The Significance of Hepatobiliary Enzymes for Differentiating Liver and Bone Diseases: A Case Control Study from Manipal Teaching Hospital of Pokhara Valley

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Original Article

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Abstract

Background

Serum alkaline phosphatase (ALP) is a member of a family of zinc metalloprotein enzymes and is secreted mainly by the liver, bone, mucosal epithelia of small intestine, proximal convoluted tubule of kidney and placenta. High mitochondrial aspartate transaminase (AST) is seen in extensive tissue necrosis during myocardial infarction and also in chronic liver diseases like liver tissue deterioration and necrosis. Marked elevations of alanine transaminase (ALT) levels are observed with diseases that involve primarily hepatocytes such as viral hepatitis, ischemic liver injury (shock liver) and toxin-induced liver damage. Serum gamma –glutamyl transferase (γ-GT) activity is mainly attributed to the hepatobiliary system and most commonly raised in alcoholic liver disease. The objective of this study is to diagnose hepotobiliary and bone diseases with the facilitation of various biochemical markers as single enzyme lacks the specificity.

Materials and methods

It was a hospital based case control study carried out in the Department of Biochemistry of Manipal Teaching Hospital, Pokhara, Nepal between 1st January 2010 and 31st July, 2011. The variables collected were age, gender, aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and gamma–glutamyl transferase (γ-GT). The One way ANOVA was used to examine the statistical significant difference between groups. Post Hoc test LSD used for the comparison of means of control versus case groups. A p-value of <0.05 (two-tailed) was used to establish statistical significance.

Results

Of 1500 subjects enrolled in our study, 1200 were cases and 300 were controls. Cases were of viral hepatitis, extrahepatic cholestasis, Paget's disease and osteomalacia.

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The values of AST and ALT were markedly raised in cases of viral hepatitis when compared to controls, Paget's disease and osteomalacia (p=0.0001). ALP was raised in cases of Paget's disease 1434.8±219.5 (CI 1409.8, 1459.8), extrahepatic cholestasis 907.6±282.8 (CI 875.5, 939.7), osteomalacia 511.8±198.9 (CI 489.2, 534.4) (p=0.0001). γ-GT values was found to be significantly raised in cases of extrahepatic cholestasis when compared to controls (p=0.0001).

Conclusion

It is not easy for clinicians to differentiate and diagnose liver and bone diseases correctly with a single hepatobiliary enzyme. Correlation of variation in several biochemical markers increases the sensitivity and specificity for segregate and identification of liver and bone diseases for proper treatment and prognosis.

Key words

Hepatobiliary Enzymes, Liver and Bone Diseases, Nepal

Background

The hepatobiliary enzymes varies substantially in viral hepatitis, extrahepatic cholestasis, Paget's disease and osteomalacia. Hepatitis types A, B, and C are the highest critical forms of viral hepatitis in the United States. Epidemics of hepatitis A and endemic transmission of both hepatitis B and hepatitis C is usually due to high-risk sexual behaviour and drug use. HCV infection was responsible for 1.3% of acute viral hepatitis in Nepal. The existence of numerous drug abusers in the country may result in the emergence of HCV as a vital cause of chronic liver disease in Nepal in future[1].

Extrahepatic cholestasis occurs outside the liver. It can be caused by bile duct tumors, cysts, narrowing of the bile duct (strictures), stones in the common bile duct, pancreatitis, pancreatic tumor or pseudocyst, pressure on an organ due to a nearby mass or tumor and primary sclerosing cholangitis. In Asia, there is a much higher incidence of extrahepatic cholestasis than in Western countries[2]. Paget's disease of bone is a chronic disorder, characterized by focal areas of excessive osteoclastic bone resorption accompanied by a secondary increase in osteoblastic bone formation. Paget's disease of bone shows an increasing frequency of occurrence with age and also varies with genetic, cultural, environmental, social, racial differences. The prevalence of Paget's disease of bone is about 3% of people aged over 40; 10% by age 80 and prevalence rate for Paget's disease of bone is approximately 1 in 33 or 3.00%in the USA[3]. Osteomalacia is the softening of the bones caused by inadequate or delayed mineralization of osteoid in mature cortical and spongy bone secondary to inadequate amounts of available phosphorus and calcium. The causes of osteomalacia are lack of calcium and vitamin D in the diet, not enough exposure to sunlight, malabsorption of vitamin D by the intestines, use of very strong sunscreen, cancer, hereditary or acquired disorders of vitamin D metabolism, kidney failure and acidosis, liver disease, phosphate depletion associated with not enough phosphates in the diet and as side effects of medications used to treat seizures[4].

