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Prognostic Role of Biochemical Markers in Severe Acute Pancreatitis – A Study of 50 cases

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Abstract **Original Research Article**

Background*:** Acute pancreatitis remains difficult to diagnose. The disease may occur at any age, with a peak in young men and older age. It is defined as an inflammatory process of the pancreas with possible peri- pancreatic tissue & multi-organ involvement inducing multi-organ dysfunction syndrome with an increased mortality rate. Majority of patients present with a mild disease, however approximately 20% run in a severe course and require appropriate management in an intensive care unit. According to the Atlanta Classification, severe acute pancreatitis is defined as an acute pancreatitis associated with local and/or systemic complications. Acute pancreatitis remains difficult to diagnose. The disease may occur at any age, with a peak in young men and older age. ***Objectives: The aim of the study was to determine prognostic role of biochemical markers in severe acute pancreatitis. ***Methods:*** The Study was conducted in the department of surgery of Dhaka Medical College Hospital, Dhaka, Bangladesh to find out the common indications of prognostic role of biochemical markers in Severe Acute Pancreatitis. Fifty cases were randomly selected for the study. Clinical examination and evaluation were done from May 2017 to November 2017. Other necessary investigations were done if clinically indicated and to prepare the patient for anesthesia. Statistical analysis of the results was obtained by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-22). ***Results*:** The maximum number of patients 23(46.0%) was found in the 31-40 years of age, the next was 16(32.0%) found in 41-50 years and the lowest percentage was 11(22.0%) in the 50-60 years. The mean age of the study group was 41.86±8.27 years, minimum age 31 and maximum 58 years. ***Conclusions:*** Clinical, biochemical parameters are related to the clinical course of acute pancreatitis and they can predict its severity. However, acute pancreatitis is a very complex disease, and despite the existence of several criteria, it is not an easy task to predict its subsequent course.

Keywords: Biochemical; Severe acute; Pancreatitis; complication.

1. INTRODUCTION

Multifactorial scoring system such as Ranson, Glasgow, and APACHE II have a similar accuracy after 48 hours of admission. Current prognostic markers of severity are valuable, but immediate evaluation is difficult. Cytokines have a central role in the pathogenesis of SAP, IL-6, IL-8, CRP are good predictors of severity. Other markers such as PMN elastase, Trypsinogen activation peptide & procalcitonin are elevated in SAP & can be used for severity assessment. They are able to predict the severity but they are not widely available. Currently CRP is the only marker applied routinely in clinical use [1]. Recently several laboratory markers including blood urea nitrogen, creatinine, serum amyloid A, haematocrit, matrix metalloproteninase 9(MMP-9) have been used as early predictors of severity within the first 24 hours.

The premature activation of trypsin in pancreatic parenchyma acting as the central step in the initiation of autodigestion of pancreatic tissue and

subsequent local and systemic inflammation is presently the most accepted theory. Whatever is the initiating event, the disease progression can be viewed as a three-phase continuum: local inflammation of the pancreas and a generalized inflammatory response followed by the final stage of multiorgan dysfunction.

Serum amylase & lipase remains the most commonly used biochemical marker for the diagnosis of acute pancreatitis. Urinary trysinogen-2 is convenient. Early prediction of the severity of acute pancreatitis can be made by well validated scoring system at 48 hours. On account of the different in outcome between patients with mild & severe disease, it is important to define that group of patients who will develop severe pancreatitis. Various scoring systems have been introduced such as Ranson & Glasgow scoring system, APACHE II can be applied. A severe attack may be heralded by an initial clinical impression of a very ill patient & an APACHE II score above 8. At 48 hours after the onset of symptoms, a Glasgow score of 3 or more, a C- Reactive protein level greater than 150 mg/L & worsening clinical state with sepsis or persisting organ failure indicate a severe attack. Severity stratifications should be performed in all patients within 48 hours of diagnosis.

Patient with a body mass index over 30 are at higher risk of developing complications. The diagnosis of acute pancreatitis was based on a consistent clinical picture, a threefold increase of serum amylase (upper limit of normal, 160 IU/A) or serum lipase (upper limit of normal, 190 IU/L) & morphological abnormalities compatible with acute pancreatitis on contrast enhanced computed tomography study of pancreas and/or ultrasound scan within the first 48 hours of hospital admission. The severity of pancreatitis was assessed by the clinical outcome that is number of complications that occurred during the course of the disease. A mild attack was uncomplicated or one with only minor complications a severe attack included at least three prognostic factors of severity according to the criteria.[2] Major organ failures, a pancreatic complication (pseudocyst, abscess, necrosis, sepsis, shock, renal failure, consumptive coagulopathy, encephalopathy) or death.

