Triglyceride/Glucose Index might be a Predictor for Delirium in ICU Patients with Various Systemic Disorders

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Abstract

Background: Delirium is a frequent event affecting intensive care unit (ICU) patients is a leading cause longer ICU stays and may compromise outcomes.

Objectives: Evaluation of the ability of the triglyceride/glucose (TyG) index estimated at ICU admission to differentiate patients vulnerable to develop delirium, morbidities and/or mortality.

Patients and methods: A Prospective observational non-randomized multicenter comparative study conducted on 300 ICU patients who were evaluated for disease severity status, the presence of risk factors for delirium using the Delirium Rating Scale-R-98 (DRS-R-98). Blood samples were obtained for estimation of blood glucose and plasma triglyceride levels to calculate the TyG index. During ICU stay, organ functions were evaluated using the Sequential Organ Failure Assessment Score and its deterioration was expressed as ΔSOFA, which equal 72-h minus 24-h scores, the development of new morbidities, mortality rate (MR), and development and severity of delirium among survivors were determined.

Results: The frequencies of new morbidities, SOFA score deterioration and mortality were 21%, 16.7% and 11%, respectively. High TyG index and ΔSOFA showed highly significant ($P<0.001$) predictive ability for new morbidities and MR. Medical ICU (MICU) patients were more vulnerable to develop delirium than surgical ICU. Statistical analyses defined high TyG index and ΔSOFA as the highly significant ($P<0.001$) predictors for oncoming delirium.

Conclusion: Delirium is common especially among MICU patients. High at-admission TyG index is a significant predictor for ICU outcomes and might identify patients vulnerable to develop delirium. High ΔSOFA might predict the morbidity and mortality rates but was less significant predictor for delirium.

Keywords: Delirium; Delirium Rating Scale-R-98; ICU patients; Mortality rate; SOFA score.

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Introduction

Altered metabolism reflected as dyslipidemia with subsequent elevation of plasma levels of triglycerides and/or hyperglycemia had been linked to multiple systemic disorders. The calculated triglyceride-glucose (TyG) index was positively associated with albuminuria, which is a risk marker of hypertension-mediated organ damage **(Tian et al., 2023)** and also showed an L-shaped association with the risk of all-cause mortality among middle-aged and elderly hypertensive patients **(Pang et al., 2023)**.

Elevated TyG index was found to be significantly associated with the occurrence of cardiac arrest (CA) and its related high mortality rate **(Boshen et al., 2023)** and independently related to the presence of coronary artery calcification in asymptomatic, non-diabetic patients maintained on hemodialysis **(Ding et al., 2023)**.

Moreover, high TyG index is an independent risk factor for the development of contrast-induced nephropathy in non-diabetic non-ST elevation acute myocardial infarction (NSTEMI) underwent coronary angiography **(Aktas et al., 2023)** and is related to the risk of acute kidney injury (AKI) in ICU patients **(Jin and Zhang, 2023)**.

Furthermore, moderate increase of the TyG index was independently associated with a higher incidence of Alzheimer's disease **(Sun et al., 2023)** and is a risk factor for bipolar disease course among women had nonalcoholic fatty liver disease **(Wang et al., 2023)**. A national wide cross-sectional survey detected significant association between TyG index and suicidal ideation especially in women and may help prevent suicide via earlier detection of suicidal ideation **(Lee et al., 2024)**.

Delirium is common among critically ill patients and is associated with extended hospital stays, increased morbidity and higher consumption of health care resources **(Jarman et al., 2023)**. Delirium is a common complication after cardiac surgery and is associated with longer ICU and hospital stay, functional decline and 30-day mortality **(Rivas et al., 2023)**. The TyG index shows promise as a novel biomarker for predicting the occurrence of POD in elderly surgical patients with T2DM **(Sun et al., 2024)**. Delirium is associated with serious short- and long-term clinical consequences **(Al Huraizi et al., 2023)**, thus defining risk factors for developing delirium is crucial for prevention and improving patients' outcomes.

The previously mentioned relation between the ability of estimated TyG index for early distinguishing people vulnerable to develop neuropsychiatric disorders arouse the possibility of using this index for early prediction and distinguishing ICU patients vulnerable to develop delirium. This study tried to evaluate the predictability of estimated TyG index at time of ICU admission for the development of delirium and oncoming outcomes.

Patients and methods

Design: Prospective observational non-randomized multicenter comparative study.

Setting: Departments of Psychiatry, Faculty of Medicine, Suez Canal University, Internal Medicine, Faculty of Medicine, Zagazig University and Anesthesia, Pain and Intensive Care, Faculty of Medicine, Al-Azhar University, in conjunction with multiple private centers.

Ethical considerations : The study protocol was approved by the Departmental Committee, Neurology and Psychiatry Department before case collection. After completion of case collection and patients' follow-up during ICU stay, the final approval by the Local Ethical Committee, Faculty of Medicine, Suez Canal University was obtained with code: Research 5621# on February 20-02-2024.

Patients: Patients admitted to ICU were eligible for evaluation for the inclusion and exclusion criteria.

Inclusion criteria: Newly patients admitted to ICU who were free of exclusion criteria were included in the study.

Exclusion criteria: Patients liable to have neuropsychiatric disorders especially diabetic patients with history of previous recurrent comas, patients with history of neurodegenerative disorders, psychiatric disorders, neurosurgical operations, maintenance on drugs altering the psychological statuses, on dialysis, hereditary metabolic disorders, metabolic syndrome, morbid obesity with body mass index (BMI) of >35 kg/m^2, impaired hepatic function, patients who were admitted in shock or coma and those who died during ICU stay were also excluded.

Patients' evaluation: At time of ICU admission, patients were evaluated to collect data concerning demographic data including age, gender, and if possible, body mass index, indication of ICU admission, previous or current medical disorders, past history of neuropsychiatric or neurological disorders. In case of patient admitted after surgical interference, the collected data included type and duration of surgery, the applied anesthetic procedure and in case of general anesthesia, it was inhalational or total intravenous and if possible, the type of anesthetic used. In case of patients who were admitted with sepsis, the collected data included the affected organ, possible source, type of sepsis and if it requires admission to isolation area of ICU or not.

