ORIGINAL ARTICLE

ROLE OF SIMPLIFIED ADMISSION CRITERIA FOR PREDICTING SEVERE COMPLICATIONS OF GALL STONE PANCREATITIS

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Background: Gallstone Pancreatitis (GP) is not an uncommon disease in our country and is associated with large number of morbidity and mortality especially if severe complications develop. Different criteria have been developed to predict the complications of GP. Simple admission criteria are better predictors of severe complications of GP than an APACHE II score of 5 or greater, a modified Imrie (Glasgow) score of 3 or greater, and a Biliary Ranson score of 3 or greater. The purpose of this study was to determine the role of simplified admission criteria in predicting severe complications of Gallstone Pancreatitis. **Methods:** This was a descriptive study conducted in Surgical 'A' Unit, Khyber Teaching Hospital Peshawar between July 16th 2007 to November 30th 2008. Total 52 patients (42 women and 10 men, aged range from 18 to 76 years, with mean age, 39 years) who presented to our unit with gallstone pancreatitis were included in the study through technique of non-probability convenient sampling. The main outcome measures were major local and systemic complications requiring intensive care unit care, and death. Physiological factors and laboratory data were collected on admission and recorded daily. **Results:** Seven patients (14%) had severe complications with mortality of 2%. On univariate analysis, a white blood cell count of 14500/dL or more (p=0.03), a serum glucose level of or more ≥150 mg/dL (8.3 mmol/L) (p<0.001), an APACHE II score of 5 or greater (p=0.008), a modified Imrie score of 3 or greater (p<0.001), and a biliary Ranson score of 3 or greater (p=0.03) were statistically associated with the development of severe complications. On multivariate analysis, only a serum glucose level of ≥150 mg/dL or more (8.3 mmol/L) was predictive of adverse events (p<0.001). **Conclusions:** Glucose level (≥150 mg/dL) is the best single admission predictor of severe complications of Gallstone Pancreatitis and is superior to an APACHE II score of 5 or greater, a modified Imrie score of 3 or greater, and a biliary Ranson score of 3 or greater.

Keywords: Gallstones pancreatitis, admission criteria, complications

INTRODUCTION

Gallstones are the most common cause of acute pancreatitis worldwide.[1] Although most patients recover uneventfully, a subgroup goes on to develop severe complications. Numerous scoring systems, including those of Ranson *et al*[2–3] and Imrie *et al*[4–6] have been devised in an effort to predict which patients will manifest severe Pancreatitis. A modified Imrie (Glasgow) or biliary Ranson score of 3 or greater has been associated with severe Pancreatitis. These scoring systems are hampered by the fact that they require measurement of multiple factors over a 48-hour period. Five variables present on admission to the hospital that predicted the development of complications of severe gallstone pancreatitis (GP) necessitating care in the intensive care unit (ICU).[7] These factors included the following admission values: white blood cell count of 14500/dL or more, blood urea nitrogen (BUN) level of ≥12 mg/dL or more (4.3 mmol/L), heart rate of 100 beats per minute or more, serum glucose level of ≥150 mg/dL or more (8.3 mmol/L), and an Acute Physiology and Chronic Health Evaluation (APACHE) II score of 5 or greater. This study prospectively validated these admission criteria in a new group of patients with GP and determined if any of these predictors of severe complications of GP are superior to an APACHE II score of 5 or greater, a modified Imrie score of 3 or greater, or a biliary Ranson score of 3 or greater.

PATIENTS AND METHODS

Between July 16, 2007, and November 30, 2008, 52 consecutive patients (42 women and 10 men aged 18 years to 76 years (mean age 39 years) with acute Pancreatitis of biliary origin seen at Surgical 'A' Ward, Khyber Teaching Hospital Peshawar, were prospectively enrolled in this study after obtaining informed patient consent. The diagnosis of acute GP was based on upper abdominal pain and tenderness, an elevated serum amylase level, documented gallstones, and the absence of other factors known to cause Pancreatitis, i.e., alcoholism, hypercalcemia, hypertriglyceridemia, and medications).[8] Physiological factors and laboratory data were collected on admission and recorded daily.

