] demonstrated that high leptin levels are associated with stroke severity and poor functional outcome; additionally, ischemic stroke patients with poor functional outcome had high serum leptin levels, supporting the hypothesis that leptin level could be a significant biomarker of poor outcome after stroke, independent of other baseline variables.

METHODS

Ethical approvals:

The study was carried out under the number (ZU-IRB #5070-23-12-2018). According to the ethical rules of the Institutional Review Board, written informed consent was obtained from all patients recruited or written assent from a relative (IRB). The patients in the study were given a clinical diagnosis of acute ischemic stroke with suspected symptom onset within the previous 24-48 hours.

Study Design:

This prospective follow-up cohort study was conducted in the Neurology Department of Zagazig University Hospitals between September 2018 and September 2019. This study included sixty first-ever acute ischemic stroke patients (19 males and 41 females), ranging in age from 33 to 90 years, with a mean age of 65 years 8. Patients were recruited prospectively from the Neurology Critical Care Unit and the Neurology Stroke Unit.

Inclusion criteria:

Patients who present with acute ischemic stroke (AIS) and are diagnosed using the World Health Organization (WHO) stroke criteria [13]. Patient's age: over the age of 18. Stroke is defined as rapidly developing clinical symptoms and signs (focal or global) of cerebral function disturbances lasting more than 24 hours (unless interrupted by surgery or death) with no apparent cause other than vascular origin. Patients with early imaging signs of a cerebral infarct or a recent infarct were included in the study. Admission within 24-48 hours of the insult's onset.

Exclusion criteria:

Hemorrhagic stroke and other non-ischemic strokes (intracerebral hemorrhage or subarachnoid hemorrhage). Patients with old infarctions and venous infarctions found on CT scan. Patients who have had a head injury or surgery. Patients with brain tumors or other forms of systemic cancer. Patients suffering from CNS infections or systemic sepsis. Patients suffering from metabolic emergencies. Patients experiencing multiple system failures. Patients who died during follow-up for any reason.

The following procedures were performed on all patients:

Clinical evaluation, which includes a detailed medical history is obtained from the patients or their relatives, with special attention paid to past medical history, to determine the presence of any risk factors such as HTN, DM, dyslipidemia, smoking, and cardiac diseases. Comprehensive general examination with emphasis on blood pressure measurement: Hypertension is defined as having a systolic blood pressure greater than 130 mmHg and/or a diastolic blood pressure greater than 80 mmHg on at least two occasions. Body mass index is calculated by dividing one's weight in kilograms by one's height in square meters. BMI classifications: -Underweight < 18.5 kg/m2. -Weight normal = 18.5-24.9 kg/m2. -Weight gain=25-29.9 kg/m2. -Obesity >30 kg/m2 [14]. ECG. Echocardiography was performed at Zagazig University's echocardiography unit, cardiology department.

Extensive neurological examination

All patients in our study underwent a thorough neurological examination. To assess the level of consciousness, stroke severity, follow-up, and short-term outcome of stroke, the following scales were used:

The Glasgow Coma Scale (GCS) was used to assess the level of consciousness.

National Institutes of Health Stroke Scale (NIHSS) assessment of stroke severity: The initial evaluation

of stroke severity was performed using the NIHSS; at admission, the stroke severity of the studied patients was classified as follows: If the NIHSS is less than 6, the stroke severity is mild. If the NIHSS score is 6-15, the stroke severity is moderate. If the NIHSS is 16-20, the stroke is moderate to severe. If your NIHSS score is 21-42, you have a severe stroke.

Assessment of functional outcome (follow-up) after 30 days using Rankin Scale Modified (mRs). We used it to assess our patients' short-term outcomes (including mortality) after 30 days from the onset of their stroke. The scale has six grades ranging from 0 to 6, with the best score 0 corresponding to no symptoms and the worst score 5 corresponding to severe disability, while death is rated 6 in the mRS. A score on the mRS ranging from 0 to 2 denotes a good outcome, while a score of 3 denotes a poor outcome [8].