Patients' evaluations include

A) **Evaluation of the disease severity status** was conveyed using the following tools:
   1. **Glasgow Coma Scale (GCS)** entails evaluation of three domains including 15 items each item is scored by one point for determination of the best eye (E), verbal (V) and motor responses (M) and a total score was calculated as the sum of the score of the 15 items with a higher score indicates the best conscious state **(Teasdale and Jennett, 1976)**.
   2. **Acute Physiology and Chronic Health Evaluation II (APACHE II) Score** consists of three domains: the Acute Physiology Score, age and the chronic health points. The total APACHE II score is the sum of the scores of the three domains with the higher total score, the worst is the patient's prognosis **(Knaus et al., 1985; Moon et al., 2014)**.
   3. **The Sequential Organ Failure Assessment (SOFA) Score** evaluates the impact of disease on body organs namely, central nervous system, cardiovascular, renal and respiratory systems in addition to the coagulation profile and liver functions. SOFA score was determined at 24-h and 72-h after ICU admission to assess patients' progress. Each organ was scored using 0-4 Likert scale with higher scores correlates with mortality rate **(Vincent et al., 1996; Vincent et al., 1998)**.

B) Lab investigations
   - At time of ICU admission blood samples were obtained aseptically and divided into:
     1. EDTA containing tube for determination of complete

blood picture including platelet count

2. Plain tube to allow sample clotting and then was centrifuged at 1500 rpm for 10 minutes to separate serum for estimation of serum creatinine and total bilirubin by photoluminescence methods.
3. Fluoride containing tube for estimation of blood glucose level in the samples obtained after 6-h fasting and free of intravenous glucose infusion by glucose oxidase method **(Tinder, 1969)**.

- , blood samples were collected in to preserve
- After 12-h fasting, samples were collected in EDTA containing tubes for enzymatic estimation of plasma triglyceride (TG) levels by modified glycerol-3-phosphate oxidase /peroxidase method **(Mcgowan, 1983)**.

C) Calculation of the TyG index

The Triglyceride/Glucose (TyG) index was calculated according to the equation: Ln [fasting triglycerides (mg/dl) × fasting plasma glucose (mg/dl)/2] **(Simental-Mendía et al., 2008)**.

D) Psychiatric evaluation

1. **Evaluation for the presence of the risk factors for delirium** using the predictive model for delirium that evaluates four items by 0 or 1 if present. These items include the presence of cognitive impairment (CI), high serum creatinine, APACHE II score >16 and vision impairment. Collective score of 0 points suggests 10% chance to develop delirium (Low risk), score of 1 or 2 indicates 25% possibility to have delirium (Intermediate risk) and score of 3 or 4 indicates high risk with 80% possibility of getting delirium **(Inouye et al., 2007)**.
2. **DSM-5 diagnostic criteria for delirium** to diagnose delirium depending on the presence of disturbed attention and awareness with CI in absence of physiological or pathological bases for these disturbances **(Kalish et al., 2014)**.
3. **Delirium Rating Scale-R-98 (DRS-R-98)** is a 13-domain scale each was scored on 0-3 scale for a maximum score of 39 and higher score indicates high delirium severity **(Trzepacz et al., 2001)**. DRS-R-98 was applied for initial assessment at time of ICU admission and at time discharge.

Study outcomes

The study outcome was evaluation of the ability of the TyG index to predict the oncoming patients' outcomes including

1. The development of new morbidities, deterioration of the of the organ function as judged by ΔSOFA score which equals SOFA score at 72-h minus SOFA score at 24-h, and mortality rate.
2. The development and severity of delirium among survivors at time of ICU discharge.

Statistical analysis

Considering the study design as an observational study predetermined sample size was not defined. The Kolmogorov-Smimov test of normality and the normal Q-Q plots were used to test the data normality. Data are presented as mean and standard deviation (SD) that were compared using unpaired t-test, while data presented as percentages were compared using Chi-square test. Pearson's Correlation analysis was applied to assess the relations between the at-admission data and patients' outcomes. The receiver operating characteristic (ROC) curve analysis was used to verify the correlated variates with the outcomes as significant predictors for these outcomes according to the significance of the difference between the area under the curve (AUC) for each variate and that under the reference line (AUC=0.5). The ability of the variates gave significant AUC to predict each outcome was verified using the regression analysis and the paired-analysis of the difference in the area under the curve to determine the highly significant predictors for the outcome. In multivariate analysis, all variates were analyzed against each other for the significant predictors in Model-1 and these significant were passed to Model-2 and variates that were still present were passed to Model-3 to define the persistently significant variates. Statistical analyses were conveyed by the IBM® SPSS® Statistics software (Ver. 26, 2019; IBM Corporation; Armonk, USA). The significance of the analysis results was evaluated at the cutoff point of P less than 0.05.

Results

During the preliminary evaluation of patients admitted to ICU, 26 patients were excluded; 5 patients had neurosurgeries, 6 patients had history of recurrent comas, 4 patients had psychiatric disorders, three patients had cerebrovascular stroke, three patients were maintained on dialysis, three patients had neurodegenerative disorders and two patients had hepatic encephalopathy. Three hundred patients fulfilled the inclusion criteria; 175 patients at surgical and 125 patients at medical parts of ICU.

Patients admitted to Medical ICU (MICU) were significantly ($P<0.001$) older, mostly females ($P=0.0017$) and more obese ($P=0.018$) than patients admitted to Surgical ICU (SICU). Regarding the applied anesthetic technique used for patients admitted to SICU; 90 patients (51.4%) had received general inhalational anesthesia using sevoflurane (n=75; 42.9%) or isoflurane (n=15; 8.5%) and 42 patients (24%) received total intravenous anesthesia that was propofol-base for 30 patients (17.1%) and dexmedetomidine-based for 12 patients (6.9%), while the remaining 43 patients (24.6%) had received epidural anesthesia. Among sepsis patients; 11 had septic shock (6.3%), 8 patients (4.6%) had severe sepsis and 12 patients (6.9%) had moderate sepsis, (**Table.1**).

