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Original Research Article

# Association between plasma adiponectin levels and severity of acute ischemic stroke

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ABSTRACT

**Background:** There is little documentation describing the correlation between plasma adiponectin and the severity of ischemic stroke in the Indian population. The present study was aimed to find the correlation between plasma adiponectin levels and severity of acute ischemic stroke using the National Institute of Health Stroke Scale (NIHSS) and Modified Rankins Scale (MRS).

**Materials and Methods:** The present prospective observational study was conducted on 109 patients of confirmed acute ischemic stroke aged ≥ 30 years presenting within 24 hours of new onset of neurodeficits. NIHSS and MRS were measured within 24 hours and 5 days after onset of symptoms respectively. Plasma adiponectin levels were measured. The primary objectives were to find the correlation of plasma adiponectin levels with severity of acute ischemic stroke using the NIHSS and neurological functional outcome using the MRS. The secondary objectives were to find an association of plasma adiponectin levels with serum lipid profile and comorbidities.

**Results:** There was a negative correlation between plasma adiponectin levels and NIHSS score (r = - 0.110, p-value = 0.253) and MRS (r = -0.041, p-value = 0.672) which was not statistically significant. The median plasma adiponectin levels were comparable between the groups of cases with co-morbidity and without co-morbidity. A significantly higher percentage of patients who had high triglyceride levels had normal plasma adiponectin levels. The distribution of other lipid parameters and hypertension did not differ significantly between the groups of cases with normal and abnormal plasma adiponectin levels.

**Conclusions:** There was no correlation between plasma adiponectin levels and severity of acute ischemic stroke.



## 1. Introduction

Multiple studies have shown various physiological effects of the hormone adiponectin, including insulin sensitizing, anti-atherogenic and anti-inflammatory.[1–4] Studies have shown that lower levels of adiponectin correlate best with chronic inflammation associated with Type 2 diabetes mellitus, obesity and cardiovascular diseases (CVD).[1,2,5] Adiponectin has been shown to have both pro inflammatory as well as anti-inflammatory properties. It was reported that adiponectin acts as a pro inflammatory mediator namely for the development of rheumatoid arthritis, chronic kidney disease, and inflammatory bowel disease.[2] It was also associated with prolonging lifespan and ageing however, higher plasma adiponectin levels were associated with adverse outcomes in people aged more than 65 years.[6]

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Globally, stroke was the second-leading cause of death (11.6% of total deaths) after ischemic heart disease (16.2%) in the year 2019. Ischemic stroke constituted 62·4% of all new strokes in 2019 (7·63 million strokes), intracerebral haemorrhage constituted 27.9% (3·41 million), and subarachnoid haemorrhage constituted 9.7%.[7] In 2019, the estimated number of incident cases of stroke in India was 1·29 million, and number of deaths due to stroke was 6,99, 000. The crude Disability Adjusted Life Years rate of stroke had a 5·5 times variation between the states in 2019, with the highest rate in West Bengal, followed by Chhattisgarh and Tripura.[8]

Currently no biomarker exists to predict the severity and prognosis of acute ischemic stroke effectively. Traditionally, various scoring systems such as the National Institute of Health Stroke Scale (NIHSS) have been used to quantify the severity of the acute ischemic stroke with the use of clinical parameters.[9] This scale has also been traditionally used to evaluate and take a decision of the use of recombinant tissue plasminogen activator (rTPA) for thrombolysis.[10]Similarly, the Modified Rankins Scale (MRS) has been used to quantify the residual neurodeficit in ischemic stroke patients.[11]

Many studies were conducted to find the correlation between plasma adiponectin levels and atherosclerotic CVD like myocardial infarction, ischemic stroke and carotid atherosclerosis. However, there are conflicting results.[12–15] There is little documentation describing the correlation between plasma adiponectin and the severity of ischemic stroke in the Indian population. This study was aimed to find the correlation between plasma adiponectin levels and severity of acute ischemic stroke patients using the NIHSS and MRS.

