



TO COMPARE TRIGLYCERIDE AND GLUCOSE (TyG) INDEX AS AN EFFECTIVE BIOMARKER WITH CTSI AND BISAP SCORE FOR SEVERE ACUTE PANCREATITIS

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ABSTRACT **Background:** Acute pancreatitis is mostly self-limiting disease with adequate management, resolves itself with few complications. Early diagnosis of severe acute pancreatitis (AP) is important to reduce morbidity and mortality. The triglyceride-glucose (TyG) index is a novel surrogate marker of insulin resistance and its related metabolic abnormalities. **Aim:** To compare triglyceride and glucose(TyG) index as an effective biomarker with CTSI and BISAP score for severe acute pancreatitis. **Methods:** An observational prospective study was carried out in department of medical gastroenterology for a period of 6 months from November 2021. This study included patients ≥ 18 years, who admitted with acute pancreatitis. The TyG index was calculated as: $\ln\{ \text{fasting triglyceride(mg/dl)} \times \text{fasting plasma glucose(mg/dl)}\} / 2$. **Results:** A total of 67 patients with acute pancreatitis were included, male 46 (68.7%) and female 21 (31.3%). The median age of presentation was 47.07 ± 11.86 years. 11 (16.4%) patients were in severe group while 56 (83.6%) patients were in non- severe group according to Atlanta classification. 9(13.4%) patients need icu treatment at admission while 58 (86.6%) patients were managed in ward. Among severe acute pancreatitis 2(3%) patients died despite ICU care. Mainly TyG index, BISAP and CTSI scores were used. BISAP score has AUROC 0.957 with standard error 0.042, p value 0.0005, AUROC for CTSI 0.941 with SE 0.044, p value 0.0005 and AUROC for TyG index 0.985 with SE 0.013, p value 0.0005. On applying t- test for equality of variance parameters which were statistically significant (p value < 0.005) were age, FBS, TyG level, BMI, duration of hospital stay, BISAP,CTSI, TyG index. In our study, TyG index shows maximum accuracy over BISAP and CTSI in predicting severity of acute pancreatitis. **Conclusion:** TyG index is superior than pre-existing scores like BISAP and CTSI for assessment of severity of acute pancreatitis as it has highest positive predictive value and can be estimated at admission without subsequent follow up.

KEYWORDS : Severe acute pancreatitis, triglyceride-glucose (TyG) index, CTSI, BISAP score.

INTRODUCTION:

Acute pancreatitis (AP) is an acute inflammatory process in which the pancreatic injury can remain localized, spread to nearby tissues, or lead to systemic inflammation through the activation of cytokine cascades.

The pathway by which local pancreatic injury extends to systemic inflammation is incompletely known. Although AP is mostly a self-limiting disease that, with adequate management, resolves itself with few complications, approximately 15% of AP cases progress to more serious conditions.

Severe AP (SAP) still has a mortality rate of 2- 9% despite developments in understanding the disease.

Therefore, predicting the severity of AP and classifying patients at high risk for progressing to SAP is important for planning the initial level of care and interventions needed for patient management.

Although several classification methods for SAP have been developed, mortality and organ failure from SAP remains unacceptably high. Thus, a more accurate AP scoring system for predicting SAP is needed in clinical practice.

The important role of metabolic disease in acute pancreatitis is increasingly recognized. Several recent studies have found that factors indicating metabolic abnormalities, such as diabetes, hypertriglyceridemia, morbid obesity, vitamin D deficiency, and a higher-than-normal ratio of serum apolipoprotein B to A-I, are closely associated with the severity and prognosis of AP.

Furthermore, recent studies have shown that insulin resistance strongly influences the prognosis and severity of AP.

Insulin resistance is itself a chronic, low-grade inflammatory status, and it is considered to play a pathogenic role in several other inflammatory diseases, including AP.

A novel surrogate marker of insulin resistance and its related metabolic abnormalities that is slowly gaining acceptance is the triglyceride-glucose (TyG) index.

The concept of the TyG index arose from a study that demonstrated that triglycerides present in skeletal muscle are inversely correlated with both skeletal muscle insulin sensitivity and whole-body insulin action.