Table 1. Patients' enrolment data and indications of ICU admission

Variables	Surgical cases		Medical cases	
Age (years)	**<40**	54 (30.9%)	**<40**	0
	40-49	48 (27.4%)	**40-49**	45 (36%)
	50-59	38 (21.7%)	**50-59**	42 (33.6%)
	60-69	31 (17.7%)	**60-69**	38 (30.4%)
	>70	4 (2.3%)	**>70**	
	Average (±SD)	48 (12.1)	**Average (±SD)**	54.6 (7.1)

Gender	**Males**	105 (60%)	**Males**	52 (41.6%)
	Females	70 (40%)	**Females**	73 (58.4%)
BMI (kg/m^2)	**Average**	29 (16.6%)	**Average**	11 (8.8%)
	Over	94 (53.7%)	**Over**	59 (47.2%)
	Obese	52 (29.7%)	**Obese**	55 (44%)
	Average (±SD)	30.3 (2.5)	**Average (±SD)**	31.2 (2.3)
Indications of ICU admission	**Major abdominal Surgeries**	55 (31.5%)	**STEMI**	10 (8%)
	CABG	49 (28%)	**Non STEMI**	23 (18.4%)
	Thoracotomy	17 (9.7%)	**Atypical angina**	6 (4.8%)
	Sepsis	31 (17.7%)	**Atrial fibrillation**	7 (5.6%)
	Trauma	23 (13.1%)	**Status asthmaticus**	8 (6.4%)
			COPD	11 (8.8%)
			Hypoglycemic coma	18 (14.4%)
			Diabetic ketoacidosis	42 (33.6%)

CABG: Coronary artery bypass-graft surgery; COPD: Chronic obstructive pulmonary disease

Patients' distribution according GCS showed insignificant difference, while the mean values of at-admission GCS were significantly higher among surgical cases. On contrary, mean value of at-admission APACHE II score was significantly lower for surgical than medical cases. At 24-h, SOFA scores of patients admitted to SICU were significantly higher among than scores of those admitted to MICU. Estimated hemoglobin concentration and platelet count were insignificantly lower, while total leucocytic count was significantly (P<0.001) higher in SICU than MICU patients. Also, estimated serum levels of direct bilirubin and creatinine were significantly (P=0.001 & 0.035, respectively) lower in surgical than medical cases, with significantly (P0.011) lower frequency of patients had serum creatinine level over the upper normal levels among surgical than medical cases (13.1% vs. 22.4%). Estimated plasma glucose and triglycerides levels were significantly (P<0.001) higher with significantly (P<0.001) higher TyG index for medical than surgical cases. Evaluation of the risk factors for getting delirium during ICU stay showed insignificant difference between surgical and medical patients as regards patients' distribution according to the frequency of these risk factors. However, the calculated mean value of the risk of getting delirium in ICU defined low risk in 42 patients (14%) and high risk in only 5 patients (1.7%), while the majority of patients (n= 253; 84.3%) showed intermediate risk with significantly (P=0.048) higher possibility of developing delirium among medical than surgical patients (**Table.2**).

Table 2. Data of disease severity and lab findings at-admission

Scores Patients			Surgical cases	Medical cases	P value
Score on Glasgow Coma Scale at ICU admission			12.5±2.1	12.2±2.2	**0.0024***
Score on APACHE II at ICU admission			28.6±8.2	31.6±9	**0.002***
SOFA score at 24-h after ICU admission			10.2±2.5	7.8±2.2	**<0.001***
Complete blood count	Hemoglobin concentration (g %)		10.1±0.74	10.22±0.69	0.142*
	Total leucocytic count (cells/µl)		8903.5±1506.7	7416.7±993.1	**<0.001***
	Platelet count (1000/µl)		208.8±61	211.6±56	0.685*
Fasting blood glucose (mg/dl)			110.7±9.6	119.8±10.9	**<0.001***
Serum levels of	Direct bilirubin (mg/ml)		0.27±0.08	0.32±0.13	**0.0001***
	Creatinine (mg/ml)	Abnormal levels	23 (13.1%)	28 (22.4%)	**0.035†**
		Mean level	0.87±0.32	0.97±0.35	**0.011***
Plasma triglycerides (mg/dl)			138.5±18.4	147.6±24.7	**<0.001***
TyG index			4.82±0.52	4.88±0.44	**<0.001***
At-admission risk for getting delirium	**Items**	Cognitive impairment	77 (44%)	51 (40.8%)	0.593†
		Serum creatinine >1.2 mg/dl	31 (17.7%)	22 (17.6%)	
		APACHE II >16	168 (96%)	122 (97.6%)	
		Vision impairment	36 (20.6%)	17 (13.6%)	
	Risk of getting delirium	Low	31 (17.7%)	11 (8.8%)	**0.048†**
		Intermediate	140 (80%)	113 (90.4%)	
		High	4 (2.3%)	1 (0.8%)	

ICU: Intensive care unit; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; TyG: Triglyceride/Glucose; * unpaired t-test; †Chi-square test; **Bold P-values:** significant

The study found that medical patients had significantly higher scores on the DRS-R-98 scale at admission and discharge from the ICU, except for the severity of delusions that showed insignificant difference at admission, but significant difference at time of discharge. Moreover, the frequency of medical patients who showed higher scores of items of the DRS-R-98 at time of discharge was significantly higher in comparison to their respective frequencies at time of ICU admission except for perceptual disturbance where the difference was insignificantly higher. Surgical patients had significantly higher scores for perceptual disturbance, delusions severity, language disturbances, orientation and attention were insignificantly higher compared to their frequencies at admission, while the differences were significant for the remaining items of the DRS-R-98 (**Table.3**).