## 2. Materials and Methods

This prospective observational study was conducted between November 2021 and October 2022 in Poona Hospital and Research Centre, Pune, India. After approval from the institutional ethics committee (Letter # RECH/ECBHR/2020-21/372), written informed consent was obtained from all the patients. One-hundred nine patients aged ≥ 30 years of either sex presenting with new onset focal neurological deficits, confirmed of acute ischemic stroke on magnetic resonance imaging (MRI) and presenting within 24 hours of onset of neurodeficits were included. Patients with haemorrhagic stroke, traumatic brain injury, spontaneous intracranial haemorrhage, demyelinating syndromes like multiple sclerosis, intracranial space occupying lesions and patients of stroke who were thrombolysed using rTPA were excluded.

Detailed history of the patient was taken, physical examination including neurological examination was done. The diagnosis of acute ischemic stroke was confirmed on GE SIGNA pioneer 3 Tesla 96 channel wide bore MRI machine (manufactured in Japan). After taking informed written consent all the required blood investigations were done within the first 24 hours of onset. NIHSS and MRS were measured within 24 hours and 5 days after onset of symptoms respectively. Plasma adiponectin levels was measured with a two-step sandwich Enzyme Linked Immunosorbent Assay (ELISA) kit, Diagnostic Biochem, Canada. NIHSS was calculated by National Institute of Health, USA guidelines,[9]whereas the severity of the stroke was labelled from Zhuo Y et al.[16] Modified Rankins Score was calculated from Banks and Marotta CA.[11]

All the patients included in the study were not candidates for intravenous thrombolysis and mechanical thrombectomy. They received standard care in the form of dual antiplatelets and statins, with control of blood sugar control and blood pressure. The primary objectives were to find the correlation of plasma adiponectin levels with severity of acute ischemic stroke using the NIHSS within first 24 hours and neurological functional outcome of acute ischemic stroke at the end of 5 days using the MRS. The secondary objectives were to find an association of plasma adiponectin levels with serum lipid profile and comorbidities. A sample size of 109 patients was calculated by a formula $N^{17} = [(Z\ \alpha + Z\ \beta)/C]\ 2 + 3$, where $Z\ \alpha$ a standard normal variate at 5% type 1 error = 1.96, $Z\ \beta$ the standard normal deviate at $\beta$ power 80 % at type II error = 0.842 and $C = 0.5 * \ln[(1+r)/(1-r)]$. The sample size was calculated from the previous study by Wang Z et al. who reported a positive correlation of 0.266 between NIHSS score and plasma levels of adiponectin.[18]

Data collected was entered in Excel 2019, and analysis of data was done using Statistical Package for Social Sciences (SPSS) for Windows, Version 24, IBM Corporation, USA. The data on categorical variables are shown as n (% of cases), and the data on continuous variables are presented as mean, and standard deviation (SD). Comparison of the distribution of categorical was done using the Chi-Square or Fisher's exact test. The medians of continuous variables were tested using Mann-Whitney U test. Spearman's correlation analysis was used to find the correlation. A p-value $< 0.05$ was considered as statistically significant.

## 3. Results

Of 181 patients who were admitted with acute neurological deficit were screened with MRI brain. Fifty-one patients were excluded; because 43 had haemorrhagic stroke, 6 had demyelinating lesions and 2 had space occupying lesions. Of 130 patients of acute ischemic stroke patients, 21 were excluded because 20 patients presented in the window period hence were thrombolysed using rTPA and one patient refused to participate in the study. In all 109 patients were included and analysed in the present research (Figure 1). The demographic and clinical profile of the study population

is depicted in Table 1. The mean ± SD of age of the study population was 54.5 ± 5.5 years. Of 109 cases studied, 26(23.9%), 30(27.5%), 20(18.3%) and 33(30.3%) patients had minor stroke (NIHSS < 5), moderate stroke (NIHSS between 5 – 15), moderate to severe stroke (NIHSS between 16 – 20) and 33 severe strokes (NIHSS between 21-42) respectively.