2. OBJECTIVE

The aim of the study was to determine prognostic role of biochemical markers in severe acute pancreatitis.

3. METHODS

The Study was conducted in the department of surgery of Dhaka Medical College Hospital, Dhaka, Bangladesh to find out the Role of Biochemical Markers in Severe Acute Pancreatitis. Fifty cases were randomly selected for the study. Clinical examination and evaluation were done from May 2017 to November 2017. Other necessary investigations were done if clinically indicated and to prepare the patient for anesthesia. Proper consent was taken before data collection. Statistical analysis of the results was obtained by using window-based computer software devised with Statistical Packages for Social Sciences (SPSS-22).

Inclusion Criteria

- Determine prognostic role of biochemical markers in severe acute pancreatitis.
- Patients aged between 31-60 years
- Participants willing to share necessary information

Exclusion Criteria

- Patients suffering from comorbid medical illness.
- Biochemical markers in severe acute pancreatitis

4. RESULTS

Table I shows that the maximum number of patients 23(46.0%) was found in the 31-40 years of age, the next was 16(32.0%) found in 41-50 years and the lowest percentage was 11(22.0%) in the 50-60 years. The mean age of the study group was 41.86±8.27 years, minimum age 31 and maximum 58 years. Regarding severity of pain on admission 76.0% patients had moderate pain, 20.0% patients had severe pain, 4.0% patients had mild pain. After 48-72 hours pain maximum 62.0% patients had moderate pain and 38.0% patients had severe pain. The serum lipase level rises 3-6 hours after the onset of symptoms, and peaks in within 24 hours of onset. The specificity of lipase level is 92.31%, but the sensitivity is 91.89%. The positive predictive value 97.14% and negative predictive value 80.0%.

Table-1: Age distribution of the patient (n=50)

Age of the patient	n=50	(%)
31 years to 40 years	23	46
41-50	16	32
51-60	11	22
Total	50	100
Mean ± SD	41.86±8.27	

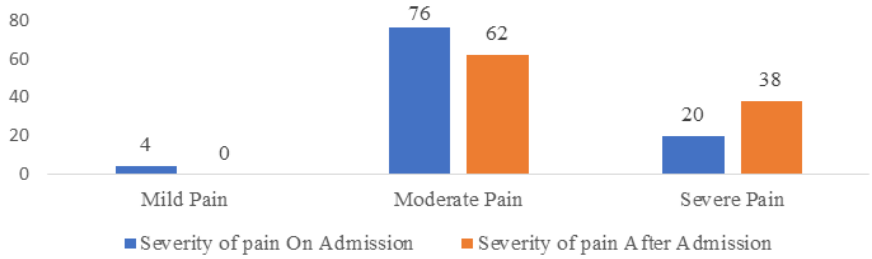

Fig-1: Distribution of the study subjects by severity of pain (n=50)

Table-2: Comparison of biochemical marker and enzyme on admission and after 48-72 hrs (n=50)

Biochemical marker	On admission Mean± SD (n=50)	After 48-72 hrs Mean± SD (n=50)	P value
Serum amylase (U/L)	902.9±474.9	1058.4±489.9	<0.001*
Serum lipase (U/L)	469.7±262.4	505.2±265.9	<0.001*
Blood glucose (mmol/L)	16.86±5.86	20.24±6.70	<0.001*
Total count	18935.2±3600.1	19023.8±3611.6	<0.001*
Neutrophil	87.22±3.25	88.04±3.68	0.037*
Lymphocyte	11.97±2.31	13.05±2.92	<0.001*
ESR	97.82±10.79	100.56±12.02	<0.001*
Hb (%)	8.47±0.83	9.67±2.18	<0.001*
Serum urea (mmol/L)	18.77±5.77	21.35±7.60	<0.001*
C-reactive protein (mg/L)	166.8±13.2	169.2±21.3	0.127
Serum Billirubin (mmol/L)	3.23±1.49	2.93±0.94	0.023*
Blood urea nitrogen (mg/dl)	2.55±0.30	2.56±0.21	0.597
LDH (U/L)	467.4±16.4	736.5±107.2	<0.001*
Serum ionized calcium (mg/dl)	7.16±0.52	6.73±0.48	<0.001*

Data were expressed as mean± SD, Data were analyzed by Paired t-test, *significant, Biochemical markers and enzymes significantly increased after 48-72 hours from admission.

