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Original Research Article

Comparison of Ranson's and Glasgow criteria with revised Atlanta in prediction of mortality in acute pancreatitis patients

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ABSTRACT

Background: To compare the performance of Ranson's Score (RS) and Glasgow Score (GS) with Revised Atlanta Classification (RAC) in prediction of mortality, and to check their suitability to replace RAC for surgical intervention of gallstone induced acute pancreatitis (GAP).
Methods: A hospital based prospective study was conducted between April 2014 and May 2017 with patients presenting with GAP. RS and GS was evaluated using data in first 24 hours and at 48 hours post admission. Patients were classified into mild, moderate and severe based on RAC at the time of hospital stay. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated for each scoring system. Receiver Operating Characteristics (ROC) curves for mortality, ICU admission, Organ Failure (OF) and Gallstone Recurrence (GR) were plotted and predictive accuracy of each scoring system was measured by the Area under Curve (AUC). AUC values were compared for statistical significance using De Long test. A p-value of <0.05 was considered statistically significant.
Results: Of 81 patients, 15 patients had OF and local complication classified as SAP, with persistent OF (16.0%). The AUC for RS was consistently the highest for predicting mortality (0.943), recurrence of gallstone (0.766), ICU-admission (0.801) and OF (0.852). RS had high specificity (61.9%), PPV (88.2%), Accuracy (90.1%) for predicting mortality, recurrence of gallstone and OF. Glasgow criteria had high sensitivity (85.1%), NPV (79.4) in predicting ICU-admission.
Conclusions: RS in comparable with RAC in predicting mortality, GR in patients with GAP and early referral for surgical intervention.

Keywords: Gallstone induced acute pancreatitis, Glasgow score, Ranson's score, Revised Atlanta classification

INTRODUCTION

Acute Pancreatitis (AP) is sudden swelling or inflammation of the exocrine pancreas causing severe and rapidly progressive abdominal pain associated with increased levels of total amylase, trypsin, pancreatic iso-amylase and lipase in the serum.[1,2] The incidence of AP has increased in the past two decades with an average annual increase of 2.7% since 1999 (27.6), in countries like the USA, UK and Europe.[3,4] Obesity, Gallstone and alcohol accounts for majority of AP cases, of which gallstone induced AP (GAP) accounts for 40%-70% cases.[5] A meta-analysis on the global incidence and mortality associated with AP, reported 33.74 cases and 2.60 deaths per 100,000 person-years respectively.[6] AP is much common among Western and Japanese population, and in India, the prevalence rate is between 8.0-8.6 per 100,000 persons.[7,8] Though majority (80%) of patients recover successfully without further complications, 10-20% develop moderate to severe forms of AP with increased complications and mortality risk.[9]

Mortality caused by AP is due to systemic inflammatory response syndrome (SIRS) which leads to OF and sepsis.[10] The overall mortality increases from 6.4% to 7.9% within 60 days to one year of disease onset.[11,12] Hence, irrespective of its level of severity, proper diagnosis helps to avoid its recurrence and death.

Gallstones are caused by excessive levels of bilirubin, cholesterol and calcium salts along with protein. The non-genetic risk factors for gallstones are given in Table 1.

Table 1: Non-genetic risk factors for gallstones.

Age
Female gender
High-calorie, low-fiber diet
High-carbohydrate diet, dietary glycemic load
Obesity
Physical inactivity
Rapid weight loss/surgery for obesity
Total gastrectomy with lymph node dissection
Spinal cord injury
Infections: enterohepatic *Helicobacter* species, malaria
Biliary strictures
Drugs: estrogens, calcineurin inhibitors, fibrates, octreotide, ceftriaxone
Total parenteral nutrition
Duodenal diverticulum
Extended ileal resection (black pigment stones)
Vitamin B_{12}/folic acid deficient diet (black pigment stones)
Pancreatic insufficiency
Cholangitis (brown pigment bile duct stones)

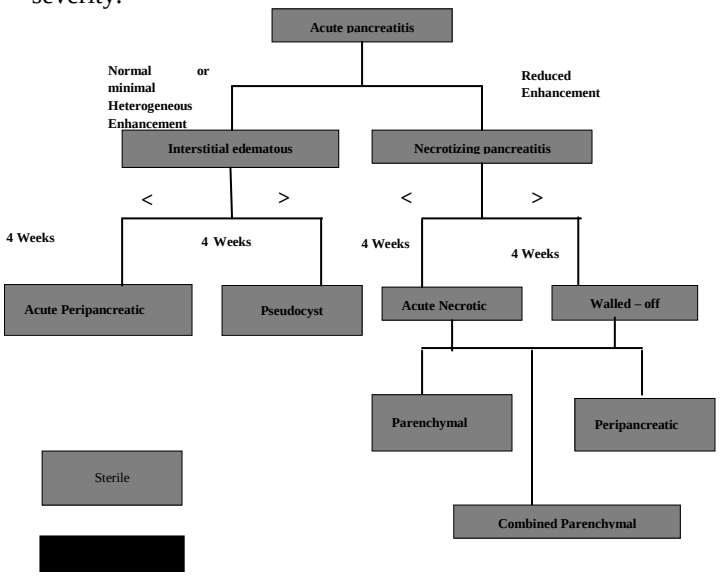
Source: Portincasa et al.[13]

When gallstones from the gallbladder, pass and obstruct ducts of the pancreas, they develop choledocholithiasis, aggravating release of pancreatic enzymes into the glandular interstitium, resulting in SAP and/or cholangitis.[14]

Since most patients are asymptomatic, diagnosis for GAP includes a combination of clinical history, physical examination, serum biochemical analysis and imaging of pancreas and gallbladder.[15,16]

GAP management is usually coupled with treatment for gallstone(s). In recent years, open surgery was replaced by aggressive intensive care management, using Non-Steroidal Anti-Inflammatory Drugs or narcotic pain relievers and Oral Dissolution Therapy (ODT).[13] However, recurrence of gallstones and inefficiency of ODT in treating Cholelithiasis cause by cholesterol, Cholecystectomy is recommended even with mild form [17,18]

RAC based on revised clinical and radiologic criteria (Contrast-Enhanced CT) was developed in 2012 (Figure 1) for accurately classification of AP based of its type and severity.[19]



Source: Adopted from Zhao et al.[20]

Figure 1: Schematic representation of AP using revised Atlanta 2012.

Table 1: Represents the grades of severity based on organ failure (OF).

Mild acute pancreatitis
No organ failure
No local or systemic complication
Moderately severe acute pancreatitis
Organ failure that resolves within 48h (transient organ failure) and or
Local or systemic complication without persistent organ failure
Severe acute pancreatitis
Persistent organ failure (>48h)
-single organ failure
-multiple organ failure

Source: Adopted from Banks et al.[21]

Though several multi-factorial prognostic scoring systems have been proposed to stratify SAP, from literatures it is understood that each of the scoring systems has its own limitations and not well validated for predicting mortality. However, with recent advancement in imaging technology there has been a major improvement in the scoring systems in predicting mortality and recurrence of gallstone in GAP.[2,19,21-23] Hence, this study aims to compare the performance of Ranson's Score (RS) and Glasgow Score (GS) scoring systems in prediction of mortality and gallstone recurrence, against RAC and to assess their suitability to replace RAC for surgical intervention of GAP.

METHODS

A hospital based prospective study was conducted between April 2014 and May 2017 with 92 patients affected with Acute Pancreatitis and admitted in the Department of General Surgery at Tertiary Care hospital in India.

Patients with Acute gallbladder pancreatitis, common bile duct stones; traumatic, idiopathic, ERCP procedure, patients undergone sphincterotomy and stone extraction; prophylactic sphincterotomy and Cholecystectomy were included in the study. Diagnosis for acute gallbladder pancreatitis was made based on abdominal pain similar to AP, three times or more elevated serum levels of pancreatic amylase and or lipase and finally radiographic diagnosis using abdominal Computed Tomography (CT), Endoscopic Retrograde Cholangiopancreatography (ERCP) or Abdominal Ultrasound (AUS) images.

Patients presenting with chronic pancreatitis, AP due to alcohol, biliary, pancreatic malignancy; pseudocysts, acute fluid collections, necrotizing pancreatitis, walled-off necrosis; AP in pediatric patients; pregnancy were excluded from the study.

Hospital ethics committee approval and informed and written consent by the patient were obtained before undertaking the study.

Demographic, Clinical, biochemical and radiographic data was prospectively collected. After detailed history and physical examination, laboratory investigations were sent at the time of admission-arterial blood gas analysis, hematocrit, kidney function test, liver function test, serum electrolytes, serum amylase, serum lipase and complete hemogram. All patients underwent abdominal ultrasonography at admission and contrast enhanced pancreatic protocol CT scan 72 hours after symptom onset.

Patients were subsequently examined daily and laboratory investigations relevant to Ranson's criteria and Glasgow criteria were sent. A Ranson and Glasgow criterion was evaluated using data in first 24 hours and at 48 hours post admission.

At time of hospital stay, discharge/death, patients were classified as having mild, moderately severe and severe acute pancreatitis, based on the Atlanta 2012 classification i.e., presence of organ failure for more than 48 hrs and local complications. Organ failure included shock (systolic blood pressure < 90 mmHg), pulmonary insufficiency (arterial PO2 < 60 mmHg at room air or the need for mechanical ventilation), or renal failure (serum creatinine level > 2 mg/dL after rehydration or hemodialysis). Patients with mild AP had neither local complications nor organ failure. Patients with moderately severe AP had transient organ failure (less than 48 hours), whereas patients with severe acute pancreatitis had persistent organ failure (more than 48 hours).

Statistical analysis

Severity of the disease was evaluated in terms of ICU admission, length of hospital stay, final grade as per Atlanta 2012 classification. Data were collected prospectively in a Microsoft Excel Database. After completion of data collection, the database was imported into SPSS software version 20.0. Categorical variables were expressed as absolute numbers and proportions. Sensitivity, specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were calculated for each scoring system. Receiver operating characteristics (ROC) curves for SAP, ICU admission, organ failure and gallstone recurrence were plotted for Ranson's score, and Glasgow criteria, and predictive accuracy of each scoring system was measured by the area under ROC curve (AUC) with 95% confidence interval. AUC values were compared for statistical significance using De Long test. A p-value of <0.05 was considered statistically significant.

RESULTS

Patient's characteristics

Of total 81 patients, the mean age of patients was 52 years with 55.6% male and 38.3% of total patients were >60 years. Majority 66.7% of the patients with BMI 30-34.9. Of 81 patients, majority 96.3% have abdominal pain, radiating (93.8%), localized pain (64.2%), diffused pain (35.8%) while least vomiting (16.0%) respectively. 43.2% of patients have diabetes mellitus, Hypertension (14.8%) and no comorbid condition (39.5%). During hospital stay, patients were stratified into mild with no organ failure (56.8%), moderate with transient organ failure (24.7%) and severe with persistent organ failure (16.0%) based on revised Atlanta 2012 classification system (Table 2).

Out of 81 patients, majority 92.6% of them was observed to have a recurrence of gallstones followed by traumatic (3.7%), idiopathic (2.5%) and post endoscopic retrograde cholangiopancreatography ERCP procedure (1.2%) (Table 3).

On the basis of the highest sensitivity and specificity values generated from the receiver-operating characteristic curves, the following cut-offs were selected for further analysis. Majority 74.1% of patients with Ranson score ≥3 and 25.9% with score <3, 66.7% with Glasgow score ≥3 and 33.3% with score <3. Majority 77.8% of patients were discharged followed by recurrence of gallstone (12.3%), Permanent organ failure (3.7%), Mortality during hospital stay and ICU-admission (2.5%) in each and Transient organ failure (1.2%) (Table 4).

Table 2: Patients characteristics.

Characteristics	Category	No. of cases	% of patients
Sex	Male	45	55.6
	Female	36	44.4
	Male: Female Ratio	5:4	
Age group (years)	>60 years	31	38.3
	50-59 years	22	27.2
	40-49 years	20	24.7
	30-39 years	8	9.9
BMI	<18.5	1	1.2
	18.5-24.9	7	8.6
	25-29.9	17	21.0
	30-34.9	54	66.7
	>35	2	2.5
Clinical Presentation	Abdominal pain	78	96.3
	radiating	76	93.8
	Localized pain	52	64.2
	Diffused pain	29	35.8
	Epigastric tenderness	67	82.7
	Nausea	23	28.4
	Vomiting	13	16.0
Comorbidities	Diabetes Mellitus	35	43.2
	Hypertension	12	14.8
	No comorbid condition	32	39.5
	others	2	2.5
Revised Atlanta 2012 grading	Mild	46	56.8
	Moderate	20	24.7
	Severe	15	18.5
	No organ failure	46	56.8
	Transient organ failure	20	24.7
	Persistent organ failure	13	16.0
	Multi-organ failure	2	2.5

Comparison of Scoring Systems in Predicting Mortality, Recurrence of gallstone, ICU-admission and Organ failure.

In prediction of Mortality according to the AUC (with 95% CI) Ranson score (0.943 (0.894–0.992)) had the highest accuracy when compared to Glasgow score (0.861 (0.783–0.940). AUCs for each scoring system in predicting Mortality, Recurrence of gallstone, ICU-admission and Organ failure are shown in Table 5.

Table 3: Etiology spectrum.

Characteristics	Category	No. of cases	Percentage (%)
Etiology spectrum	Gallstones	75	92.6
	Traumatic	3	3.7
	Post ERCP procedure	1	1.2
	Idiopathic	2	2.5

ERCP: Endoscopic retrograde cholangiopancreatography

Table 4: Ranson's criteria and Glasgow criteria scoring for AP.

Characteristics	Category	No. of cases	Percentage (%)
Ranson's score	≥3	60	74.1
	<3	21	25.9
Glasgow criteria	≥3	54	66.7
	<3	27	33.3
Clinical outcome	Discharged	63	77.8
	Mortality during hospital stay	2	2.5
	Recurrence of gallstone	10	12.3
	ICU-admission	2	2.5
	Transient organ failure	1	1.2
	Permanent organ failure	3	3.7

In our study we have found high sensitivity, specificity, and accuracy of 100%, 61.9%, and 90.1% of Ranson criteria for prediction of Mortality and 100%, 38.2%, and 74.1% for Glasgow. Similar result has been found for prediction of recurrence of gallstone, ICU-admission and organ failure.

For Ranson score we have found high sensitivity, specificity, and accuracy of 90%, 80.9%, and 87.7% when compared to Glasgow 87.2%, 50.0% and 71.6%. In predicting ICU-admission Glasgow score have high sensitivity, specificity, and accuracy of 85.1%, 79.4%, and 82.7% when compared to Ranson 83.3%, 80.9% and 82.7% and in organ failure Ranson score have high sensitivity, specificity, and accuracy of 91.7%, 71.4%, and 86.4% when compared to Glasgow 89.4%, 44.1% and 70.4% (Table 6).

The Formula for calculating the Sensitivity, Specificity, PPV, NPV and Accuracy are:

$$\text{Sensitivity} = \frac{TP}{TP+FN} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(1)$$

$$\text{Specificity} = \frac{TN}{FP+TN} \quad \ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots\ldots(2)$$

$$PPV = \frac{TP}{TP+FP} \quad \text{.....(3)}$$

$$NPV = \frac{TN}{FN+TN} \quad \text{.....(4)}$$

$$Accuracy = \frac{TP+TN}{TP+FN+FP+TN} \quad \text{.....(5)}$$

The mortality of the patients was interpreted based on the biochemical markers as shown in Table 7.

For both Ranson and Glasgow criteria, the ranges for each characteristic have been taken from the previous studies.

Table 5: AUC (area under curve) of different prognostic markers in predicting mortality, recurrence of gallstone, need for ICU admission and organ failure.

Area under curve (AUC) (95% CI)	Mortality	Recurrence of gallstone	ICU-admission	Organ failure
Ranson	0.943 (0.894-0.992)	0.766 (0.617-0.916)	0.801 (0.704-0.898)	0.852 (0.739-0.964)
Glasgow	0.861 (0.783-0.940)	0.724 (0.609-0.839)	0.782 (0.676-0.888)	0.707 (0.587-0.826)

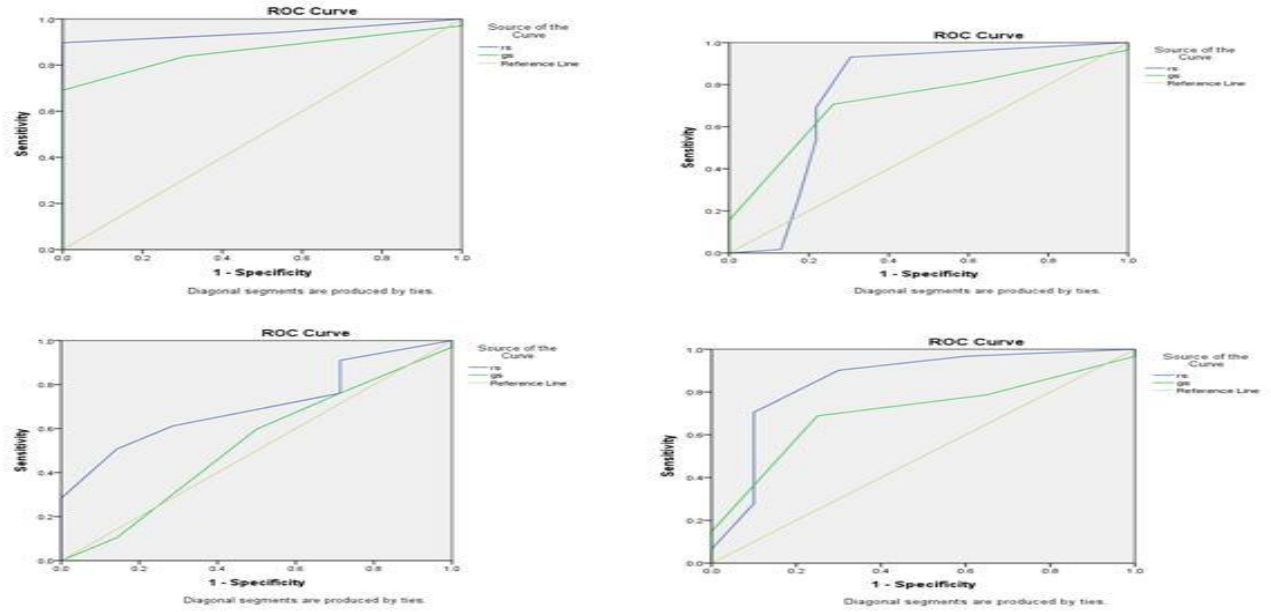


Figure 2: AUC comparison of various scoring systems in predicting Mortality (a), Recurrence gallstone (b), ICU admission (c) and organ failure (d). Diagonal segments are produced by ties.

Table 5: Sensitivity, specificity, PPV, NPV, and accuracy of different markers in predicting mortality, recurrence of gallstone, need for ICU admission and organ failure.

	TP	FN	FP	TN	Sensitivity	Specificity	PPV	NPV	Accuracy
Mortality									
Ranson	60	0	8	13	100	61.9	88.2	100	90.1
Glasgow	47	0	21	13	100	38.2	69.1	100	74.1
Recurrence of gallstone									
Ranson	54	6	4	17	90	80.9	93.1	73.9	87.7
Glasgow	41	6	17	17	87.2	50	70.7	73.9	71.6
ICU-admission									
Ranson	50	10	4	17	83.3	80.9	92.6	63	82.7
Glasgow	40	7	7	27	85.1	79.4	85.1	79.4	82.7
Organ failure									
Ranson	55	5	6	15	91.7	71.4	90.2	75	86.4
Glasgow	42	5	19	15	89.4	44.1	68.9	75	70.4

TP=True Positive, FN=False Negative, FP=False Positive, TN=True Negative, PPV=Positive Predictive Value, NPV=Negative Predictive Value.

Table 7: Biochemical markers.

Characteristics	Modified RC for gallbladder pancreatitis	GC[24]
PaO2 (mmHg)	<70 within 48 hours	<59.3
Age (years)	>55	>55
WBC (uL)	>18 x 10^3	>15 x 10^3
Calcium (mg/dL)	<8 within 48 hours	<8
Urea (mg/dL)		>44.8
LDH (IU/L)	>400	>600
Albumin (g/dL)		<3.2
Glucose (mg/dL)	>220	>180
AST	>250	
hematocrit drop	>10% from admission	
BUN (mg/dL)	≥2 from admission	>45
Fluid needs (L)	> 4 within 48 hours	

Interpretation for mortality

Based on the biochemical markers, the interpretation for mortality has been scored. In RC if the patients has PaO2 (mmHg) <70 within 48 hours and Age (years) >55 then the score is 0 to 2 points with RC 0% to 3%, similarly PaO2 (mmHg) <70 within 48 hours, Age (years) >55, WBC (uL) >18 x 10^3 and Calcium (mg/dL) <8 within 48 hours then the score is 3 to 4 points with RC 15%. If the patients has all the characteristics then the scores ranges from 7 to 10 points that is close to 100% which is predicting mortality (Table 8).

Table 8: Score interpretation for mortality.

Scores	RC (%)	GC (%)
0 to 2 points	0 to 3	2
3 to 4 points	15	15
5 to 6 points	40	40
7 to 10 points	Close to 100	100

DISCUSSION

GAP is the most common form of acute pancreatitis encountered by physicians in emergency departments globally. It is important to identify patients with severe GAP who shall benefit upon early diagnosis, referral and intensive care. Hence, it is important to include a combination of clinical history, physical examination, biochemical analysis and imaging techniques for diagnosing the severity of GAP which is often tailor-made based on the underlying etiology.[16]

Several prognostic scores have been developed and used for predicting severity of acute pancreatitis. In this study we have assessed and compared the performance of traditional multi-factorial scoring systems RS and GS in prediction of mortality, gallstone recurrence, ICU-admission and OF in GAP based on RAC. In this context, RS was found to be more specific, sensitive and accurate in prediction in comparison to GC. This finding was concordant with several previous studies.[25,26]

The mean age of the study population was 52 years and the male-to-female ratio was 1.2 (55.6% males). 38.3% of the study population was above 60 years of age. Gallstone disease and biliary pathology is increasingly is common among geriatric population which is evident in our study.[27–29] Majority (66.7%) of patient had BMI between 30-34.[9] From Erlinger 30 and Stender et al it is evident that increased body mass index (BMI) increases the risk of gallstone formation.[31] Majority of patients had abdominal pain (96.3%) which is mostly radiating (93.8) a most common symptom of GAP.[32]

Though studies have reported that gallstone disease is related to several diabetes risk factors, there is no proof that diabetic patients have more gallstones.[33] However, in this study it was found that 43.2% patient suffered with diabetes mellitus as comorbid condition. This could be due to fact that about 50.9 million people suffer from diabetes and India being the diabetic capital of the world.[34]

Gall stone disease (92.6%) followed by traumatic (3.7%) were the most common etiology spectrum in our study. There are many possible underlying causes of acute or sudden onset pancreatitis, but 60 to 75 percent of all cases are caused by gallstones. However, only 3 to 7 percent of patients with gallstones develop pancreatitis.[12] The higher incidence of gall stone disease in our study indicates higher prevalence of gall stone in South India, where our institute is located.

RS had high specificity (61.9%), PPV (88.2%), Accuracy (90.1%) for predicting mortality, high sensitivity (90%), specificity (80.9%), PPV (93.1%) accuracy (87.7%) for predicting recurrence of gallstone, high sensitivity (91.7%), specificity (71.4%), PPV (90.2%), accuracy (86.4%) for predicting OF. Glasgow criteria had high sensitivity (85.1%), NPV (79.4) in predicting ICU-admission.

RS and GS are simple, easy and best predictive scoring systems for GAP related mortality, recurrence in resource limited setting with no external funding and lack of advanced imaging techniques availability. When compared to RS, GS has 8 out of 11 lab indices however, both are taken in timely fashion with results available post 48 hours of admission due to the time interval required for its calculation.[25] Based on RAC, patients at the time of hospital stay were classified into mild with no OF (56.8%), moderate with transient OF (24.7%) and severe (18.5%) with persistent OF (16%) and multi-OF (2.5%). Based on RS and GS 74.1% and 66.7% of patients were classified as moderately severe to severe GAP of which 2.5% were dead during hospital stay, 12.3% had recurrence of gallstone, 2.5% had ICU-

admission 1.2% had transient OF and 3.7% had permanent OF. The cause of death in those 2 cases was multiple OF. Similar mortality rate was observed in study by Kumar and Griwan.[19] When the performance of RS and GS was compared with that of RAC, it was found that the AUC for RS was consistently the highest for predicting mortality (0.943), recurrence of gallstone (0.766), ICU-admission (0.801) and OF (0.852). Similar results was observed in previous studies by Maheshwar et al and Ghimire and Ghimire.[26,35]

Limitations of the study: the strength of the study is that it included an adequate number of patients with necessary investigations. However, RS and GS predict severity of disease post 48 hours of admission. This limits its utility in time-sensitive situations like the emergency department. Also, the study was conducted in a resource limited setting with no external funding, hence, we could not repeat initial lab values for all patients. Moreover, ≥10 parameters for RS and GS, makes it difficult to use it conveniently and we could not calculate the scores at different times of hospital stay. However, detailed scoring systems offer significant advantage of risk assessment and prediction of morbidity and mortality. Finally, the age range considered in RS and GS is 30 to 75 years of age, hence, its application for a pediatric or adolescent population was limited.[36]

CONCLUSION

RS in comparable with RAC in predicting mortality, gallstone recurrence, ICU-admission and OF in patients with GAP. It is a useful predictive scoring system for group of patients who have high chance of gallstone recurrence which needs early intervention and referral, especially in resource limited settings. Hence, it can be concluded that RS can suitably replace RAC for surgical intervention of GAP.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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