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Biochemical Investigation in Prediction of Acute Pancreatitis

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Abstract
Acute pancreatitis is a common clinical presentation. Gall stone disease and alcohol consumption are most common etiologies. Detection of biliary etiology is important in order to provide definite management in the form of cholecystectomy to prevent attacks .Sensitivity for abdominal ultrasound to detect cholelithiasis is decreased to 67-87% in presence of acute pancreatitis. Difference in biochemical investigations of acute biliary and non biliary pancreatitis has been proposed to increase the suspicion of biliary etiology.

A Cross sectional study was conducted in the Department of Biochemistry, Government Medical College, Jammu, J&K, India, with a diagnosis of first episode of acute pancreatitis during a period of 3 months i.e. May 2017 to July 2017. Alanine Transaminase levels were found higher in biliary group but not statistically significant. Meanwhile mean of serum amylase was found much higher in biliary group. Further investigations suggested that the biliary etiology of Acute Pancreatitis should be considered in female patients with deranged Lever Function Test and highly raised serum amylase level even if initial Abdominal Ultra Sound do not detect cholelithiasis. Negative for cholelithiasis in this subset of patient should not be accepted. Thus definite management of cholelithiasis may be based upon early derangement of biochemical investigations while Endoscopic Ultra Sound seems to be a non mandatory investigation to detect the biliary cause of Acute Pancreatitis.

Keywords: *Acute Pancreatitis, Cholelithiaisis, Amylase.*

Introduction

Acute pancreatitis (AP) is an acute inflammatory process of pancreas that frequently affects the pancreatic tissues and less frequently affects the systemic organs.(1) Identification of biliary cause of pancreatitis is important to provide definite management in the form of cholecystectomy to prevent the further attacks.(2) Biliary tract diseases such as cholecystitis, cause up to four fold elevations of the serum amylase activity a result of either primary or secondary pancreatic involvement Abdominal ultrasound is the most important tool to detect cholelithiasis wih sensitivity of almost 100% in uncomplicated situation which decreases to 67% to 87% in AP.(3) Endoscopic ultrasound has higher rate of detecting biliary etiology resulting in 75% of initially diagnosed idiopathic acute pancreatitis to be biliary pancreatitis but endoscopic ultrasound is currently not available in Jammu. Several

biochemical parameters such as bilirubin , alkaline phosphatise, alanine transaminase, serum amylase have been proposed to identify a biliary etiology.[4]

Aim of the study is to investigate the difference in biochemical parameters between biliary and non-biliary acute pancreatitis and its role in detection of biliary etiology.

Materials and Methods

A Cross sectional study was conducted in the department with a diagnosis of first episode of acute pancreatitis during a period of 3 months i.e. May 2017 to July 2017. Patients with chronic liver diseases and those not giving consent were excluded in this study. Written informed consent was taken from the patients. Ethical approval was taken from institutional review board.

Diagnosis of acute pancreatitis was made if two of the following three features were made.

Abdominal pain consistent with acute pancreatitis; serum amylase values corresponding to more than three times than normal; characteristics finding of AP by Abdominal Ultra Sound (AUS), contrast enhanced computed tomography, CECT abdomen or Magnetic Resonance Imaging (MRI).

Diagnosis of biliary and alcoholic pancreatitis was confirmed by the presence of gallstones by AUS and history of alcohol binge without gall stones respectively. Patients with dyslipidemia, hypercalcemia, history of drug intake known to cause acute pancreatitis, trauma, endoscopic retrograde cholangio pancreatography (ERCP) in the absence of other cause were considered to have acute pancreatitis related to these causes. Patient without any identifiable cause were labelled as idiopathic pancreatitis.

Acute pancreatitis is common and significant disorder. Most of the cases (around 75%) are caused by biliary stones and heavy drinking. It approximately affects 200,000 individuals in US alone.

The current British Society of Gastroenterology Guidelines for the management of acute pancreatitis has also suggested a preference towards the measurement of lipase levels for the diagnosis of acute pancreatitis. At present due to the availability of serum amylase, tests are frequently requested concurrently in patients presenting with acute abdominal pain. The purpose of test is to confirm the diagnosis of pancreatitis, irrespective of etiology. All the subjects were admitted in the surgery Ward with first episode of abdominal pain, some advised for serum total bilirubin, Aspartate Transaminase (AST), Alanine Transaminase (ALT), Alkaline Phosphatase (ALP), serum amylase investigations. Investigations done were included in the study irrespective of age. 2ml of venous blood was collected from antecubital vein under aseptic conditions and serum was separated for above written investigations.