Table 3. Distribution of surgical and medical cases according to the frequency of the DRS-R-98 detected at time of admission to and discharge from ICU

Patients		Surgical cases				Medical cases				P value
Item Score		0	1	2	3	0	1	2	3	
Sleep disturbance	Admission	139	23	13	0	81	30	14	0	**0.017†**
	Discharge	118	40	15	2	62	38	20	5	**0.0095†**
	P1	**0.038†**				**0.023†**				
Perceptual disturbance	Admission	132	33	10	0	85	22	18	0	**0.039†**
	Discharge	115	47	13	0	73	31	21	0	**0.041†**
	P1	**0.134†**				**0.263†**				
Delusions	Admission	162	13	0	0	110	12	3	0	**0.092†**
	Discharge	156	19	0	0	92	27	6	0	**0.0003†**
	P1	**0.266†**				**0.015†**				
Labiality of affect	Admission	149	22	4	0	90	26	9	0	**0.013†**
	Discharge	130	35	9	0	70	41	14	0	**0.0027†**
	P1	**0.045†**				**0.031†**				
Language disturbances	Admission	161	14	0	0	104	21	0	0	**0.019†**
	Discharge	152	22	1	0	94	25	6	0	**0.0093†**
	P1	**0.219†**				**0.033†**				
Thought abnormalities	Admission	141	20	14	0	83	25	17	0	**0.021†**
	Discharge	122	38	15	0	61	43	21	0	**0.001†**
	P1	**0.030†**				**0.014†**				
Motor agitation	Admission	149	23	3	0	91	29	5	0	**0.029†**
	Discharge	130	37	8	0	72	44	9	0	**0.010†**
	P1	**0.033†**				**0.040†**				
Motor retardation	Admission	140	26	9	0	80	33	12	0	**0.018†**
	Discharge	122	49	12	0	60	46	19	0	**0.0021†**
	P1	**0.014†**				**0.037†**				
Orientation	Admission	152	20	3	0	98	17	10	0	**0.023†**
	Discharge	141	26	8	0	75	29	21	0	**0.0001†**
	P1	**0.177†**				**0.0064†**				
Attention	Admission	157	17	1	0	97	21	7	0	**0.0039†**
	Discharge	145	25	5	0	78	37	10	0	**0.0003†**
	P1	**0.097†**				**0.030†**				
Short-term memory	Admission	141	31	3	0	76	37	12	0	**0.0002†**
	Discharge	122	44	9	0	56	53	16	0	**0.00006†**
	P1	**0.036†**				**0.040†**				
Long-term memory	Admission	161	14	0	0	94	21	8	0	**0.0001†**
	Discharge	149	26	0	0	72	32	21	0	**<0.001†**
	P1	**0.044†**				**0.004†**				
Visuospatial ability	Admission	165	8	2	0	103	16	6	0	**0.0016†**
	Discharge	149	21	5	0	86	31	8	0	**0.0032†**
	P1	**0.019†**				**0.037†**				

† Chi-square test; **Bold P-values:** significant

The total severity score of the items of the DRS-R-98 scale was significantly (P < 0.001) lower in surgical than medical patients both at-admission to (2.24 ± 1.61 vs. 4.38 ± 2.18) and discharge from (6.79 ± 2.912 vs. 10.6 ± 3.2) ICU. Moreover, the calculated percentage of change of the total DRS-R-98 score at time of ICU discharge in relation to at-admission score was insignificantly (P = 0.568) lower for cases of SICU than that of MICU (167.8 ± 134.1 vs. 187.3 ± 163, respectively) (**Fig.1**).

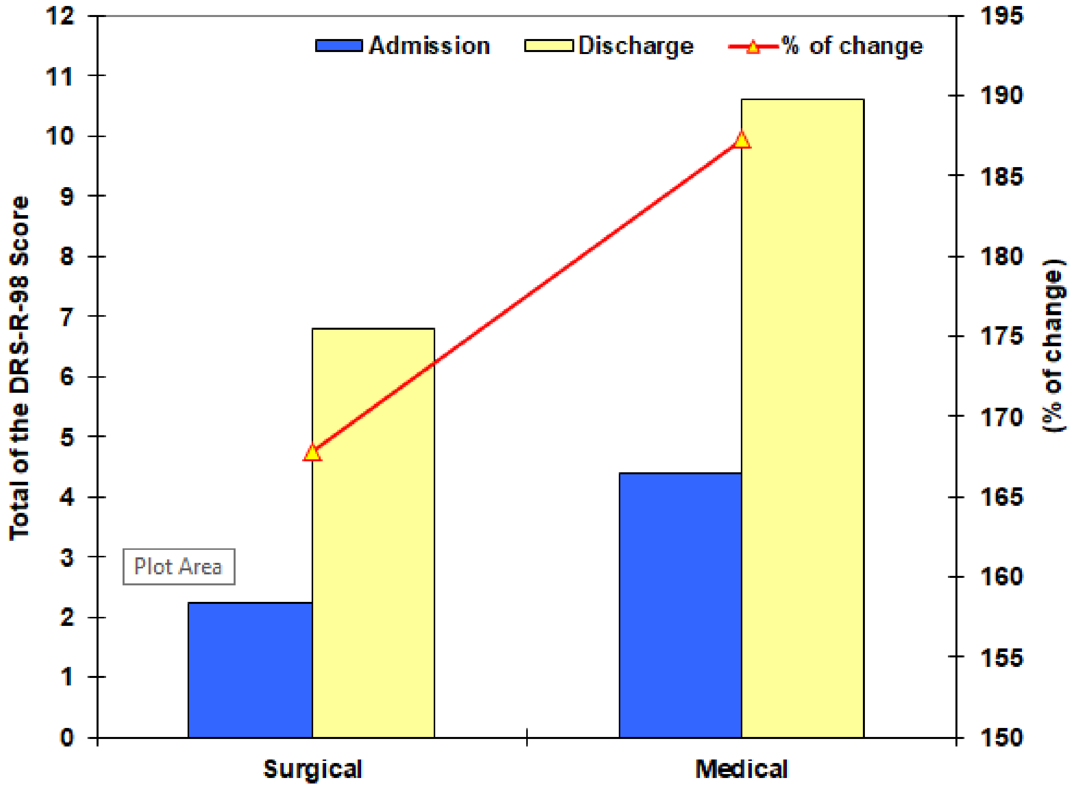

Fig.1: Total value of the DRS-R-98 score of surgical and medical ICU patients at time of admission to and discharge.

