Evaluation of Prothrombin Time and Activated Partial Thromboplastin Time among Patients with Obstructive Jaundice in Federal Medical Center Yola, Nigeria

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ABSTRACT

Background: Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) are medical tests used to evaluate the degree of hepatocellular failure and the integrity of haemostasis system. Obstructive jaundice is a post hepatic problem cause by blockage in the bile duct. Aim: This study aims to evaluate the PT and APTT profile of patients with obstructive jaundice in Northeastern Nigeria for better monitoring and management of these patients. Methods: 156 subjects comprising of 79 patients with obstructive Jaundice (41 females and 38 males with mean age of 53.46± 6.64) and 77 apparently healthy subjects (with a mean age of 51.23±4.14 years comprising of 45 female and 32 males.) participated in the study. PT and APTT values of the studied subjects were determined using standard methods. Result: The mean level of APTT test in patients with obstructive jaundice was 54.29±4.31 seconds while that of the control group was 39.47±5.3 seconds, P< 0.05. The mean value of the PT of patients was 21.17± 3.12 seconds while that of the control group was 13.05±2.0 seconds (P<0.05). The correlation of PT versus APTT value was significant with the correlation coefficient (r) of 0.34 at P<0.05. Conclusion: APTT and PT were prolonged in patients with obstructive jaundice compare with the control group. Therefore, in Northeastern Nigeria, patients with obstructive jaundice may be predisposed to bleeding events which may get complicated especially in palliative surgery and may require coagulation process support and monitoring.

Key words: Prothrombin Time, Activated Partial Thromboplastin Time, Obstructive-Jaundice, liver function, haemostasis, hepatocellular failure

INTRODUCTION

Activated Partial Thromboplastin Time (APTT), Prothrombin Time (PT) and International Normalized Ratio (INR) are Coagulation profile tests usually performed to determine if a person have enough coagulation activity for efficient blood clotting process.[1] They are used to test the integrity of the haemostasis system of the human body.[2] In patients with liver disease, PT and APTT tests can be used to evaluate the degree of hepatocellular failure and the severity of liver function impairment. [3]
of haemostasis disorders manifesting as bleeding, or bleeding risk.\[3\] Prothrombin Time determination may be sufficient to evaluate the degree of hepatocellular failure\[4\] but usually the Activated Partial Thromboplastin Time (APTT) is used in conjunction with the Prothrombin Time (PT) test.\[5\] The APTT measures the speed of blood clotting by means of the intrinsic pathway, while PT measures blood clotting by means of the extrinsic pathway.\[6\] In addition, APTT has been used as research tool for elucidating the interaction of coagulation factors, thrombin generation and fibrin formation.\[2\]

Haemostasis is closely related to liver function because coagulation factors that are required for efficient coagulation process are produced by the liver.\[7\] The degree of coagulation disorder depends upon the degree of impairment of liver function\[8\] and liver problem like obstructive jaundice plays important role in promoting coagulation disorder.\[7\]

Obstructive Jaundice is a medical problem that occurs when there is blockage of the bile duct resulting in an obstruction to the passage of vitamin K from the liver into the intestine.\[9\] Bile duct obstruction which is usually caused by a stone in the bile duct or carcinoma of the head of the pancreas has been reported to be the commonest cause of obstructive jaundice.\[10\] Obstructive jaundice is mostly complicated by bleeding events, which may be due to unavailability of vitamin K dependent clotting factors\[11\] as a result of blockage of the bile duct.\[12\] Vitamin K is a fat soluble vitamin requiring bile salts for its absorption from the gut\[3\] and Vitamin K is essential for the synthesis of many clotting factors\[6\] which are required for effective clot formation in the hemostatic process.\[2\]

The aetiology of obstructive jaundice varies from place to place.\[11,12,14\] However, in Nigeria, carcinoma of the head of pancreas and periampullary cancer are the commonest causes of obstructive jaundice\[13\] and most of these patients with obstructive jaundice usually with late presentation requires palliative surgeries.\[16\] It becomes imperative to assess the hemostasis function of patients with obstructive jaundice for better treatment and monitoring. This study aims at providing information on the PT and APTT of patients with obstructive jaundice from the Northeastern part of Nigeria.