The TyG index has been reported as a predictor of diabetes, hypertension, nonalcoholic fatty liver disease (NAFLD), and cardiovascular events. However, little is known about the association between the TyG index and the severity of AP.

AIM OF THE STUDY:

To compare Triglyceride and glucose (TyG) index as an effective biomarker with CTSI and BISAP score for severe acute pancreatitis.

Methods:

Study Place: Department of medical gastroenterology Stanley Medical College Chennai.

Study Design: An observational prospective study.

Sample size: 67

Study duration: Nov 2021 to April 2022.

Inclusion Criteria:

All patients with more than 18 years of age admitted with acute pancreatitis.

Exclusion criteria:

- 1) Age below 18 years.
- 2) Not willing to participate in study.
- 3) Aetiology of acute pancreatitis no established.
- 4) Comorbidities limiting fluid management: CKD/CHF/CLD
- 5) Pre-existing pulmonary/neurological disorders.

AP was diagnosed based on the presence of two of the following three features:

1)Typical abdominal pain, (2) serum amylase and/or lipase ≥ 3 times the upper normal limit, and (3) radiologic findings.

The etiologies of AP were gallstone, alcohol and hypertriglyceridemia.

Peripheral blood samples were obtained at the time of admission to assess clinical laboratory parameters: hemoglobin, hematocrit, white blood cell count, calcium, phosphorus, blood urea nitrogen, creatinine, lactate dehydrogenase, aspartate aminotransferase, C-reactive protein, USG abdomen, HBsAg, anti- HCV.

An abdominal computed tomography (CT) scan was performed on all patients upon admission to differentiate AP from other diseases.

Once AP was diagnosed, the levels of fasting insulin, glucose, and triglyceride (TG) were verified using the baseline blood sampling.

The TyG index was calculated as: $\ln [\text{fasting TG (mg/ dL)} \times \text{fasting plasma glucose (mg (dL)}] / 2$.

As additional scoring systems, CT scoring index (CTSI), and Bedside Index of Severe Acute Pancreatitis (BISAP) were applied.

The severity of AP was classified as mild, moderately severe, or severe per the revised Atlanta 2012 criteria.

Mild AP was defined by the absence of organ failure (OF) and local or systemic complications. Moderately severe AP was defined as transient OF that resolved within 48 h and was accompanied by local or systemic complications. Severe AP was defined as persistent OF.

This study protocol was approved by the institutional ethics committee. Informed consent was obtained from all patients.

Statistical Analysis:

The collected data were analysed with IBM SPSS Statistics for Windows, Version 23.0.(Armonk, NY: IBM Corp).To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & S.D were used for continuous variables. To find the significant difference between the bivariate samples in Independent groups the Unpaired sample t-test was used. To find the significance in categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2x2 tables then the Fisher's Exact was used. To find the efficacy of the Scores to predict the Severe Acute Pancreatitis the Receiver Operating Characteristics curve(ROC) was used with Sensitivity, Specificity & accuracy. In all the above statistical tools the probability value .05 is considered as significant level.

RESULTS

Demographic Analysis

A total of 67 patients with acute pancreatitis were included in this study, male 46 (68.7%) and female 21 (31.3%). Median age of presentation was 47.07 ± 11.86 years with a minimum age of 21 years and while maximum age of 69 years. Most common etiology was gall stone followed by alcohol consumption and hypertriglyceridemia.

Table: 1 Base Line Characteristics Of Patients.