Investigations:

Laboratory Investigations:

On admission, all routine laboratory tests are performed. Full blood count (CBC). Examinations of liver function (ALT, AST, S. Albumin, and Total Bilirubin). Kidney function examinations (S. Creatine, S. Urea). In diabetic patients, random plasma glucose level on admission, followed by fasting and 2 hours post-prandial plasma glucose assessment. Total cholesterol (TC), triglycerides (TGS), high density lipoprotein (HDL), and low-density lipoprotein (LDL) are the lipid profiles (LDL). Coagulation profile: prothrombin time (PT), prothrombin concentration (PC), international normalized ratio (INR), international normalized ratio (INR), international normalized ratio (INR), international normalized ratio (INR) (INR).

Leptin concentrations in the blood:

Participants' 3 ml peripheral venous blood samples were collected on plain vacationer tubes and centrifuged at 1000g for 10 minutes. The serum samples were then collected and stored at -80 C until leptin analysis. The enzyme-linked immunosorbent assay was used to determine the serum leptin concentration (ELISA). Serum leptin levels were measured twice: once within 48 hours of admission and again after 30 days.

Principle of testing:

To determine the level of Human Leptin (LEP) in samples, the kit employs a double-antibody sandwich enzyme-linked immunosorbent assay (ELISA). Incubate Leptin (LEP) in a monoclonal antibody Enzyme well pre-coated with human Leptin (LEP) monoclonal antibody; then, incubate Leptin (LEP) antibodies labeled with biotin and Streptavidin-HRP to form an immune complex; then, repeat incubation and washing to remove the uncombined enzyme. When you add Chromogen Solution A, B, the color of the liquid changes to blue, and when you add acid, the color changes to yellow. The color chrome and the concentration of the human substance Leptin (LEP) in the sample were found to be positively correlated.

Other investigations:

On admission, a chest x-ray was performed to rule out acute pulmonary embolism. Carotid Doppler ultrasonography is used when necessary.

Brain imaging:

A CT scan of the brain was performed.

To confirm the diagnosis of AIS, all patients underwent a plain CT scan of the brain using a Philips scanner (Tom scan 350) with scanning time = 4.8, matrix size = 512 x 512, and slice thickness = 9 mm. Supine positioning was used for all axial scans. The CT brain was examined for early infarction signs, as defined by Wardlaw and Mielke (2005) [18].

Brain magnetic resonance imaging (MRI)

Magnetic Resonance Imaging (MRI) of the brain was performed in cases of early AIS or suspected brain stem lesions. Within 2-3 days, a second plain CT scan or MRI of the brain was performed for volumetric analysis to determine the location and size of the infarct. The infarct size was estimated (Size = 0.5 x an x b x c x number of slices), where a and b represent the largest perpendicular diameters detected by the CT scan and c represents the slice thickness (9 mm) [9], the size of an ischemic stroke lesion is classified as small (less than 1.5 cm3), medium (1.5 cm3 to 3 cm3), or large (size more than 3 cm3).

Statistical Analysis:

The statistical analysis was carried out by computer using (SPSS) version 24. Shapiro Walk test was used to check the data for normal distribution. To calculate the difference between qualitative variables, the Chi square test (2) and Fisher exact were used, as indicated. For non-parametric data, quantitative data were expressed as the median and interquartile range (not normally distributed).

For non-parametric variables, the Mann Whitney test was used to calculate the difference between quantitative variables in two groups. For non-parametric variables, the Kruskal-Walli's test was used to calculate the difference between quantitative variables in more than two groups, and Dunn's Post hoc test was used for multiple comparisons. For non-parametric variables, the

Wilcoxon Signed Ranks test is used to compare changes before and after follow-up.

A multivariate logistic regression analysis model was used to identify independent predictors of neurological deterioration. Non-parametric variables were correlated using Spearman's correlation tests. A receiver operating characteristic curve (ROC) curve was created to allow for the selection of threshold values for test results as well as the comparison of various testing strategies.