During ICU stay, 52 patients developed new morbidities: 27 in SICU and 25 in MICU. Acute kidney injury was the commonest with significantly (P = 0.044) higher incidence among surgical than among medical cases (11.4% vs. 4.8%). Nine patients got cardiac insults with significantly (P=0.025) higher incidence among medical than surgical cases (5.6% vs. 1.1%). Seventeen patients developed respiratory complications; 12 developed ARDS and 5 got acute respiratory failure with significant difference between SICU and MICU (P = 0.039). SOFA score at 72-h after admission to ICU (72-h SOFA) and the mean value of change (ΔSOFA) between 72-h and 24-h SOFA were significantly (P = 0.0033 & 0.0004, respectively) higher among patients of SICU. Moreover, 50 patients; 32 (18.3%) in SICU and 18 (14.4%) in MICU showed deterioration, while only 13 patients showed no change of SOFA score between 72-h and 24-h and the remaining 237 patients showed improved SOFA score at 72-h with insignificant (P = 0.249) difference between both patients' groups. Unfortunately, 24 patients (8%) died during ICU stay with insignificantly (P = 0.666) higher mortality rate among surgical patients (**Table.4**).

Table 4. Clinical outcomes for the studied cases

Estimated parameters				Surgical cases	Medical cases	P
New morbidities	Acute kidney injury			20 (11.4%)	6 (4.8%)	**0.044 †**
	Cardiac insult			2 (1.1%)	7 (5.6%)	**0.025 †**
	Respiratory complications	ARDS		4 (2.3%)	8 (6.4%)	**0.039 †**
		ARF		1 (0.6%)	4 (3.2%)	
72-h SOFA score	Score			7.3±4.1	6±2.9	**0.0033***
	ΔSOFA	Significance	Improvement	138 (71.4%)	99 (79.2%)	0.249 †
			No change	5 (10.3%)	8 (6.4%)	
			Deterioration	32 (18.3%)	18 (14.4%)	
		Value		2.94±3.03	1.81±2	**0.0004***
Mortality rate				15 (8.6%)	9 (7.2%)	0.666*

SOFA: Sequential Organ Failure Assessment; ARDS: Adult Respiratory Distress Syndrome; ARF: Acute renal failure; * unpaired t-test; † Chi-square test; **Bold P-values:** significant

Statistical analyses showed a highly significant (P<0.001) predictive ability of high 72-h ΔSOFA for the oncoming development of new morbidities during ICU stay, irrespective of the indication for ICU admission. In conjunction with the 72-h ΔSOFA, high calculated TyG index in blood samples obtained at ICU admission indicated high positive probability for getting new morbidities during ICU stay and was found to be the significant (P<0.001) early predictor for this event. The ROC curve analysis assured the highly predictive ability of high TyG as an at-admission predictor for development of new morbidities during ICU stay with highly significant (P<0.001) AUC, while high ΔSOFA as a highly significant (P<0.001) predictor during ICU stay with AUC for the possibility of getting new morbidities for all patients admitted to ICU as shown in (**Table.5, Fig.2**).

The incidence of ICU mortalities was positively correlated with old age (P=0.005) and high at-admission APACH II score (P=0.045), TyG index (P<0.001) and high ΔSOFA (P=0.006). Regression analysis assured that high TyG index is a highly significant (P<0.001) predictor for ICU mortality, while excluded other variate. The ROC curve analysis defined high ΔSOFA (P<0.001) and high at-admission TyG index as the significant (P<0.001) predictor for ICU mortality (**Table.5, Fig. 3**).

Table 5. Statistical analyses for predictors of clinical outcomes of patients admitted to ICU

Analyses	Correlation analysis		Multivariate Regression analysis		The Receiver Operating Characteristic Curve analysis			
Variates	"r"	P	β	P	AUC	Std.	P	95% CI
New morbidities								
Age	0.096	0.099	0.031	0.557	0.379	0.043	0.715	0.496-0.657
Males	-	0.622	0.002	0.916	0.	0.045	0.925	0.397-

gender	0.029				504			0.575
BMI	0.054	0.356	0.092	0.068	0.436	0.046	0.158	0.361-0.528
APACHE II	0.086	0.140	0.028	0.591	0.456	0.044	0.328	0.447-0.640
ΔSOFA at 72-h	-0.386	**<0.001**	-0.233	**<0.001**	0.705	0.044	**<0.001**	0.160-0.332
TyG index	0.486	**<0.001**	0.377	**<0.001**	0.824	0.040	**<0.001**	0.755-0.893
Mortality rate								
Age	0.161	**0.005**	0.010	0.859	0.379	0.043	0.078	0.295-0.464
Males gender	0.008	0.892	0.076	0.184	0.504	0.045	0.925	0.416-0.593
BMI	0.092	0.111	0.021	0.718	0.436	0.046	0.158	0.346-0.526
APACHE II	0.116	**0.045**	0.078	0.175	0.456	0.044	0.328	0.371-0.541
ΔSOFA at 72-h	0.159	**0.006**	0.091	0.145	0.705	0.040	**<0.001**	0.625-0.784
TyG index	0.295	**<0.001**	0.202	**<0.001**	0.713	0.042	**<0.001**	0.632-0.495

Bold P-values: significant

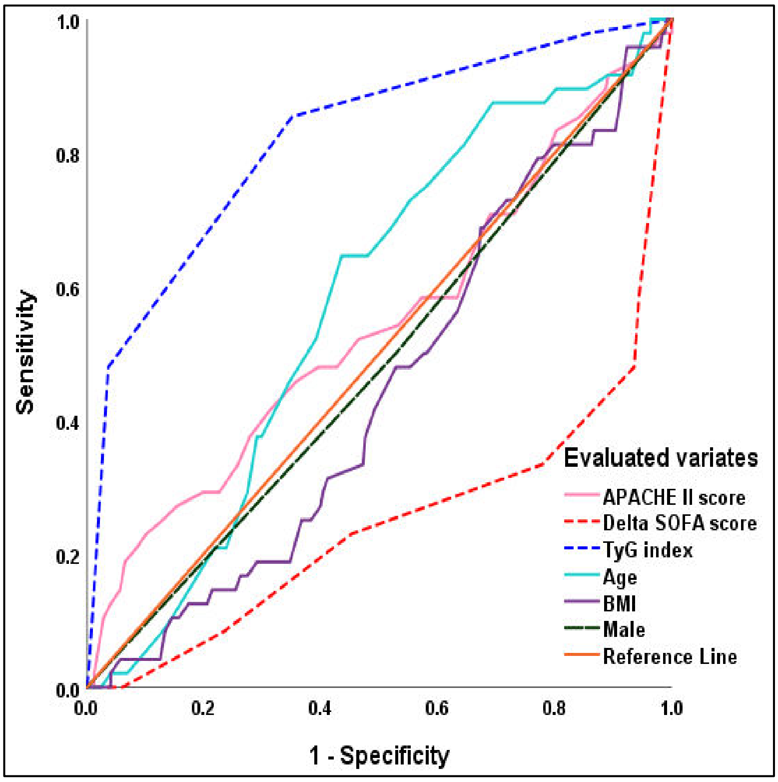

Fig. 2. ROC curve for evaluating clinical variate for prediction of the possibility of getting new morbidities during ICU stay

