

ORIGINAL RESEARCH ARTICLE

A STUDY OF THE CORRELATION BETWEEN HISTOPATHOLOGICAL EXAMINATION OF THEHEPATOBILIARY TISSUE WITH SERUM ALANINE AMINOTRANSFERASE AND ALKALINE PHOSPHATASE

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Abstract

Background: Several biochemical tests are useful in the evaluation and management of patients with hepatic dysfunction. These tests can be used to detect the presence of liver disease, distinguish among different types of liver disorders, gauge the extent of known liver damage, and follow the response to treatment. ALT reflects damage to hepatocytes and it is found primarily in liver in low concentrations and get released into the blood in greater amount when there is damage to liver cell membrane resulting in increased permeability. The activity of ALP in a pathological condition is usually elevated in cholestasis.Non-pathologically it is also elevated in children and adolescents undergoing rapid bone growth and in late pregnancy. The main objective of this study was to correlate these serum biomarkers with the histopathological reports of the resected gallbladder specimen.

Methodology: This study was conducted prospectively on 493 patients in a tertiary care hospital in eastern Uttar Pradesh (India). In year 2019, from January to December, patients admitted for cholecystectomy in surgery ward of this hospital were included in this study. After surgery, about 3-4 ml of the blood sample was obtained and analyzed in the biochemistry laboratory after proper control and calibration, meeting the quality standard of the laboratory. Results thus obtained were correlated with the histopathological report of the gallbladder specimen provided by the pathology department of the institute.

Results: In our study, out of 493 patients it was observed that 70 (14.2%) patients were males with mean age of 39.6 years and 423 (85.8%) patients were females with mean age of 37.6 years. 'Chronic cholecystitis with cholelithiasis' was reported in 284 (57.6%) patients with mean values of serum ALT as 79.9 IU/L and serum ALP as 263.9 IU/L. 'Chronic cholecystitis' was reported in 79 (16%) patients with mean values of serum ALT as 59.1 IU/L and serum ALP as 228.1 IU/L. **Conclusion:** From our study, we concluded that in patients of chronic cholecystitis with cholelithiasis, observed values of serum ALT and serum ALP were much higher than in chronic cholecystitis.

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Introduction:-

Liver function tests (LFT) are one of the most commonly requested screening or diagnosing blood tests which are used for the investigation in suspected liver disease, for monitoring a disease or simply as routine blood analysis. For evaluation and management of patients with hepatic dysfunction, some biochemical tests may prove very useful to detect the presence of liver disease, distinguish among different types of liver disorders, gauge the extent of known liver damage, and follow the response to treatment.^[1]Many biochemical functions performed by liver may not be easily measured by these blood tests. In fact, many tests like the aminotransferases or alkaline phosphatase, do not measure liver function at all.Rather, they detect liver cell damage or interference with bile flow.The aminotransferases includes the aspartate aminotransferases (AST) and the alanine aminotransferases (ALT) which are sensitive indicators of liver cell injury and are most helpful in recognizing acute hepatocellular diseases such as hepatitis.AST is found within the liver, heart muscle, skeletal muscle, kidneys, brain, pancreas, lungs, leucocytes and erythrocytes in decreasing order of concentration, whereas ALT is found primarily in the liver.Normally, aminotransferases are present in the serum in low concentrations and get released into the blood in greater amounts when there is damage to the liver cell membrane resulting in increased permeability. However, aminotransferase level starts decreasing quickly and the liver function tests rapidly evolve into one typical of cholestasis.^{[2][3]}The normal serum alkaline phosphatase consists of many distinct isoenzymes found in the liver, bone, placenta, and less commonly small intestine. Normally, it is elevated in children and adolescents undergoing rapid bone growth because of bone alkaline phosphatase, and late in normal pregnancies due to the influx of placental alkaline phosphatase. If an elevated serum alkaline phosphatase is the only abnormal finding in an apparently healthy person, or if the elevation is higher than expected, identification of the source of elevated isoenzymes is helpful. First, and most precise is the fractionation of the alkaline phosphatase by electrophoresis. The second approach is based on the observation that alkaline phosphatases from individual tissues differ in susceptibility to inactivation by heat. The finding of an elevated serum alkaline phosphatase level in a patient with heat stable fraction strongly suggests that the placenta or a tumor is the source of elevated enzyme in the serum. Susceptibility to inactivation by heat increases respectively for the intestinal, liver, and bone alkaline phosphatase, bone being by far the most sensitive.

