The predictive validity of serum biochemical markers in case of acute biliary pancreatitis.

Adnan Riaz¹, Sumera Saghir², Roomana Anwar³, Sabeen Khalid⁴, Muhammad Shakil⁵, Tabinda Fatima⁶

ABSTRACT... Objective: To analyze the detection validity of serum biochemical markers in the suspicion of acute biliary disease. Study Design: Retrospective study. Setting: Department of Biochemistry, Islam Teaching Hospital, Sialkot. Period: January 2023 till June 2023. Methods: In a retrospective analysis of 70 patients, there were 35 patients suffering from acute biliary pancreatitis and 35 patients were suffering from non-biliary pancreatitis in group A and B respectively. The patients were identified based on high serum amylase levels. Age, gender, and history were examined, and patients with persistent abdominal pain and abnormal amylase levels were included. Computed tomography detected gallstones, and patients with chronic liver issues were excluded. Results: Comparative analysis conducted using Chi-square and Mann-Whitney tests in SPSS 15.0. A significant result was defined as a P value under 0.005. The sample collection was done from Islam teaching hospital Sialkot and the study was conducted at biochemistry lab of Islam medical college Sialkot. Conclusion: The study, involving 70 patients, aimed to predict acute biliary pancreatitis using serum biochemical markers. The two groups, one with acute biliary pancreatitis and other non-biliary, showed significant differences in key markers (total bilirubin, ALT, direct bilirubin, ALP, AST and serum amylase). These findings suggest the potential diagnostic relevance of these markers.

Key words: Acute Pancreatitis, Alanine Transaminase, Bilirubin, Biochemical Markers, Serum Amylase.

INTRODUCTION

Acute pancreatitis is a diagnostic condition with serious consequences that includes sepsis, systemic inflammatory response and in some cases multi-organ failure.¹ The diagnosis of this condition is due to the extent of pancreatic inflammation, necrosis, hemorrhage and abscess formation. In some cases, there is presence of peripancreatic fluid that could be one of the prognostic marker.²-³ Biliary pancreatitis is known to be due to movement of bile into the bile duct (common). In particular, the blockade of Ampulla of Vater due to biliary sludge or gallstones can be triggering factor for patients.⁴ The extent or degree of obstruction in both pancreatic bile duct or and the bile duct (common) have significant ramifications for the resolution of the disease. The nature of obstruction can be either chronic, mild or in some cases acute.⁵ The obstruction can be transient or temporary, and the factors like stones or tumors are important to determine the prognosis and subsequent management of the disease. It is worth noting that the rate pf complications arise if the obstruction persists beyond 48 hours. The condition takes place when the bile acids to cholesterol ratio is disturbed to abnormal levels.⁶-⁷ One of the most common primary bile acids are cholic acid and chenodeoxycholic acid that are called as the precursor of cholesterol. The primary bile acids undergo conversion into secondary and tertiary bile acids by the intestinal microbiota through hydroxylation and deconjugation.⁸ These reserves of bile salts are kept under a constant level by intestinal-hepatic circulation. The concentration of bile acids in the blood indicates about the hepatic activity. Under normal circumstances liver removes 20g of bile salts from the blood. Until recently it was known that the expensive and specialist methods like HPLC are used to detect bile acids in blood.⁹

1. MBBS, M.Phil (Biochemistry), Assistant Professor Biochemistry, Islam Medical College, Sialkot.
2. MBBS, M.Phil (Biochemistry), Associate Professor Biochemistry, Rashid Latif Medical College.
3. MBBS, M.Phil (Biochemistry), Assistant Professor Biochemistry, Islam Medical College, Sialkot.
4. MBBS, M.Phil (Biochemistry), Assistant Professor Biochemistry, M. Islam Medical College, Gujranwala.
5. MBBS, M.Phil (Biochemistry, PhD Biochemistry), Associate Professor Biochemistry, King Edward Medical University, Lahore.
6. Pharm D, M.Phil (Biochemistry), Assistant Professor Biochemistry, Grand College of Pharmacy, Sialkot.

Correspondence Address:
Dr. Adnan Riaz
Department of Biochemistry
Islam Medical College, Sialkot.
dradnanriaz@gmail.com

Article received on: 16/11/2023
Accepted for publication: 17/01/2024
Total bilirubin, AST, ALP, Direct bilirubin and ALT are some of the biochemical markers used for the prognosis of acute biliary pancreatitis. Serum amylase Abdominal ultrasound is considered to be one of the ways to detect acute pancreatitis however, its sensitivity decreases up to 60-70 % as the disease severity increases as in case of acute pancreatitis. In many cases endoscopic ultrasound is used as it has a higher rate to detect acute pancreatitis as compared to abdominal ultrasound but it is not commonly found for the patients. There are several easy and less expensive biochemical testings that are proposed to detect acute pancreatitis so that early prognosis and management of the disease can be done. The goal of this study was to analyze the importance of biochemical markers (serum) in detecting acute biliary pancreatitis.

