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Serum Bile Acids and Standard Liver Enzymes in Hepatobiliary Disorders

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Abstract

The study included 20 normal individuals as control group and 58 cases (13 cases with hepatitis, 17 cases with chronic cholycystitis, 14 cases with obstructive jaundice and 14 cases with hepatoma). The mean value of serum levels of post-prandial bile acids and standard liver enzymes for each diseased group showed statistically significant difference except in ALP,GGT and 5'N in chronic cholycystitis group when compared with the control group. The sensitivity and accuracy of serum post-prandial bile acids were 100% and 97% in both hepatoma and obstructive jaundice groups. While in hepatitis, were 100% and 96% and as regard the cases of chronic cholycystitis were 23.5% and 62% respectively.

Introduction

DETERMINATION of functional impairment of liver offers unusual difficulties for several reasons, the main reason is that there is no uniform degree of failure of different liver functions, some may still be normal while others are impaired. Moreover, the liver has considerable functional reserve capacity to regenerate. These are particulary true in chronic conditions [1].

Estimation of serum bile acids level in hepatobiliary disease is becoming more wide spread, although the potential value of having the information has not been clearly defined. Almost without exception, the increased sensitivity of 2 - hours post prandial bile acid level compared to the fasting level has been confirmed, considering that it is the most practical and least invasive procedure that would be suitable for the over whelming majority of the population, the test is generally useful [2,3].

The aim of this study is to evaluate the value of serum post-prandial bile acids measurements, its sensitivity and accuracy in comparison with other standard liver enzymes in diagnosis of hepatitis, chronic cholycystitis, obstructive jaundice and hepatoma.

Materials and Methods

The study included 78 individuals:

1. *Control Group*: included 20 apparantely normal healthy individuals from medical laboratory staff. They gave no history of liver affection and their liver function tests were normal.

2. *Diseased Group*: included 58 patients with liver diseases admitted to Surgical and Internal Medicine Departments of El-Minia University Hospital. They were not received treatment before.

The diseased group was divided into the following:

A) *Hepatitis Group (Group I)*: included 13 patients, their ages ranged from 18-35 years.

B) *Chronic Cholycystitis Group (Group II)* : included 17 patients, their ages ranged from 25-40 years.

C) *Obstructive Jaundice Group (Group III)*: included 14 patients, their ages ranged from 40-55 years.

D) *Hepatoma Group (Group IV)*: included 14 patients, their ages ranged from 50-60 years.

Both patients and control groups were subjected to the followings:

1. Standard liver enzymes which included: Transaminases (AST and ALT) [4] alkaline phosphatase (ALP) [5], gamma glutamyl transferase (GGT) [6] and 5'nucleotidase (5'N) [7]

2. 2- Hours post-prandial total serum bile acids using enzyme immunoassay kits (EIA) (Immunotech-corporation, Gowindom street, Allston, NA 02134 USA).

Statistical Analysis:

Means and standard deviations ($X \pm SD$) were calculated and compared using unpaired t-test. P value of < 0.05 was taken as the level of statistical significance. Also the results of the different tests were evaluated by using the sensitivity and accuracy. The cut off value was the mean of normal control $\pm$ 2 SD.

$$\text{Sensitivity (TN)} = \frac{\text{No. of true positive (TP)}}{\text{No. of (TP) + No. of true negative}} \times 100$$

$$\text{Accuracy} = \frac{\text{True positive + True negative}}{\text{Total}} \times 100$$

Results

The mean ± SD of all studied parameters are illustrated in tables (I, II, III and IV), the sensitivity & accuracy percentage in table (V) and figure (I) in all diseased and control groups.

There is statistically significant increased levels in all studied parameters in diseased groups when compared with control one except in the levels of ALP, GGT, and 5'N in cases of chronic cholycystitis there is no statistically significant difference when compared with control group ($p < 0.05$) (Table I).

Also hepatitis group showed statistically significant difference when compared different studied parameters with that of chronic cholycystitis, obstructive jaundice and hepatoma except GGT in cases of obstructive jaundice and alkaline phosphatase (ALP). In cases of hepatoma, there was no significant difference ($p < 0.05$) (Table II).

Table (1): Mean ± SD of Different Studied Parameters in Control, Hepatitis, Chronic Cholycystitis, Obstructive Jaundice and Hepatoma Groups.