Serum alkaline *phosphatase* (ALP) is a member of a family of zinc metalloprotein enzymes and is expressed mainly from the liver, bone, mucosal epithelia of small intestine, proximal convoluted tubule of kidney, and placenta[5]. It carries out calcification in bone. The serum ALP activity is mainly from the liver with 50% contributed by bone. The most frequent basis of augmentation of serum ALP level is found in obstructive liver disease and metabolic bone diseases[6]. AST exists in two genetically different isoenzymes, mitochondrial and cytoplasmic forms[7]. AST is present in higher concentration in the heart as compared to other tissues of the body such as liver, skeletal muscle and kidney. High mitochondrial AST can be seen in extensive tissue necrosis including myocardial infarction and chronic liver diseases like liver cirrhosis in which tissue deterioration and necrosis occurs[8]. Though ALT is found in kidney, heart and muscle, its greater concentration is in liver when compared to other tissues of the body. ALT is purely a cytoplasmic enzyme and it catalyses the transamination reaction. Marked elevations of ALT levels are observed with diseases that involve primarily hepatocytes such as viral hepatitis, ischemic liver injury (shock liver) and toxin-induced liver damage[9]. γ-GT is a membrane bound enzyme present in hepatocytes and biliary epithelial cells, renal tubules, pancreas and intestine. It also helps in transport of peptides into the cell across the cell membrane and involves in glutathione metabolism[10]**.** Serum γ-GT activity is mainly attributed to hepatobiliary system and is most commonly seen in alcoholic liver disease. The objective of this study is to diagnose the hepotobiliary and bone diseases with the help of various biochemical markers as a single enzyme lacks specificity.

Materials and methods

Study design and the participants

A hospital based case control study was carried out in the Department of Biochemistry of Manipal Teaching Hospital, Pokhara, Nepal. It was chosen for the study because Manipal teaching hospital is a tertiary care 825 bedded

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hospital and it was expected that most of the patients will come to this hospital from Western Nepal.

Data collection

The present study was undertaken between 1st January 2010 and 31st July, 2011 in the Department of Biochemistry at Manipal Teaching hospital. The variables collected were age, gender, aspartate transaminase, alanine transaminsase, alkaline phosphatase, γ-glutamyl transferase. The transaminases (AST and ALT) were estimated by liquid UV test[11]. Estimation of serum alkaline phosphatases was done by standard enzymatic method[12]. Assay of serum gamma-glutamyl transferase activity was based on the hydrolysis of the substrate L-gamma-glutamyl-3-carboxy-4-nitranilide[13]**.** All these laboratory parameters were analyzed using Human reagent kits and with the help of semi autoanalyser (Human, Germany).

Inclusion criteria

Patients with increased aminotransferase levels (greater than 1.5 times normal) for at least six months, presence of anti-HCV and anti-HBV in serum, minimal to nil alcohol consumption (less than 30 g/day for men and less than 20 g/day for women) with chief complaints related to vomiting, hepatomegaly, jaundice or ascites were included in our study. Extrahepatic cholestasis group comprised of 300 subjects with intraluminal, intramural or extraluminally obstruction. Patients have a diagnosis of Paget's disease, bone deformities and radiological signs of Osteomalacia were also included. Control group comprised of 300 healthy subjects with age and sex distribution similar to the clinical groups.

Exclusion criteria

Exclusion criteria were patients with history of an alcohol intake of more than 40 g per day, severe cardiac or renal disease, and active intravenous drug abuse. Patients receiving previous treatment with interferon or immunosuppressive agents or were taking medication that could cause steatosis (i.e. salicylates, nonsteroidal anti-inflammatory drugs, corticosteroids, valproic acid, amiodarone, perhexiline maleate), treated with zoledronic acid who relapsed and was retreated with anti-resorptive bisphosphonate or calcitonin therapy within the last 12 months, Bisphosphonate hypersensitivity, patients with suspected/ proven metastases at retreatment, Active primary hyperparathyroidism, hypoparathyroidism, presence of tubulopathy, hypercalciuria were also excluded from the study.

