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Study of biochemical markers in jaundice : our experience

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ABSTRACT

Back ground and objectives : Jaundice is a common clinical disorder in tropical countries like India. It is defined as yellowish discolouration of skin, sclera and mucus membrane due to increase in serum bilirubin concentration which affects the liver function. The objective is to evaluate the liver function parameters in jaundice. Methods : Liver function parameters were estimated in 100 subjects suffering from jaundice to evaluate the clinical utility of these tests to differentiate hepatocellular jaundice from obstructive jaundice. 50 normal healthy subjects were studied as control group. Serum total bilirubin with its fractions(both conjugated and unconjugated bilirubin), ALT, AST,ALP, GGT and albumin were analysed by standared methods. Statistical analysis was done by student 't' test(unpaired-t test) and 'p' value was elicited. Results : We observed a significant increase in serum total bilirubin with its fractions($p < 0.001$) in both the types of jaundice compared to controls. Conjugated bilirubin, ALP & GGT were much more significantly increased in obstructive jaundice($p < 0.001$). Unconjugated bilirubin, ALT & AST were significantly increased and albumin levels were significantly decreased in hepatocellular jaundice($p < 0.001$). Conclusions : our results suggest that increase in unconjugated bilirubin, transaminases and decrease in albumin are in favour of hepatocellular jaundice. Increase in conjugated bilirubin, ALP & GGT are in favour of obstructive jaundice.

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1.Introduction

Jaundice is defined as yellowish discolouration of skin, sclera and mucus membranes which result from increase in serum bilirubin concentrations[1]. It is clinically detectable when plasma bilirubin exceeds by 3 mg/dl which is the catabolic end product of heme after removal of its iron component[2].

Jaundice is classified into 3 types : (a) prehepatic or haemolytic (b) hepatic or hapatocellular and (c) post hepatic or cholestatic or obstructive jaundice. Hepatocelular jaundice results from injury to the hepatocytes caused by various viral infections, drugs, chemicals and toxins. This results in decreased hepatocellular function and synthesis of albumin is decreased. Damaged liver cells release transaminases into blood circulation which reflects as increased serum transaminase levels[3]. Cholestasis is defined as a decrease in canalicular bile flow from the basolateral membrane of the hepatocyte to the entry of the bile duct into the duodenum

which may be due to intra hepatic or extra hepatic obstruction[4]. ALP is located at calicular and sinusoidal membrane(space of Disse)[5]. GGT is present in cell membranes in tissues like liver, kidney, pancreas, brain, spleen and seminal vesicles. Due to obstruction, damaged hepatocytes regurgitates bile with ALP and GGT back into blood circulation there by its levels are increased in serum[6].

It is necessary in all cases of jaundice to decide the type of expectant management which will bring best results in medical or hepatic jaundice or whether surgery is required in surgical or obstructive jaundice. Therefore differentiation between both the types of jaundice is very important for the clinician.

So the present study is aims to differentiate the type of jaundice by analysing a battery of liver function parameters.

2.Materials and methods

In order to help the clinician in differentiating the type of jaundice, a study was conducted in Department of Biochemistry in collaboration with Departments of medicine and surgery at Prathima Institute of Medical Sciences, Karimnagar, Andhra Pradesh. 100 patients who were admitted to medical and surgical wards of Prathima Hospital with in 2-3 weeks of onset of jaundice

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or suspected hepatobiliary disease i.e., hepatomegaly, right abdominal pain in the age group of 20-70 years were included along with 50 normal healthy subjects and grouped as follows:

Group – I : 50 normal healthy subjects as controls.

Group – II : 50 cases of hepatic jaundice.

Group – III : 50 cases of obstructive jaundice.

Both the sexes were included. Subjects below 20 and above 70 years, pregnant women, diabetes mellitus, hypertension, any type of malignancies, cardiovascular, respiratory disorders were excluded.

5 ml of venous blood was drawn from all the subjects of the study by venepuncture under all aseptic conditions. Blood was allowed to clot for 30 minutes, then centrifuged at 3000 rpm for 10 minutes to obtain a clear serum. This serum was used for various biochemical assays.

