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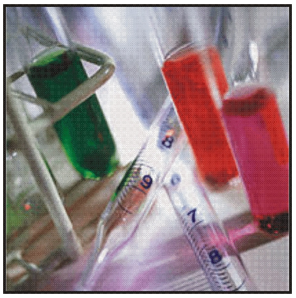

SERUM ALT;
CLINICAL SIGNIFICANCE OF BORDERLINE HIGH LEVELS

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ABSTRACT … tariqtbk@yahoo.com **Aim:** To assess the cases of borderline high serum ALT. **Objectives:** To find out underlying pathology causing borderline high serum ALT cases using noninvasive methods, and to evaluate their significance. **Method and Material:** A total of 30 patients fulfilling the selection criteria were included at convenience. **Study design:** This was an observational study. **Setting and Period:** This study was conducted in PMA hospital Kakul during 2004. **Results:** The results of the study showed that fatty liver was present in 36.6% of the cases. Hepatitis C infection was detected in 13.4%, while in most of the patients (50%) no specific cause could be detected. **Conclusions:** On the basis of these observations it was concluded that in patients detected to have borderline high serum ALT on routine evaluation the chances of diagnosing steatohepatitis were more than chronic hepatitis and that the possibility of serious underlying liver disease was uncommon.

Key Words: Serum ALT, Fatty liver, Hepatitis.

INTRODUCTION

Incidence of hepatitis C is gradually increasing in our country and so is the awareness and concerns of general public. It has been observed that a normal to a borderline high serum ALT is frequently detected in patients suffering from chronic hepatitis. As a result many healthy people unnecessarily undergo frequent assessment of liver function tests for screening purposes. Those found to have a borderline high serum ALT are stuck with a series of evaluations and laboratory investigations. These tests, usually unwarranted, not only are expensive but also put the patient to risk of multiple pricks. Abnormal LFTs are also frequently detected in asymptomatic patients since many screening test panels now routinely include them. Studies evaluating the clinical significance of these abnormalities have produced variable findings. The differences among individual studies reflects variation in the prevalence of liver disease in the populations that have been studied and the degree to which an underlying cause of the abnormalities was sought. Consensus on the cost-effective approach to the evaluation of patients with abnormal LFTs has also not been established. This study was designed to evaluate the patients presenting with borderline high ALT with the aim to find its causes and evaluate its significance.

METHODS

This was an observational study in which patients were enrolled at convenience after informed consent. This study was conducted in PMA Hospital Kakul during 2004. Study period was 6 months. The patients who

were detected to have a borderline high serum ALT, defined as less than twofold higher than the upper limit of normal, were selected using an inclusion and exclusion criteria. Reasons for inclusion were; first time detected to have a high serum ALT, no history of jaundice in past, or known to have any illness likely to cause a high serum ALT.

Evaluation protocol was as follows:

Step 1: A complete medical history for evaluation of the patient with elevated LFTs was taken, inquiring the use of or exposure to any chemical or medication (including prescription and over-the-counter medications as well as herbal therapies) which may be temporally related to the onset of LFT abnormalities. The duration of LFT abnormalities and presence of any accompanying symptoms such as jaundice, arthralgias, myalgias, rash, anorexia, weight loss, abdominal pain, fever, pruritus, and changes in the urine and stool. The patients were carefully questioned about possible parenteral exposures including transfusions, intravenous and intranasal drug use, tattoos, and sexual activity. Other important questions included recent travel history, exposure to people with jaundice, exposure to possibly contaminated foods, occupational exposure to hepatotoxins, and alcohol consumption. The physical examination was focused upon findings suggesting the presence of liver disease.

a. Blood complete picture.
b. Liver function tests. serum AST/ALT ratio was done to screen alcoholic hepatitis[1,2]
c. Serology for Hepatitis B and C
d. Screening for hemochromotosis serum iron /TIBC ratio
e. Evaluation for fatty liver: USG abdomen.

Step 2: If the above tests were normal, the protocol was as follow:

a Tests to exclude muscle disorders, Muscle enzymes (serum CK and Aldolase)
b Thyroid function tests[3,4]
c Tests to exclude autoimmune hepatitis. Serum protein electrophoresis, ANA, and Anti Smooth Muscle Antibodies.
d Tests to exclude Wilsons disease: Examination for KF rings, serum ceruloplasmin.

Liver biopsy was not kept as an option in patients' evaluation. Firstly, because it was invasive and secondly because studies have concluded that the biopsy results only infrequently clarify the presumptive diagnosis and that no proven therapy exists for many such patients[5].

