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RESEARCH ARTICLE

BIOCHEMICAL MARKERS AS PROGNOSTIC INDICATORS IN CHOLELITHIASIS AMONG ALCOHOLICS

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ABSTRACT

Gallstones disease provides significant input to surgical opd and cause morbidity worldwide. Cholelithias is develops because of an imbalance in the chemical composition of bile inside the gallbladder and it is due to multifactorial etiology which include chronic alcoholism. Symptomatic patient's will undergo cholecystectomy. The important complications of long term gallstones are acute pancreatitis, cholecystitis, obstructive jaundice which alter the liver function and decrease the life expectancy. The present study was conducted in vinayaka mission medical college and hospital, karaikalto assess the biochemical markers as prognostic indicators in patients with cholelithiasisamong alcoholics. A total of 22 patients (case) in which 11 alcoholics and 11 non alcoholics who were age and sex matched with multiple stones in gall bladder, symptomatic and undergoing cholecystectomy were recruited for this study. 25 normal individuals as controls were recruited for this study. Serum total and direct bilirubin were estimated by DMSO method. Serum SGPT, SGOT, GGT, Lipase, Amylase and Serum alkaline phosphatase level were estimated .In the present study liver function biochemical parameters were found to increase in alcoholic gallstone disease individuals when compared to healthy individuals and also compared to gallstone disease nonalcoholic subjects. ALP and Direct billirubin were significantly elevated in alchoholic gallstone disease subjects ($p=0.01$,$p=0.04$) when compared to healthy individuals. Thus elevated biochemical parameter levels in blood could predict the presence of liver damage and also indicates the severity of gallstone disease and its complications among alcoholics.

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INTRODUCTION

Gallstones are among the most common gastrointestinal disorders in Western as well as asian populations. Approximately 80 percent of gallstones contain cholesterol (as cholesterol monohydrate crystals). The remaining 20 percent are pigment stones, which consist mainly of calcium bilirubinate (Bosma *et al*., 1995). Cholesterol-containing gallstones are divided into two subtypes: cholesterol stones (which contain 90- to 100-percent cholesterol) and mixed stones (which contain 50- to 90-percent cholesterol). Each sub type may also contain varying amounts of calcium salts, bile acids, and other components of bile. Gallstone formation results from a combination of several factors, including super saturation of bile with cholesterol, accelerated nucleation of cholesterol monohydrate in bile, and bile stasis or delayed gallbladder emptying due to impaired gallbladder motility (Thomsen, 1981). Cholesterol supersaturation can result from an excessive concentration of cholesterol in bile, a deficiency of substances that keep cholesterol in solution (i.e., bile salts and phospholipids), or a combination of these factors.While most gallstones are asymptomatic, some patients experience biliary colic, which is characterized by sudden and severe colicky right-upper-quadrant pain (often accompanied by nausea and vomiting), occurs after a fatty meal and lasting one to four hours. Acute or chronic cholecystitis may also occur in association with gallstones. Complications of cholecystitis may include infection, perforation, and gangrene (Van Hootegem, 1985). Cholecystectomy is the most frequently recommended conventional treatment for symptomatic gallstones. Bile acids (ursodeoxycholic acid or chenodeoxycholic acid) are also used in some cases to dissolve radiolucent stones, but these drugs can cause gastrointestinal side effects and there is a high rate

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of stone recurrence after treatment is discontinued. Lithotripsy is used in some cases in conjunction with ursodeoxycholic acid for patients who have a single symptomatic non-calcified gallstone. There is evidence that dietary factors influence the risk of developing cholesterol gallstones (Doumas, 1997).

MATRIALS AND METHODS

A total of 22 patients in which 11alcoholics and 11 non alcoholics who were age and sex matched with multiple stones in gall bladder, symptomatic and undergoing cholecystectomy were recruited for this study. 25 normal individuals as controls were recruited for this study. Serum total and direct bilirubin were estimated by DMSO method. Serum SGPT, SGOT, GGT, Lipase, Amylase and Serum alkaline phosphatase level were estimated for research purpose in-patients from general and laparoscopic surgery department of vinayaka mission medical college and hospital karaikal. To verify the diagnosis of diabetes and NASH, determining the functional state of the liver using complex clinical laboratory, biochemical and instrumental methods. Statistical analysis Results were expressed as mean ± SD and mean ± SEM. Students t test was used to compare the data between patients and control groups

RESULTS

Table 1. Show the Comparison of Plasma Biochemical Changes between Case or Group A And Control Group B

Parameters	Case group with gall stones [GROUP A]	Control group healthy subjects GROUP [B]	P value
Total bilirubin [mg/dl]	0.93	0.52	<0.001*
Direct bilirubin [mg/dl]	0.62	0.32	<0.001*
SGPT [IU/L]	3.84	3.3	<0.001*
SGOT[IU/L]	34.1	32.3	<0.001*
ALP [IU/L]	15.3	11.0	<0.001*
GGT[IU/L]	75.4	35.2	<0.002*
LIPASE [IU/L]	61.2	42.1	<0.001*
AMYLASE [IU/L]	94.2	75.2	<0.001*