METHODS
This retrospective research included 70 patients among which 35 were suffering from acute biliary pancreatitis and 35 patients were suffering from non-biliary pancreatitis, who visited tertiary care unit between the period of six months from January 2023 to June 2023. The diagnosis was made after analyzing the enhanced serum amylase levels among patients. The age, gender history of patients was studied and only those patients who fulfilled the inclusion criteria were made part of the study. Patients showing constant abdominal pain, abnormal serum amylase levels were included on the study. Computed tomography was done to detect gallstones among patients. The patients who had chronic liver issues or those who were not willing to participate were excluded from the study. Patients were asked to give consent in the written form.

The study was conducted after Ethical board approval (IMDC/ERC/2023/05) (04.01.23). Serum levels of ALT, ALP, AST, direct bilirubin, amylase and total bilirubin were measured. Results are depicted in Table-II. Patients were divided into two groups for a comparative analysis. The results were compared for both acute biliary pancreatitis and non-biliary patients. Mann-Whitney test and Chi square test were carried out for comparison of the parameters of groups. In order to analyze the data, SPSS 15.0 was used. Probability value < 0.005 was significant.

RESULTS
The research was carried out on two groups to find the significance of serum biochemical markers for acute biliary pancreatitis. There were 35 patients in acute biliary pancreatitis and non-biliary group respectively. Acute biliary pancreatitis group had patients who were suffering from acute biliary pancreatitis who follow inclusion criteria. There were 15 males and 20 females in acute biliary pancreatitis and there were 12 males and 23 females in non-biliary group. The mean age of patients was 64.5 ± 14 and 61.4 ±12 for acute biliary and non-biliary groups respectively. The features are shown in Table-I.

<table>
<thead>
<tr>
<th>Features</th>
<th>Acute Biliary Pancreatitis n=35</th>
<th>Non-biliary Group n=35</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>15 (42%)</td>
<td>12 (34%)</td>
</tr>
<tr>
<td>Female</td>
<td>20 (57%)</td>
<td>23 (65%)</td>
</tr>
<tr>
<td>Mean Age</td>
<td>64.5 ± 14</td>
<td>61.4 ±12</td>
</tr>
</tbody>
</table>

Table-I. Features of acute biliary pancreatitis and non-biliary group

Table-II presents a comparative analysis of concentration of serum biochemical markers in biliary and non-biliary patient groups. The biochemical markers used were total bilirubin, direct bilirubin, AST, ALT, ALP and serum amylase. In patients with acute biliary pancreatitis, the mean concentration of total bilirubin was 2.21 mg/dl, while in the non-biliary group, it was 1.626 mg/dl. The difference was statistically significant with a P value of 0.005. The average concentration of direct bilirubin was 1.09±1.5 mg/dl in acute biliary pancreatitis patients and 0.81±2.4 mg/dl in the non-biliary group, with a statistically significant difference (P value = 0.003). Patients with acute biliary pancreatitis exhibited a higher mean AST concentration of 202.1±1.9 U/I, while the non-biliary group had a mean concentration of 114.7±2.0 U/I. The difference was considered to be significant statistically (P value = 0.001). The mean ALT concentration was 177.8±2.1 U/l in acute biliary pancreatitis patients and 99.1±1.7 U/l in the non-biliary group, with a statistically significant p value (P value = 0.002).
Patients with acute biliary pancreatitis had a higher mean ALP concentration of 442.1±16.3 U/l, while the non-biliary group had a mean concentration of 342.9±21.3 U/l. In patients with acute biliary pancreatitis, the mean serum amylase concentration was notably elevated at 3433.8±21.9 U/l, compared to the non-biliary group, where it was 1988.1±19.9 U/l. This difference was statistically significant (P value = 0.002).