Parameter	Control group (I) n = 20 x ± SD	Hepatitis group (II) n = 13 x ± SD	Ch.cholycy. group (III) n = 17 x ± SD	Obst. Jaund. group (IV) n = 14 x ± SD	Hepatoma group (V) n = 14 x ± SD
Bile acids (μg / ml)	0.52 ± 0.35	4.0 ± 1.3	1.45 ± 0.38	18.2 ± 14.3	21.8 ± 32.2
P-value		< 0.0001	< 0.05	< 0.0001	< 0.0001
Ast (IU/ L)	13.6 ± 3.3	286 ± 36	36.7 ± 7.2	100 ± 84	71 ± 32.4
P-value		< 0.0001	< 0.0001	< 0.0001	< 0.0001
ALT (IU/ L)	7.9 ± 2.7	275 ± 96.5	29.7 ± 2.0	106 ± 70	40 ± 37.1
P-value		< 0.0001	< 0.0001	< 0.0001	< 0.0001
ALP (KAU)	7.8 ± 2.0	28.2 ± 4.2	8.4 ± 1.1	51.7 ±20.4	29 ±18.8
P-value		< 0.0001	> 0.05	< 0.0001	< 0.0001
GGT (IU/ L)	15 ± 2.8	67 ± 9.5	18.7 ± 1.7	62.2 ± 7.6	119 ± 8.1
P-value		< 0.0001	> 0.05	< 0.0001	< 0.0001
5'N (IU/ L)	1.6 ± 0.93	13 ± 1.1	1.7 ± 0.1	17.1 ± 1.3	18.8 ± 1.1
P-value		< 0.0001	> 0.05	< 0.0001	< 0.0001

Table (II): Comparison of the Mean ± SD of Different Studied Parameters Between Hepatitis, Chronic Cholycystitis, Obstructive Jaundice and Hepatoma Groups.

Parameter	Hepatitis group (I) n = 13 x ± SD	Ch.cholycy. ggroup (II) n = 17 x ± SD	Obst. Jaund. group (III) n = 14 x ± SD	Hepatoma group (IV) n = 14 x ± SD
Bile acids (µg / ml)	4.0 ± 1.3	1.45 ± 0.38	18.2 ±14.3	21.8 ± 32.2
P-value		< 0.0001	< 0.0001	< 0.0001
Ast (IU/ L)	286± 36	36.7 ± 7.2	100 ± 84	71 ± 32.4
P-value		< 0.0001	< 0.0001	< 0.0001
ALT (IU/ L)	275 ± 96.5	29.7 ± 2.0	106 ± 70	40 ± 37.1
P-value		< 0.0001	< 0.0001	> 0.0001
ALP (KAU)	28.2 ± 4.2	8.4 ± 1.1	51.7 ± 20.4	29 ±18.8
P-value		< 0.0001	< 0.0001	< 0.05
GGT (IU/ L)	67 ±9.5	18.7 ± 1.7	62.2 ± 7.6	119 ± 8.1
P-value		< 0.0001	> 0.05	< 0.0001
5'N (IU/ L)	13 ±1.1	1.7 ± 0.1	17.1 ± 1.3	18.8 ± 1.1
P-value		< 0.0001	< 0.01	< 0.01

On comparing results of chronic cholycystitis with that of obstructive jaundice and hepatoma groups there was significant decreased levels ($p < 0.0001$) except in ALT in cases of hepatoma ($p < 0.01$) (Table III).

Also in obstructive jaundice group there was significant difference when compared with that of hepatoma groups except in total serum bile acids and 5'N ($p < 0.05$) (Table IV).

Table (III): Comparison of the Mean ± SD of Different Studied Parameters Between Chronic Cholycystitis, Obstructive Jaundice and Hepatoma Groups.

Parameter	Ch.cholycy. group (I) n = 17 x ± SD	Obst. Jaund. group (II) n = 14 x ± SD	Hepatoma group (III) n = 14 x ± SD
Bile acids (μg / ml)	1.45 ± 0.38	18.2 ± 14.3	21.8 ±32.2
P-value		< 0.0001	< 0.0001
Ast (IU/ L)	36.7± 7.2	100 ± 84	71 ± 32.4
P-value		< 0.0001	< 0.0001
ALT (IU/ L)	29.7 ± 2.0	106 ± 70	40 ± 37.1
P-value		< 0.0001	< 0.01
ALP (KAU)	8.4 ± 1.1	51.7 ± 20.4	29 ± 18.8
P-value		< 0.0001	< 0.0001
GGT (IU/ L)	18.7 ± 1.7	62.2 ± 7.6	119 ± 8.1
P-value		< 0.0001	< 0.0001
5'N (IU/ L)	1.7 ± 0.1	17.1 ± 1.3	18.8 ± 1.1
P-value		< 0.0001	< 0.0001

As regards the sensitivity percentages of the post-prandial serum bile acids was 100% in all groups except in chronic cholycystitis was 23.5%. While the accuracy in hepatitis was 96%, in chronic cholycystitis 62%, in obstructive jaundice and in hepatoma group was 97% (Table V).