For statistical analysis, we used the Statistical Package for Social Sciences (SPSS) 24.0 software (SPSS, Inc., Chicago, IL, USA). For statistical significance, an alpha level of less than 0.05 was used.

RESULTS

Table (1) reveals that there is highly statistically significant association between leptin serum level and diabetes mellitus, hypertension, obesity and cardiac patients (<0.001), also it shows that serum leptin level was significantly higher among cardioembolic type of ischemic stroke with P value equal 0.007.

Table (2) demonstrates that patients with severe stroke (as accessed by NIHSS score) was associated with higher serum leptin level after 30 days of follow up with statistically significantly higher in patients with poor functional outcome as detected by mRS after 30 days with P value (0.05).

Table (3) shows that the significant risk factors for unfavorable outcome in the studied patients were diabetes mellitus, higher serum leptin level, higher NIHSS score and poor mRS after 30 days.

Figure (1) reveals that a cutoff ≤12.45 had an AUC of 0.663 (95% CI,0.529 to 0.780) with a sensitivity of 71.43% (95% CI, 29.0 - 96.3%) and a specificity of 75.47% (95% CI,61.7 - 86.2%), P= 0.193.

Table 1: The relationship between serum leptin level and both ischemic stroke risk factors and stroke subtypes among the studied AIS patients.

		Serum Leptin, ng/mL.		Test	P-value
		Median	IQR		
Gender	Female	15.14	(12.34-17.21)	-0.405*	0.685¶
	Male	13.68	(11.26-18.1)		
Diabetes mellitus	No	12.34	10.46-13.23	-6.456*	<0.001¶
	Yes	17.23	16.2-18.8		
Hypertension	No	11.26	10.34-12.45	-6.645*	<0.001¶
	Yes	16.38	15.24-18.36		
Smoking	No	15.46	(12.37-17.23)	-0.961*	0.336¶
	Yes	13.54	(11.26-16.78)		
Cardiac diseases	No	12.31	10.46-12.56	-6.553*	<0.001¶
	Yes	17.21	15.53-18.8		
Obesity	No	11.27	10.36-12.5	-6.457*	<0.001¶
	Yes	16.47	15.46-18.38		
Hyperuricemia	No	15.19	(12.475-17.355)	-0.902*	0.367¶
	Yes	12.9	(11.77-16.625)		
Dyslipidemia	No	13.96	(11.36-16.995)	-0.870*	0.384¶
	Yes	15.39	(12.42-17.92)		
Ischemic Stroke subtypes		S. Leptin, ng/mL. Median	IQ range	KW Test	P
Undetermined		12.65	(11.64-18.2)	-3	0.007
Cardio embolic		19.35	(16.36-24.05)		
Large artery atherosclerotic		14.71	(10.36-17.48)		
Lacunar		12.31	(10.46-13.68)		

* Compared using Mann Whitney test; ¶ = Significant.

Table 2: Association between serum Leptin level and both stroke severity and functional outcome after 30 days.

		S. Leptin, ng/mL		KW Test	P
		Median	IQ range		
Initial NIHSS	Moderate	15.89	(13.37-18.37)	2	0.872
	Moderate to severe	17.48	(11.64-21.3)		
	Severe	21.79	(12.5-23.57)		
NIHSS. after 30 days	Minor	14.94	(11.47-16.46)	3	0.04
	Moderate	16.47	(12.6-18.38)		
	Moderate to severe	14.7	(11.53-23.55)		
Functional. Outcome (mRS) after 30 days		Serum Leptin, ng/mL Median	IQ range	MW Test	P
mRS 0-2 (n=19)		15.24	(12.31-18.34)	-1.92	0.05
mRS 3 -5 (n=41)		17.48	(13.25-22.47)		

P ≤ 0.05= significant and P >0.05 non-significant. *mRS (0-2) is good, (3-5) is poor.