**METHODOLOGY**

This study was carried out at Federal Medical Center of Yola, in Adamawa State, Northeast Nigeria from April 2015 to November 2016. A total of 156 subjects participated in the study. 79 were patients with mean age of 53.5 ± 6.6 years and clinical diagnosis of obstructive jaundice. 41 of them were females while 38 were males. 77 of the studied group were apparently healthy subjects with a mean age of 51.2±4.1years comprising of 45 females and 32 males. Three milliliters (3mls) of blood was collected from subjects into vacutainer bottle containing 200ul of 3.2% buffered sodium citrate. Plasma was obtained from the blood by centrifugation. The Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) of all subjects were determined using quick one stage method and Modified Kaolin Method respectively.\[17\] The reagent for APTT test was a commercial rabbit brain extract phospholipid containing an activator which is ellagic acid in buffered medium. The reagent for PT was commercial freeze-dried calcium thromboplastin obtain from a rabbit brain extract. All analyses were performed in duplicate.

**Informed consent**

All subjects gave their informed consent prior to their inclusion in the study.

**Inclusion criteria**

Only patients with clinical diagnosis of obstructive Jaundice with an average age 53.46± 6.64 were included in this study.

**Exclusion criteria**

Patients with non-obstructive jaundice and those above 65 years of age were excluded from the study. Obstructive jaundice patients who have undergone surgery were also excluded.

**Sample collection**

Three (3.0)mls of blood was aseptically collected through the antecubital vein of all the subjects and put in a vacutainer bottle containing 200μl of 3.2% buffered sodium citrate; the bottles were further labeled with the patient number, sex and age. Plasma was obtained from the blood...
through centrifugation. Prothrombin Time (PT) and Activated Partial Thromboplastin Time (APTT) values were determined in the plasma of all subjects within one hour of collection. INR of each subject was calculated using the Prothrombin Time values and the international sensitivity index (ISI). The ISI for this tissue factor was 1.5.

**Sample analyses**

**Activated Partial Thromboplastin Time (APTT) test**

Using the Modified Kaolin Method, the procedure of test was as follows:
1. All reagents were brought to required working room temperature.
2. Test tubes were labeled with the sample number and pre-incubated in a water bath set at the temperature of 37°C for 15 minutes.
3. 50µl of plasma was added to all the tubes in the water bath.
4. 50µl of APTT reagent was further added to all the tubes in the water bath.
5. The tubes containing the plasma and liquid APTT reagent were incubated in the water bath for further 3 minutes.
6. 50µl of 0.025M liquid Calcium Chloride was added to each tube and a stop-watch was started simultaneously.
7. The time it takes for the clot to form in the tubes was noted and recorded in seconds.

**Prothrombin Time Test**

Using the one stage Prothrombin test method, the procedure for the test was as follow:
1. 2.5mls of distilled water was added to 2mls of freeze-dried calcium thromboplastin to obtain a rehydrated solution.
2. The rehydrated solution was allowed to stand at room temperature for 30 minutes.
3. The rehydrated solution was further incubated at 37°C for 15 minutes in a water bath.
4. 100µl of plasma was dispensed into test tubes and incubated at 37°C for 5 minutes.
5. 200µl of the rehydrated solution was added to the tubes containing the plasma and a stopped watch was started simultaneously.
6. The time it takes for clot to form in the tubes was noted and recorded in seconds.

**International Normalized Ratio (INR)**

The INR was calculated as the PT ratio raised to the power of the ISI used (INR = R^{ISI}). The Prothrombin time (PT) ratio (R) was calculated by dividing the PT values of the subject by the PT value of the control. The PT Control value, was 13.5 seconds.

**Statistical analysis**

Statistical analysis was performed using the SPSS (Statistical Package for Social Sciences) computer software version 20.0. Descriptive values were given as mean and standard error of mean. Categorical variables were expressed as the number of cases and the percentage value. The Student's t-test was used to compare the means differences of the estimated parameters while the Pearson's correlation coefficient was used to calculate the relationship between PT and APTT values in this group of patients.

**RESULTS**

The mean level of Activated Partial Thromboplastin Time test value was higher than the normal reference range in patients with obstructive jaundice when compared with that of the control group as shown in table 1.