Sample size calculation

For the sample size calculation with 95% confidence interval and significance level α = 5%. We conducted a pilot study of 100 cases each of all the diseases included in this study. In extra hepatic cholestasis, σ= SD of the ALP = 285, allowable error = 35, and required sample size was 255. In Paget's disease, σ= SD of the ALP = 220, allowable error = 25, and required sample size was 298. In Osteomalacia, σ= SD of the ALP = 200, allowable error = 24, and required sample size was 267. σ= SD of the ALP in Osteomalacia cases. In Viral hepatitis, σ=500, allowable error = 57, and required sample size was 296. σ= SD of the ALT in cases of viral hepatitis[14-17].

Outcome variables

The levels of AST, ALT, ALP, γ-gt were assessed in cases of viral hepatits, extra hepatic cholestasis, Paget's disease osteomalacia and controls.

Explanatory variables

Factor at individual level were age, gender (male and female).

Ethical committee approval

Preceding the study, approval for the study was obtained from the institutional research ethical committee.

Data management and statistical analysis

Analysis was done using descriptive statistics and testing of hypothesis. The data was analyzed using Excel 2003, R 2.8.0, Statistical Package for the Social Sciences (SPSS) for Windows Version 16.0 (SPSS Inc; Chicago, IL, USA) and the EPI Info 3.5.1 Windows Version. The One way ANOVA was used to examine the statistical significant difference between groups. Post Hoc test LSD used for the comparison of means of control versus case groups. A p-value of <0.05 (two-tailed) was used to establish statistical significance**.**

Results

Of 1500 subjects enrolled in our study, 1200 were cases and rest 300 were controls. Cases taken were of viral hepatitis, extraheaptic cholestasis, Paget's disease and osteomalacia. For all subjects, mean values and confidence interval was calculated with all variables taken into our study.

Table 1 illustrates that values of AST and ALT were markedly raised in cases of viral hepatitis when compared to controls, Paget's disease, osteomalacia. The difference observed was found to be statistically significant (p Value). ALP was maximally raised in cases of Paget's disease 1434.8±219.5(CI 1409.8,1459.8), extrahepatic cholestasis 907.5±282.7(CI 875.5,939.7), osteomalacia 511.7±198.9 (CI 489.2,534.4). ALP values were within normal limits in controls 140.2 ±28.4 (CI 137.0, 143.5). The difference in between cases and controls for ALP was found to be statistically significant. γ-GT values was found to be significantly raised in cases of extrahepatic cholestasis 205.6 ±44.0(CI 200.6,210.6) when compared to controls 18.4±3.9(CI 17.9,18.9). The difference was found to be statistically significant. γ-GT values for viral

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hepatitis, Paget's disease, osteomalacia and controls were within reference range .

Table 1: Detailed evaluation of mean values of variables in cases and controls.

Variables	AGE (Yrs)	AST (0-40 IU/L)	ALT (0-45 IU/L)	ALP (145-310 U/L)	γ-GT (0-60 IU/L)
Controls (300)	62.6±4.4 (61.7,63.4)	25.7±3.6 (25.3,26.1)	27.6±3.6 (27.2,28.1)	140.2±28.4 (137.0,143.4)	18.4±3.9 (17.9,18.9)
Viral hepatitis (300)	60.5±4.4 (60.1,61.1)	429.3±513.1 (371.1, 487.6)	395.6±525.5(335.9, 455.3)	251.5±45.1 (241.8, 261.1)	19.5±3.8 (19.1, 19.9)
Extrahep cholestasis(300)	63.9±0.1 (63.5, 64.4)	59.1±8.9 (58.1, 60.1)	84.5 ±13.5 (83.1, 86.1)	907.5±282.7(875.4, 939.7)	205.6±44.0 (200.6, 210.6)
Paget's Disease (300)	64.4±2.9 (64.1, 64.8)	26.4 ±3.8 (26.1, 26.9)	31.3±5.2 (30.7, 31.9)	1434.8±219.5(1409.8, 1459.8)	20.4±4.2 (20.01, 20.97)
Osteomalacia (300)	62.7±4.7 (62.2, 63.3)	22.5±4.2 (22.1, 23.1)	26.0±4.1 (25.5, 26.5)	511.7±198.9 (489.1, 534.3)	19.0±3.7 (18.5,19.4)
p Value	0.0001†	0.0001†	0.0001†	0.0001†	0.0001†

† p value <0.001 statistical significance between groups

Table 2: Detailed evaluation of mean values of variables in cases and controls of males