TBI method was evaluated for interference according to CLSI/NCCLS EP7-A.[5] It is a modification of Doumas reference method[6] (which is a modification of Diazo method described by Jendrassik and Grof in 1938).[7] Briefly, diazotized suphanilic acid is formed by combining sodium nitrite and suphanilic acid at low pH. Bilirubin (unconjugated) in the sample is solubilized by dilution in a mixture of EDTA. Upon addition of diazotized suphanilic acid the solubilized bilirubin including conjugated bilirubin and the delta forms is converted to diazobilirubin, a red chromophore which absorbs at 540nm.Sampling, reagents delivery, mixing, processing and printing of results were automatically performed by the Siemens Dimension Clinical Chemistry system.

Reference range [5]:

Normal subjects: total serum bilirubin: 0.2-1mg/dl.

Clinical jaundice: total serum bilirubin ≥2 mg/dl.

AST method

Aspartate aminotransferase catalyse the transamination of L-aspartate to alpha ketoglutarate, forming oxaloacetate reduced to malate by malate dehydrogenase with simultaneous oxidation of reduced NADH change

in absorbance with time due to the conversion of NADH to NAD is directly proportional to AST activity and is measured using a bichromatic (340, 700nm).[8] Sampling, reagents delivery, mixing, processing and printing of results were automatically performed by the Siemens Dimension Clinical Chemistry system.
Expected value 15-37 U/L[8]

ALT
Alanine aminotransferase catalyse the transamination of L-alanine to alpha ketoglutarate and pyruvate and is reduced to lactate by Lactate Dehydrogenase (LDH) with simultaneous oxidation of reduced NADH change in absorbance to ALT activity is measured using bichromatic rate technique.[8] Sampling, reagents delivery, mixing, processing and printing of results were automatically performed by the Siemens Dimension Clinical Chemistry system.
Expected value 30-65 U/L[9]

ALP
Alkaline phosphatise catalyzes the transphosphorylation of p-nitrophenol in the presence of the transphosphorylating buffer, 2amino-2methyl-1-propanolol the reaction is enhanced through the use of magnesium and zinc ions .the change in absorbance at 405nm due to the formation of p-nitrophenol is directly proportional to ALP activity, since other reactants are present in non rate limiting quantities and is measured using a bichromatic (405, 510nm).[10] Sampling, reagents delivery, mixing, processing and printing of results were automatically performed by the Siemens Dimension Clinical Chemistry system.
Expected value. 50-136U/L[11]

Amylase
Alpha amylase catalyze the hydrolysis of a defined synthetic substrate 2-chloro-4-nitrophenyl, D-maltoside, maltriose and glucose. After an incubation of 70seconds at 37 c the absorbance due to the formation of 2-chloro-4-nitrophenol is measured using a bichromatic (405, 577 nm) rate technique.[12]
A simple rapid and accurate prediction of cholelithiasis as etiology of acute pancreatitis can be provided by changes in biochemical parameters. EUS is not always necessary to detect the biliary cause of acute pancreatitis.
Expected value: 25-115 IU/L[13]

Results
Total 120 patients were found admitted with diagnosis of acute pancreatitis (AP) out of which 77 and 42 had biliary and non biliary etiology. The etiology in non-biliary groups included alcoholic, traumatic, malignancy and idiopathic (Table 1)

Table 1: Etiologies in non-biliary group

Etiology	Number	Percentage
Alcoholic	19	45.24 %
Idiopathic	20	47.62 %
Traumatic	2	4.76 %
Malignancy	1	2.38 %