Table (IV): Mean ± SD of Different Studied Parameters Between Obstructive Jaundice, and Hepatoma Groups.

Parameter	Obst. Jaund. group (I) n = 14 x ± SD	Hepatoma group (II) n = 14 x ± SD
Bile acids (μg / ml)	18.2 ± 14.3	21.8 ± 32.2
P-value		> 0.05
Ast (IU/ L)	100± 84	71 ± 32.4
P-value		< 0.01
ALT (IU/ L)	106 ±70	40 ± 37.1
P-value		< 0.0001
ALP (KAU)	51.7 ± 20.4	29 ± 18.8
P-value		< 0.0001
GGT (IU/ L)	62.2 ± 7.6	119 ±8.1
P-value		< 0.0001
5'N (IU/ L)	17.1 ± 1.3	18.8 ± 1.1
P-value		> 0.05

Table (V): Sensitivity and Accuracy Percentage of Total Bile Acids and Standard Liver Enzymes in Different Groups.

Parameter	Hepatitis group (I) n = 13		Ch.cholycy. group (II) n = 17		Obst. Jaund. group (III) n = 14		Hepatoma group (IV) n = 14	
	Sens.	Accu.	Sens.	Accu.	Sens.	Accu.	Sens.	Accu.
Bile acids	100 %	96 %	23.5 %	62 %	100 %	97 %	100 %	97 %
Ast	92 %	96 %	88 %	94 %	78.5 %	91 %	71 %	88 %
ALT	93 %	96 %	76 %	89 %	71 %	88 %	78 %	91 %
ALP	76 %	90 %	11.7 %	59 %	85 %	94 %	71 %	88 %
GGT	76 %	87 %	35 %	67 %	78.5 %	88 %	85 %	91 %
5'N	84 %	93 %	11.7 %	59 %	78.5 %	91 %	85 %	94 %

N.B:

Sens. = Sensitivity Accu = Accuracy

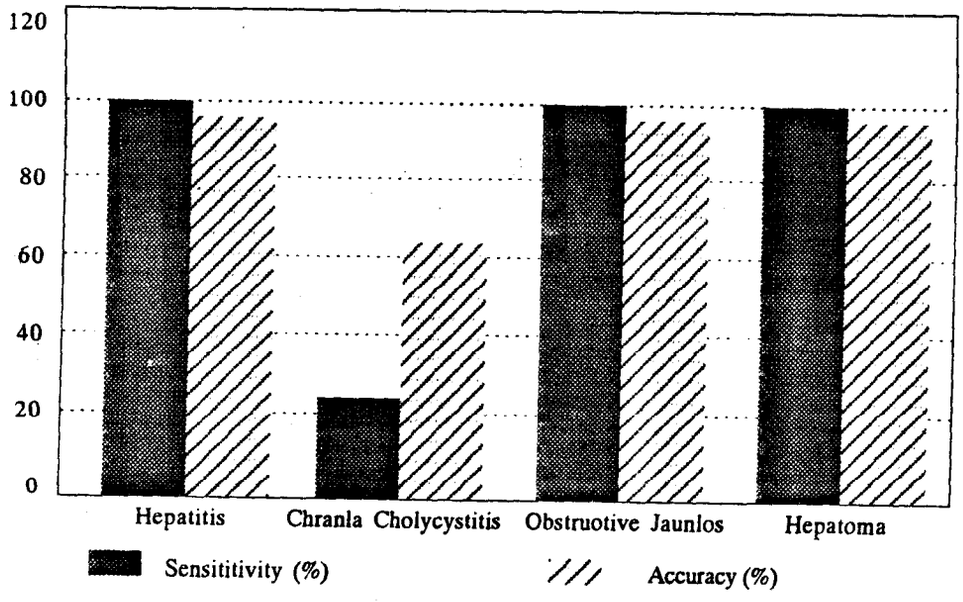

Fig. 1: Sensitivity and accuracy of bile acids in hepatitis, obst. jaund., ch. cholycystitis and hepatoma.

