Evaluation of lipid profile and liver function in acute pancreatitis patients: a case control study

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Abstract:
Pancreatitis is described as any inflammation that manifests in acute or chronic forms in the pancreas. Acute pancreatitis is a sudden attack that leads to inflammation of the pancreas and affects the peripancreatic tissue and surrounding organ. In this study, liver function and lipid profile tests were evaluated in acute pancreatitis patients in order to find any relationship between liver function and lipid profile impairment and the etiology of acute pancreatitis. A total of 65 patients with acute pancreatitis, mean age 46.81 years, along with 65 healthy volunteers, mean age 43.06 years, were included in this study. Serum levels of T. protein, T. bilirubin, D. bilirubin, blood urea nitrogen, lipid profile, AST, ALT, and ALP were determined and statistical analysis was performed on the collected data. The results obtained indicated a significant decrease in serum levels of BUN and a significant increase in serum levels of AST, ALT, ALP, T. protein, T. Bilirubin, and D. Bilirubin. The results also indicated a highly significant increase in serum levels of triglycerides and VLDL, and a highly significant decrease in HDL levels for patients group when compared with control. The present study concluded that there is a clear relationship between disturbances of liver function and the promotion of acute pancreatitis. Therefore, we can suggest that liver enzymes (AST, ALT, and ALP) are good indicators for pursuing acute pancreatitis. Additionally, the results confirm that triglycerides, HDL, and VLDL may be helpful in identifying patients at risk of acute pancreatitis.

Keywords: lipid profile, liver function, acute pancreatitis, AST, ALT, ALP

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Introduction:
The pancreas is an organ located in the abdomen. It lies in the upper abdomen behind the stomach. The pancreas is a part of the gastrointestinal system that makes and secretes digestive enzymes in the intestine, as well as an endocrine organ that makes and secretes hormones into the blood to control energy metabolism and storage throughout the body. It plays a key role in turning the food we eat into fuel for the body cells. The pancreas has two main functions: the exocrine function that helps in digestion and the endocrine function that regulates blood sugar.

Pancreatitis, which is generally described as an inflammation of the pancreas, is a serious condition that manifests in acute or chronic forms. Acute pancreatitis (AP) is a sudden attack that causes inflammation to the pancreas and affects the peripancreatic tissue and surrounding organ, the global frequency of incidence is 12-73/100000. AP is usually associated with severe upper abdominal pain. The pain may be severe and last several days. Other symptoms of acute pancreatitis include nausea, vomiting, diarrhea, bloating and fever.

The etiologic and pathogenesis of acute pancreatitis have been intensively investigated for centuries worldwide. It can be initiated by several factors, including gallstones, alcohol, trauma, infections and hereditary factors. It has been reported that about 75% of pancreatitis is caused by gallstones or alcohol.

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[7]. In developed countries, it has found that the most common causes of AP are obstruction of gallstone in common biliary duct (about 38%) and alcohol intake (about 36%) [8, 9]. In fact, acute pancreatitis occurs suddenly and can lead to life-threatening complications; however, the majority of patients (about 80%) recover completely. AP is divided by the disease severity into mild AP and severe AP [4].

Acute pancreatitis was diagnosed based on clinical, laboratory, and imaging findings. Although there is no standard gold diagnostic method, amylase and lipase released from pancreatic acinar cells are the main laboratory tests in the diagnosis of AP. However, one of the important indicators of inflammation is C-reactive protein (CRP), an acute-phase reactant released from liver cells. Increased CRP in the early stages of pancreatic necrosis is significant in terms of being an indicator of disease severity. Other parameters such as serum alanine transaminase (ALT) and aspartate transaminase (AST) are also elevated; increased bilirubin levels and elevated leukocyte levels have also been investigated as clinical laboratory parameters for AP [10-12].