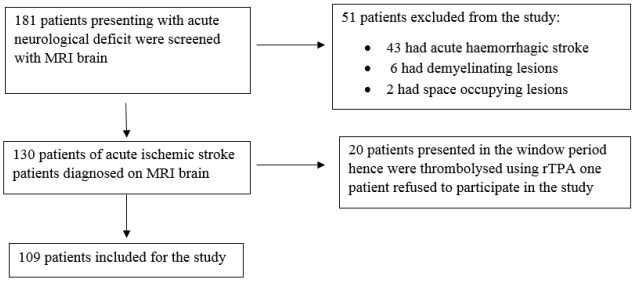


**Fig. 1:** CONSORT flow diagram

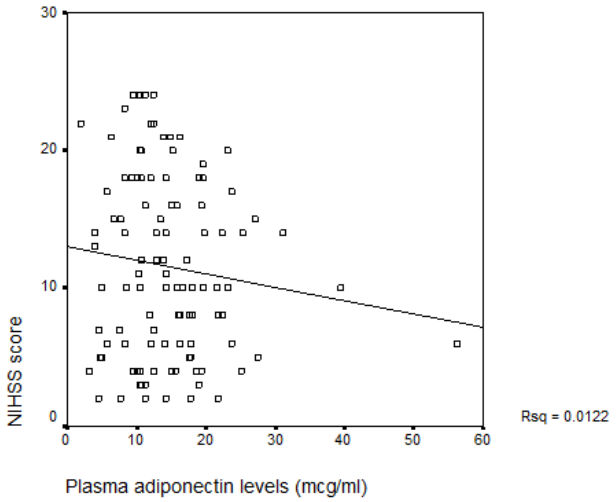


**Fig. 2:** Correlation between plasma adiponectin levels with NIHSS, **NIHSS** - National Institute of Health Stroke Scale

Of 109 cases studied, 33(30.3%), 18(16.5%), 17(15.6%), 9(8.3%), 18(16.5%), and 14(12.8%) patients had no significant disability (MRS score 1), slight disability (MRS score 2), moderate disability (MRS score 3), moderately severe disability (MRS score 4), severe disability (MRS score 5) and died (MRS score 6) respectively. Of 109 cases studied, 71 cases (65.1%) had normal plasma adiponectin levels and 38 cases (34.9%) had abnormal plasma adiponectin levels. Out of 109 patients included in the study 14(12.8%) died.

There was no statistically significant difference in the median plasma adiponectin levels in relation to co-morbidity, obesity and mortality (Table 2). A significantly higher percentage of patients who had high

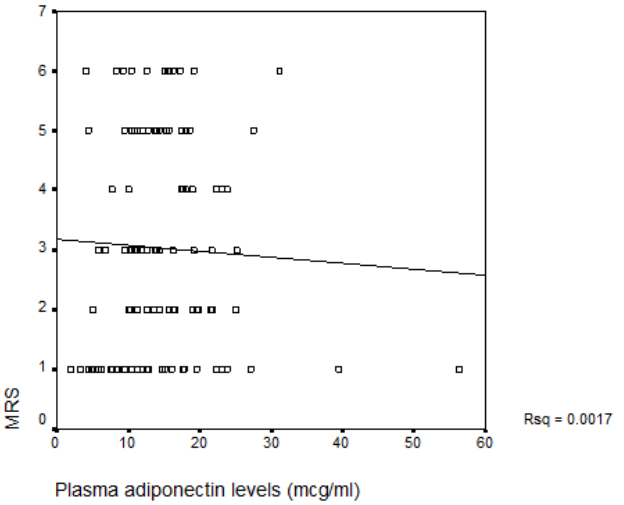


**Fig. 3:** Correlation between plasma adiponectin levels with MRS; **MRS**- Modified Rankins Scale

**Table 1:** Demographic and clinical profile

| **Variables** | **n (%)** |
|---|---|
| **Age group in years** | |
| 30 – 39 | 6 (5.5) |
| 40 – 49 | 12 (11.0) |
| 50 – 59 | 25 (22.9) |
| 60 – 69 | 22 (20.2) |
| 70 – 79 | 30 (27.5) |
| >80 | 14 (12.8) |
| **Gender** | |
| Male | 78 (71.6) |
| Female | 31 (28.4) |
| **Co-morbidity** | |
| Nil | 21 (19.3) |
| Diabetes mellitus | 34 (31.2) |
| Hypertension | 68 (62.4) |
| Ischemic heart disease | 8 (7.3) |
| Chronic kidney disease | 5 (4.6) |
| Other | 9 (8.3) |
| **BMI in Kg/m** $^2$ | |
| <18.50 | 13 (11.9) |
| 18.50 – 23.99 | 40 (36.7) |
| 24.00 – 29.99 | 42 (38.5) |
| ≥30.00 | 14 (12.8) |

**BMI**- Body mass index

triglyceride levels had normal plasma adiponectin levels. The distribution of total cholesterol (TC), high density lipoprotein (HDL) cholesterol, low density lipoprotein (LDL) cholesterol, very-low density lipoprotein (VLDL) cholesterol and hypertension did not differ significantly between group of cases with normal plasma adiponectin and group of cases with abnormal plasma adiponectin levels (Table 3). Distribution of severity of acute ischemic stroke (as measured by NIHSS score) did not differ significantly

**Table 2:** Distribution of median plasma adiponectin levels according to co-morbidity, obesity and mortality.

| Variables | n | Median plasma adiponectin levels (mcg/mL) | p-value |
|---|---|---|---|
| **Comorbidity** | | | |
| Present | 88 | 12.50 | 0.572 |
| Absent | 21 | 13.90 | |
| **Obesity** | | | |
| Present (BMI ≥ 30.0 kg/m$^2$) | 14 | 12.37 | 0.690 |
| Absent (BMI < 30.0 kg/m$^2$) | 95 | 13.75 | |
| **Mortality** | | | |
| Survived | 95 | 13.75 | 0.511 |
| Dead | 14 | 13.75 | |

Mann-Whitney U test was used
**BMI**- Body mass index

**Table 3:** Association between levels of plasma adiponectin with lipid profile and comorbidities

| Variables | Plasma adiponectin levels | | | p-value |
|---|---|---|---|---|
| | Normal | Abnormal | Total | |
| **Total cholesterol (mg/dL)** | | | | |
| Normal (< 200) | 60 (84.5) | 33 (86.8) | 93 (85.3) | 0.743 |
| Abnormal (≥ 200) | 11 (15.5) | 5 (13.2) | 16 (14.7) | |
| **Triglycerides (mg/dL)** | | | | |
| Normal (< 150) | 47 (66.2) | 33 (86.8) | 80 (73.4) | 0.020 |
| Abnormal (≥ 150) | 24 (33.8) | 5 (13.2) | 29 (26.6) | |
| **HDL cholesterol (mg/dL)** | | | | |
| Normal (> 40) | 23 (32.4) | 19 (50.0) | 42 (38.5) | 0.072 |
| Abnormal (≤ 40) | 48 (67.6) | 19 (50.0) | 67 (61.5) | |
| **LDL cholesterol (mg/dL)** | | | | |
| Normal (< 130) | 54 (76.1) | 31 (81.6) | 85 (78.0) | 0.507 |
| Abnormal (≥ 130) | 17 (23.9) | 7 (18.4) | 24 (22.0) | |
| **VLDL cholesterol (mg/dL)** | | | | |
| Normal (< 30) | 61 (85.9) | 35 (92.1) | 96 (88.1) | 0.536 |
| Abnormal (≥ 30) | 10 (14.1) | 3 (7.9) | 13 (11.9) | |
| **Hypertension** | | | | |
| Absent | 26 (63.4) | 15 (36.6) | 41 (100.0) | 0.769 |
| Present | 45 (66.2) | 23 (33.8) | 68 (100.0) | |

Chi-square test was used
**HDL**- High density lipoprotein
**LDL**- Low density lipoprotein
**VLDL**- Very low-density lipoprotein

**Table 4:** Correlation of plasma adiponectin levels withlipid profile

| Correlation between | r-value | p-value |
|---|---|---|
| Plasma adiponectin and total cholesterol | -0.106 | 0.272 |
| Plasma adiponectin and triglycerides | -0.219 | 0.022 |
| Plasma adiponectin and HDL cholesterol | 0.176 | 0.068 |
| Plasma adiponectin and LDL cholesterol | -0.102 | 0.292 |
| Plasma adiponectin and VLDL cholesterol | -0.120 | 0.212 |