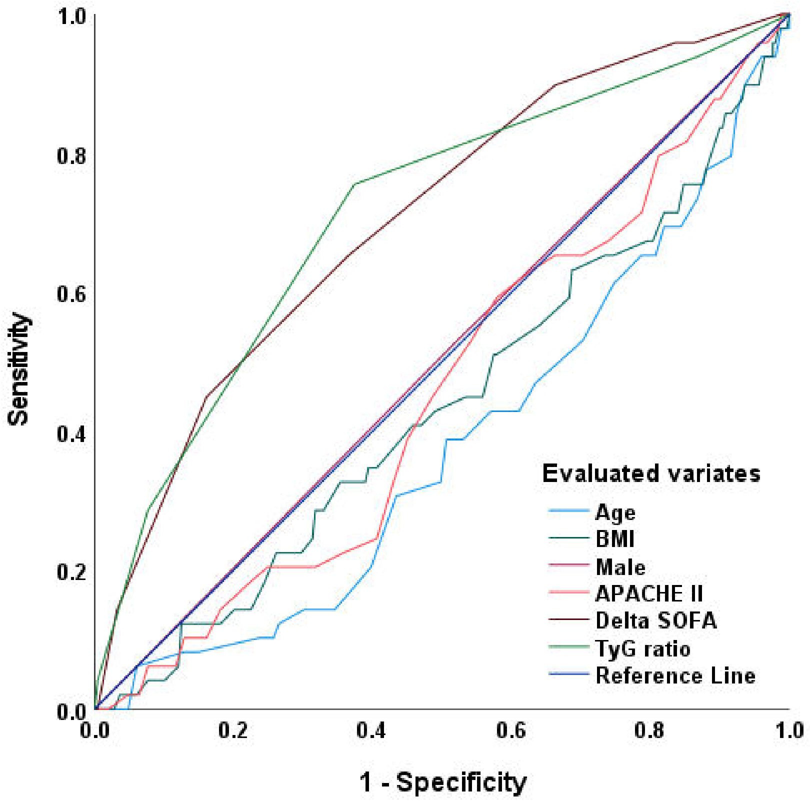

Fig. 3.ROC curve for evaluating clinical variates for prediction of the possibility of mortalities during ICU stay

The percentage of change in DRS-R-98 score at-discharge in relation to at-admission score showed positive significant correlation with high BMI (P=0.002), high at-admission SOFA score (P=0.007) and the calculated risk for getting delirium (P=0.001) and the TyG index (P<0.001). Regression analysis for the correlated variate assured the value of high at-admission TyG index (P<0.001), and the calculated risk for getting delirium (P<0.001) as significant predictors for deterioration of the DRS-R-98 as a measure for delirium severity. On contrary, ROC curve analysis assured the predictability of high TyG index (P<0.001), high 72-h ΔSOFA (P=0.001) and the calculated delirium risk (P=0.018) as early predictors for oncoming delirium at-discharge from the ICU with significant AUC (**Table.6, Fig. 4**).

Table 6. Statistical analyses for variate as predictors of development of delirium at ICU

Analyses / Variates	Correlation analysis		Regression analysis		The Receiver Operating Characteristic Curve analysis			
	"r"	P	β	P	AUC	Std.	P	95% CI
Age	0.063	0.279	0.027	0.614	0.536	0.060	0.503	0.418-0.654
Males gender	0.080	0.165	0.056	0.291	0.594	0.053	0.083	0.490-0.698
BMI	0.015	0.790	0.004	0.944	0.548	0.054	0.373	0.443-

									0.653
At admission	GCS	0.072	0.214	0.022	0.676	0.485	0.051	0.781	0.386-0.584
	APACHE II	0.042	0.466	0.054	0.312	0.479	0.057	0.698	0.368-0.590
	SOFA	0.035	0.541	0.026	0.625	0.334	0.045	0.153	0.246-0.422
ΔSOFA at 72-h		0.073	0.213	0.106	0.081	0.885	0.046	**0.001**	0.765-0.945
The calculated risk		0.388	**<0.001**	0.404	**<0.001**	0.629	0.054	**0.018**	0.522-0.735
TyG index		0.493	**<0.001**	0.382	**<0.001**	0.731	0.043	**<0.001**	0.647-0.816

BMI: Body mass index; GCS: Glasgow Coma Scale; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; TyG: Triglyceride/Glucose; **Bold P-values:** significant

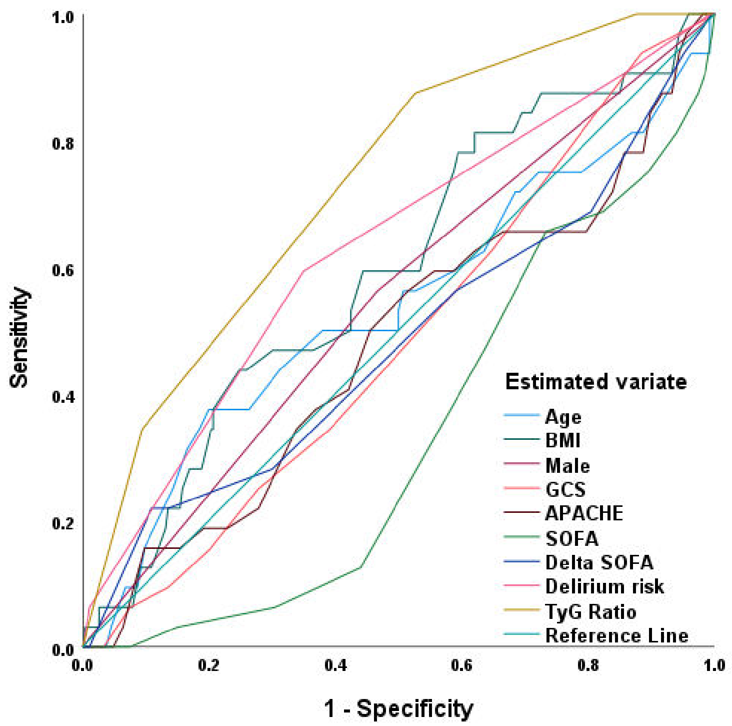

Fig. 4. ROC curve for evaluating clinical variate for prediction of the possibility of development of delirium during ICU stay