Serum total bilirubin with its fractions were estimated by modified Jendrassik and Grof technique, ALT & AST were estimated by UV-kinetic test according to IFCC, ALP by kinetic photometric test, albumin by BCG method(7). GGT was estimated by kinetic szasz method(8).

Statistical analysis was done by using standard student 't' test (unpaired 't'-test) and 'p' value was elicited. 'p' <0.05 was considered as significant.

3.Results

This study included 50 cases of normal healthy subjects as control group-I, 50 cases of hepatocellular jaundice as group-II and 50 cases of obstructive jaundice as group-III.

The mean and SD of serum total bilirubin in control group-I was 0.67 ± 0.2 , in hepatic jaundice group-II was 9.02 ± 1.3 and in obstructive jaundice group-III was 16.52 ± 2.5 . Significant increase in total bilirubin was found with the 'p' value of <0.001 in both the types of jaundice compared to that from controls group-I.

The mean and SD of conjugated bilirubin in controls group-I was 0.15 ± 0.05 , in hepatic jaundice group-II was 1.16 ± 0.6 and in obstructive jaundice group-III was 12.20 ± 1.92 . The mean and SD of unconjugated bilirubin in group-I was 0.53 ± 0.2 , in group-II was 6.86 ± 1.0 and in group-III was 4.34 ± 1.2 . Both the fractions of bilirubin were significantly increased ($p < 0.001$) in both the types of jaundice compared to that from controls. But conjugated bilirubin was more raised in obstructive jaundice and unconjugated bilirubin was more raised in hepatic jaundice.

The mean and SD of ALT and AST in group-I were 28.1 ± 8.1 & 28.3 ± 6.8 , in group-II were 394 ± 56.6 & 366 ± 41.8 and in group-III were 84.8 ± 9.7 & 76.4 ± 10.9 U/L respectively. Both ALT & AST were significantly increased in both the types of jaundice compared to group-I. But transaminases were more raised in group-II than that from group-III ($p < 0.001$).

Serum ALP levels in group-I was 83.2 ± 12.1 , in group-II was 108.2 ± 25.6 and in group-III was 404.4 ± 30.7 IU/L. Significant increase ($p < 0.001$) in ALP was observed in both the types of jaundice than from group-I, but the raise was more in group-III than that from group-II ($p < 0.001$).

The mean and SD of GGT in group-I was 21.5 ± 4.1 , in group-II was 44.4 ± 5.7 and in group-III was 180.5 ± 21.6 U/L. GGT increased in both the types of jaundice than the group-I ($p < 0.001$), but raise was more in group-III than that from group-II ($p < 0.001$).

The mean and SD of albumin in group-I was 4.1 ± 0.46 , in group-II was 2.5 ± 0.55 and in group-III was 2.5 ± 0.87 mg/dl. Albumin was decreased ($p < 0.001$) in both the types of jaundice than that from group-I, but there was no significance of albumin levels in group-II from group-III.

4.Discussion

Differentiation between the type of jaundice is important for the clinician to decide the treatment modality to the patient. Raise in serum total bilirubin levels indicate jaundice. Conjugated bilirubin much more increased in obstructive jaundice and unconjugated bilirubin increased in hepatic jaundice, but, they have limited diagnostic role as these fractions cannot particularly differentiate hepatic from obstructive jaundice[9].

Transaminases are commonly employed to ascertain liver function. Increase in transaminase level is the first and only signal of liver disease[10]. Stenmadson et al, Wroblewski et al in their study showed striking elevations in transaminases in hepatic jaundice. Though the raise was parallel to each other, increase in ALT was more than AST in hepatic jaundice. This raise in transaminases begins during early prodromal phase of the disease and reaches peak elevation which is usually 10-100 times greater than the normal and followed by gradual decrease towards normal range during recovery phase. Increase in transaminase activity upto 10 times the reference limit observed in obstructive jaundice and both ALT and AST were altered in the same direction. Marked elevation of transaminases show better discriminant power between hepatic from obstructive jaundice[11, 12, 13]. Our study was very well correlated with these earlier workers.