Table 3: Binary logistic regression analysis of neurological deterioration and poor outcome with associated risk factors

Covariates		Odds ratio	(95% CI)	Sig.
Age		0.910	0.76-1.09	0.305
Sex		0.263	0.003-24.946	0.565
DM		1.166	0.04-14.352	0.022*
HTN		0.0003	0.0001-0.009	0.999
Smoker		0.690	0.015-31.274	0.849
Obesity		36.950	0.976-1399.035	0.052
Dyslipidemia		5.581	0.121-256.41	0.379
S. Leptin, ng/mL.		1.104	0.432-1.146	0.008*
NIHSS		3.12	0.151-7.24	0.032*
mRS		2.712	0.128-4.213	0.014*
Size	(Medium vs small)	0.177	0.004-7.076	0.358
	(Large vs small)	0.226	0.008-6.137	0.377
Constant		1687.5		

*Significant, (CI)confidence interval.

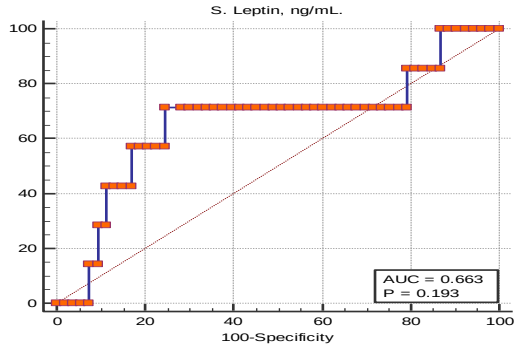

Figure 1: The Area under the ROC curve (AUC) of initial serum Leptin as a prognostic marker for neurological deterioration.

DISCUSSION

The aim of the current study was to assess the serum levels of leptin and its association with severity of acute ischemic stroke and functional outcome as well. The study included 60 first ever acute cerebrovascular ischemic stroke patients (68.3% were females while 31.7% were males). Their mean age was 65 ± 8years with a range 60-70 years.

On studying the distribution of underlying vascular risk factors in our AIS patients, the results of the current study reported that hypertension was found in 48 patients (80%) of AIS patients, diabetes was found in 40 AIS patients with percentage of (66.7%), while dyslipidemia was reported in (33.3%) of our patients. Regarding cardiac risk factors in our study, 19 (31.7%) patients were smoker, 51.70% of patients were obese and 41.70% of AIS patient had Leukoaraiosis.

Regarding the relationship between ischemic stroke risk factors and serum leptin level, we found that there is statistically significant association between serum leptin level and diabetes mellitus and statistically significant positive correlation between leptin serum level and random blood sugar (RBS), consistent with these observations [6] in quartiles of leptin associated with increase in random blood sugar (RBS).

In our study, we found no significant association between serum leptin level and smoking, a finding that was opposite to results of [10-11]. As regards dyslipidemia, we found no statistically significant association between leptin serum level and history of dyslipidemia. Obesity is a known risk factor for the development of atherosclerosis and is considered a health burden. Regarding obesity as a risk factor, the present study reported highly statistically significant association between serum leptin level and obesity in patients with increased body weight, this finding was in accordance with [12-14].

Correlation analysis showed that BMI positively correlated with leptin, implicating leptin's role in stroke via visceral adiposity. The positive correlation between body mass index and serum leptin is probably explained primarily by the increased release of leptin from large fat cells.

In fact, some studies have proposed that leptin can serve as an indicator of fat content and that its levels increase exponentially with increasing body fat percentage. Leptin levels decrease by reduction of body fat even though BMI values remain unchanged. In contrary to that result, [15] showed no significant correlation between serum leptin level and obesity.

On studying the relationship between cardiac diseases as risk factors for ischemic cerebrovascular stroke and serum leptin, we found that serum leptin level was highly significantly elevated among patients with history of cardiac diseases (with P value was<0.001), consistent with our findings, [9].