Variables	AGE (Yrs)	AST (0-40 IU/L)	ALT (0-45 IU/L)	ALP (145-310 U/L)	γ-GT (0-60 IU/L)
Controls (160)	63.8±3.7 (62.9, 64.7)	25.4±3.5 (24.8, 25.9)	28.5±3.6 (27.9, 29.10)	140.1±28.2 (135.7, 144.5)	18.3±3.9 (17.6,18.9)
Viral hepatitis (197)	62.2±4.3 (61.6, 62.8)	515.6±528.6 (441.3, 589.9)	474.6±549.4 (397.5, 551.9)	252.0± 55.6 (240.1, 264.1)	20.1± 3.8 (19.5, 20.6)
Extrahep cholestasis(37)	63.7±3.1 (62.7, 64.8)	58.8±8.7 (55.9, 61.7)	84.4±13.8 (79.7, 89.0)	910.9 ±281.7 (816.9, 1004.8)	210.4±45.2 (195.4, 225.5)
Paget's Disease (169)	64.2±3.1 (63.7,64.6)	26.3± 3.7 (25.7,26.9)	32.4±5.1 (31.7,33.2)	1431.6±233.5 (1396.1, 1467.1)	21.1±4.1 (20.4,21.7)
Osteomalacia (39)	63.8±4.5 (62.3,65.3)	20.8±3.4 (19.7 21.9)	21.4±0.9 (21.11,21.76)	491.6±199.0 (427.1,556.1)	18.3± 2.8 (17.3, 19.2)
p Value	0.0001†	0.0001†	0.0001†	0.0001†	0.0001†

† p Value <0.001 statistical significance between groups

Table 2 illustrates that in cases of males, variation in values of all variables were somewhat similar to those of total cases. Out of total 300 cases, 197 cases of viral hepatitis were males. In cases of Paget's disease, the number of males (169) suffering were more than females (131). The mean values of AST (515.6 ±528.6) and ALT (474.6±549.4) were markedly raised in cases of viral hepatitis. ALP was maximally increased in cases of Paget's disease (1431.6±233.5). In cases of extrahepatic cholestasis, ALP was also markedly raised (910.9±281.7) and values of ALP were somewhat less than that of Paget's disease (1431.6±233.5). In cases of osteomalacia, ALP was moderately raised (491.6±199.0) and values were less than that of Paget's disease (1431.6±233.5) and extrahepatic cholestasis (910.9 ±281.7). γ-GT values was maximally increased in cases of extrahepatic cholestasis (210.4± 45.1). The mean values of γ-GT was found to be in normal range in cases of viral hepatitis (20.1± 3.8) Paget's disease (21.1± 4.1) and osteomalacia(18.2± 2.8).

Table 3 illustrates that in cases of females, variation in values of all variables were somewhat similar to those of total cases. Out of total 300 cases, 261 cases of osteomalcia were females. Furthermore, number of females(263) were more than males(37) in cases of extrahepatic cholestasis. The mean values of AST (264.3±439.3) and ALT (244.5± 440.7) were markedly raised in cases of viral hepatitis. ALP was maximally increased in cases of Paget's disease (1440.6±200.8). In cases of extrahepatic cholestasis, ALP was also markedly raised (907.1±283.4) and values of ALP were somewhat less than that of Paget's disease (1440.6±200.8). In cases of osteomalacia, ALP was moderately raised (514.7± 199.1) and values were less than that of Paget's disease (1440.6±200.8) and extrahepatic cholestasis (907.1±283.4). γ-GT values was maximally increased in cases of extrahepatic cholestasis (204.9±43.9). The mean values of γ-GT was found to be in normal range in cases of viral hepatitis (18.42±3.65) Paget's disease (19.7±4.3) and osteomalacia (19.1± 3.8).

Table 3: Detailed evaluation of mean values of variables in cases and controls of females

Variables	AGE (Yrs)	AST (0-40 IU/L)	ALT (0-45 IU/L)	ALP (145-310 U/L)	γ-GT (0-50 IU/L)
Controls (140)	60.1±4.4 (59.5,60.6)	26.1±3.8 (25.4,26.7)	26.5±3.4 (26.0,27.1)	140.3±28.7 (135.5, 145.1)	18.0±3.8 (17.8, 19.1)
Viral hepatitis (103)	59.8±4.4 (58.9,60.6)	264.3±439.3(178.4,350.2)	244.5± 440.7(158.3, 330.6)	250.4±54.2 (233.9, 266.9)	18.4±3.6 (17.7, 19.1)
Extrahep cholestasis(263)	64.2±4.0 (63.7,64.1)	59.1±9.0 (58.1,60.2)	84.5±13.4 (82.9,86.2)	907.1±283.4 (872.7, 941.5)	204.9±43.9(199.5, 210.2)
Paget's Disease (131)	64.4±3.2 (63.8,65.0)	26.6±3.9 (25.9,27.3)	29.8±5.1 (28.9, 30.7)	1440.6±200.8 (1405.8, 1475.3)	19.7±4.3 (19.0, 20.4)
Osteomalacia (261)	62.6±4.7 (62.0,63.1)	22.8± 4.3 (22.3, 23.3)	26.7 ±3.8 (26.2, 27.2)	514.7± 199.1 (490.5,539.1)	19.1±3.8 (18.6,19.5)
p Value	0.0001†	0.0001†	0.0001†	0.0001†	0.0001†