Striking elevations in ALP observed in extra hepatic obstruction than liver disease. Extra hepatic obstruction means simple mechanical obstruction of biliary tract with no destruction of hepatocytes with alteration in liver architecture. Marked increase in ALP i.e., more than 4 times to normal indicate obstructive jaundice[14]. Our study also showed the same.

GGT is a sensitive indicator of obstructive jaundice[15]. Increased GGT levels observed in extra hepatic biliary obstruction where as only mild elevation in GGT levels observed in liver disease. The raised GGT levels parallel with raised ALP levels in biliary obstruction and much higher GGT levels than ALP levels during obstruction of biliary tract. Our study also showed the increased levels of GGT, which is very well correlated with these

earlier workers. Disproportionate raise in transaminases compared to GGT indicate acute hepatic cellular necrosis a feature of acute viral hepatitis a cause for hepatic jaundice. Disproportionate raise in GGT compared to transaminase activity suggest biliary obstruction[16].

Liver is the primary organ for synthesis of most of the plasma proteins except immunoglobulins. Especially albumin levels indicate the synthetic function of liver[17]. Albumin levels were decreased in hepatocellular jaundice which shows decreased hepatocyte function in hepatic jaundice due to hepatocyte necrosis in viral hepatitis[18]. In our study also we observed decreased albumin in both the types of jaundice, but no much significance was observed between both the types of jaundice.

TABLE - 1 Total bilirubin with its fractions

| | Controls Group-I | Hepatic jaundice Group-II | p'-value | Conrols Group-I | Obstructive jaundice Group-III | p'-value |
|--------------|------------------|---------------------------|----------|-----------------|--------------------------------|----------|
| Total | Mean±SD | Mean±SD | | | | |
| Bilirubin | 0.67±0.2 | 9.02±1.3 | <0.001 | 0.67±0.2 | 16.51±2.5 | <0.001 |
| Conjugated | 0.15±0.05 | 1.16±0.8 | <0.001 | 0.15±0.05 | 12.16±1.9 | <0.001 |
| Bilirubin | | | | | | |
| Unconjugated | | | | | | |
| Bilirubin | 0.53±0.1 | 6.86±1.0 | <0.001 | 0.53±0.1 | 4.3±1.2 | <0.001 |

'p' value <0.001 was considered as statistically significant.

TABLE - 2 SERUM ENZYMES - ALT, AST ALP & GGT AND ALBUMIN

| | Controls Group-I | Hepatic jaundice Group-II | p'-value | Conrols Group-I | Obstructive jaundice Group-III | p'-value |
|---------|------------------|---------------------------|----------|-----------------|--------------------------------|----------|
| | Mean±SD | Mean±SD | | | | |
| ALT | 28.1±8.1 | 394±56.6 | <0.001 | 28.1±8.1 | 84.8±9.7 | <0.001 |
| AST | 28.3±6.8 | 366±41.8 | <0.001 | 28.3±6.88 | 76.3±10.9 | <0.001 |
| ALP | 83.2±12.1 | 108.2±25.6 | <0.001 | 3.2±12.1 | 404.4±30.7 | <0.001 |
| GGT | 21.5±4.1 | 44.4±5.7 | <0.001 | 21.5±4.1 | 180.5±21.6 | <0.001 |
| Albumin | 4.1±0.5 | 2.5±0.6 | <0.001 | 4.1±0.5 | 2.5±0.8 | <0.001 |

'p' value <0.001 was considered as statistically significant.

5. Conclusions

From this study, it can be concluded that increased unconjugated bilirubin, transaminases and decreased albumin levels are in favour of hepatic jaundice. Increased conjugated bilirubin, ALP (more than 4 times to the normal) and GGT levels are in favour of obstructive jaundice, which helps the clinician to differentiate the type of jaundice to give appropriate treatment to the patients

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