Parameters	Severe AP (n=11)	Non-severe AP (n=56)	P-value
Sex(male:female)	7(63.6%): 5(45.4%)	39(69.4%): 17(30.3%)	0.321
Age(years)	59.45 ± 6.22	44.64 ± 11.18	.0005
Hb	11.77 ± 2.02	11.28 ± 1.60	0.378
TLC	8619.09 ± 5271.10	7368.89 ± 4067.95	0.471
Platelet count	2.36 ± 0.88	2.37 ± 0.66	0.961
BUN	16.27 ± 7.42	13.20 ± 4.37	0.209
urea	33.09 ± 15.29	26.43 ± 8.87	0.188
creatinine	1.22 ± 0.82	0.85 ± 0.45	0.180
Total bilirubin	2.32 ± 1.86	1.07 ± 0.62	0.052
Direct bilirubin	1.00 ± 0.78	0.41 ± 0.36	0.031
SGOT	74.09 ± 45.77	52.61 ± 23.61	0.157
SGPT	72.00 ± 49.34	48.13 ± 22.56	0.144
amylase	611.45 ± 447.22	337.45 ± 71.05	0.070
lipase	707.55 ± 594.57	343.25 ± 68.10	0.070

Hospital stay(days)	14.73 ± 4.13	6.18 ± 1.75	0.0005
Fasting TG	677.45 ± 360.12	150.29 ± 55.99	0.001
FBS	207.18 ± 69.67	96.64 ± 17.72	0.0004
BISAP score	3.64 ± 0.67	1.84 ± 0.50	0.0005
CTSI	8.27 ± 1.68	4.63 ± 1.29	0.0005
TyG index	5.82 ± 0.43	4.75 ± 0.26	0.0005
BMI	25.86 ± 1.88	23.29 ± 1.67	0.0005

Characteristics of the study subjects according to TyG index:

The TyG index scores were significantly higher in the SAP group than the non-SAP group (5.82 ± 0.43 vs. 4.75 ± 0.26 , $p < 0.0005$). The TyG index scores were also higher (1) in patients requiring ICU admission ($n = 09$) than those not admitted to an ICU ($n = 58$) and (2) in those who subsequently died of AP-related complications ($n = 2$) than those who did not ($n = 65$)

Severity Assessment

11 (16.4%) patients were in severe group while 56 (83.6%) patients were in non- severe group according to Atlanta classification. 9(13.4%) patients need icu treatment at admission while 58 (86.6%) patients were managed in ward. Among severe acute pancreatitis 2(3%) patients died despite ICU care.

Scoring System For Acute Pancreatitis

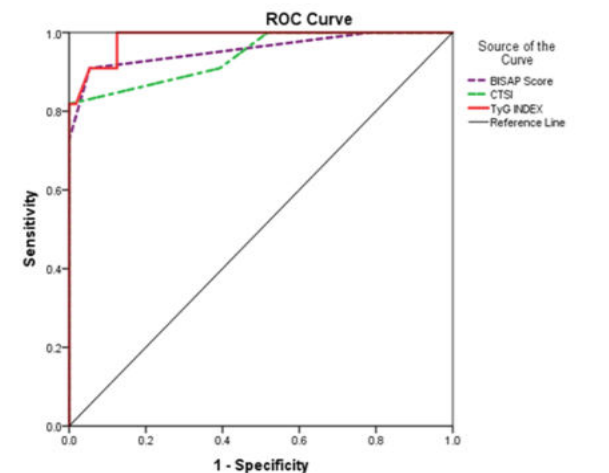
We calculated the AUCs of TyG index, CTSI, BISAP scores for predicting severe acute pancreatitis (Table 2). TyG index showed the greatest accuracy for predicting severe acute pancreatitis. BISAP score has AUROC 0.957 with standard error 0.042, p value 0.0005, AUROC for CTSI 0.941 with SE 0.044, p value 0.0005 and AUROC for TyG index 0.985 with SE 0.013, p value 0.0005.

Table 2 TyG Index And Scoring Systems For Predicting Severe Acute Pancreatitis:

Test Result Variable(s)	Area Under the Curve				
	Area	Std. Error ^a	p-value	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
BISAP Score	.957	.042	.0005	.875	1.000
CTSI	.941	.044	.0005	.854	1.000
TyG INDEX	.985	.013	.0005	.960	1.000

On applying t- test for equality of variance parameters which were statistically significant (p value <0.005) were age, FBS, TyG level, BMI, duration of hospital stay, BISAP,CTSI, TyG index.