† p Value <0.001 statistical significance between groups

Table 4 depicts that there was statistically significant difference for AST in cases of viral hepatitis when compared to controls. There was statistically significant difference for ALT in cases of viral hepatitis and extraheaptic cholestasis when compared to controls. There was statistically significant difference in ALP in cases of viral hepatitis, extrahepatic cholestasis, Paget's disease and osteomalacia

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when compared to controls. There was a statistically significant difference for γ-GT in cases of extrahepatic cholestasis when compared to controls.

Table 4: Significance of variables in cases when compared to controls

Dependent variable controls Vs cases	Mean Difference (I-J)	p value	95% Confidence Interval	
			Lower Bound	Upper Bound
AST				
C VH	-403.604*	0.0001	-440.41	-366.80
EC	-33.374	0.076	-70.18	3.43
PD	-.731	0.969	-37.54	36.08
OM	3.169	0.866	-33.64	39.98
ALT				
C VH	-368.023*	0.0001	-405.69	-330.35
EC	-56.943*	0.003	-94.61	-19.27
PD	-3.718	0.847	-41.42	33.98
OM	1.573	0.935	-36.10	39.24
ALP				
C VH	-110.110*	0.087	-139.28	-81.22
EC	-767.340*	0.0001	-797.37	-737.31
PD	-1295.28*	0.0001	-1325.3	-1265.2
OM	-371.523*	0.0001	-401.55	-341.49
γ-GT				
C VH	--1.12	0.493	--4.33	-2.09
EC	-187.217*	0.0001	-192.01	-182.42
PD	-2.113	0.388	-6.91	2.68
OM	-.610	0.803	-5.41	4.19

C-Controls; VH-Viral hepatitis; EC-Extrahepatic cholestasis; PD-Paget's disease; OM-Osteomalacia

* p Value <0.05 statistical significance between groups

Discussion

Prevalence and Diagnosis of viral hepatitis, extrahepatic cholestasis, Paget's disease, and osteomalacia

Viral hepatitis infects millions of persons worldwide putting it at the leading cause of liver cirrhosis and hepatocellular carcinoma. These complications can be prevented if the diagnosis is made near the beginning and patients are given adequate treatment[18-20]. The incidence of cholangiocarcinoma in US which remains the most frequent cause of extrahepatic cholestasis is approximately 0.8 per 100000 people per year. The annual incidence per 100000 population is 7.3 in Israel, 6.5 in American Indians and 5.5 amongst the Japanese[21]. Paget's disease is not known to exhibit a proclivity for any race. Nonetheless, remarkable patterns of prevalence have been illustrated. The prevalence of Paget disease is maximum in Europe (predominantly England, France, and Germany). The disease is infrequent in Asian countries, particularly China, India, and Malaysia, and in the Middle East and Africa[22-23]. The overall incidence of osteomalacia is 1 in every 1,000 individuals. Pregnancy and breastfeeding increase a woman's need for vitamin D and therefore increase the risk of deficiency. Women are affected slightly more often than men[24]. Isolated alterations of biochemical markers of liver damage can present a challenge for the clinician. Individual markers may correctly identify a cause but appear to have insufficient specificity and sensitivity[25]. Our present study illustrates that accurate and precise diagnosis after interpreting alterations of various biochemical markers could improve the outcomes through early detection, monitoring intervention and selection of appropriate treatment strategies[26].