Methodology:-

It was a prospective study conducted at Uttar Pradesh university of medical sciences (U.P.U.M.S.) Saifai-Etawah, one of the largest tertiary care hospital and medical college of eastern Uttar Pradesh, India, after the clearance of the institute's ethical committee. The duration of the study was one year i.e., from January 2019 to December 2019. The study was carried out on all male and female patients of age above 18 years and who were diagnosed as having gallstones, or any other benign biliary disease which requires simple cholecystectomy. All elective patients undergoing cholecystectomy either by open or by laparoscopic method, were included in our study. All those patients who were below 18 years, pregnant ladies, and non-cooperative patients who refused to give written consent for participation in the study were excluded from the study.Brief history of the patients were taken as per the proforma from the OPD of general surgery and blood samples of those patients were obtained from the ward by venipuncture after 12-24 hrs of the surgery for gallbladder resection. Around 3-4 ml of the venous blood was collected in a plain vial and it was then allowed to clot at room temperature for about 1 hour and then centrifuged in the biochemistry laboratory of the institute at 4000 rpm for 4 min. The serum thus formed was analysed immediately for ALT and ALP on Selectra pro XL with commercial kits manufactured by ELITech group. To assess serum ALT, UV kinetic method without pyridoxal phosphate (P-5'-P), based on IFCC was used, which works on the principle of kinetic determination of alanine aminotransferase (ALT) activity. Serum ALP was analysed by kinetic enzymatic method based on DGKC and SCE method. It works on the principle that in presence of Mg2+ and diethanolamine as phosphate acceptor, p-nitrophenylphosphate is transformed by alkaline phosphatase into phosphate and pnitrophenol (vellow compound). To check the accuracy of assays, control sera such as ELITROL I and ELITROL II were used. These controls were performed and validated before the patient samples are assayed. Out of control values were calibrated to get the results within the defined ranges. For staining, hematoxylin and eosin staining, a 10 step procedure was used for formalin-fixed, paraffin embedded (FFPE) tissue of gallbladder.

Results:-

In our study, it was observed that out of total 493 patients, 423 (85.8%) were females and 70 (14.2%) were males. The mean age of female patients was 37.6 years and that of male patients was 39.6 years. Also, 284 (57.6%) patients were of 'chronic cholecystitis with cholelithiasis' and 79 (16%) patients were of 'chronic cholecystitis constitutes nearly about three-fourth of the total pathologies, so the rest

one-fourth were not reported here in this study. The mean value of serum ALT and serum ALP in patients of chronic cholecystitis with cholelithiasis was 79.9 IU/L and 263.9 IU/L respectively and these values in patients of chronic cholelithiasis was 59.1 IU/L and 228.1 IU/L respectively.

	TOTAL PATIENTS	PERCENTAGE	MEAN AGE (years)
MALE	70	14.2 %	39.6
FEMALE	423	85.8 %	37.6

Table 1:- Total number of male and female patients with their percentage and mean age.

Discussion:-

The gall bladder is amongst the most common surgically resected organs, and the number of cholecystectomies has increased by more than 50% in the past decade worldwide. The layers that comprise the gallbladder wall are mucosa (surface epithelium and its lamina propria), smooth muscle, perimuscular subserosal connective tissue (also referred to as subserosa or adventitia), and serosa, the latter being present only on the free surface. There is no submucosa or muscularis mucosa in the gallbladder.^{[4][5][6]}The mucosal layer is thrown into variably sized branching folds which are more prominent when the organ was contracted. The surface epithelium consists of a single layer of tall columnar cells containing abundant pale, eosinophilic, apical cytoplasm and basally located nuclei with inconspicuous nucleoli.In diseased gallbladders, a spectrum of gastric and intestinal metaplasia may appear, including argyrophilic and argentaffin cells, which are not present normally.^{[7][8][9]}Because the epithelium is quite susceptible to bile related autolysis, prompt fixation of gallbladders was done. A total of three full-thickness sections (one each from the fundus, body and neck/cystic duct region) of the gallbladder were routinely taken and placed in one cassette. Several full-thickness sections were taken from larger masses, to include the area of deepest mural penetration. The cystic duct resection margin ought to be examined routinely because both in situ and invasive carcinomas can be subtle and difficult to identify by macroscopic examination.^{[10][11]}Chronic cholecystitis^{[12][13]} is the most commonly encountered disease of the gallbladder and the overwhelming majority of cholecystectomies are performed for chronic cholecystitis. It is associated with cholelithiasis in more than 90% of the cases. Therefore, as with gallstones and other researcher's studies, there is a female predominance. The pathologic findings vary depending on the severity and the duration of the disease.Calculi are present in more than 90% of the cases.The gallbladder itself may appear nearly normal or show thickening of the wall.In more severe cases, the gallbladder may be shrunken, with marked fibrous thickening of the wall and serosal scarring associated with adhesions to adjacent organs. In additions, the mucosa may appear granular, ulcerated, or exhibit regenerative polyploid areas.

Cholelithiasis^{[14][15]} is a common disorder afflicting 10% to 20% of adult populations in developed countries. It occurs predominantly in females and the incidence increases with age, possibly resulting from a progressive increase in the secretion of biliary cholesterol.^{[16][17][18]}Cholesterol stone formation requires the supersaturation of bile with cholesterol, which results from increased biliary cholesterol output, decreased bile acid synthesis, or both gall bladder hypomotility and mucinhypersecretion promote the precipitation and agglomeration of cholesterol monohydrate crystals into stones. The appearance of cholesterol stones varies depending on the cholesterol content.^{[19][20][21]}In our study, out of total 493 patients, 463 (93.9%) cases were reported for chronic cholecystitis and out of these 463 chronic cholecystitis cases 355 (76.6%) were found to be associated with cholelithiasis.

Conclusion:-

In the light of findings, it was concluded that most of the pathologies were of chronic cholecystitis with cholelithiasis and chronic cholecystitis. These two together constitutes for>75% of the total pathologies. More than three-fourth of the total patients were females which follows the rule of fat, fertile, female of forty is more susceptible for gallbladder diseases. In patients of chronic cholecystitis with cholelithiasis, values of ALT and ALP were raised much more than in chronic cholecystitis. Values of serum ALT in more than 65% of patients lied between 41-100 IU/L and values of serum ALP in more than 68% of patients lied between 101-300 IU/L. This indicates that the hepatic injury due to any obstruction in the hepatobiliary system is mild and transient.

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