To find the efficacy of the Scores to predict the Severe Acute Pancreatitis the Receiver Operating Characteristics curve (ROC) was used with Sensitivity, Specificity & accuracy(Fig.1).The AUC of the ROC for predicting severe acute pancreatitis with TyG index is highest than CTSI and BISAP score.



scores	AUC of ROC
TyG index	0.998
BISAP	0.963
CTSI	0.818

Fig. 1. Receiver operative characteristic curve comparison

Mortality:

Correlation of duration of hospital stay and mortality with Atlanta and TyG index. Pearson Chi-Square test showed statically significant results for duration of hospital stay (P value<0.004), while it was non-significant for assessing mortality.

DISCUSSION:

Acute pancreatitis is seen across all age groups, though it is more common in 3rd to 5th decade .Rare causes such as pancreatic divisum, familial pancreatitis are more common in the pediatric age group. There are various scores and parameters to decide about the severity of acute pancreatitis, however none of them is accurate to determine severity. Ranson score requires 24 hours to 48 hours for assessing severity, which leads to loss of crucial period for i/v fluid management and decision about ICU need. CTSI require around 5 days waiting period for development of necrosis in pancreatic parenchyma, BISAP require daily monitoring. TyG index is newly devised index, which predict future risk of severity by measuring glucose and triglyceride at admission. In our study, TyG index shows maximum accuracy over BISAP and CTSI in predicting severity of acute pancreatitis.

Over and above it has more specificity in determining hospital stays and mortality of patients at admission.

We have demonstrated that the TyG index, a surrogate marker of insulin resistance and metabolic abnormalities, is significantly associated with SAP in patients with AP.

Clinically, AP has many causes including gallstones, alcohol consumption, and hyperlipidemia. Inflammation of the pancreatic adipose tissue is an important component of the pathophysiology of AP.

Metabolic disease and insulin resistance increase both the incidence of AP and the risk of SAP. Obesity and diabetes, as surrogate phenotypes of metabolic disease, are known to be closely associated with incident AP and SAP.

The TyG index has also been reported as a predictor of diabetes, hypertension, NAFLD, and cardiovascular events.

There is a biologically plausible mechanism underlying the significant association between the TyG index and SAP. Ectopic fat (e.g., NAFLD or fatty pancreas) and SAP have a strong relationship.

Our study illustrates several important and novel findings. First, the TyG index was higher in the SAP group than in the non-SAP group. . The cut-off of TyG index for severe acute pancreatitis is 5.39. Study d by Jin Myung Park et al. also showed that Triglyceride and glucose (TyG) index is an effective biomarker to identify severe acute pancreatitis with cut-off of TyG index for severe acute pancreatitis was 4.92. The mean TG level was also significantly higher in patients with ICU admission and AP-related mortality. Therefore, the TyG index could be a good combination to predict the severity of AP.

Second, the predictive value of traditional models for SAP increased significantly after adding the TyG index. We extensively investigated the predictive ability of TyG for SAP using various statistical methods, including a comparison of AUCs and model fitness statistics. This finding implies that a simple, single measurement of serum chemistry at clinical baseline can reliably compensate traditional prognostic indices of AP that require multiple clinical measurements. Our result strongly supports the prognostic value of the TyG index in patients with AP.

Limitations:

(1) Small sample size (2) Single center study (3) Long-term follow up for delayed complications not done. Despite these limitations, this study also has several strengths. This study investigating the predictive value of the TyG index in AP and suggesting the TyG index be incorporated to improve upon previously established severity-scoring systems. Replacing the blood glucose level with the TyG index in traditional prognostic scoring systems could improve their performance.

CONCLUSION:

TyG index is superior than pre-existing scores like BISAP and CTSI for assessment of severity of acute pancreatitis as it has highest

positive predictive value and can be estimated at admission without subsequent follow-up.