Pearson's correlation was used.
**HDL**- High density lipoprotein
**LDL**- Low density lipoprotein
**VLDL**- Very low-density lipoprotein

between group of cases with normal plasma adiponectin and group of cases with abnormal plasma adiponectin levels (p-value = 0.164). Distribution of neurological functional outcome (as measured by MRS) of acute ischemic stroke did not differ significantly between group of cases with normal plasma adiponectin and group of cases with abnormal plasma adiponectin levels (p-value = 0.644). There was a negative correlation between plasma adiponectin levels and NIHSS score (r = - 0.110) which was not statistically significant (p-value = 0.253) [Figure 2]. There was a negative correlation between plasma adiponectin levels and MRS (r = -0.041) which was not statistically significant (p-value = 0.672) [Figure 3]. Plasma adiponectin levels had a significantly negative correlation with serum triglyceride levels (r = - 0.219, p-value = 0.022), but there was no statistically significant correlation between plasma adiponectin levels with TC, HDL, LDL and VLDL cholesterol (Table 4).

## 4. Discussion

Acute ischemic stroke continues to be an important cause of mortality and morbidity in the developing and developed countries. Moreover, no plasma biomarker exists which can accurately predict the severity of ischemic strokes and their prognosis in terms of neurological outcome and residual morbidity. The present research was a prospective observational study conducted on 109 patients at a single centre aimed to determine the correlation between plasma adiponectin levels with the severity of acute ischemic stroke. In the present study, there was no statistically significant correlation between the plasma adiponectin levels and severity of acute ischemic stroke measured using the NIHSS and residual disability measured by the MRS.

Wang Z et al. concluded that that high adiponectin was associated with stroke severity and stated that adiponectin can serve as a biomarker of poor outcome after stroke, independent of baseline variables. The study further stated that there was a positive correlation between NIHSS score and serum levels of adiponectin levels (r[spearman]=0.266; p-value < 0.001).[18] Efstathiou SP et al. reported that NIHSS score on admission and adiponectin values had an inverse correlation which was not significant (r= - 0.20; p-value = 0.066), but after adjustment for age the correlation was statistical significance (r= - 0.29; p-value = 0.035).[19] Kuwashiro T et al. in a prospective study of 171 ischemic stroke patients reported that adiponectin values at day 0 were positively associated with neurological severity as assessed by the NIHSS on admission (r = 0.420, p-value = 0.003).[20]

In the present study, distribution of severity of acute ischemic stroke (as measured by NIHSS score) did not differ significantly between group of cases with normal plasma adiponectin and group of cases with abnormal plasma adiponectin levels. Wang Z et al. stated that the median adiponectin levels in minor stroke were significantly lower than that observed in patients with moderate-to-high stroke (6.0 $\mu$g/ mL vs. 7.8 $\mu$g/mL, p-value < 0.001).[18] A prospective study conducted by Khalili P et al. with 3885 participants reported that adiponectin levels did not independently predict the risk of stroke, coronary events, or a combination of these two outcomes.[21] Kizer JR et al. reported that both total and high molecular weight (HMW) adiponectin were significantly directly associated with CVD after adjustment for confounding variables.[22]

In the present study, distribution of neurological functional outcome (as measured by MRS) of acute ischemic stroke did not differ significantly between group of cases with normal plasma adiponectin and group of cases with abnormal plasma adiponectin levels. Wang Z et al. stated that at 3-month follow-up, 58 patients (25.6%) had poor functional outcomes (median adiponectin level 10.0 $\mu$g/mL) whereas 169 patients (74.4%) had good outcomes (median adiponectin level 6.3 $\mu$g/mL) (p-value < 0.001).[18] Kuwashiro T et al. reported that adiponectin values were higher in the groups with poor outcomes (MRS) ≥ 3 on day 90.[20] Marousi SG et at. in a prospective study of 82 acute ischemic stroke patients which were followed up for 6 months concluded that serum adiponectin measured shortly after an acute ischaemic stroke does not seem to reliably predict disease severity, progression or outcome. The study further stated that higher adiponectin levels (12. 57 versus 8. 83 mg/ dL, p-value = 0. 053) was indicative of greater disability (MRS) at one month follow-up, but not by the next follow-up months.[23]

In a study conducted by Wang Z et al. among the 227 patients, 28 (12.3%) died. The median adiponectin levels in 28 patients who died were greater as compared with patients who survived (11.2 vs. 6.8 $\mu$g/mL; p-value < 0.001).[18] In the present study, out of 109 patients 14 (12.8%) died. There was no statistically significant difference in the median plasma adiponectin levels in patients who died and survived.