DISCUSSION

The mortality rate of acute biliary pancreatitis is increasing worldwide. It is important to distinguish biliary pancreatitis from non-biliary for its proper management.11 The duration between incidence of disease and ERCP is of great significance, therefore it is important to detect the biliary origin at an early stage. The sensitivity and accuracy of procedure like USG to detect biliary disease reduces as the disease severity increases.12-13 In case of pancreatitis the biochemical analysis presented low predictive scores. The presence of occult biliary stones indicate that majority of the idiopathic pancreatitis are originally biliary in nature.14 In some cases, the use of endoscopic ultrasonography proves to be an accurate method to detect occult stones, sand or any biliary material. As the biliary sludge is described as echogenic substance made of cholesterol, muco-glycoproteins and calcium bilirubinate. If the serum amylase levels are increased three folds that is considered as an indication of acute pancreatitis.15-16 In our study it was found that the total bilirubin, direct bilirubin, ALT, AST, ALP and serum amylase are the biomarkers that have different concentrations in the acute biliary pancreatitis patient and any non-biliary person. These biomarkers can be considered as prognostic markers for acute biliary pancreatitis. Serum lipase predominantly originates from pancreatic acinar cells. It begins to elevate 4–8 hours following symptom onset, reaching its peak at 24 hours.17 Lipase exhibits a strong correlation with levels of serum amylase, demonstrating similar kind of sensitivity and specificity. Biliary pancreatitis, unlike hypertriglyceridemia-linked and alcohol related pancreatitis, is marked by an intact pancreas suddenly impacted by biliary sludge or stones.18 In cases of alcoholic pancreatitis, amylase levels tend not to rise as significantly as in biliary pancreatitis. Approximately 25% of alcoholic pancreatitis patients exhibit normal amylase levels. A lipase-to-amylase ratio exceeding 3 may suggest alcohol linked pancreatitis, albeit with limited sensitivity. Lipase levels surge fourfold more than amylase in chronic pancreatitis. Sensitivity for lipase in acute pancreatitis can range from 55% leading to 100%. In patients with initial pancreatitis and those with post-ERCP pancreatitis, where amylase, total bilirubin, and direct bilirubin values were estimated after ERCP clearance, all these parameters showed declines post-obstruction relief in biliary ducts. The mean half-lives of amylase and lipase were prolonged in early pancreatitis, whereas the higher scores were elevated in case of pancreatitis (post ERCP). This underscores the significance of amylase, lipase, and bilirubin levels in biliary pancreatitis, along with the respective half-lives. Combining EUS with biochemical studies may enhance the biliary pancreatitis diagnosis.19 Biochemical indicators hinting at the biliary origin of pancreatitis may guide healthcare providers toward endoscopic evaluation and treatment, particularly in the absence of cholelithiasis identified by ultrasound in acute pancreatitis.20 In this study, we investigated the predictivity of serum biochemical markers for acute biliary pancreatitis using two

<table>
<thead>
<tr>
<th>Features</th>
<th>Mean Values of Acute Biliary Pancreatitis</th>
<th>Mean Values of Non Biliary Group</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total bilirubin</td>
<td>2.21±2.4 mg/dl</td>
<td>1.626±3.4 mg/dl</td>
<td>0.005</td>
</tr>
<tr>
<td>Direct bilirubin</td>
<td>1.09±1.5 mg/dl</td>
<td>0.81±2.4 mg/dl</td>
<td>0.003</td>
</tr>
<tr>
<td>Aspartate Aminotransferase (AST)</td>
<td>202.1±1.9 U/l</td>
<td>114.7±2.0 U/l</td>
<td>0.001</td>
</tr>
<tr>
<td>Alanine Transaminase (ALT)</td>
<td>177.8±2.1 U/l</td>
<td>99.1±1.7 U/l</td>
<td>0.002</td>
</tr>
<tr>
<td>Alkaline phosphatase (ALP)</td>
<td>442.1±16.3 U/l</td>
<td>342.9±21.3 U/l</td>
<td>0.000</td>
</tr>
<tr>
<td>Serum amylase</td>
<td>3433.8±21.9 U/l</td>
<td>1988.1±19.9 U/l</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Table-II. Concentration of serum biochemical markers in biliary and non-biliary patients
groups. Table-II presents a comparative analysis of serum biochemical markers. Patients with acute biliary pancreatitis showed significantly higher levels of total bilirubin, direct bilirubin, ALP, ALT, AST, and serum amylase compared to the non-biliary group. These differences were statistically significant, with P values < 0.005, indicating the potential diagnostic value of these markers.

CONCLUSION
In summary, the study suggests that serum biochemical markers, particularly total bilirubin, direct bilirubin, ALP, ALT, AST, and serum amylase, have high detection validity for identifying acute biliary pancreatitis. Their distinctive patterns of elevation may aid in prompt and accurate characterization between biliary and non-biliary forms of the disease, contributing to more effective clinical management and treatment decisions.

CONFLICT OF INTEREST
The authors declare no conflict of interest.

SOURCE OF FUNDING
This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Copyright© 17 Jan, 2024.

REFERENCES


**AUTHORSHIP AND CONTRIBUTION DECLARATION**

<table>
<thead>
<tr>
<th>No.</th>
<th>Author(s) Full Name</th>
<th>Contribution to the paper</th>
<th>Author(s) Signature</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Adnan Riaz</td>
<td>Main researcher and Author</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Sumera Saghir</td>
<td>Research methods and experimentation.</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Roomana Anwar</td>
<td>Experimentation and sample collection.</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Sabeen Khalid</td>
<td>Analysis of data.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Muhammad Shakil</td>
<td>Idea conception and writing of manuscript.</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Tabinda Fatima</td>
<td>Sample collection and analysis of data.</td>
<td></td>
</tr>
</tbody>
</table>