Materials and methods
Subjects and study design
Blood samples were taken from all patients with acute pancreatitis and control Volunteers. From each individual, 10 ml of blood were drawn by vein puncture using disposable syringes. The blood sample divided into two parts, 5 ml in a gel tube and 5 ml in EDTA tube. Blood samples were taken from all patients with acute pancreatitis and controls Volunteers. From each individual, 10 ml of blood were drawn by vein puncture using disposable syringes. The blood sample divided into two parts, 5 ml in a gel tube and 5 ml in the EDTA tube. This study includes 65 patients with acute pancreatitis, male and female, age ranging from (35 - 60) years with a mean age 46.81 years. The samples were collected from patients referred to a gastrointestinal tract hospital (GIT)/ Medical city in Baghdad, Iraq. The control group consisted of 65 healthy volunteers, males and females, age ranging from (35 - 60) years, with mean age 43.06 years old), none of whom had any history of acute pancreatitis.

Sample collection:
Blood samples were taken from all patients with acute pancreatitis and control volunteers. From each individual, 10 ml of blood were drawn by vein puncture using disposable syringes, and collected in a gel tube and then separated by centrifugation at 5000 rpm for 10 minutes.

Evaluation of Biochemical tests
The colorimetric method for determination of serum T. Protein (TP), T. Bilirubin (TSB), D. Bilirubin, Blood Urea Nitrogen (BUN), Lipid profile, AST, ALT, and ALP were carried out following the protocol of the commercially available kits supplied by Siemens, Germany. Also, the C-reactive protein test was carried out using the protocol of the commercially available kit supplied by Spinreact Company, Spain.

Statistical analysis:
Statistical analysis was achieved using the SPSS statistical software, version 20.0. Independent-Samples Student t-test and Pearson’s correlation analysis for assessment of mean differences between patients and control groups were performed with considered p <0.05 to be significant.

Results and Discussion:
The calculated values for quantitative analysis of liver function tests (T. Bilirubin, D. Bilirubin, AST, ALT, ALP and TP), as well as BUN in health control and patients with acute pancreatitis groups are summarized in Table 1. The results indicated the presence of a significant decrease in serum levels of BUN and significant increase in serum levels of ALT and TP (p<0.05), as well as a highly significant increase in serum levels of TSB, D. Bilirubin, AST and ALP (p<0.001), as seen in Table 1 and Figure 1.
Table 1: Levels of BUN and liver function tests for patients with acute pancreatitis and healthy volunteers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>sample</th>
<th>Mean</th>
<th>Std. Deviation</th>
<th>Std. Error</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN (mg/dl)</td>
<td>patient</td>
<td>10.24</td>
<td>4.55</td>
<td>0.57</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>13.97</td>
<td>2.84</td>
<td>0.35</td>
<td></td>
</tr>
<tr>
<td>TSB (mg/dl)</td>
<td>patient</td>
<td>1.15</td>
<td>0.89</td>
<td>0.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>0.59</td>
<td>0.26</td>
<td>0.03</td>
<td></td>
</tr>
<tr>
<td>D. Bilirubin</td>
<td>patient</td>
<td>0.67</td>
<td>0.86</td>
<td>0.11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>(mg/dl)</td>
<td>control</td>
<td>0.15</td>
<td>0.05</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>patient</td>
<td>42.53</td>
<td>20.29</td>
<td>2.52</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>26.95</td>
<td>9.05</td>
<td>1.12</td>
<td></td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>patient</td>
<td>38.12</td>
<td>16.38</td>
<td>2.03</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>30.61</td>
<td>11.18</td>
<td>1.39</td>
<td></td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>patient</td>
<td>146.45</td>
<td>70.67</td>
<td>8.76</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>65.43</td>
<td>17.58</td>
<td>2.18</td>
<td></td>
</tr>
<tr>
<td>TP(g/dl)</td>
<td>patient</td>
<td>6.64</td>
<td>1.09</td>
<td>0.14</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>8.16</td>
<td>0.88</td>
<td>0.11</td>
<td></td>
</tr>
</tbody>
</table>

Figure 1: Diagram shows serum BUN and liver function tests (TSB, D. Bilirubin, AST, ALT, ALP and TP) of patients with acute pancreatitis in comparison with control subjects.

For the assessment of the lipid profile, all obtained data were analyzed statistically and presented in Table 2. The p-values were also included to verify differences in levels of study parameters between patients and control. The results indicated the presence of a highly significant increase in serum levels of triglyceride and VLDL, and a highly significant decrease in serum levels of HDL for patients with acute pancreatitis when compared with control. While no significant differences were found in cholesterol and LDL levels, as seen in Table 2 and Figure 2.
Farhan et al. (2020): Lipid profile, liver function, and acute pancreatitis

Table 2: Levels of BUN and liver function tests for patients with acute pancreatitis and healthy volunteers.