Regression analysis of the studied variate, showed that at-admission TyG index is the highly significant (P<0.001) predictor for development or deterioration of delirium. Also, the at admission calculated risk of delirium, 72-h ΔSOFA and high BMI are significant (P=0.001) predictors for development or deterioration of delirium as shown in (**Table.7**).

Table 7. Multivariate Regression analysis for variate as predictors of development of delirium at ICU

Variate		β	P
Age		0.050	0.382
Males gender		0.021	0.708
BMI		0.182	**0.001**
At admission	GCS	0.098	0.076
	APACHE II	0.058	0.295
	SOFA	0.090	0.089
72-h ΔSOFA		0.174	**0.001**
The calculated risk		0.189	**0.001**
At-admission TyG index		0.237	**<0.001**

BMI: Body mass index; GCS: Glasgow Coma Scale; APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment; TyG: Triglyceride/Glucose; **Bold P-values:** significant

The Paired-Sample analysis of the difference in the AUCs for these four variates detected significant differences between AUC for at-admission TyG index and AUCs for the delirium risk, BMI and the 72-ΔSOFA and between the AUC for ΔSOFA in comparison to that for BMI. However, the AUC-difference was insignificant between AUCs for delirium risk and both of BMI and the 72-h ΔSOFA. Thus, these results excluded BMI and the delirium risk as predictors for oncoming delirium and stratified high at-admission TyG as the highly significant predictor and followed by high 72-h ΔSOFA score (**Table.8, Fig. 5).**

Table 8. Paired-Sample Area Difference under the ROC curves for variates defined as predictors of development of delirium at ICU

Variates		AUC difference	Std.	P	95% CI
At-admission TyG index vs.	The calculated risk	-0.266	0.394	0.038	[-0.518] – [-0.014]
	BMI	-0.403	0.412	0.001	[-0.643] – [-0.163]
	72-h ΔSOFA	-0.575	0.389	<0.001	[-0.779] – [-0.370]
The calculated risk vs.	BMI	-0.137	0.501	0.464	[-0.505] – [0.230]
	72-h ΔSOFA	-0.309	0.480	0.067	[-0.640] – [0.022]
BMI vs.	72-h ΔSOFA	-0.171	0.470	0.003	[-0.286] –[-0.057]

TyG: Triglyceride/Glucose; SOFA: Sequential Organ Failure Assessment; BMI: Body mass index; AUC: Area under the ROC curve; **Bold P-values:** significant

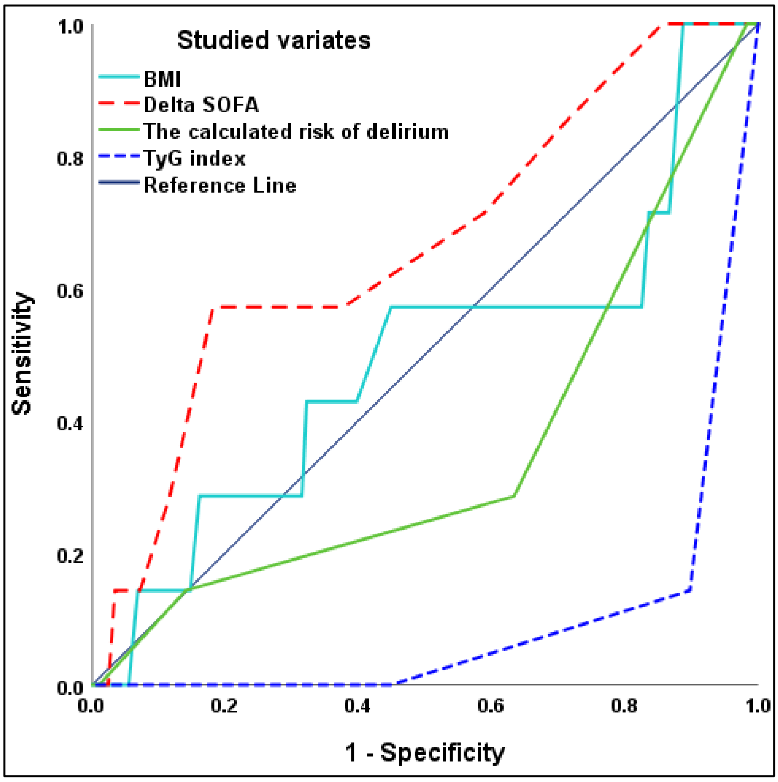

Fig. 5. ROC curve for evaluating the significance of AUCs for predictors for the possibility of getting delirium during ICU stay

Discussion

During ICU stay, the incidence rate of new morbidities was 21% and AKI was the commonest (12.3%). Moreover, 16.7% of patients showed deteriorated SOFA score and mortality rate among the studied patients was 11%. Correlation analysis defined positive relation between at-admission TyG index and 72-h ΔSOFA and both morbidity and mortality rates, but the ROC curve analysis defined TyG index as the predictor for the events might occur during ICU stay with the highest AUC.