Most patients having 1 or more of the 4 simple criterions (i.e., white blood cell count, ≥14,500/dL; BUN level ≥12 mg/dL; heart rate, ≥100 beats per minute; or serum glucose level, ≥150 mg/dL) on admission were admitted in the Ward. However, the ultimate decision on ICU placement was at the discretion of the admitting surgeon. Initial management of all patients included fluid resuscitation, bowel rest, parenteral analgesia, and

cholecystectomy once the acute phase of pancreatitis resolved. Patients were monitored daily for evidence of severe systemic and local complications, including pulmonary, cardiovascular, infectious, renal, haematological, neurological, and gastrointestinal tract. A complication was considered to be severe if the patient required ICU care beyond the initial 24 hours (Table-1).[7]

Table-1: Definition of severe complications requiring ICU monitoring and treatment

System	Complications
Pulmonary	Mechanical ventilation; pneumonia with hypoxemia ($P_{aO_2} \leq 60$ mm Hg); and hypoxemia ($P_{aO_2} \leq 60$ mm Hg) or dyspnoea requiring frequent assessment of need for intubation.
Cardiovascular	Hypotension requiring pressor support; ischemia or acute myocardial infarction noted on electrocardiogram or cardiac enzymes; and new onset arrhythmia other than sinus tachycardia.
Infections	Sepsis of any origin.
Renal	New onset oliguric or non-oliguric renal failure or new onset dialysis.
Haematologic	Disseminated intravascular coagulation and platelet counts $<50\times10^9$/L.
Neurologic	Glasgow Coma Scale score ≤9 and diminished responsiveness or agitation (requiring significant sedation) with need for frequent airway monitoring.
Gastrointestinal	Stress ulcer with hematemesis or melena (requiring 2 units of blood per 24 hours)

Potential univariate correlates of severe complications were identified using χ^2 or Fisher exact tests wherever appropriate. The sensitivity, specificity, positive and negative predictive values for each of the 4 single criteria, the APACHE II score of 5 or greater (Table-2)[9], the modified Imrie score of 3 or greater (Table-3)[6], and the biliary Ranson score of 3 or greater (Table-4)[3] were calculated. Factors found to be significant on univariate analysis were entered into a multivariate logistic regression analysis and $p<0.05$ was considered statistically significant. No adjustment was made for multiple comparisons.

Table-2: The APACHE II Scoring System*

Physiologic variable	Reference range
Rectal temperature, °C	36–38.4
Mean arterial pressure, mmHg	70–109
Heart rate (ventricular response), beats/min	70–109
Respiratory rate, breaths/min	12–24
Oxygenation, mm Hg	$P_{AO_2}-P_{aO_2}$ <200 or P_{O_2} >70
Arterial *p*H	7.33–7.49
Serum sodium level, mmol/L	130–149
Serum potassium level, mmol/L	3.5–5.4
Serum creatinine level, μmol/L (mg/dL) (double point score for acute renal failure)	0.6–1.4 (53–123)
Haematocrit	0.30–0.46
Leukocyte count, $\times10^9$/L	0.003–0.015
Glasgow Coma Scale score (GCS)	15−actual GCS score

To calculate the Acute Physiology and Chronic Health Evaluation (APACHE) II score, the 12 physiological variables are assigned points between 0 and 4, with 0 being normal and 4 being the most abnormal.[9] The sum of these values is added to a point weighting for patient age (≤44 years=0; 45–54 years=2; 55–64 years=3; 65-74 years=5; ≥75 years=6) and a point weighting for chronic health problems. $PA_{O_2}-Pa_{O_2}$ indicates alveolar-arterial difference in partial pressure of oxygen.