<table>
<thead>
<tr>
<th>Variable</th>
<th>sample</th>
<th>Mean</th>
<th>Std.Deviation</th>
<th>Std. Error</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHOL (mg/dl)</td>
<td>patient</td>
<td>163.74</td>
<td>57.19</td>
<td>7.09</td>
<td>0.826</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>165.46</td>
<td>26.63</td>
<td>3.31</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>TRI (mg/dl)</td>
<td>patient</td>
<td>207.41</td>
<td>85.26</td>
<td>10.57</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>138.23</td>
<td>76.41</td>
<td>9.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL (mg/dl)</td>
<td>patient</td>
<td>37.28</td>
<td>12.01</td>
<td>1.48</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>47.05</td>
<td>9.99</td>
<td>1.24</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LDL (mg/dl)</td>
<td>patient</td>
<td>84.98</td>
<td>48.33</td>
<td>5.99</td>
<td>0.438</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>90.76</td>
<td>35.57</td>
<td>4.41</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VLDL (mg/dl)</td>
<td>patient</td>
<td>41.48</td>
<td>17.05</td>
<td>2.12</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>control</td>
<td>27.65</td>
<td>15.28</td>
<td>1.89</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Figure 2: Diagram shows serum lipid profile (cholesterol, triglyceride, HDL, LDL and VLDLD) of patients with acute pancreatitis in comparison with control subjects.

The correlation between all variables included in the current work was studied for acute pancreatitis patients using Pearson correlation analysis, and the data analysis was displayed in Table 3. The results showed that the BUN level was positively correlated with TRI and VLDL levels. The analysis also revealed the presence of a positive correlation between the levels of D. bilirubin, AST, ALT, and ALP, with the TSB level. Furthermore, the current study revealed a positive correlation of D. bilirubin with AST, ALT, ALP and HDL levels, and positive correlation of AST with ALT and ALP as shown in Table 3.

The results obtained showed the presence of a positive correlation between the levels of ALT and ALP, as opposed to the negative correlation between the levels of ALP with HDL of patients with acute pancreatitis. It also showed the presence of a positive correlation between the level of cholesterol and the levels of TRI, HDL, LDL, and VLDL, while showed a positive correlation between the TRI level with HDL and VLDL levels of patients with acute pancreatitis. There was also a positive correlation between the levels of HDL and VLDL of the patients.
Table 3: correlations between variables in acute pancreatitis patients group (R-value).