Age

The mean age of patients of viral hepatitis was 60.5±SD4.4 (60.1, 61.04). The mean age of patients of extrahepatic cholestasis 63.9±SD0.1 (63.5, 64.5) was little higher than those of viral hepatitis. Paget's disease is noticeably unusual in persons younger than 25 years and augments in occurrence with increasing age. Paget's disease mostly develops in persons in the fifth decade of life and is most frequently diagnosed in the sixth decade. The incidence of Paget's disease in persons older than 80 years is approximately 10%. The mean age of the patients in our study was 64.5±SD2.9 (64.2,64.8) and it concurred with the selection of patients of Poor G et al[27]. The mean age of patients of osteomalacia 62.8±SD4.7 (62.2, 63.3) was similar to that of controls 62.6±SD4.4 (61.7, 63.5) and less than the patients of extra hepatic cholestasis 63.9±SD0.1 (63.5, 64.5) and Paget's disease 64.5±SD2.9 (64.2, 64.8).

Gender

Our results specify that the mean values of all variables did not illustrate any significant difference in relation to gender. In our present study, females were more prone to suffer from extrahepatic cholestasis than males. The above findings concurred with Trifan[28]. Number of males were more in cases of Paget's disease than females[29].

AST and ALT

The current study signifies that in cases of Paget's disease and osteomalacia, aminotransferases were in normal range. The mean values of AST (429.4±SD513.2) and ALT (395.6 ±SD525.5) were found to be noticeably raised in cases of viral hepatitis when compared with the cases of extrahepatic cholestasis, Paget's disease and osteomalacia[30]. Elevated ALT levels in extrahepatic cholestasis reflect the damage to liver as aminotranferases are typically concentrated in cytosol and mitochondria of hepatocytes. Our results concurred with the findings of Souza et al[31].

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ALP

ALP was highly elevated in cases of Paget's disease[32]. The mean values of ALP in extrahepatic cholestasis (907.6±SD282.8) was less than that of Paget's disease(1434.8 ±SD219.5). In Paget's disease, increased ALP was due to osteoblastic activity[33]. Likewise, in extrahepatic cholestasis, accumulating bile salts increase ALP synthesis and liberation from surface of bile duct epithelia[34]. Further, we found that values of ALP in cases of osteomalacia (511.8± SD198.9) was lesser than both Paget's disease and extrahepatic cholestasis. The level of ALP was within normal range in controls and cases of viral hepatitis.

γ-GT

γ-GT is a membrane bound enzyme present in hepatocytes and biliary epithelial cells. γ-GT was significantly raised in cases of extrahepatic cholestasis(205.6±SD 44.1) when compared to viral hepatitis 19.5±SD3.8), Paget's disease(20.5±SD4.2), osteomalacia (19.0±SD3.7) and controls(18.4±SD3.9). Our results concurred with the findings of Castro-e-Silva et al[35]. An increase in γ-GT levels in patients with obstructive liver disease is associated with bile duct damage and fibrosis. Thus, because of its lack of specificity but high sensitivity for liver disease, γ-GT can be valuable for identifying causes of altered ALP levels, in concert with other biochemical abnormalities. An elevated alkaline phosphatase with normal γ-GT in cases of Paget's disease and osteomalacia stalwartly imply the bone origin.

Clinical relevance

Our study signifies that AST and ALT are the foremost specific markers of viral hepatitis. ALP is the main marker of Paget's disease and osteomalacia. γ-GT and ALP together are most important markers of extrahepatic cholestasis. Thus, deviation in levels of hepatobiliary enzymes precisely distinguishes between liver and bone diseases.

What this study adds

In regular clinical practices, there is an inclination of diagnosing bone and liver diseases with single hepatobiliary enzymes. The present study emphasizes that comparing the values of various hepatobiliary enzymes increase the sensitivity and specificity of accurately differentiating and obtaining the diagnosis of disease.

Future scope of study

Isoenzymes of different enzymes can be studied for the differentiation of liver and bone diseases. Moreover, by observing the serum levels of different enzymes, causes and diagnosis of hepatobiliary disorders and different types of liver diseases can be established.

Conclusion

It is not easy for clinicians to differentiate and diagnose liver and bone diseases correctly with single hepatobiliary enzyme. If a systematic approach is adopted, based on additional non-invasive serological tests and imaging procedures covering the most frequent liver diseases, the cause is often apparent. Correlation of variation in several biochemical markers increases the sensitivity and specificity for segregate and identification of liver and bone diseases for proper treatment and prognosis.

Conflict of Interests

The authors do not have any conflict of interest arising from the study.

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Authors' contributions

AM designed the study, deduced the data, drafted the manuscript, and revised it. AH, KS and SKY acquired the data with AM. BP and SMF planned the study with AM, conducted the data analysis, interpreted the data, and revised the manuscript. BS participated in statistical analysis, interpreted the data, and revised the manuscript. NC critically revised the manuscript. All the authors approved the final document.

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