Efstathiou SP et al. stated that there was a significant inverse correlation between adiponectin levels and body mass index (r = - 0.31; p-value = 0.033), whereas there was no significant correlation with hypercholesterolemia (r = - 0.13; p-value = 0.177).[19] Matsumoto M et al. conducted a study on 5243 subjects which were followed over 9.7 years, reported that adiponectin levels were not independently associated with stroke or brain infarction. The study further stated that adiponectin levels were negatively correlated with body mass index (r = - 0.21, p-value < 0.01), triglyceride (r = - 0.22, p-value < 0.01) and positively correlated with HDL cholesterol (r = 0.25, p-value < 0.01). In the present study, plasma adiponectin levels had a significantly negative correlation with serum triglyceride levels (r = - 0.219, p-value = 0.022), but there was no statistically significant correlation between plasma adiponectin levels with TC, HDL, LDL and VLDL

cholesterol.[24] Khalili P et al. stated that mean body mass index, mean systolic blood pressure, mean diastolic blood pressure and mean triglyceride levels were significantly higher in patients who had lowest adiponectin levels, whereas there was no statistically significant difference between mean TC and adiponectin levels.[21] Kizer JR et al. stated that the mean body mass index, mean diastolic blood pressure, and mean triglyceride were significantly higher in patients who had lowest adiponectin levels, whereas there was no statistically significant difference between mean LDL cholesterol, systolic blood pressure and adiponectin levels. The mean HDL cholesterol was significantly higher who had highest adiponectin levels.[22]

Kuwashiro T et al. concluded that plasma adiponectin values may help to classify stroke subtypes and predict neurological severity and functional outcome in ischemic stroke patients.[20] Gairolla J et al. in their study reported that the process of atherosclerosis and stroke are multifactorial and involve the interplay of various other mediators apart from adiponectin in the pathogenesis of atherosclerosis and stroke.[25] Yanai H et al.concluded that adiponectin reduces inflammatory cytokines and oxidative stress, which lead to an improvement of insulin resistance.[26]

## 5. Limitations

The sample size of this study is small. The study was conducted in a single centre. Longer follow up was not done to find the residual neurological deficit. Since the disease pathogenesis of acute ischemic stroke is multifactorial, case control studies with adjustments for comorbidities, age, gender, smoking, etc., will provide better information about the association between adiponectin and ischemic stroke. This study measured only the total plasma adiponectin levels, isoforms of adiponectin such as HMW, low molecular weight adiponectin levels were not measured.

We did not further classify brain infarction to analyze subcategories of brain infarction separately, because of the limited number of cases. Past investigators have reported that each of the subcategories of brain infarction have different associations with lipids.[27] Therefore, each of the subclasses of brain infarction may have a different link to adiponectin.

We did not measure local adipose tissue of adipocytokines and/or plasma expression of adipocytokines, such as retinol-binding protein-4, leptin, fatty acid binding protein 4, omentin-1 and irisin. The association between plasma adiponectin, other adipocytokines and stroke should be clarified. We only measured baseline plasma levels of adiponectin, which might not represent the long-term levels of these marker. The validity of the ELISA assay of adiponectin was also questioned by Bluher M et al.,[28] that reported significant differences between different commercially available assays. We also did not measure the activity of the adiponectin receptor and, thus, cannot directly test the adiponectin resistance hypothesis in the present study. Variant in the adiponectin gene was not tested. Chen XL et al.,[29] reported a relationship between the rs2241766 variant in the adiponectin gene and ischemic stroke risk in Han population women from northern China.

## 6. Conclusions

There was a negative correlation between plasma adiponectin levels and NIHSS score (r = - 0.110) which was not statistically significant (p-value = 0.253) and MRS (r = -0.041, p-value = 0.672). The median plasma adiponectin levels were comparable between group of cases with co-morbidity and without any co-morbidity (p-value = 0.572), with obesity and without obesity (p-value = 0.690), and who survived and who died (p-value = 0.511). A significantly higher percentage of patients who had high triglyceride levels had normal plasma adiponectin levels. The distribution of TC, HDL cholesterol, LDL cholesterol, VLDL cholesterol and hypertension did not differ significantly between group of cases with normal plasma adiponectin and group of cases with abnormal plasma adiponectin levels. Multi-centric studies with large sample size and longer duration of follow-up should be undertaken to substantiate the research findings described in this paper. Further studies using the isoforms of adiponectin such as HMW and low molecular adiponectin should be undertaken.

## 7. Source of Funding

None.

## 8. Conflict of Interest

None.

## References

1. Frankenberg ADV, Reis AF, Gerchman F. Relationships between adiponectin levels, the metabolic syndrome, and type 2 diabetes: a literature review. *Arch Endocrinol Metab*. 2017;61(6):614–22. doi:10.1590/2359-3997000000316.
2. Ryu J, Galan AK, Xin X, Dong F, Abdul-Ghani MA, Zhou L, et al. APPL1 potentiates insulin sensitivity by facilitating the binding of IRS1/2 to the insulin receptor. *Cell Rep*. 2014;7(4):1227–38. doi:10.1016/j.celrep.2014.04.006.
3. Berg AH, Combs TP, Du X, Brownlee M, Scherer PE. The adipocyte-secreted protein Acrp30 enhances hepatic insulin action. *Nat Med* . 2001;7(8):947–53. doi:10.1038/90992.
4. Ahima RS. Adipose tissue as an endocrine organ. *Obesity (Silver Spring)*. 2006;14(5):242–9. doi:10.1038/oby.2006.317.
5. Yang WS, Lee WJ, Funahashi T, Tanaka S, Matsuzawa Y, Chao CL, et al. Weight reduction increases plasma levels of an adipose-derived anti-inflammatory protein, adiponectin. *J Clin Endocrinol Metab*. 2001;86(8):3815–9. doi:10.1210/jcem.86.8.7741.
6. Gulcelik NE, Halil M, Ariogul S, Usman A. Adipocytokines and aging: adiponectin and leptin. *Minerva Endocrinol*. 2013;38(2):203–10.
7. Feigin VL, Stark BA, Co J, Roth GA, Bisignano C, Abady GG. Global, regional, and national burden of stroke and its risk factors,