The current study showed that serum leptin level was statistically significantly higher among cardio embolic subtype of ischemic stroke, this finding was consistent with [16-17]. A statistically significant of higher level for serum leptin in AIS patients was found, moreover serum leptin level was significantly positively correlated with NIHSS score, this agrees with [18].

On studying the relationship between the radiological findings among the studied AIS patients and serum leptin level both at admission and after 30 days of follow up, the present study showed that AIS patients with large sized infarction had significantly higher serum leptin level than those with small and moderate sized lesions, in addition, a significant positive correlation was recorded between size of brain infarction and serum leptin level, a result that was matching to that of [19].

Also, our results showed that 41.7% of our patients had early signs of middle cerebral artery (MCA) infarction, while the percentage was 20.8% by [20]. Moreover, ischemic stroke of anterior circulation had a higher percentage (81.7%), these results were consistent with that of [21-23].

In addition, the results of the current study reported that left sided weakness (LSW) were more frequent than right sided weakness (RSW). This agrees with Pan et al. (2005) who reported 53.1 % of ischemic stroke patients with LSW, 46.8 % with RSW and [24] in which 50% of cases presented with LSW, in comparison with 38% presented with RSW.

To assess the prognostic role of serum leptin level as a significant and reliable biomarker of poor functional outcome among our study patients, a binary logistic regression analysis of neurological deterioration and poor outcome was done and the results of the current study demonstrated that both diabetes, high NIHSS score, poor mRS and elevated serum leptin level were the most independent important predictors for neurological deterioration and poor functional outcome after 30 days with adjusting for other confounding study variables.

This result was in accordance with [25] who demonstrated that elevated serum leptin level and

fasting blood sugar were the most important risk factors for neurological deterioration.

CONCLUSIONS

In conclusion, and in view of our results in the present study, we reached to a conclusion that elevated serum leptin level was significantly associated with vascular risk factors, infarct size, and severity of acute ischemic stroke as well as poor functional outcome, supporting the hypothesis that serum leptin can be served as a significant and reliable biomarker of poor outcome after ischemic stroke, independently of other baseline variables.

Conflicts of Interest/ Financial Disclosures: Nothing to declare.

REFERENCES

(1) Amelia K, Charles E, Mitchell S. Stroke risk factors, genetics, and prevention. Circ Res 2017; 120(3): 472–95.

(2) Guo Y, Li P, Guo Q, Shang K, Yan D, Du S, Lu Y. Pathophysiology and biomarkers in acute ischemic stroke. Trop J Pharm Res 2013 ; (6) : 1097-105.

(3) Savopoulos C, Michalakis K, Apostolopoulou M, Miras A, Hatzitolios A. Adipokines and stroke: a review of the literature. Maturitas. 2011; 70: 322-7.

(4) Kantorova E, Jesenska L, Cierny D et al. The intricate network of adipokines and stroke. Int J Endocrinol 2015;15: 47-54.

(5) Wannamethee SG, Whincup PH, Lennon L, Rumley A, Lowe G. Fibrin D-dimer, tissue-type plasminogen activator, von Willebrand factor, and risk of incident stroke in older men. Stroke. 2012; 43(5): 1206-11.

(6) Soderberg S, Stegmayr B, Stenlund H Ågren A, Johansson L, Weinehall L, Olsson T. Leptin, but not adiponectin, predicts stroke in males. J Int Med 2004; 2: 128–36.

(7) Wang Z, Li B, Wang Y, Maimaitili A, Qin H, Dangmurenjiafu G, Wang S. The association between serum adiponectin and 3-month outcome after ischemic stroke. Cardiovasc Diabetol 2019; 18: 105.

(8) Bogousslavsky J, Diserens K, Rothacher G. Stroke selected topics in seminars in clinical neurology. 2006; 4: 1-65.

(9) Alemam AI, Elwan ME, and Alahmar IA. Prognostic value of hypothalamic copeptin in acute ischemic stroke. J Neurol Res 2016; (6):41-5.