REFERENCES

- [1] Oiva J, Mustonen H, Kyllänpää M-L, Kyhälä L, Kuuliala K, Siitonen S, et al. Acute pancreatitis with organ dysfunction associates with abnormal blood lymphocyte signaling: controlled laboratory study. *Crit Care* 2010;14:R207.
- [2] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis 2012: revision of the atlanta classification and definitions by international consensus. *Gut* 2013;62:102e11.
- [3] Bradley EL. A clinically based classification system for acute pancreatitis: summary of the international symposium on acute pancreatitis, atlanta, ga, september 11 through 13, 1992. *Arch Surg* 1993;128:586e90.
- [4] Huh JH, Jeon H, Park SM, Choi E, Lee GS, Kim JW, et al. Diabetes mellitus is associated with mortality in acute pancreatitis. *J Clin Gastroenterol* 2018;52:178e83.
- [5] Nawaz H, Koutroumpakis E, Easler J, Slivka A, Whitcomb DC, Singh VP, et al. Elevated serum triglycerides are independently associated with persistent organ failure in acute pancreatitis. *Am J Gastroenterol* 2015;110:1497e503.
- [6] Huh JH, Kim JW, Lee KJ. Vitamin d deficiency predicts severe acute pancreatitis. *United European Gastroenterol J* 2019;7:90e5.
- [7] Huh JH, Jung S, Cho SK, Lee KJ, Kim JW. Predictive value of apolipoprotein b and a-i ratio in severe acute pancreatitis. *J Gastroenterol Hepatol* 2018;33:548e53.
- [8] Ranson JH, Rifkind KM, Roses DF, Fink SD, Eng K, Spencer FC. Prognostic signs and the role of operative management in acute pancreatitis. *Surg Gynecol Obstet* 1974;139:69e81.
- [9] Cho SK, Huh JH, Yoo JS, Kim JW, Lee KJ. Homa-estimated insulin resistance as an independent prognostic factor in patients with acute pancreatitis. *Sci Rep* 2019;9:14894.
- [10] Lee Y-H, Pratley RE. The evolving role of inflammation in obesity and the metabolic syndrome. *Curr Diabetes Rep* 2005;5:70e5.
- [11] Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. *Metab Syndr Relat Disord* 2008;6:299e304.
- [12] Pan DA, Lillioja S, Kriketos AD, Milner MR, Baur LA, Bogardus C, et al. Skeletal muscle triglyceride levels are inversely related to insulin action. *Diabetes* 1997;46:983e8.
- [13] Zhang S, Du T, Zhang J, Lu H, Lin X, Xie J, et al. The triglyceride and glucose index (tyg) is an effective biomarker to identify nonalcoholic fatty liver disease. *Lipids Health Dis* 2017;16:15.
- [14] Zheng R, Mao Y. Triglyceride and glucose (tyg) index as a predictor of incident hypertension: a 9-year longitudinal population-based study. *Lipids Health Dis* 2017;16:175.
- [15] Sánchez-Iñigo L, Navarro-González D, Fernández-Montero A, Pastrana-Delgado J, Martínez JA. The tyg index may predict the development of cardiovascular events. *Eur J Clin Invest* 2016;46:189e97.
- [16] Mikolasevic I, Milic S, Orlic L, Poropat G, Jakopic I, Franjic N, et al. Metabolic syndrome and acute pancreatitis. *Eur J Intern Med* 2016;32:79e83.
- [17] Szentesi A, Parniczky A, Vincze A, Bajor J, Gódi S, Sarlósi P, et al. Metabolic syndrome elevates the risk for mortality and severity in acute pancreatitis. *Pancreatol* 2018;18:S14.
- [18] Krishna SG, Hinton A, Oza V, Hart PA, Swee E, El-Dika S, et al. Morbid obesity is associated with adverse clinical outcomes in acute pancreatitis: a propensity-matched study. *Am J Gastroenterol* 2015;110:1608e19.
- [19] Wu DC, Zhang M, Xu SX, Wu KY, Wang NZ, Wang YZ, et al. Nonalcoholic fatty liver disease aggravated the severity of acute pancreatitis in patients. *BioMed Res Int* 2019;(1):9583790.
- [20] Vege SS, Gardner TB, Chari ST, Munukuti P, Pearson RK, Clain JE, et al. Low mortality and high morbidity in severe acute pancreatitis without organ failure: a case for revising the atlanta classification to include "moderately severe acute pancreatitis". *Am J Gastroenterol* 2009;104:710e5.