Legend: 1 All the parameter are increased in group A (case) when compared to group B(control)and direct bilirubin ,alkaline phosphatase (ALP) and gamma glutamyl transepeptidase (GGT) were significantly increases in group B when compared to group A

Table 2. Show the comparison of plasma biochemical changes between group 1(Alcoholic) and group (2) (non alcoholic) Gallstone diseased individuals in group A

Parameters	GROUP 1	GROUP 2	P value
Total bilirubin [mg/dl]	0.93	0.42	<0.006*
Direct bilirubin [mg/dl]	0.61	0.3	<0.002*
SGPT [IU/L]	3.62	3.31	<0.003*
SGOT[IU/L]	35.6	33.1	<0.006*
ALP [IU/L]	16.3	9.8	<0.001*
GGT[IU/L]	9.8	76.3	<0.002*
LIPASE [IU/L]	59.3	32.1	<0.006*
AMYLASE [IU/L]	93.2	73.2	<0.006*

Legend: 2 All the parameter are increased in group1 when compared to group 2, and direct bilirubin, alkaline phosphatase (ALP), SGPT and gammaglutamyltrance peptidase (GGT) were significantly increases in group 1(alcoholic) then group 2 (non alcoholic)

DISCUSSION

We discovered that gallstone disease affects the course of nonalcoholic steatohepatitis and accompanied by decompensation of carbohydrate, protein and lipid metabolism, as in patients of the third study group (nonalcoholic steatohepatitis without pathology of the gallbladder) changes in clinical and laboratory parameters were the most insignificant compared to first group and second group (Pugh *et al*., 1973). The amount of cholesterol in the bile is supposed to increase with age. This is caused by dyslipoproteinemia that results in a linear increase in cholesterol excretion into the bile and by the reduced synthesis of bile acids due to the dropped activity of the enzyme cholesterol 7α-hydroxylase (CYP7A1) (Bonis *et al*., 1999).

The xenobiotic receptor, pregnant X receptor (PXR), has a role in the pathogenesis of cholesterol GD. PXR prevents cholesterol GD via its coordinated regulation of the biosynthesis and transport of bile salts in the liver and intestine. Cholesterol precipitation is prevented by increases in concentrations of biliary bile salts and a reduced cholesterol saturation index (CSI). Loss of PXR sensitized mice to lithogenic diet-induced cholesterol GD, characterized by decreases in biliary concentrations of bile salts and phospholipids and increases in the CSI and formation of cholesterol crystals (Kamath *et al*., 2001). The decreased bile acid pool size in PXR-/- mice that received lithogenic diets was associated with reduced expression of CYP7A1, the rate-limiting enzyme of cholesterol catabolism and bile acid formation. The reduced expression of CYP7A1 most likely resulted from activation of PXR and induction of fibroblast growth factor 15 in the intestine. Normal bile consists of 70% bile salts (mainly cholic and chenodeoxycholic acids), 22% phospholipids (lecithin), 4% cholesterol, 3% proteins, and 0.3% bilirubin. An increased expression of gel-forming mucin, such as MUC5AC and MUC2, was found in patients with hepatolithiasis (Williams *et al*., 1998).

Giannini E and coworkers described a positive correlation between MUC1 and MUC5A **C**expression, indicating a gene-gene interaction that might affect the accumulation of mucin gel and cholesterol GS formation. Bile mucin is derived from pure hepatic bile, gallbladder-concentrated bile, and mucin secreted by the bile duct epithelium. In patients with biliary sludge, mucin concentration was higher in bile collected by endoscopic retrograde cholangiography than in gallbladder bile. Cholestasis enhances the synthesis and release of ALP, and accumulating bile salts increase its release from the cell surface.ALP half-life in the circulation is about 1 week (Doumas, 1997). These characteristics explain why ALP levels usually rise late in bile duct obstruction and decrease slowly after resolution (Giannini, 1999). Elevated GGT levels can be observed in a variety of nonhepatic diseases, including chronic obstructive pulmonary disease and renal failure, and may be present for weeks after acute myocardial infarction. Increased serum levels observed in alcoholic liver disease can be the result of enzyme induction and decreased clearance (Giannini *et al*., 2003).

Conclusion

Alterations in liver biomarkers levels are most commonly used prognostic indicators in patients with cholelithiasis which will be more significantly elevated in alcoholics. we can asses the severity and predicit the difficulties during cholecystectomy by assesing the biomarkers in combination with other investigations. Finding the way through the multiple diagnostic pathways can challenge even the experienced

clinician. The pattern of enzyme abnormality, interpreted in the context of the patient's characteristics, can aid in directing the subsequent diagnostic work-up.

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