<table>
<thead>
<tr>
<th>Variables</th>
<th>BUN</th>
<th>TSB</th>
<th>D. Bilirubin</th>
<th>AST</th>
<th>ALT</th>
<th>ALP</th>
<th>TP</th>
<th>CHOL</th>
<th>TRI</th>
<th>HDL</th>
<th>LDL</th>
<th>VLDL</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUN</td>
<td>1</td>
<td>.054</td>
<td>.071</td>
<td>.030</td>
<td>-.053</td>
<td>.057</td>
<td>.132</td>
<td>.165</td>
<td>.251</td>
<td>.348</td>
<td>.021</td>
<td>.251</td>
</tr>
<tr>
<td>TSB</td>
<td>.054</td>
<td>1</td>
<td>.490</td>
<td>.302</td>
<td>.285</td>
<td>.405</td>
<td>-.218</td>
<td>.020</td>
<td>-.025</td>
<td>-.232</td>
<td>.091</td>
<td>.025</td>
</tr>
<tr>
<td>D. Bilirub</td>
<td>.071</td>
<td>.400</td>
<td>1</td>
<td>.550</td>
<td>.438</td>
<td>.586</td>
<td>.092</td>
<td>.209</td>
<td>-.009</td>
<td>.345</td>
<td>.337</td>
<td>.009</td>
</tr>
<tr>
<td>AST</td>
<td>.030</td>
<td>.302</td>
<td>.550</td>
<td>1</td>
<td>.665</td>
<td>.553</td>
<td>-.081</td>
<td>.076</td>
<td>.010</td>
<td>-.186</td>
<td>.132</td>
<td>.010</td>
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<tr>
<td>ALT</td>
<td>.053</td>
<td>.285</td>
<td>.438</td>
<td>.665</td>
<td>1</td>
<td>.415</td>
<td>.022</td>
<td>.213</td>
<td>.074</td>
<td>-.038</td>
<td>.236</td>
<td>.074</td>
</tr>
<tr>
<td>ALP</td>
<td>.057</td>
<td>.405</td>
<td>.586</td>
<td>.553</td>
<td>.415</td>
<td>1</td>
<td>.118</td>
<td>-.005</td>
<td>.011</td>
<td>.360</td>
<td>.080</td>
<td>.011</td>
</tr>
<tr>
<td>TP</td>
<td>.132</td>
<td>.218</td>
<td>-.092</td>
<td>-.081</td>
<td>.022</td>
<td>.118</td>
<td>.067</td>
<td>1</td>
<td>.558</td>
<td>.316</td>
<td>.908</td>
<td>.558</td>
</tr>
<tr>
<td>CHOL</td>
<td>.165</td>
<td>.020</td>
<td>.209</td>
<td>.076</td>
<td>.213</td>
<td>.005</td>
<td>.067</td>
<td>1</td>
<td>.558</td>
<td>.316</td>
<td>.908</td>
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<td>TRI</td>
<td>.251</td>
<td>.025</td>
<td>-.009</td>
<td>.010</td>
<td>.074</td>
<td>.011</td>
<td>-.237</td>
<td>.558</td>
<td>1</td>
<td>.373</td>
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<tr>
<td>HDL</td>
<td>.348</td>
<td>.232</td>
<td>-.345</td>
<td>-.186</td>
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<td>.360</td>
<td>.086</td>
<td>.316</td>
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<td>1</td>
<td>-.006</td>
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<td>LDL</td>
<td>.021</td>
<td>.091</td>
<td>.337</td>
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<td>.236</td>
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<td>.142</td>
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<td>-.006</td>
<td>1</td>
<td>.215</td>
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<tr>
<td>VLDL</td>
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<td>.010</td>
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<td>.011</td>
<td>-.237</td>
<td>.558</td>
<td>1.000</td>
<td>.373</td>
<td>.215</td>
<td>1</td>
</tr>
</tbody>
</table>

*Correlation is significant at the 0.05 level.
** Correlation is significant at the 0.01 level.

Many modern scoring systems, in addition to the original Ranson standards, include blood urea nitrogen (BUN) to predict death rates in AP [13-16]. Early changes in the BUN level may reflect many important physiological processes in acute pancreatitis. In addition to intravascular volume depletion, elevated BUN levels may be secondary to impaired renal function or potentially concurrent upper gastrointestinal haemorrhage. Renal failure is a relatively common form of organ dysfunction among patients with acute pancreatitis [17].

The persistent rise in BUN may either reflect a failure to adequately resuscitate patients early in the course of the disease, a deterioration of renal function, or a persistent negative nitrogen balance related to increased protein-catabolism caused by AP [18-20]. This is consistent with our study regardless of the specific mechanism type, we have clearly shown that patients with early elevation in BUN are at increased risk of acute pancreatitis. The highest level of BUN should be a signal for clinicians to initiate intense early recovery efforts because these early signs in BUN anticipate mortality in AP. Close monitoring of BUN levels during the first 24 hours of AP helps to identify patients at increased risk of mortality and provides important information on the effectiveness of primary treatment [21].

In populations with a high incidence of biliary pancreatitis, the sensitivity of biochemical parameters may increase. The levels of total and direct bilirubin had the highest levels of specificity and positive negative predictive values among other biochemical laboratory measurements [22]. Of course, the total bilirubin increase is associated with the direct bilirubin increase. In agreement with our results, it has been found that bilirubin levels (especially direct bilirubin) were the most important signs of pancreatitis [23]. This indicates that pancreatitis may occur after very little obstruction of the common bile duct. It is very difficult to detect obstruction of the pancreatic duct or any other pathophysiological mechanism that causes pancreatitis and its deterioration during the initial periods of development of pancreatitis. A little obstruction in the pancreatic duct may cause reduced drainage of pancreatic secretions leading to pancreatitis [22].