Table-3: Diagnostic test for serum lipase (n=50)

	Value	95% CI
Sensitivity	91.89%	78.07% to 98.20%
Specificity	92.31%	63.90% to 98.72%
Positive Predictive Value	97.14%	85.03% to 99.52%
Negative Predictive Value	80.00%	51.91% to 95.43%

5. DISCUSSION

Various methods have been used to predict the progress of severe acute pancreatitis, such as clinical evaluation and testing of various serological markers [3, 4]. In our series, we investigated the correlation between the changes of the clinical predictors, pancreatic enzyme, and the biochemical markers. In this study, we present some other aspects of the correlation among clinical, biochemical, and evaluate their prognostic value in the early assessment of severity and outcome of severe acute pancreatitis. In present study maximum 68.0% patients had severe and 32.0% had acute pancreatitis?

Our results showed statistically significant higher serum concentrations of CRP in patients with severe disease. Also, changes of the CRP level during the treatment reflect the disease prognosis. Serum CRP is an acute-stage protein, i.e., synthesized in the liver. It is elevated in various inflammatory conditions, and serves as a nonspecific inflammation marker. This parameter is usually used because it is simple and cheap [5, 6]. Also, CRP is a proven predictor of severity for AP when serum level of over 150 mg/L is measured within 48 hours after the onset of symptoms [7-9]. The pancreatic enzymes derived from pancreatic acinar cells [amylase, lipase] are the cornerstone in the laboratory diagnosis of acute pancreatitis.[10] Serum lipase is a more sensitive and specific biochemical marker of acute pancreatitis than the more frequently used amylase. A raised level of serum amylase activity, at least three times the upper limit of normal, supports the diagnosis of acute pancreatitis. Its activity rises quickly within the first 12 hours after the onset of symptoms and returns to normal within three to five days. Serum amylase activities may be normal at the time of hospital admission, as a result of delayed presentation [11].

Serum amylase activities can be increased in other intra-abdominal inflammatory conditions and salivary gland pathologies, and also where there is decreased renal clearance because of renal impairment or macroamylasaemia where amylase is bound to immunoglobulins or polysaccharides to form large molecular weight complexes. In this study, the specificity of amylase level is 76.9%, but the sensitivity is 94.59%. The positive predictive value 92.11% and negative predictive value 83.3% by the cut off value 800 IU/I. Described the sensitivity and specificity of amylase as a diagnostic test for acute pancreatitis depends on the chosen threshold value, by raising the cut off level to 1000 IUI (more than three times the upper limit of normal), amylase has a specificity approaching 95%, but a sensitivity as low as 61% in some studies.

Compared with serum amylase, serum lipase activity remains increased for longer (up to 8 to 14 days), thereby giving greater sensitivity in patients with a delayed presentation. Pancreatic lipase activities are more than four times that of amylase and as such are less likely to be affected by chronic pancreatic insufficiency. The recent UK guidelines for the management of pancreatitis state: "Where lipase is available it is preferred for the diagnosis of acute pancreatitis".[12] Serum Lipase level may also be raised in other intra-abdominal pathologies or in renal insufficiency. Hypertriglyceridaemia does not interfere with laboratory measurement, but drugs such as frusemide can increase lipase activity. The diagnostic accuracy of lipase appears to be better than that of amylase.

In our study, the serum lipase level rises 4-8 hours after the onset of symptoms, and peaks at the 24th hour of onset. The specificity of lipase level is 92.31%, but the sensitivity is 91.89%. The positive predictive value 97.14% and negative predictive value 80.0% with the cut off value 590 IU/I. In accordance other studied showed at a cut off activity of 600 IU/A, specificities above 95%, with sensitivities ranging between 55% and 100% [13].

Limitations of the Study

During this study, some limitations could not be overcome despite of most sincere effort. So, it is the honest duty to admit these limitations. This study was conducted in a limited of patients which could not represent the total population effectively. Duration of study was short (six months) and single center. So, Present study was not comparing other local study.

6. CONCLUSION

Clinical, biochemical parameters are related to the clinical course of acute pancreatitis and they can predict its severity. However, acute pancreatitis is a very complex disease, and despite the existence of several criteria, it is not an easy task to predict its subsequent course.

7. RECOMMENDATION

Studies with larger numbers of patients, with more homogenous patient populations, and better correlation between the onset of symptoms and blood Sampling and more similarity in the assay techniques are required in order to resolve the issue.

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