The mean value of the prothrombin time was also higher in patients compared with the control group (P<0.05; table 1).

The correlation of PT versus APTT was significant (P<0.05) with coefficient (r) of 0.34 as shown in table 3.

**DISCUSSION**

In this present study, it was observed that the mean APTT and PT values were prolonged in patients with obstructive jaundice than that of the control group (p<0.05); this implies the presence of abnormal haemostasis in obstructive jaundice. The abnormality was observed in both the intrinsic and extrinsic pathway of coagulation as reflected by the APTT and PT values. The prolong APTT and PT may be due to deficiency of vitamin K-dependent coagulation factors that usually follows poor absorption of vitamin K as a result of absence of bile in the intestine. This is because in obstructive jaundice, the passage of bile from the liver to the intestine is block. The vitamin K is essential for the synthesis of important
coagulation factors\textsuperscript{[20]} which are required for effective clot formation in the haemostasis process.\textsuperscript{[21]}  

Table 1: Demography of the studied population

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>PATIENTS (n = 79)</th>
<th>Control group (n = 77)</th>
<th>P- Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>53.46 ± 6.6</td>
<td>51.23 ± 4.1</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>38</td>
<td>32</td>
<td>0.01</td>
</tr>
<tr>
<td>Female</td>
<td>41</td>
<td>45</td>
<td>0.01</td>
</tr>
<tr>
<td>Obstructive jaundice due to head of pancreas and periampullary cancer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prothrombin time (sec)</td>
<td>21.17±3.1</td>
<td>13.05± 2.0</td>
<td>0.05</td>
</tr>
<tr>
<td>APTT (sec)</td>
<td>54.29±4.3</td>
<td>39.47± 5.3</td>
<td>0.05</td>
</tr>
</tbody>
</table>

Table 2: The mean values of APTT, PT and INR of patients with Obstructive jaundice

<table>
<thead>
<tr>
<th>PARAMETERS</th>
<th>Patient (N = 79)</th>
<th>Control (N = 77)</th>
<th>Normal Values</th>
<th>P VALUE</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT (secs)</td>
<td>21.17±3.1</td>
<td>13.05± 2.0</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Normal range 12 – 14.5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>APTT (secs)</td>
<td>54.29±4.31</td>
<td>39.47± 5.3</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>Normal range 34.0 – 45.0</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PT Ratio</td>
<td>2.08±0.23</td>
<td>1.82 ± 0.40</td>
<td></td>
<td>0.05</td>
</tr>
<tr>
<td>INR</td>
<td>3.75±0.92</td>
<td>4.17 ± 3.10</td>
<td>0.8-8.0</td>
<td>0.05</td>
</tr>
</tbody>
</table>
Table 3: Correlation of PT values with APTT and INR in patients with Obstructive jaundice

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Correlation coefficient (r)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PT versus APTT</td>
<td>0.34</td>
<td>0.05</td>
</tr>
</tbody>
</table>

A prolonged APTT implies that in patients with obstructive jaundice, the integrity of the intrinsic pathway is poor, it could therefore be inferred that the exclusive coagulation factor of the intrinsic pathway such as factor XII, XI, IX, and VIII \(^7\) could be deficient, malfunction or inhibited in patients with obstructive jaundice. High value of the APTT occur as a result of the deficiency of vitamin K dependent clotting factors because in obstructive jaundice, uptake of vitamin K is impaired due to blockage of bile in the bile duct and this process by extension affects the efficient functioning of the vitamin K dependent clotting factors in the intrinsic pathway which is manifesting as prolong APTT values that is seen in this study.

Nevertheless, in this study, there is a significant correlation between PT and APTT values with correlation coefficient of 0.34 at \(P<0.05\) indicating that, the PT and APTT are related to each other in patients with obstructive jaundice and since APTT has been used as research tool for elucidating the interaction of coagulation factors, \(^2\) the result of the correlation of PT versus APTT implies that some of the clotting factors in the extrinsic pathway may also be involved in the intrinsic pathway of coagulation.

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CONFLICT OF INTEREST
There is no conflict of interest regarding this work among the authors.

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Conflict of Interest: None declared
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