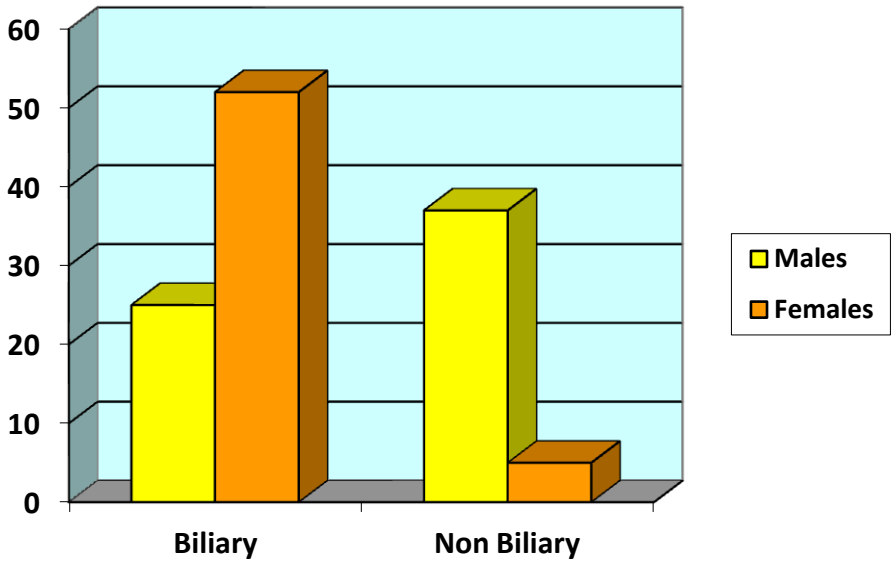
As regards the distribution of severity of pancreatitis, i.e. mild, moderate or severe, both the biliary and non-biliary groups showed the similar pattern and diversity. (Table 2)

Table 2: Distribution of Severity of pancreatitis

Etiology	Biliary	Non Biliary
Mild Acute Pancreatitis	45	29
Moderately Severe Acute Pancreatitis	21	9
Severe Acute Pancreatitis	11	4

Regarding the distribution of patients on the basis of gender, the number of female patients was higher and statistically very significant in Biliary group (52 : 5, P=0.00) (Figure 1) Considering the fact that Alcoholic being the primary etiology amongst men, Ideopathic assumes more significance amongst females.

Figure 1



Bar Chart showing distribution of patients on the basis of sex

Mean values of total bilirubin, direct bilirubin, AST, ALT and ALP levels were higher in biliary group. However mean of serum amylase was much higher in biliary group and statistically significant (Table 3)

Table 3: Mean values of various biochemical investigations

Investigation	Biliary	Non-Biliary	P Value
Total Bilirubin	2.16 mg/dl	1.88 mg/dl	.073
Direct Bilirubin	1.07 mg/dl	0.91 mg/dl	.043
Serum Amylase	2646.92 U/l	1272.45 U/l	.007
ALP	461.25 U/l	321.67 U/l	.112
ALT	168.0 U/l	102.08 U/l	.101
AST	189.43 U/l	106.92 U/l	.093

Discussion

Most common etiologies of Acute Pancreatitis are gallstone disease and alcohol consumption which accounts for almost 80 to 90% of cases. Other eliologies included infections, and metabolic disorders, trauma, endoscopic retrograde cholangio pancreatography, etc. Distinction of biliary pancreatitis is important in order to provide specific treatment like cholecystectomy or ERCP in the patient. The association between rise in hepatic transaminase level and biliary pancreatitis was first suggested by McMohan and Pickford.[14] ALT is the most commonly used to predict biliary etiology and is thought to be the most useful of the available biochemical investigations in predicting gall stone etiology of AP, however in current study ALT levels was higher in biliary group but not statistically significant (0.101). Anderson et al[15] suggested that ALT rather than AUS alone is an important investigation to justify cholecystectomy in patient presenting with AP.

Biliary etiology of AP should be considered in female patients with deranged LFT and Highly raised serum amylase level even if initial AUS do not detect cholelithiasis. Negative AUS for cholelithiasis in this subset of patient should not be accepted. Definite management of cholelithiasis may be based upon early derangement of biochemical investigations. EUS is recommended in patients with idiopathic pancreatitis with normal LFT. There were 20 patients of idiopathic pancreatitis, if they were subjected to further investigations like EUS, biliary cause could have been identified, which tantamount to the limitations of the current study.

Conclusion

Biochemical investigations are providing a thorough and accurate route towards detecting AP and predictions towards cholelithiaisis, thus

making EUS as a non mandatory investigation to detect the biliary cause of AP.

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