Table-3: Imrie (Glasgow) Scoring System*

Within 48 Hours of Hospital Admission†	Original[4]	Modified[6]
Age, (Yr)	>55	>55
White blood cell count, $\times10^9$/L	>15	>15
Serum glucose level, mmol/L (mg/dL)	>9.9 (180)	> 9.9 (>180)
Serum LDH level, U/L	>600	> 600
Serum transaminase level, mU/mL	>100	. . .
BUN, mmol/L (mg/dL)	>16.1 (45)	>16.1 (> 45)
Serum calcium level, mmol/L (mg/dL)	<2 <(8)	<2 (< 8)
P_{aO_2}, mmHg	<60	<64
Serum albumin level, g/L	<32	<32

*Zero to 2 criteria met indicates mild pancreatitis; 3 or more criteria, severe pancreatitis, †LDH indicates lactate dehydrogenase; BUN, blood urea nitrogen; and ellipsis, not applicable

Table-4: Ranson Scoring System for Acute Pancreatitis[2,3]*

Criterion†	All Causes	Biliary Origin
On Hospital Admission		
Age, year	>55	>70
White blood cell count, $\times10^9$/L	>16	>18
Serum glucose level, mmol/L (mg/dL)	>11.1 (200)	>11.1 (>220)
Serum LDH level, U/L	>350	>400
Serum AST level, U/L	>250	>250
Within 48 Hours of Hospital Admission		
Hematocrit decrease	>0.1	>0.1
BUN level increase, mmol/L (mg/dL)	>1.8 (>5)	>0.7 (>2)
Serum calcium level, mmol/L (mg/dL)	<2 (<8)	<2 (<8)
P_{aO_2}, mm Hg	<60	. . .
Base deficit, mmol/L	>4	>5
Estimated fluid sequestration, L	>6	>4

*Zero to 2 criteria met indicates mild pancreatitis; 3 or more criteria, severe pancreatitis, †LDH indicates lactate dehydrogenase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; and ellipsis, not applicable

RESULTS

There were 52 patients with documented GP, of whom 42 (84%) were women and 10 (16%) were men. The mean age of these patients was 39 years (age range, 18–76 years). The mean admission serum amylase level was 1701 U/L (reference range, 181–2526 U/L). Four patients (2%) had severe systemic complications requiring ICU monitoring and therapy (Table-5). The most frequent systemic complications were pulmonary and infectious followed by haematological and neurological.

Three patients had a total of 6 local complications. All of these patients had concomitant systemic complications requiring ICU care. One patient had a pancreatic abscess requiring operative

debridement, with associated sepsis and adult respiratory distress syndrome. Another patient had sterile pancreatic necrosis and pulmonary failure requiring prolonged mechanical ventilatory support. Both of these patients later developed pancreatic pseudo cysts. The remaining 1 patient had necrotising Pancreatitis associated with fatal multiple system organ failure. This patient was the only death in the series (overall mortality, 2%).

Table-5. Complications of gall stones pancreatitis

	Patients	Type of complication
Total 4		
Pulmonary	1	Respiratory distress with Hypoxemia (PaO2 <60mmHg)
Cardiovascular	Nil	
Infectious	1	Sepsis
Hematologic	1	Disseminated Intravascular Coagulation
Neurologic	1	Depressed Mentation (GCS <9)
LOCAL 3		
	1	Pancreatic Abscess
	1	Pancreatic Pseudocyst
	1	Necrotizing Pancreatitis

On univariate analysis a white blood cell count of 14500/dL or more (p=0.03), a serum glucose level of ≥150 mg/dL or higher (p<0.001), an APACHE II score of 5 or greater (p=0.008), a modified Imrie score of 3 or greater (p<0.001), and a biliary Ranson score of 3 or greater (p=0.03) were statistically associated with the development of severe complications; whereas a BUN level of 12 mg/dL or higher and a heart rate of 100 beats per minute or more were not (Table-6). Admission serum glucose level of ≥150 mg/dL or higher had the highest sensitivity (79%), positive predictive value (41%), and negative predictive value (95%). On multivariate analysis of the 4 criteria, only the serum glucose level of ≥150 mg/dL (8.3 mmol/L) or higher was statistically significant (p<0.001).