In accordance with these findings, **Jin and Zhang (2023)** reported an AKI incidence of 25.1% among ICU patients with an independent relationship with the TyG index and concluded that the TyG index might be a predictor for the risk of AKI among ICU patients. Also, **Yang et al. (2023)** suggested TyG index as an independent predictor of the incidence of AKI and poor renal outcome in heart failure patients admitted to ICU. Moreover, **Zhang et al. (2023)** showed that the TyG index was an independent risk factor for coronary artery diseases (CADs) and its stratification according to severity. Recently, **Liu et al. (2024)** found high TyG-BMI index was independently linked to the major adverse cardiovascular events (MACE) in STEMI patients undergoing percutaneous coronary intervention (PCI) and might be used for risk assessment and prediction of prognosis. Also, **Li et al. (2024)** showed that the TyG-BMI index was an independent predictor for slow coronary flow phenomenon in ischemia and non-obstructive coronary arteries patients, but TyG ratio showed better predictive value than BMI or TG level. Moreover, **Sun et al. (2024)** defined the TyG index as predictor for the risk of MACE and all-cause mortality after PCI.

The reported mortality rate goes in hand with **Zheng et al. (2023)** who through an observational study detected an ICU mortality rate of 15.43% especially among sepsis patients and found high TyG index was independently associated with elevated risk of in-hospital and ICU mortalities. Also, **Boshen et al. (2023)** found TyG index was significantly higher in post-cardiac arrest (CA) patients than in those without CA and showed moderate ability to identify CA from overall patients' population, act as independent risk factor for in-hospital and ICU mortality and negatively correlated with the neurological status of post-CA patients. Further, **Chen et al. (2023)** documented that the TyG index is a significant predictor for severe consciousness impairment and in-hospital death in ICU patients with cerebrovascular disease. In support of the efficacy of TyG index for prediction of outcomes of ICU patients, **Cheng et al. (2023)** documented that dynamic changes of TyG index during hospital stay may be superior to TyG index for prediction of the in-hospital and 1-year all-cause mortality of ICU patients.

The obtained results illustrated the impact of the disease state that indicated ICU admission, the deterioration of organ functions and possibly the medications used during ICU stay on patients' psychological statuses especially that of patients admitted to MICU who were more vulnerable to psychological deterioration and were at higher risk to get delirium diagnosed at MICU discharge than patients admitted to SICU.

Correlation analysis showed positive significant association between the extent of deterioration of the DRS-R-98 score and BMI, at-admission SOFA score, the delirium risk score and TyG index, while ROC curve analysis defined high 72-h ΔSOFA and TyG index as predictors for oncoming deterioration of the DRS-R-98 score. In support of the variates defined to be related to deteriorated patients' psychological statuses during ICU stay, **Boncyk et al. (2024)** detected increased odds of recurrent delirium with older age, admission to medical ICU, shock at time of admission, admission to surgical or trauma ICU, propofol-based anesthesia and propofol sedation during mechanical ventilation.

Regression analysis defined high at TyG index as the highly significant predictor for the possibility of getting delirium at ICU discharge, followed by high delirium risk score, BMI and ΔSOFA, but paired analysis of the difference of the AUC showed significantly higher AUC for TyG index than that of other variates and between ΔSOFA and BMI in favor of ΔSOFA.

These findings go in hand with **Iribarren-Diarasarri et al. (2023)** who detected significant deterioration of the five domains of the EuroQol health index and showed that delirium and need for tracheostomy were associated with drop in score and associated with post-intensive care syndrome. Also, **Huang et al. (2023)** through a database review assured the presence of an independent relationship between the TyG index and the risk of critical delirium in patients aged ≥65 years and concluded that this index is a reliable marker for risk assessment of cardio-cerebrovascular patients admitted to ICU. Through long-term follow-up, **Seo et al. (2023)** found patients with metabolic syndrome had higher TyG index and exhibited higher delayed-match-to-sample task total time, as a measure of memory and reaction time than those without metabolic syndrome. Moreover, **Sun et al. (2023)** assured that moderate increases in TyG index were independently associated with higher incidence of Alzheimer's disease and suggested using this index as indicator for Alzheimer's disease high-risk persons. Also, among patients with major depressive disorders (MDD), **Jin et al. (2023)** detected higher TyG index values than in those without MDD with significantly higher the morbidity rate and concluded that the TyG index could be a valuable marker for identifying MDD patients.

Recently, evaluation of dementia-free people older than 65 years by **Tian et al. (2024)** showed significant inverse relation between TyG index and scores of memories, attention, verbal fluency, executive function, and global cognition and concluded that high TyG index was associated with poor function in multiple cognitive domains. Also, **Cheng et al. (2024)** detected significantly higher at-admission TyG index in patients with post-stroke cognitive impairment (CI) than those without CI and found this index was independently correlated with higher risk of CI within 3-m of having stroke and might be used as predictor for post-stroke CI, with significantly high area under the ROC curve.

Objectively, **Zhang et al. (2022)** found attendants of memory clinic with age ≥65 years and high TyG index were more likely to have lacunes, higher grades of deep white matter hyperintensity, higher cerebral small vessel disease score than those had low TyG index and concluded that implementation of TyG index into traditional risk factors significantly improved prediction and risk stratification of moderate to severe cerebral small vessel disease. Thereafter, **Tian et al. (2024)** detected reduced volumes of total brain tissue, gray and white matter on MRI subsample of dementia-free people older than 65 years and found these changes inversely related to the TyG index, so concluded that high TyG index was associated with global brain atrophy.

Limitation: The incidence of delirium for each disease state is required to define the disease state as predictor for delirium is the study limitation

Recommendation: Wider scale studies are required to determine the cutoff points of TyG index for medical and surgical ICUs patients and for each disease state.

Conclusion

Delirium during ICU is a common event especially among patients admitted to MICU. High at-admission TyG index is a significant predictor for ICU outcomes and might identify patients vulnerable to develop delirium. Deterioration of SOFA score at 72-h after ICU admission might predict the morbidity and mortality rates, but is less significant predictor for delirium.

Authors' contributions: Patients' evaluation, determination of their admission data and follow-up during ICU stay was the duty of two authors: Osman HA and Hashem MM. The calculation of the risk for developing delirium was the duty of Hashem MM, while Osman HA was responsible for the determination of the 28-day ICU stay outcomes. Patients' at-admission cognitive function (CF) for the calculation of the risk for getting delirium was evaluated by Ahmed AZ who was not responsible for calculation of the risk and was blinded about it. Also, Ahmed AZ was responsible for assessment of patients for the criteria of DSM-5 for diagnosis of delirium and of Delirium Rating Scale-R-98 to determine the severity of delirium at time of discharge of patients who were discharged alive to home or ward.

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