ALP, a major parameter in biliary pancreatitis, also increases in obstructive jaundice. The significance of the increase in ALP more than 246 U / L may indicate obstruction of the ducts that cause biliary pancreatitis. We identified a significant increase in some biochemical variables that are associated with acute pancreatitis. These are AST, ALT, ALP, total bilirubin and direct bilirubin. In the literature, individual clinical parameters that are associated with biliary pancreatitis and biliary stones are identified [23-26]. Age, bilirubin, ALP and ALT levels were found to be significantly increased in biliary pancreatitis [27], and this was consistent with the results of the current study. Several studies showed that total bilirubin, ALP, and ALT are significant variables in pancreatitis [23, 28]. ALT or AST levels more than three times the normal upper limit indicate gallstones as the cause of acute pancreatitis. ALT
Hypertriglyceridemia (HTG) is the third most common cause of acute pancreatitis after alcohol consumption and gallstones. It accounts for 1–7% of patients with AP. Severe hypertriglyceridemia, including chylomicronaemia, is the underlying cause of up to 7% of all cases of AP. Persistently elevated serum triglycerides, for weeks, can reflect underlying lipid disorders.

It was proposed that pancreatic lipase hydrolyzes triglycerides and the resulting free fatty acids provoke inflammatory changes and free radicals damage that promote acute pancreatitis. Chylomicrons are triglyceride-rich lipoproteins. Poor flow of fat in the pancreatic capillaries, leading to ischemia, may disturb the acinar structure that exposes triglyceride-rich molecules to the pancreatic lipase. The proinflammatory non-esterified free fatty acids generated from the enzymatic degradation of chylomicrons-HTG may lead to more damage to pancreatic acinar cells and microvasculature. Subsequent amplification of released inflammatory mediators and free radicals eventually leads to necrosis, edema, and pancreatitis. HTG has also been shown to aggravate other experimental models of acute pancreatitis.

The exact mechanism of the HTG that causes the AP is not clearly understood. Most accepted theories rely on animal models describing the metabolism of excess TGs by pancreatic lipase to release fatty acids that lead to pancreatic cell injury and ischemia. HTG is more likely to be associated with acute pancreatitis compared to other causes however no difference in mortality has been reported. In agreement with our study, contrary HTG, there is no correlation between and AP.

However, in a clear relationship though, it may still be difficult to distinguish between mild to moderate hyperlipidemia (HLP) as secondary comorbidity in AP from acute HTG that primarily induces AP, especially in patients with hereditary HLP. Also, the effect of HLP on the development of AP is still unclear, despite the well-documented association between high serum triglyceride levels and some molecular mechanisms of pancreatic acinar cell damage. It has been reported that HTG independently affects the severity and deterioration of necrotizing AP. On the other hand, and inconsistent with the result of the present study, some reports indicated that HLP does not affect the outcome of AP. It has been clearly demonstrated that patients with hyperlipidemia, especially hypertriglyceridemia, have more severe acute pancreatitis, higher incidence of complications and poorer outcomes compared to patients with normolipidemic.

In conclusion, valuable information is available on liver function and lipid profile, but its association with acute pancreatitis is yet to be studied further. The present study shows a clear relationship between disturbances in liver function and the promotion of acute pancreatitis. The results indicated that the total serum bilirubin level, more precisely direct bilirubin, of acute pancreatitis patients is substantially affected relative to those in healthy subjects. Furthermore, the results indicated that liver enzymes (AST, ALT, and ALP) are good indicators for pursuing acute pancreatitis. These findings give a positive indication of the presence of a significant association between liver function and the promotion of acute pancreatitis. Moreover, the results showed that patients with early elevation in BUN are at increased risk of acute pancreatitis. The present work proved that the distortions in lipid profile (especially triglycerides, HDL and VLDL) are highly associated with the etiologic of acute pancreatitis. Pearson correlation analysis demonstrated that there is a relationship between the etiologic of acute pancreatitis and the fatty personality. Lastly and more importantly, the results confirm that triglycerides in the blood, HDL and VLDL may be helpful in identifying patients at risk of acute pancreatitis. More studies are recommended to understand the exact mechanism of the relationship between liver function and lipid profile with the etiologic of acute pancreatitis.

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References:


