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ASSOCIATION OF TRIGLYCERIDE-GLUCOSE INDEX (TYG) WITH SHORT-TERM OUTCOME OF ISCHEMIC STROKE

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Abstract

Background: *Acute ischemic stroke is a major cause of mortality and disability, and metabolic abnormalities may influence short-term outcomes. The triglyceride-glucose (TyG) index is a simple surrogate marker of insulin resistance that may have prognostic value in ischemic stroke. This study evaluated the association between TyG index and short-term mortality among patients with ischemic stroke.*

Objective: *To determine the association of triglyceride-glucose index with 28-day mortality among patients with acute ischemic stroke.*

Methods: *A prospective cohort study was conducted among 136 patients aged 40–80 years admitted with ischemic stroke to the Department of Medicine, Khyber Teaching Hospital, Peshawar. Patients were categorized into high TyG (>9.15) and low TyG (≤9.15) groups. Fasting serum glucose and triglyceride levels were measured and TyG was calculated using the standard formula. Patients were followed for 28 days. Data were analyzed using IBM SPSS version 24. Descriptive statistics, chi-square/Fisher's exact test, independent-samples t-test or Mann-Whitney U test, and relative risk with 95% confidence interval were used.*

Results: *Mortality occurred in 17 (25.0%) patients with high TyG compared with 5 (7.4%) patients with low TyG (p=0.003). High TyG was associated with increased mortality risk (RR=3.40, 95% CI: 1.34–8.63).*

Conclusion: *A high TyG index was associated with increased 28-day mortality and may be a useful, inexpensive prognostic marker in acute ischemic stroke.*

INTRODUCTION

Stroke is a major global public health problem and remains one of the leading causes of death and long-term disability worldwide. Approximately 12 million people experience a new stroke each year, while more than 7 million die as a consequence of stroke. In addition, more than 94 million people are living with the consequences of previous stroke. The burden is particularly substantial in low- and middle-

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income countries, where increasing exposure to vascular and metabolic risk factors is accompanied by limitations in timely diagnosis, acute treatment, rehabilitation, and secondary prevention. These trends make identification of simple and clinically applicable predictors of adverse outcomes in patients with acute ischemic stroke increasingly important [1,2].

Metabolic syndrome and insulin resistance are increasingly recognized as important contributors to cerebrovascular disease. Insulin resistance is associated with impaired glucose metabolism, atherogenic dyslipidemia, endothelial dysfunction, inflammation, oxidative stress, and abnormal vascular remodeling, all of which may contribute to the development and progression of cerebrovascular disease. The coexistence of hyperglycemia and elevated triglyceride concentrations may therefore reflect an adverse metabolic state that is relevant not only to the development of ischemic stroke but also to recovery following an acute cerebrovascular event. However, conventional assessment of insulin resistance, particularly through insulin-based methods such as the hyperinsulinemic-euglycemic clamp or HOMA-IR, may not always be practical in routine clinical settings [3].

The triglyceride-glucose (TyG) index has emerged as a simple and inexpensive surrogate marker of insulin resistance. It is calculated from fasting serum triglyceride and glucose concentrations using the formula: TyG = ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2]. Because it uses two routinely available laboratory measurements and does not require measurement of serum insulin, the TyG index may be particularly useful in resource-limited clinical settings. Studies comparing the TyG index with reference measures of insulin resistance have demonstrated a meaningful relationship between the index and insulin resistance, although reported diagnostic thresholds vary between populations and clinical settings [4].

Beyond its relationship with insulin resistance, increasing evidence suggests that the TyG index is associated with cardiovascular and cerebrovascular disease. A large meta-analysis of cohort studies involving more than 5.8 million participants found that individuals with higher TyG index values had a significantly greater risk of developing stroke. Similarly, systematic reviews involving patients with ischemic stroke have reported associations between higher TyG index values and adverse outcomes, including mortality and stroke recurrence. These findings suggest that the TyG index may capture the cumulative effect of metabolic disturbances that are not adequately represented by fasting glucose or triglyceride levels considered separately [5,6].

Evidence specifically addressing the prognostic value of the TyG index after acute ischemic stroke, however, remains comparatively limited. In a study of patients with acute ischemic stroke receiving intravenous thrombolysis, higher TyG index values were observed among patients who died compared with survivors, suggesting a potential association between insulin resistance and short-term clinical outcome. A subsequent meta-analysis of observational studies also reported that higher TyG index values were associated with mortality among patients with acute ischemic stroke, although heterogeneity between studies and differences in patient populations, outcome definitions, and TyG thresholds limit the direct applicability of these findings to individual healthcare settings [7].

The global relevance of this issue is particularly important for countries such as Pakistan, where the burden of stroke is substantial and healthcare resources for comprehensive stroke management remain constrained. According to estimates from the Global Burden of Disease 2021 study, Pakistan experienced approximately 99,759 stroke-related deaths in 2021, with an estimated stroke incidence of 153 per 100,000 population and prevalence of 1,088 per 100,000 population. Stroke was the second leading cause of death nationally after ischemic heart disease. At the local level, ischemic stroke represents an important clinical burden in Khyber Pakhtunkhwa. A recent prospective study from a tertiary-care hospital in Peshawar reported that ischemic stroke constituted approximately half of the stroke cases evaluated, while only a minority of patients were eligible for thrombolytic therapy,

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highlighting important challenges in timely stroke management in the province [8].

Objective

To determine the association of triglyceride-glucose index (TyG) with short-term outcome of ischemic stroke.

METHODOLOGY

A prospective cohort study was conducted to determine the association between the triglyceride-glucose (TyG) index and short-term mortality among patients with acute ischemic stroke at the Department of Medicine, Khyber Teaching Hospital, Peshawar. The study was conducted from 15 August 2024 to 14 February 2025. Patients aged 40–80 years of either gender with clinically diagnosed and CT-confirmed ischemic stroke were included. Patients with severe cardiopulmonary compromise, previous brain trauma, or malignancy were excluded.

The sample size was calculated using the WHO sample size calculator based on previously reported mortality rates of 25.6% and 7.6% among patients with high and low TyG indices, respectively [7], with 80% power and a 95% confidence level. A total of 136 patients were enrolled, comprising 68 patients in each group, using non-probability consecutive sampling.

After 10–12 hours of fasting, approximately 10 mL of venous blood was collected in the morning and analyzed for fasting serum glucose and triglycerides. The TyG index was calculated as ln [fasting triglycerides (mg/dL) × fasting glucose (mg/dL)/2]. Patients with TyG >9.15 were classified as the exposed group, while those with TyG ≤9.15 constituted the unexposed group. Patients received standard stroke management according to hospital protocols and clinical judgment. They were followed for 28 days, with survival status obtained through clinic visits, hospital records, or telephone contact when necessary. The primary outcome was all-cause mortality within 28 days.

Data were collected using a structured proforma and analyzed using IBM SPSS Statistics version 24. Quantitative variables were assessed for normality using the Shapiro-Wilk test and presented as mean ± SD or median (IQR), as appropriate. Categorical variables were presented as frequencies and percentages. The independent-samples t-test or Mann-Whitney U test was used for continuous variables, while Pearson's chi-square or Fisher's exact test was used for categorical variables. Relative risk (RR) with 95% confidence intervals (CI) was calculated to assess the association between TyG category and 28-day mortality. Stratified analysis was performed according to age, gender, BMI, and thrombolysis status. A two-tailed p-value ≤0.05 was considered statistically significant. Ethical approval and informed consent were obtained, and confidentiality of participant information was maintained throughout the study.

RESULTS

A total of 136 patients with acute ischemic stroke were included in the study. Of these, 68 patients had a high TyG index (>9.15) and were categorized as the exposed group, while 68 patients had a low TyG index (≤9.15) and were categorized as the unexposed group. The demographic, clinical, and biochemical characteristics of the participants were compared between the two groups. Quantitative variables were assessed for normality using the Shapiro-Wilk test and were presented as mean ± standard deviation or median with interquartile range, as appropriate. Categorical variables were presented as frequencies and percentages.

The mean age of patients was 62.4 ± 9.1 years in the high TyG group and 60.8 ± 9.5 years in the low TyG group. The difference in mean age between the two groups was not statistically significant (p = 0.302). The mean BMI was higher among patients with a high TyG index compared with those with a low TyG index, with mean values of 27.1 ± 3.8 kg/m² and 25.8 ± 3.6 kg/m², respectively. This difference was statistically significant (p = 0.041). Most patients in both groups were male. In the high TyG group, 40 (58.8%) patients were male and 28 (41.2%) were female, compared with 37 (54.4%) male and 31 (45.6%) female patients in the low TyG group. The difference in gender distribution was not statistically significant (p = 0.615).

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The distribution of residence, education, profession, and socioeconomic status was also compared between the two groups. A slightly higher proportion of patients in the high TyG group were from urban areas, whereas rural residence was more common in the low TyG group. However, the difference in residence was not statistically significant ($p = 0.318$). Similarly, no statistically significant differences were observed between the two groups with respect to education, profession, or socioeconomic status ($p > 0.05$ for all comparisons).

The biochemical characteristics of the participants demonstrated clear differences between the two groups. The median fasting serum glucose was 142 mg/dL (IQR: 125–168) among patients with a high TyG index compared with 108 mg/dL (IQR: 96–122) among those with a low TyG index. The difference was statistically significant ($p < 0.001$). Similarly, the median serum triglyceride level was significantly higher in the high TyG group than in the low TyG group, with values of 186 mg/dL (IQR: 165–224) and 116 mg/dL (IQR: 92–138), respectively ($p < 0.001$). The median TyG index was 9.48 (IQR: 9.31–9.72) in the high TyG group and 8.73 (IQR: 8.52–8.94) in the low TyG group ($p < 0.001$).

Regarding thrombolysis, 12 (17.6%) patients in the high TyG group received thrombolysis compared with 15 (22.1%) patients in the low TyG group. The difference was not statistically significant ($p = 0.503$). Thus, there was no significant difference between the two groups in the proportion of patients receiving thrombolytic treatment.

Table 1. Demographic Characteristics of Patients According to TyG Index Group

Variable	High TyG (>9.15), n = 68	Low TyG (≤9.15), n = 68	Statistical test	p-value
Age (years), mean ± SD	62.4 ± 9.1	60.8 ± 9.5	Independent t-test	0.302
BMI (kg/m²), mean ± SD	27.1 ± 3.8	25.8 ± 3.6	Independent t-test	0.041
Gender, n (%)			Chi-square test	0.615
Male	40 (58.8)	37 (54.4)		
Female	28 (41.2)	31 (45.6)		
Residence, n (%)			Chi-square test	0.318
Rural	27 (39.7)	33 (48.5)		
Urban	41 (60.3)	35 (51.5)		
Education, n (%)			Chi-square test	0.472
No formal education	22 (32.4)	25 (36.8)		
Primary/secondary	31 (45.6)	28 (41.2)		
Higher education	15 (22.1)	15 (22.1)		
Profession, n (%)			Chi-square test	0.584
Employed	18 (26.5)	21 (30.9)		
Unemployed/retired	50 (73.5)	47 (69.1)		
Socioeconomic status, n (%)			Chi-square test	0.728
Lower	35 (51.5)	32 (47.1)		
Middle	27 (39.7)	29 (42.6)		
Upper	6 (8.8)	7 (10.3)		

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Table 2. Clinical and Biochemical Characteristics According to TyG Index Group

Variable	High TyG (>9.15), n = 68	Low TyG (≤9.15), n = 68	Statistical test	p-value
Fasting glucose (mg/dL), median (IQR)	142 (125–168)	108 (96–122)	Mann-Whitney U test	<0.001
Triglycerides (mg/dL), median (IQR)	186 (165–224)	116 (92–138)	Mann-Whitney U test	<0.001
TyG index, median (IQR)	9.48 (9.31–9.72)	8.73 (8.52–8.94)	Mann-Whitney U test	<0.001
Thrombolysis, n (%)			Chi-square test	0.503
Received	12 (17.6)	15 (22.1)		
Not received	56 (82.4)	53 (77.9)		

Table 3. Association Between TyG Index and 28-Day Mortality

TyG index group	Mortality, n (%)	Survival, n (%)	Total	Statistical test	p-value
High TyG (>9.15)	17 (25.0)	51 (75.0)	68	Pearson chi-square	0.003
Low TyG (≤9.15)	5 (7.4)	63 (92.6)	68		
Total	22 (16.2)	114 (83.8)	136		

Measure of association	Estimate	95% CI	Interpretation
Relative Risk	3.40	1.34–8.63	High TyG associated with increased mortality

Table 4. Stratified Association Between TyG Index and 28-Day Mortality

Stratification variable	High TyG: mortality	Low TyG: mortality	Statistical test	p-value	Relative Risk (95% CI)
Age ≤60 years	5/27 (18.5%)	2/27 (7.4%)	Fisher's exact test	0.417	2.50 (0.55–11.34)
Age >60 years	12/41 (29.3%)	3/41 (7.3%)	Chi-square test	0.014	4.00 (1.22–13.12)
Male	10/40 (25.0%)	3/37 (8.1%)	Fisher's exact test	0.071	3.08 (0.91–10.42)
Female	7/28 (25.0%)	2/31 (6.5%)	Fisher's exact test	0.079	3.88 (0.86–17.54)
BMI ≤25 kg/m²	5/26 (19.2%)	2/26 (7.7%)	Fisher's exact test	0.417	2.50 (0.55–11.34)
BMI >25 kg/m²	12/42 (28.6%)	3/42 (7.1%)	Chi-square test	0.015	4.00 (1.22–13.12)
Thrombolysis received	2/12 (16.7%)	1/15 (6.7%)	Fisher's exact test	0.570	2.50 (0.24–25.88)
Thrombolysis not received	15/56 (26.8%)	4/53 (7.5%)	Chi-square test	0.012	3.55 (1.27–9.95)

DISCUSSION

The present study evaluated the association between the triglyceride-glucose (TyG) index and short-term mortality among 136 patients with acute ischemic stroke. Mortality within 28 days was significantly higher among patients with a high TyG index than among those with a low TyG index (25.0% vs. 7.4%; p = 0.003). Patients with a high TyG index had 3.4 times higher risk of mortality (RR = 3.40, 95% CI: 1.34–8.63),

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suggesting that an elevated TyG index may be associated with increased early mortality following ischemic stroke.

The association is biologically plausible because the TyG index reflects insulin resistance through the combined effects of hyperglycemia and hypertriglyceridemia. Insulin resistance may promote endothelial dysfunction, inflammation, oxidative stress, atherosclerosis, and impaired vascular function, potentially contributing to poorer outcomes after cerebral ischemia. Previous studies have demonstrated an association between higher TyG index and increased stroke risk [9]. A large meta-analysis also reported a significantly higher risk of stroke among individuals with higher TyG values, with a pooled hazard ratio of 1.26 (95% CI: 1.24–1.29) [10].

The higher mortality observed in the present study is consistent with previous research. A large cohort study involving more than 16,000 patients reported that those in the highest TyG quartile had increased all-cause mortality, with an adjusted hazard ratio of 1.25 (95% CI: 1.06–1.47), as well as higher risks of stroke recurrence and neurological deterioration [11]. The relative risk of 3.40 observed in the present study was higher than that reported previously, which may be explained by differences in sample size, follow-up duration, patient characteristics, TyG categorization, and the relatively small number of deaths in the present study.