(10) Bokarewa M, Erlandsson M, Bjersing J, Dehlin M, Mannerkorpi K. Smoking is associated with reduced leptin and neuropeptides Y levels and higher pain experience in patients with fibromyalgia. Mediat Inflamm 2014; doi.org/10.1155/2014/627041.

(11) Huang ZX, Qi-Zhang Wang, Ying-Yi Dai a, Hai-Ke Lu, Xiao-Yu Liang, Huan Hu, et al. Early neurological worsening in acute ischemic stroke patients. Acta Neurol Scand 2016; 133: 25-9.

(12) Fernández-Riejos P, Najib S, Santos-Alvarez J, Martín-Romero C, Pérez-Pérez A, González-Yanes C, Sánchez-Margalet V. Role of leptin in the activation of immune cells. Mediat Inflamm 2010; Article ID 568343.

(13) O'Donnell M, Xavier D , Diener C, Liu L ,Chin S, Melacini P, et al. Rationale and design of INTER `STROKE: a global case-control study of risk factors for stroke. Neuro Epidemiology 2010; 35: 36-44.

(14) Payne GA, Tune JD, Knudson JD. Leptin-induced endothelial dysfunction: A target for therapeutic interventions. Curr Pharm Des 2014; 20: 603-8.

(15) Kim B, Lee S, Ryu W, Kim C, Yoon B. Adipocytokines and ischemic stroke: differential associations between stroke subtypes. J Neurol Sci 2012; 312:117-22.

(16) Ghantous CM, Azrak Z, Hanache S, Abou-Kheir W, Zeidan A. Differential role of leptin and adiponectin in cardiovascular system. Int J Endocrinol 2015; Article ID 534320.

(17) Szczepańska-Szerej A, Kurzepa J, Grabarska A, Bielewicz J, Wlizło-Dyś E, Rejdak K. Correlation between CH_2DS_2-VASc score and serum leptin levels in cardio embolic stroke patients: The impact of metabolic syndrome. Int J Endocrinol 2017; Article ID 7503763.

(18) Yoo J, Castonguay A, Zaidat O et al. Influence of age on clinical and revascularization outcomes in the North American solitaire stent-retriever acute stroke Rregistry. Stroke 2014; 45(12): 3631–6.

(19) Kelesidis T, Kelesidis L, Chou S, Mantzoros C. Narrative Review: The role of leptin in human physiology: Emerging Clinical Applications. 2010; 152(2): 93-100.

(20) Fathy S, Abd El Gawad E, El Motayam A, Mohammed W. Blood biomarkers; brain naturistic peptide, d-Dimer and creatine kinase-MB in patients with cardio embolic stroke. 2018; MD thesis. Zagazig University.

(21) Kang DW, Yoo SH, Chun S, Kwon K, Kwon S, Koh J, Kim J. Inflammatory and hemostatic biomarkers associated with early recurrent ischemic lesions in acute ischemic stroke. Stroke 2009; 40: 1653–8.

(22) Abdel Ghani A, Zaitoun A, Gawish H. Prognostic value of d-Dimer in diffusion weighted-MRI defined early ischemic stroke recurrence. Egypt J Neurol Psychiatry Neurosurg 2011; 48: 215-222.

(23) Jung KW, Shon YM, Yang DW, Kim BS, Cho A. Coexisting carotid atherosclerosis in patients with intracranial small-or large-vessel disease. J Clin Neurol 2012; (8): 104-8.

(24) Danthala M, Lakshmaiah V. Correlative study of serum cystatin C levels with severity of acute ischemic stroke. J Clin Biomed Sci. 2013; 3(4): 188-92.

ORGINAL ARTICLE
ZAGAZIG UNIVERSITY MEDICAL JOURNAL

To Cite:
Fathy, H., Abd-Elgawad, E., Amin, K., Said, S., Khalil Ibraheem, G. The role of serum leptin as a prognostic biomarker for short term outcome in acute ischemic stroke. *Zagazig University Medical Journal*, 2023; (238-244): -. doi: 10.21608/zumj.2022.138123.2567