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Original article

Triglyceride and glucose index as a predictor of Acute Pancreatitis

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Abstract:

Early detection of severe acute pancreatitis (AP) is an urgent need to reduce complications and early mortality, and helps in early selection of patients for proper interventions. **Aim of study:** to assess the value of TyG index as a severity predictor of acute pancreatitis. **Methods:** The study was done on 54 patients who were admitted to hepatology**,** gastroenterology and Infectious diseases department, Beni-suef University hospital with acute pancreatitis. The collected data of patients within 24 hours of admission were: gender, age, CBC, aspartate aminotransferase, alanine aminotransferase, total bilirubin, albumin, BUN, creatinine, lipase, amylase, CRP, total calcium, ABGs, fasting plasma glucose level, cholesterol, and triglyceride, imaging with abdominal US and chest X-ray. The TyG index and Albumin corrected calcium level were

calculated and were used in evaluated as a risk predictors of acute Pancreatitis. **Results:** 32 males and 22 females, were divided according to BIS- AP score into two groups: (**group 1)** 47 patients with mild acute pancreatitis and (**group2)**7 patients with moderate to severe acute pancreatitis. The TyG index, fasting Blood glucose, BUN, CRP, potassium, white blood cells, calcium and Albumin corrected calcium level showed statically significant differences between two groups. TyG index at cut off (4.94) showed high AUC (0.827), sensitivity (71.4%) and specificity (85.1%), with statically significant differences between . **Conclusion**: TyG index showed to be promising predictor of severe acute pancreatitis

1. Introduction:

Acute pancreatitis (AP) Known as an inflammation of pancreas associated with inflammation of regional organ system. AP is a complicated event in which, the activated pancreatic enzymes resulting in inflammatory response and damage of the pancreases. AP is a frequent disease with a much cases of hospital admissions all over the world (1, 2). Prediction of the sever AP is possible by using risk factors, such as clinical examination, laboratory tests and imaging. Multiple grading systems and serological markers can also be used. No laboratory test exists perfectly for predicting severe AP. The difficulty is that most of models and systems have low specificity in prediction of severe cases (3).

Calcium has an important role in the incidence of pancreatitis and still evolving to understand it. Calcium has a role in secretory function of the pancreatic acinar cells, so increase of cytosolic Ca++ is associated with premature activation of trypsinogen and death of acinar cell. [4], recent insight as calcium-causes injury of acinar cell suggests that severe acute pancreatitis resulting in hypocalcemia which has a protective role in severe cases (5).

Insulin resistance itself, has a chronic inflammatory status [6], and associated with inflammatory diseases, such as acute pancreatitis. Triglyceride-glucose (TyG) index is a novel surrogate marker of insulin resistance and so, in patients with AP [7].

BISAP score in 2008 that was used for the recognition of patients with high risk of early mortality. It is comprised of 5 variables, as BUN level >25 mg/dl, Impaired mental status, occurrence of (SIRS), Age > 60 years and occurrence of effusion of the pleura. (8)

Aim of study: to evaluate TyG index as a predictor of AP severity to provide a help in early hospital admission and selection of specific interventions for patients with severe AP.

2. Patients and Methods:

Type of the study: observational cross-sectional prospective study of patients with AP

Site of the study: Hepatology, gastroenterology and Infectious diseases Department at Beni-Suef University Hospital, Egypt.

Date and period of the study: from (June 2023) for 6 months duration**.**

Inclusion criteria: AP was clinically diagnosed with 2 of the following 3 criteria: (1) symptoms (e.g. epigastric pain), (2) a serum amylase or lipase level more than 3 times the laboratory's ULN and (3) CT or MRI imaging that consistent with pancreatitis.

Exclusion criteria: Patients with history of admission after 24 hours of the onset of the AP, chronic pancreatitis , pancreatic cancer, history of debilitating severe disease ,or pregnancy.

Procedure Techniques:

Clinical and laboratory assessment

All patients on admission:

1. Sex, age, medical history, DM, HTN and current drugs were recorded.
2. Blood pressure will be measured in the sitting position on both arms.
3. (CBC), liver function tests (AST), (ALT), total bilirubin, INR), fasting blood sugar, HgA1c, triglyceride and cholesterol, (BUN), creatinine, (ESR), (CRP), lipase and amylase, total serum calcium ,Na , K, ABG,. Scores as (ACC)) **(9)** and The TyG index were calculated [**7**].
4. Abdominal ultrasonography and chest X-ray.

The patients according to BIS- AP score were divided, into two groups: group (1) mild AP and group (2) moderate to severe AP.

Ethical Consideration:

A consent was obtained from each patient. The study was performed after approval of the Ethical Committee of Beni Suef faculty of medicine. Approval No FMBSUREC/02052023/shaker

Statistical Analysis:

The data was coded to fit the program of statistical analysis (SPSS) Statistical Package for Special Sciences version 26 under windows.

3. Results:

Table 1. Demographic characteristics of participants

Variables	BIS-AP Score		Total No=54 (%)	P-value
	Mild degree (0-2) N= 47(87%)	Moderate to severe (3-5) N= 7(13%)		
Current age (years)				
Mean±SD	40.93±17.26	50±15.47	42.11±17.33	**0.196**
range	14-86	21-65	14-86	
Sex				
Male	28 (87.5)	4 (12.5)	32 ()	**0.903**
Female	19 (86.4)	3 (13.6)	22 ()	
HTN				
Yes	17 (85)	3 (15)	20 ()	**0.732**
No	30 (88.2)	4 (11.8)	34 ()	
DM				
Yes	4 (50)	4 (50)	8 ()	**0.001***
No	43 (93.5)	3 (6.5)	46 ()	

*P-value is significant at ≤0.05, * by $\chi 2$ test and t test for age

Diabetes Mellitus (DM) was significantly present in moderate to severe group (P= 0.001).But P-value not significant regarding sex, age and presence of hypertension between the two groups.

Table 2: Bio-chemical parameters among mild group and moderate to severe group.

Variables	BIS-AP Score		Total No=54	P-value
	Mild degree (0-2) N= 47(87%)	Moderate to severe (3-5) N= 7(13%)		
Mean ± SD				
ALT(U/L)	123.12±119.21	172.14 ±140.15	129.48 ±121.79	0.325
AST(U/L)	78.27±75.29	118.42 ±94.85	83.48±78.26	0.208
ALB	3.33 ± ٠.44	3.08± ٠.37	3.30 ± .43	0.168
Albumin corrected Ca	8.67± 0.703	7.76±0.49	8.55±٠.74	0.002*
Serum Lipase(U/L)	1405.46±2031.30	1354.28±1031.55	1398.83±1924.05	0.980
Serum Amylase (U/L	1503.48±2108.94	2106.0±2132.67406	1581.59±2101.62	0.484
T Bilirubin(mg/dL)	1.82±2.144	1.74±2.159	1.81± 2.126	0.920
TG	140.74±89.404	159.57 ±125.49	143.18±93.59	0.624
CHOL	160.87 ±54.03	161.14 ±78.44	160.90 ±56.83	0.991
TYG index	4.66±.250	4.94±0.214	4.69±0.262	0.007*
FBS	95.40±37.35	166.42±76.19	104.61 ±49.47	0.0001*
HbA1c	5.50±1.77	5.57±2.07	5.51±1.79	0.930
HG	12.74±2.022	11.80±1.94	12.61±2.019	0.254
WBCs	10.67±3.59	19.57±4.03	11.82±4.71	0.0001*
PLT	263.0±83.43	280.85 ±177.85	265.31±98.28	0.658
CRP(mg/L)	111.82 ±69.70	171.0±73.25	119.50 ±72.29	0.042*
ESR	79.97±15.24	88.0±10.06	81.018±14.84	0.186
BUN	34.53±16.76	53.28±15.34	36.96±17.63	0.007*
Creatinine	0.799±0.220	0.82± 0.325	0.80±0.232	0.762
INR	1.11±0.142	1.21±0.25	1.131±0.161	0.147
Na	138.82±4.082	136.42±5.061	138.51±4.24	0.165
K	3.78±0.58	3.2±0.73	3.71±0.632	0.02*
Total Serum Ca	8.14±0.641	7.02± 0.34	7.99±0.716	0.0001*
PH	7.41±0.047	7.42±0.034	7.41±0.045	0.836
PCO2mmHg)	35.87±4.59	32.28±5.67	35.40±4.84	0.067
HCO3) mEq/L	23.18±2.819	21.42±3.53	22.95±2.94	0.143

*P-value is significant at ≤0.05; (HS) highly significant*by Student t test*

TYG index, FBS, WBCs, CRP and BUN were significantly higher in severe cases while Albumin corrected, K and Total calcium were significantly lower in severe cases (P< 0.05). Other parameters were similar in both groups.

Table 3: causes of acute pancreatitis

Variables	BIS-AP Score		Total No=54 (%)	P-value
	Mild degree (0-2) N= 47(87%)	Moderate to severe (3-5) N= 7(13%)		
Causes of AP				
gall stone	28 (87.5)	4 (12.5)	32	**0.960**
hyper triglyceridemia	14 (87.5)	2 (12.5)	16	
post ERCP	5 (83.3)	1 (16.7)	6	

*P-value is significant at ≤0.05, by $\chi 2$ test

Presence of Gall stone, hyper triglyceridemia previous ERCP were similar in both groups

Table 4: Pleura effusion among mild and moderate to severe group

Variables	BIS-AP Score		Total No=54 (%)	P-value
	Mild degree (0-2) N= 47(87%)	Moderate to severe (3-5) N= 7(13%)		
Pleura effusion				
without Pleura effusion	47 (95.9)	2 (4.1)	49	0.0001*
with Pleura effusion	0	5 (100)	5	

Pleura effusion as a complications was significantly more with severe cases (P=0.0001).

Parameter	Cut off	AUC	S (%)	SP (%)	p-value
TYG index	4.94	0.827	71,4	85,1	0.0006*

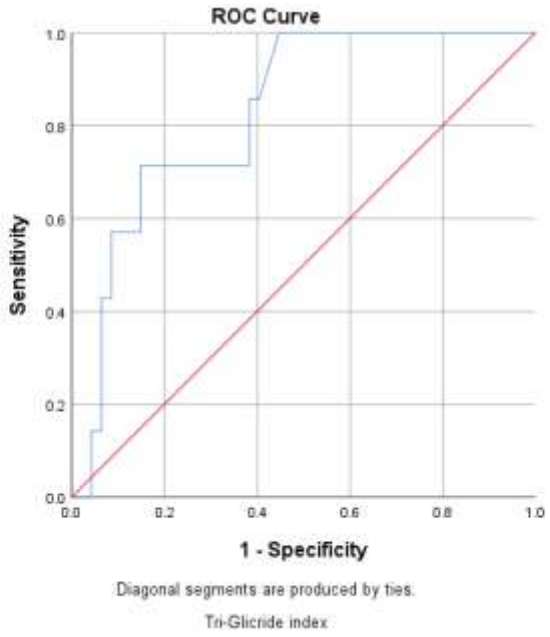

Figure 1: ROC sensitivity, specificity, of TyG index

Figure 1: ROC showing progression to sever AP. concluded that the cutoff value of **TyG index**. (4.94), the sensitivity (S) 71, 4%, specificity (Sp) 85, 1%, AUC (0.827), P= (0.0006) *high statically significance.*

4. Discussion:

BISAP score has been used to predict death in patients with AP after admission within the first 24 hours. (10). This is study was done to assess the value of Triglyceride and glucose index for prediction of severity in patients with AP in correlation with BISAP to early predict the disease severity to potentially prevent adverse outcomes.

Atlanta classification system has limitations as definitions of local complications and severity of AP were not used consistently and it is only based on presence of organ failure (11, 12).

Patients with mild AP may be undetected and complications may happen before the diagnosis is done in case of fulminant and severe pancreatitis. So the accurate incidence of diagnosis of Pancreatitis cannot be achieved and so is difficult. (13)

Early identification of risky patients (within the first 24 hours of symptoms) is important to initiate rapid and more aggressive

interventions and proper supportive management (14).

Multiple predictive models based with clinical and radiologic risk factors, with serological markers and grading systems of severity have been developed to predict the severity of AP (15).

In our study we found that hypocalcaemia and low ACC were more evident in group 2 (sever acute pancreatitis) with high statistical significance [(P=0.0001), (P= 0.002) respectively] and so, it can predict severity of AP. Similarly, Edakkepuram et al. found that low ACC and hypocalcaemia, as with BISAP score can predict severity of AP, but not superior to BISAP score. (16) in addition Gutierrez-Jz et al. noted that total calcium in the first 24 hours is a good predictor of severity (17).

Hypertriglyceridemia is an etiology of AP, and in cases of AP it is proportionally correlated with persistent organ failure regardless of the cause [18]. Also, hyperglycemia predisposes patients to organ failure whose complaint is AP [19].

We found a several novel and important findings that there was a significant higher TyG index in patients with SAP than in mild ones (P= 0.007). Similarly, J.M. Park, et al concluded that TyG index is a simple prognostic predictor of sever AP, which was elevated in the Severe AP group than in the Mild AP group. Therefore, the TyG index can be an important predictor of severe AP, (20)

Several studies reported that there is an association between SAP and the TyG index, due to an underlying biologically plausible mechanism. Also visceral fat (e.g., fatty pancreas or NAFLD) is associated with severe AP [21, 22].

Fasting Blood glucose in our study was significantly elevated in patients with SAP (G 2), (P= 0.0001). This was in agreement with Remes-Troche JM, et al. who found that elevated blood glucose is a poor prognostic factor of organ failure with severe acute pancreatitis (23).

In this study, BUN level on admission was significantly elevated in SAP patients (P=0.007), as the amount of third space fluid loss is correlated to the elevated BUN level and reduction of renal perfusion which is correlated to the severity of the AP. So more severity of pancreatitis, associated with more raising the level of BUN, this was similar to several studies as the study performed by Wu B.U.et al. who concluded that the most useful routine test for prediction of the mortality was serial BUN measurements (24). Regarding C-reactive protein, it was significantly higher in SAP patients, (P=0.042), The CRP level is correlated with

the severity of the inflammations that matches with our study. This is matching the study of Wilson C et al. Who Found that at 48 hours after attack of AP, CRP more than 150mg/L can differentiate severe AP from mild AP (25). In the our study, white blood cells was significantly higher in SAP patients , (P= 0.0001) , as white blood cells is correlated with the severity of the AP and extent of immune response .

Amylase is an enzyme produced primarily by the pancreas and the salivary glands. Amylase level within six hours of onset of AP increases rapidly. Clinical symptoms of AP does not correlate as level of amylase as it falls from the peak value to its normal levels early which means that correlation with disease severity and ultimate prognosis of amylase level not statistically significant, (P=0.484). (26).The level of Lipase increases with the onset of disease and remains for 7 to 14 days constant before it decrease to the normal level, so in patients with delayed presentation giving greater sensitivity. Lipase also increases in case of intra-abdominal disease such as appendicitis, cholecystitis, intestinal ischemia, and obstruction so there is a weak correlation with disease severity and lipase level. (27), this matches this study , as the level of serum amylase and lipase were similar in both groups (p=0.484). (p=0.980) respectively. Similarly Meher S, et al found that the concentration of lipase and amylase cannot detect complicated and severe AP as detected by imaging methods. (28). in addition Manes, G. et al, also concluded thatthe levels of lipase and amylase cannot detect the etiology or to predict severe AP (29). Also, Lankisch et al. noted that the elevation of serum amylase and lipase on admission were independent of the severity of AP. Patients with slight increased levels of amylase and lipase can also develop severe AP (30). In our study the total bilirubin levels was similar in both groups. matching the study of Maher, M. et.al who noted that the level of total bilirubin is statistically insignificant as a predictor of sever AP (31). Our study showed that liver enzymes (AST, ALT) were similar in both groups, in contrast Blum Tet al. explained that inflammatory mediators that associated with insult of liver is increased as in severe AP than with mild cases which means that in severe group have more increased level of liver enzymes than the mild one (32). in the current study, TyG index had the highest AUC(0.827), sensitivity, specificity, and accuracy among other predictors of severity with statically significance and helps in detection of severe acute pancreatitis. Higher value(4.94) would be able to identify patient

with sever AP. In agreement with our study , Jin Myung Park, et al found that, the AUC significantly increased when adding the TyG index, to a predictive Severe AP from(0.738 to 0.830) and The level of TyG index is >(4.92) with severe AP patients (20). In our study Pleura effusion occurred significantly more in severe AP (G2), (P= 0.0001)in agreement with study, that Pleural effusion has been found to be associated with poor outcome in patients with severe AP (33). Our study found that arterial pH, bicarbonate levels were similar in both groups. In contrast Vishal Sharma, et al. concluded that Arterial pH and bicarbonate levels at presentation are helpful for prediction of outcome of AP (34)

Limitation of study

Our study was done on a small number of cases with severe AP and short time of follow-up. Secondly, some important parameters that should have been involved in diagnosis of severe acute pancreatitis , including BMI, waist circumference, HOMA-IR score and HSCRP, were not available, Third, unrecognized the transport time from onset to the hospital. Fourth our data came from a single hospital, , so multicenter, large cohort farther studies are recommended.

5. Conclusion:

Triglyceride and glucose index, corrected calcium, total calcium, Fasting blood sugar, urea, white blood cells, C-reactive protein and Potassium are significantly related to AP severity.. TYG index is a good test for early predication of severe AP because it has good AUC. TYG index with BSAP scoring can be used for predicting of severity of AP with an added advantage in assessment of daily practice.

Declarations

Ethics declarations

Ethics Approval and consent to participate

Ethics Approval by Research Ethical Committee, faculty of Medicine, Beni-suef University, FWA#:FWA00015574, Approval No; FMBSUREC/02052023/shaker;.

Informed consent was obtained from each patient who had participated in the study.

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Conflict of interest

The authors declared, no conflict of interest

Consent for publications:

Approved for publications

Not applicable as no individual data, images or were included in the study.

Availability of data and material: all data is available

Please contact author for data requests.

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Code availability: available

Authors contribution:

ASS: Study design, manuscript preparation and Editing.

MSA: Plan the study design and discussion.

AM :Collected and analyzed the data .

ShN: Helped in Data analysis, reviewed the manuscript

Abbreviations

BIS- AP, Bedside Index for Severity in Acute Pancreatitis

HTN **, Hypertension**

DM, Diabetes Mellitus

ALT, Alanine amino transferase.

AST ,Aspartate amino transferase,

ALB, albumin

T.Bilirubin, Total bilirubin

TG— triglyceride;

CHOL cholesterol

TYG index , Triglyceride and glucose index

FBS, Fasting Blood glucose

HbA1c—hemoglobin A1C;

CBC. Complete Blood Count,

HGB, Hemoglobin,

WBC—white blood cell.

PLT—platelets;

CRP, C-reactive protein,

ESR, Erythrotic sedimentation Ratio,

BUN (blood urea nitrogen)

INR International normalized Ratio,

Na sodium,

K potassium,

Ca, calcium,

ABGs (arterial blood gases)

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