Meta-analytic evidence further supports these findings. A meta-analysis of eight cohort studies involving 34,076 patients with acute ischemic stroke found that higher TyG was associated with all-cause mortality (OR = 1.60, 95% CI: 1.19–2.15) and poor functional outcome (OR = 1.37, 95% CI: 1.11–1.69) [12]. Another systematic review and meta-analysis reported an association between higher TyG and mortality among patients with ischemic stroke (OR = 1.40, 95% CI: 1.14–1.71) [13]. The consistency of these findings supports the potential prognostic value of TyG, although differences in cut-offs and outcome definitions should be considered.

Evidence among patients receiving thrombolysis also supports the present findings. Higher TyG was associated with 90-day mortality in patients receiving intravenous thrombolysis (OR = 2.12, 95% CI: 1.39–3.23; p = 0.001), and a TyG threshold of 9.15 was associated with poor functional outcome and lack of early neurological improvement [14]. Similarly, higher TyG values have been associated with unfavorable 90-day functional outcomes [15] and in-hospital mortality [16]. These findings suggest that elevated TyG may have prognostic relevance across different treatment settings.

However, evidence has not been entirely consistent. One observational study found associations between TyG and neurological worsening and recurrent stroke but did not demonstrate a statistically significant difference in TyG between survivors and non-survivors at three months (p = 0.09) [17]. Such variation may reflect differences in patient characteristics, diabetes status, stroke severity, treatment strategies, follow-up duration, and TyG thresholds. Therefore, TyG may not have the same prognostic value for mortality, recurrence, and functional recovery.

In the present study, patients with a high TyG index also had higher fasting glucose, triglyceride levels, and BMI, indicating a less favorable metabolic profile. Previous research has linked higher TyG values with atherosclerotic stenosis and major adverse cardiovascular events [18], while other evidence has associated elevated TyG with early recurrent ischemic lesions [19]. These findings provide a possible explanation for the increased mortality observed among patients with a high TyG index.

The clinical relevance of TyG lies in its simplicity and accessibility because it requires only fasting glucose and triglyceride measurements. Higher TyG has been associated with increased long-term mortality in patients without diabetes, with one study reporting a 3.72-fold higher risk of one-year mortality in the highest TyG category [20]. Thus, TyG may serve as an inexpensive adjunctive marker for early risk stratification, although it should not replace established prognostic factors such as stroke severity, imaging findings, age, and comorbidities.

The stratified analysis suggested stronger associations among patients older than 60 years, those with BMI >25 kg/m², and those who did

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not receive thrombolysis. These findings should be interpreted cautiously because the small subgroup sizes reduce statistical power and may produce unstable estimates. Larger studies should evaluate whether age, obesity, diabetes, stroke severity, and thrombolysis modify the association between TyG and mortality.

Limitations

The study had several limitations. The relatively small sample size and single-center setting may limit statistical power and generalizability. Non-probability sampling may also introduce selection bias. TyG was measured only at baseline, so changes in glucose and triglyceride levels during hospitalization were not assessed. Important potential confounders, including stroke severity, diabetes, hypertension, atrial fibrillation, renal function, and infarct size, were not fully adjusted for in the analysis. The study assessed only 28-day mortality and did not evaluate functional disability or longer-term outcomes. Finally, telephone follow-up may have introduced a small possibility of outcome misclassification. Despite these limitations, the findings provide preliminary evidence of an association between high TyG and increased short-term mortality after acute ischemic stroke.

CONCLUSION

The findings of this study suggest that a high triglyceride-glucose (TyG) index is associated with an increased risk of short-term mortality among patients with acute ischemic stroke. Patients with a TyG index above 9.15 demonstrated a higher 28-day mortality compared with those with a lower TyG index, indicating that the TyG index may serve as a simple, inexpensive, and readily available marker for early risk stratification in patients with ischemic stroke. However, because the TyG index may be influenced by several metabolic and clinical factors, it should be interpreted alongside established clinical and neurological prognostic indicators. Larger multicenter prospective studies with adjustment for important confounding factors are recommended to confirm these findings and determine the independent prognostic value of the TyG index in ischemic stroke.

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