There were 4 patients who had diabetes mellitus and 48 patients who did not. The overall complication rates were 50% (2 of 4 patients) for the patients who had diabetes mellitus and 12.5% (6 of 48 patients) for the patients who did not. The difference was not statistically significant (p=0.13). An analysis was performed to determine whether the presence of diabetes mellitus altered the predictive value of the admission serum glucose level of ≥150 mg/dL (8.3 mmol/L) or higher. Among the 26 patients who had an admission serum glucose level of ≥150 mg/dL or higher (8.3 mmol/L) were 4 with known pre-existing diabetes mellitus and 22 who did not have diabetes mellitus. When all patients with diabetes mellitus were excluded from consideration, the complication rate was 42% (9 of 22 patients) for patients with a serum glucose level of ≥150 mg/dL or higher (8.3 mmol/L) and only 8% (2 of remaining 26 patients) for patients without an elevated serum glucose level (p<0.001). For those 48 patients who did not have diabetes mellitus, the sensitivity, specificity, and positive and negative predictive values for a serum glucose level of ≥150 mg/dL or higher L (8.3 mmol/L) were 82%, 85%, 45%, and 97%, respectively. As all of the 4 patients with diabetes mellitus had a serum glucose level of 8.3 mmol/L or higher (≥150 mg/dL), the criterion was not predictive in this group.

Table-6: Univariate Analyses

	Complication		
Factor	**Severe (n=4)**	**NO (n=48)**	***p***
Heart rate >100 beats/min	3	6	0. 06
White cell count >14500	4	8	0.03
BUN > 12mg /dL	3	22	0.44
Serum Glucose level >150mg /dL	3	8	<0.001
APCHE II score >5	3	30	0.008
Modified Imrie (Glasgow) score >3	3	7	<0.001
Biliary Ranson score >3	3	11	0.03

DISCUSSION

Early assessment of the severity of Pancreatitis is useful, both for prognostication and determination of the need for ICU monitoring and aggressive physiological support. Multiple scoring systems have been devised to assist in this assessment. In 1974, Ranson *et al*[2] described a scoring system using 11 objective factors collected within 48 hours of admission to predict the severity of Pancreatitis. This study was based on 100 patients with acute Pancreatitis, of whom 14 had gallstones and 74 had alcoholism as the origin. Of 79 patients with fewer than 3 signs, 2 died and 9 were seriously ill. However, of 21 patients with 3 or more signs, 13 died and 7 were seriously ill. Based on a later study of 450 patients, with the majority (70%) again of alcoholic origin, Ranson[3] revised the criteria for patients with biliary Pancreatitis. Although these criteria are most frequently cited for assessment of prognosis in the United States, some authorities believe the number of patients with GP in the study was inadequate to provide an accurate prognostic scoring system.[10]

In Europe, Imrie *et al*[4] published a study of 134 patients with acute Pancreatitis, of which 84 (63%) had biliary stone disease and 51 (38%) were alcohol abusers (1 patient had both biliary disease and alcoholism). From this study, 9 factors were determined to be of prognostic significance in determining the severity of the disease. Later, the number of factors was reduced to 8,[5,6] and subsequently, the predictive value of this modification has been confirmed[11–13]. Other scoring systems that have been recommended include the APACHE II and the multiple system organ failure scores.[7,9,10,13–15]

The above scoring systems have several shortcomings. First, 48 hours are required to complete the data collection for the Imrie and Ranson systems. Not surprisingly, the database for all the factors is often incomplete, Blamey *et al*,[6] in 405 episodes of acute Pancreatitis, reported complete information in only 36% of the patients. Second, some investigators have suggested that by 48 hours after admission, clinical evaluation alone is equivalent to the scoring systems, making them superfluous.[14] In addition, the APACHE II scoring system is more complicated than either the Ranson or Imrie scoring systems and, therefore, disadvantageous for routine clinical application.[10] Furthermore, the definitions of severe Pancreatitis used in the various studies have not been clear or consistent. The Glasgow group defined severe Pancreatitis as Pancreatitis that 'failed to settle'.[5] Ranson *et al*[2] defined it as Pancreatitis associated with the development of 'life-threatening complications or requiring more than 7 days of ICU monitoring'. In another study that compared the 3 versions of the Imrie (Glasgow) scoring system, severe Pancreatitis was defined as the 'development of a major complication requiring more than 20 days hospitalization'.[11] From these examples, it is apparent that the criteria for defining severe Pancreatitis have not been uniform. Since pulmonary complications are most frequent and typically occur early in the course of Pancreatitis, it would also be more useful if the prognostication could be made on admission so as to stratify patients at high risk for these and other severe complications.