The patients were followed up for 6 months for serum ALT levels. The data was collected and the underlying causes were calculated in percentage of the patients with raised serum ALT levels.

RESULTS

A total of 30 patients were included in the study and were evaluated as per protocols. The results are as follows. Among them 36.6% of the patients had fatty liver detected on ultrasonography and 39% of these patients were obese or had been on a diet programme while 29% of the patients detected to have fatty liver, clinically had palpable hepatomegaly that was confirmed on sonography.

Hepatitis C was detected in 13.4% of cases. There was no past history of blood transfusion or any surgical or dental procedure. Almost all of them had received intramuscular injections, mostly for vaccination, in the recent past. A 30% of these cases had been vaccinated against hepatitis B. Clinically there were no stigmata of chronic liver disease and ultrasonography of abdomen did not reveal any abnormality. PCR for HCV RNA was positive in 100% of these cases , while serum ALT levels varied over 6 months.

Majority of the cases (50%) had no detectable cause over 6 month of follow up while 57% of these cases had symptoms of chronic dyspepsia and had been on infrequent usage of antacids/H2 receptor blockers.

One patient had chronic diarrhea. His endoscopy and

colonoscopy was done. The biopsy revealed eosinophilic proctitis. The patient was placed on steroids and he responded well with normalization of symptoms and serum ALT.

Table-I. Summary of results		
HBV infection	0	0%
HCV infection	4	13.4%
Fatty liver	11	36.6%
No cause found	15	50%

DISCUSSION

The results of this study were similar to the findings in studies carried out at other centres. Advances in the noninvasive tests to identify the cause of liver disease have permitted a greater understanding of the spectrum of liver disease encountered in various patient populations. Abnormal serum aminotransferase levels (ALT >2.25 SD above normal; >55 IU/L) were detected in 99 of 19,877 (0.5%) Air Force recruits beginning basic training[6]. Of these, a cause was found in only 12 (including chronic hepatitis B and C, autoimmune hepatitis, and cholelithiasis). No specific diagnosis was established in the remaining 87 patients. The diagnoses observed in two studies that included a total of 249 blood donors with abnormal serum ALT values included, alcoholic liver disease (11 to 48%); fatty liver (22 to 56%), hepatitis C (17 to 20%); miscellaneous causes (4 to 8%) and no specific diagnosis (2 to 9%)[7,8]. Another study focused on 81 of 1124 patients who were referred for abnormal serum aminotransferase levels in whom a diagnosis could not be inferred non-invasively[9]. A liver biopsy revealed steatosis or steatohepatitis in the majority of patients (84%); six patients had fibrosis or cirrhosis and eight had normal histologic findings[10]. One of the most recent studies included 354 patients who underwent a liver biopsy to investigate abnormal LFTs, defined as an alanine aminotransferase, gamma glutamyl transferase, or alkaline phosphatase more than twice the upper limit of normal for a least six months[11]. Patients with clinical or serologic features suggesting a specific diagnosis were excluded. The most frequent finding on liver biopsy was nonalcoholic steatohepatitis or fatty liver (66%).

The sensitivity and specificity of the serum aminotransferases (particularly serum ALT) for discriminating those with and without liver disease depends upon the cut off values chosen to define an abnormal test. At least two large studies suggested that the cut off values should be adjusted for gender and body mass index[12,13]. However, most patients identified with the lower cut off values had only mild liver disease or no identifiable cause of the abnormal laboratory values. Thus, the overall benefit is unclear since it would translate into a large increase in the absolute numbers of patients who would require evaluation for an uncertain clinical benefit[14].

It is important to emphasize that false positive results are more likely in patients who have a low pretest probability of having liver disease. This is a particular concern when abnormal LFTs are detected as part of a panel of laboratory tests drawn for other reasons. Normal test reference values are usually arbitrarily defined as those occurring within two standard deviations from the mean. As a result, 5% of healthy individuals who have a single screening test will have an abnormal result (2.5% will have an abnormally high result). As more tests are ordered, the likelihood of a false positive test increases; a screening panel containing 20 independent tests in a patient with no disease will yield at least one abnormal result 64 percent of the time.

CONCLUSIONS

The above study helps us to conclude that serious underlying liver disease is uncommon in patients detected to have borderline high ALT on routine evaluation. It has also been observed that in a patient where diagnosis remains unclear, after obtaining a history and laboratory testing, chances of underlying alcoholic liver disease, steatosis, or steatohepatitis are more. It is recommended that the routine use of laboratory tests in patients with low pretest probability of the disease should be avoided so as to reduce the

frequency of false positivity. Appropriate testing guided by the pretest probability of the disease should be preferred in clinics.

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