Discussion

The concentration of total serum bile acids indicates the fraction reabsorbed from the intestine and has escaped extraction of its first passage through the liver, its value reflects instantaneous balance between intestinal absorption and hepatic uptake and raised levels are specific for hepatobiliary disease [8].

Although, sensitivity of serum bile acids estimation is less than originally thought for detecting hepatocellular damage in viral hepatitis or chronic liver disease it is however, better than serum albumin or prothrombin time because the value depends not only on hepatic injury but also on excretory function [9].

In this study, when compared control group with diseased groups as regards total serum bile acids, it was found to be significantly higher in hepatitis, obstructive jaundice and hepatoma groups ($p < 0.0001$) while in chronic cholycystitis group ($p < 0.05$). These results are in agreement with those reported by Fausa and Gjone [10] and Vucelic et al. [11] who found that total serum bile acids level was significantly increased in hepatitis patients than in control group. Also Agha and Zuberi [12] found that total serum bile acids were significantly higher in hepatitis and hepatoma patients with ($p < 0.001$) when compared with normal control group.

Ogawa et al. [13] found that serum bile acids were increased in obstructive jaundice patients and were correlated with serum ALP levels. Also Changbumrung et al. [14] reported a highly significant increase in total serum bile acids in hepatocellular carcinoma patients when compared with control group. Ali and Housni [1] Found that post-prandial total serum bile acids and ammonia (sensitivity 100% for both) were superior to other conventional liver function tests for detection of liver cirrhosis even in the anicteric phase (bilirubin < 3 mg/dl) as well as in cirrhotic cases with normal transferases.

In hepatitis group, we found that total serum bile acids was the most sensitive and accurate parameter (sensitivity 100%, accuracy 96%) when compared with liver enzymes, AST sensitivity was 92% and accuracy was 96%. ALT sensitivity was 93% and accuracy was 96%. ALP sensitivity was 76% and accuracy was 90% and 5'N sensitivity was 84% and accuracy was 93%. While GGT sensitivity was 76% and accuracy was 87%.

As regards obstructive jaundice, our results showed that total serum bile acids had a sensitivity of (100%) and accuracy of (97%) being more sensitive and accurate than accuracy of (97%) being more sensitive and accurate than routine liver enzymes. AST sensitivity was (78.5%), accuracy was (91%), ALT sensitivity was (71%), accuracy was (88%), ALP sensitivity was (85%) accuracy was (94%), GGT sensitivity was 78.%, accuracy was (88%), and 5'N had a sensitivity of (78.5%) and accuracy of (91%).

Also in hepatoma group, total serum bile acids level was found to be the most sensitive (100%) and accuracy (97%) while AST sensitivity was (71%) and accuracy was (88%), ALT sensitivity was (78%) accuracy was (91%), ALP sensitivity was (71%) and accuracy was (88%), GGT sensitivity was (85%) and accuracy was (91%) and 5'N had a sensitivity of (85%) and accuracy of (94%).

In contrast to the above mentioned groups in chronic cholycystitis, total serum bile acids was found to have a low sensitivity (23.5%) and accuracy (62%). On the other hand, AST was found to be the most sensitive (88%) and accuracy (94%), ALT sensitivity was (76%) and accuracy was (89%), ALP had a sensitivity of (11.7%) and accuracy of (59%), GGT sensitivity was (35%) and accuracy was (67%) while 5'N sensitivity was (11,7%) and accuracy was (59%).

With the exception of chronic cholycystitis group, our results come in concordance with those reported by Kaplowitz et al. [15], who found that total serum bile acids (2 hours post-prandial) to be more sensitive in detecting an abnormality than the fasting bile acids and other tests of liver function, and reported a sensitivity of 2-hours total serum bile acids of (100%) and other liver function tests as follows: BSP

(81%), ALP (74%) fasting bile acids (62%), 5'N (58%), AST (58%), ALT (41%) and serum bilirubin (35%).

In conclusion, our data demonstrate the superiority of sensitivity and accuracy of post-prandial total serum bile acids over the conventional liver enzymes in case of hepatitis, obstructive jaundice and hepatoma groups. While in chronic cholycystitis the most sensitive and the most accurate test is AST.

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