In this study, we evaluated the ability of 4 previously determined single criterion (i.e., a white blood cell count of ≥14500, a BUN level of ≥12 mg/dL (≥4.3 mmol/L), a heart rate of ≥100 beats per minute, and a serum glucose level of ≥150 mg/dL (≥8.3 mmol/L) readily available at the time of admission, to predict severe local and systemic complications of GP requiring ICU monitoring and treatment. On multivariate analysis, only the admission serum glucose level of ≥150 mg/dL (≥8.3 mmol/L) was predictive of a subsequent adverse outcome, with a sensitivity of 79%, specificity of 79%, a positive predictive value of 41%, and a negative predictive value of 95%. When patients with diabetes mellitus were excluded, the predictive value of serum glucose level of 8.3 mmol/L or higher (≥150 mg/dL) was further increased. This single, easily measured admission value had a better predictive power than the APACHE II, biliary Ranson, or modified Imrie scoring systems.

Others have previously reported the value of simplified prognostic criteria for acute Pancreatitis. In 2 studies, Fan *et al*[16–17] demonstrated that both an admission serum glucose level of 11.0 mmol/L or higher (>200 mg/dL) as well as a BUN level of 7.4 mmol/L or higher (>20 mg/dL) were comparable to the Imrie multifactoral scoring system for predicting severe complications. Importantly, the criteria for adverse outcome in the studies by Fan *et al* were very similar to those of the present study. In the earlier study by Fan *et al*,[17] only 203 (55.7%) of the patients had Pancreatitis of biliary origin. The sensitivity and specificity of the combined levels of serum glucose and BUN criteria were only 79% and 67%, respectively.

The reason that an admission serum glucose level of ≥150 mg/dL or higher (8.3 mmol/L) might accurately predict severe and complicated Pancreatitis is because, in previously non-diabetic patients, the hyperglycaemia may be indicative of severe islet cell damage and dysfunction.[16] Many studies have assessed the effects of acute or chronic Pancreatitis on the future development of diabetes mellitus, serum glucose intolerance, and markers of pancreatic endocrine and exocrine dysfunctions (i.e., the levels of serum glucose, insulin, glucagon, pancreatic polypeptide, and others). It seems as if both a decreased insulin response and an excess glucagon level have been implicated in the abnormal serum glucose metabolism associated with acute Pancreatitis. Seligson *et al*[18] showed that gross changes of the pancreatic ducts on endoscopic retrograde cholangiopancreatography seen after an acute episode of Pancreatitis was associated with deficient B-cell function and decreased serum glucose tolerance. Solomon *et al*[19] found that acute Pancreatitis was characterised by fasting hyperglycaemia, hyperglucagonemia, and relative hypoinsulinemia. They also found that at 3 weeks after the acute episode, there was a return to normal of plasma glucose, glucagon, and the primary response of insulin levels; however, the secondary response of insulin remained abnormal. Donowitz *et al*[20] found that basal glucagon levels in patients with acute Pancreatitis was 9 times higher than in control subjects, and also found that the glucagon response to alanine was 3 to 4 times greater in patients with acute Pancreatitis. Other authors have also shown a higher incidence of diabetes mellitus and glucose intolerance in patients with a history of acute Pancreatitis suggesting some permanent pancreatic damage remains.

CONCLUSION

A single admission laboratory value –a serum glucose level of ≥150 mg/dL or higher (8.3 mmol/L), was the best single, simple predictor of severe complications of GP requiring care. This value was a better predictor than an APACHE II score of ≥5, and a modified Imrie or

biliary Ranson score of 3 or greater. In addition to being less cumbersome than standard multifactorial scoring systems, use of this single measurement allows rapid assessment of Pancreatitis severity in the emergency department and, thus, facilitates immediate triage to the appropriate level of hospital monitoring and care.

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