1990-2019: A systematic analysis for the Global Burden of Disease Study. *The Lancet Neurology*. 2019;20:795–820.
8. Singh G, Sharma M, Kumar GA, Rao NG, Prasad K, Mathur P, et al. The burden of neurological disorders across the states of India: The Global Burden of Disease Study 1990-2019. *Lancet Global Health*. 2021;9:1129–44. doi:10.1016/S2214-109X(21)00164-9.
9. National Institute of Health, USA Govt. NIH Stroke scale. Available from: https://www.stroke.nih.gov/resources/scale.htm.
10. National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med*. 1995;333(24):1581–7. doi:10.1056/NEJM199512143332401.
11. Banks JL, Marotta CA. Outcomes Validity and Reliability of the Modified Rankin Scale: Implications for Stroke Clinical Trials A Literature Review and Synthesis. *Stroke*. 2007;38(3):1091–6. doi:10.1161/01.STR.0000258355.23810.c6.
12. Arregui M, Buijsse B, Fritsche A, Giuseppe R, Schulze MB, Westphal S, et al. Aadiponectin and Risk of Stroke. Prospective Study and Meta-analysis. *Stroke*. 2014;45(1):10–7. doi:10.1161/STROKEAHA.113.001851.
13. Stott DJ, Welsh P, Rumley A, Robertson M, Ford I, Sattar N, et al. Adipocytokines and risk of stroke in older people: a nested case-control study. *Int J Epidemiol*. 2009;38(1):253–61. doi:10.1093/ije/dyn215.
14. Wannamethee SG, Shaper AG, Whincup PH, Lennon L, Sattar N. Adiposity, adipokines, and risk of incident stroke in older men. *Stroke*. 2013;44:3–8.
15. Kanhai DA, Kranendonk ME, Uiterwaal C, Van Der Graaf Y, Kappelle LJ, Visseren FIJ. Adiponectin and incident coronary heart disease and stroke. A systematic review and meta-analysis of prospective studies. *Obes Rev*. 2013;14(7):555–67. doi:10.1111/obr.12027.
16. Zhuo Y, Qu Y, Wu J, Huang X, Yuan W, Lee J, et al. Estimation of stroke severity with National Institutes of Health Stroke Scale grading and retinal features: A cross-sectional study. *Medicine (Baltimore)*. 2021;100(31):26846. doi:10.1097/MD.0000000000026846.
17. Hulley SB, Cummings SR, Browner WS, Grady D, Newman TB. Designing clinical research: an epidemiologic approach. Philadelphia, PA: Lippincott Williams & Wilkins; 2013. p. 79.
18. Wang Z, Li B, Wang Y, Maimaitili A, Qin H, Dangmurenjiafu G, et al. The association between serum adiponectin and 3-month outcome after ischemic stroke. *Cardiovasc Diabetol*. 2019;18:105. doi:10.1186/s12933-019-0908-z.
19. Efstathiou SP, Tsioulos DI, Tsiakou AG, Gratsias YE, Pefanis AV, Mountokalakis TD, et al. Plasma adiponectin levels and five-year survival after first-ever ischemic stroke. *Stroke*. 2005;36:1915–20. doi:10.1161/01.STR.0000177874.29849.f0.
20. Kuwashiro T, Ago T, Kamouchi M, Matsuo R, Hata J, Kuroda J, et al. Significance of plasma adiponectin for diagnosis, neurological severity and functional outcome in ischemic stroke - Research for Biomarkers in Ischemic Stroke (REBIOS). *Metabolism*. 2014;63(9):1093–103. doi:10.1016/j.metabol.2014.04.012.
21. Khalili P, Flyvbjerg A, Frystyk J, Lundin F, Jendle J, Engström G, et al. Total adiponectin does not predict cardiovascular events in middle-aged men in a prospective, long-term follow-up study. *Diabetes Metab*. 2010;36(2):137–43. doi:10.1016/j.diabet.2009.10.004.
22. Kizer JR, Benkeser D, Arnold AM, Djousse L, Zieman SJ, Mukamal KJ, et al. Total and high-molecular-weight adiponectin and risk of coronary heart disease and ischemic stroke in older adults. *J Clin Endocrinol Metab*. 2013;98(1):255–63. doi:10.1210/jc.2012-2103.
23. Marousi SG, Theodorou GL, Karakantza M, Zampakis P, Papathanasopoulos P, Ellul J. Acute post-stroke adiponectin in relation to stroke severity, progression and 6 month functional outcome. *Neurol Res*. 2010;32:841–845.
24. Matsumoto M, Ishikawa S, Kajii E. Association of adiponectin with cerebrovascular disease: a nested case-control study. *Stroke*. 2008;39(2):323–8. doi:10.1161/STROKEAHA.107.497552.
25. Gairolla J, Kler R, Modi M, Khurana D. Leptin and adiponectin: pathophysiological role and possible therapeutic target of inflammation in ischemic stroke. *Rev Neurosci*. 2017;28(3):295–306. doi:10.1515/revneuro-2016-0055.
26. Yanai H, Yoshida H. Beneficial Effects of Adiponectin on Glucose and Lipid Metabolism and Atherosclerotic Progression: Mechanisms and Perspectives. *Int J Mol Sci*. 2019;20(5):1190. doi:10.3390/ijms20051190.
27. Tanizaki Y, Kiyohara Y, Kato I, Iwamoto H, Nakayama K, Shinohara N, et al. Incidence and risk factors for subtypes of cerebral infarction in a general population: the Hisayama study. *Stroke*. 2000;31(11):2616–22. doi:10.1161/01.str.31.11.2616.
28. Bluher M, Brennan AM, Kelesidis T, Kratzsch J, Fasshauer M, Kralisch S, et al. Total and high-molecular weight adiponectin in relation to metabolic variables at baseline and in response to an exercise treatment program: comparative evaluation of three assays. *Diabetes Care*. 2007;30(2):280–5. doi:10.2337/dc06-1362.
29. Chen XL, Cheng JQ, Zhang RL, Liu JP, Li XX, Tong YQ, et al. Study on the relationship between polymorphism of adiponectin gene and risk of ischemic stroke among Han population in the Northern parts of China. *Zhonghua Liu Xing Bing Xue Za Zhi*. 2010;31(2):129–32.

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