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A CLINICAL EVALUATION OF SERUM FERRITIN, GAMMA-GLUTAMYLTRANSFERASE (GGT) AND VITAMIN D WITH ALCOHOLIC LIVER DISEASES FOR DIAGNOSIS

Biochemistry

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ABSTRACT

Background: Alcohol is most common substance abused. Alcoholic liver disease is a major health care problem in India. Alcohol consumption is directly associated with liver disease mortality and accounts for increased social and economic costs. Alcoholic liver disease may take the forms of acute involvement (alcoholic hepatitis) or chronic liver disease (steatosis, steatohepatitis, fibrosis and cirrhosis. The severity and prognosis of alcohol- induced liver disease depends on the amount, pattern and duration of alcohol consumption, as well as on the presence of liver inflammation, diet, nutritional status and genetic predisposition of an individual.

Aims & objective: The aim of the current study was to analyze the correlation of gamma-glutamyltransferase (GGT); vitamin D; and ferritin with alcoholic liver disease and clinical presentation to access the severity of alcoholic liver disease and their treatment response and outcome among patients using laboratory.

Material and Methods: It is observational case control study, was included 100 subjects. Out of 100 subjects, 50 subjects were patients of alcoholic liver disease and another 50 normal subjects, were age and sex matched healthy volunteers as control group. 50 ALD patients were studied and their clinical profile, laboratory parameters and radiological investigations were taken.

Results: Alcoholic liver disease was seen among the productive age group with high morbidity and mortality. The statistically inverse significant correlations were recorded between serum vit.D and ferritin. While, serum Vit.D and GGT besides that highly statistically significant inverse correlation and ferritin with GGT positive significant correlations were found in alcohol liver disease subjects.

Conclusion: Alcoholic liver disease was seen among the productive age group with high morbidity and mortality. Mortality and morbidity associated with this disease is matter of serious economic loss to the nation and grief for the society.

KEYWORDS

Alcoholic Liver Disease; gamma-glutamyltransferase (GGT); vitamin D; and ferritin

INTRODUCTION

Alcoholic liver disease spans a clinical and histological spectrum, from fatty liver to alcoholic hepatitis to alcoholic cirrhosis. Fatty liver develops in most people who abuse alcohol for a period of days. However, this condition is generally asymptomatic and entirely reversible with abstinence. Although the majority of people who abuse alcohol for an extended duration do not develop advanced lesions of alcoholic liver disease, approximately 15% to 20% develop alcoholic hepatitis and/or cirrhosis, which may develop in succession or exist concomitantly. The level of alcohol consumption necessary for the development of these advanced forms of alcoholic liver disease is probably 80 g of alcohol per day, the equivalent to 6 to 8 drinks daily for several years.[1]

The concentration of serum ferritin is used clinically as an indicator of body iron stores[2] and plays a central role in the diagnosis of haemochromatosis. However, increased serum levels of ferritin have been associated with other liver diseases[3-5] and certain malignancies.[6-8] High serum ferritin has also been reported in acute and chronic inflammation[9-10]without evidence of increased iron stores. Kristenson *et al.*[11] found increased serum ferritin value in 67% of middle-aged males who were heavy drinkers and with increased gammaglutamyl transpeptidase (GGT) activities. In alcoholics with significant liver disease, serum ferritin levels are of little value in assessing iron stores.[12]

Alcoholic liver disease encompasses a spectrum of injury, ranging from simple steatosis to frank cirrhosis.[13,14] It may well represent the oldest form of liver injury known to mankind. Evidence suggests that fermented beverages existed at least early as the Neolithic period (cir. 10,000 BC).[15]Chronic and excessive alcohol ingestion is one of the major causes of liver disease in western world.[16,17] Alcohol remains most common cause of liver disease in India. Alcoholic liver disease encompasses a clinical histological spectrum, including fatty liver, alcoholic hepatitis and alcoholic cirrhosis. Fatty liver is a benign condition but progression to alcoholic hepatitis and cirrhosis is life threatening. Alcoholic hepatitis is diagnosed predominantly on clinical history, physical examination and laboratory findings.

The possible factors that can affect the development of liver injury include the dose, duration and type of alcohol consumption, drinking patterns, gender, ethnicity, and associated risk factors, including obesity, iron overload, nutritional deficiency esp. protein, pregnancy, concomitant infection with viral hepatitis and genetic factors.

In our present study, we have focused on alcoholic liver disease and its various complications using laboratory and radiological investigations.

MATERIALS AND METHODS

This study was carried out in department of Biochemistry in collaboration with department of Medicine of Sardar Patel Medical College and attached Hospital from 2017-18 at Bikaner.

It is observational case control study, was include 100 subjects. Out of 100 subjects, 50 subjects were patients of alcoholic liver disease and another 50 normal subjects, were age and sex matched healthy volunteers as control group. The control group was taken from patient's attendants, staff, students and private laboratories which conduct routine serum check up of healthy persons.

Clinical survey of alcoholic liver disease was carried out and total one hundred patients with diagnosis of alcoholic liver disease are included in study. Patient's details including occupation, socio economic status, risk factors, clinical features, complications, laboratory and radiological investigations were carried out.

Inclusion criteria

- Clinically confirmed cases of alcoholic disease.
- Age between30 to 60 years.

Exclusion criteria

- Very sick patients.

- Age less than 30 years and more than 60 years.
- Those receiving calcium and Vitamin D supplementations.
- Patients taking drugs which affecting serum level of Ferritin, GGT, and Vitamin D.
- Haemolysed blood samples.

A case of Alcoholic liver disease is diagnosed in patients with history of significant alcohol intake, physical signs of liver disease, and supporting laboratory investigations.**[9]** Alcoholic cirrhosis is diagnosed in a patients with H/o alcohol consumption > 80 g/dl in men and 40 g/dl in female and at least one clinical sign of hepatocellular failure and one of the sign of portal hypertension along with at least three ultrasound finding of cirrhosis of liver.[18]

RESULTS

The present study, though not probably first of its kind in world population, it is an attempt forward in series of previous studies done internationally, to study the concentration of Ferritin, Vitamin D and Gamma-glutamyltransferase (GGT) in patients with diagnosis of alcoholic liver disease. The data obtained from this study is to be compared with age and sex matched control group and is discussed here and results have been compared with other similar studies. The demographic profile of the study population has also been analyzed with reasonable wisdom.

In the present study, we observed that there were highly significant positive correlations between Ferritin and GGT in both men and women. The acute phase response that occurs during inflammation or infection produces a decrease in serum iron as well as an increase in serum Ferritin.Several studies have reported elevated serum Ferritin levels in patients of chronic alcohol abuse. Yang SQ et al. (1998)[19] found that serum Ferritin is frequently reported to be elevated in chronic alcoholics. Rogers JT et al. (2007)[20] found that Serum Ferritin levels have been shown to increase during inflammation and the acute phase response.

In accord with our findings, many previous studies have suggested inverse relationships between vitamin D and Alcoholic liver disease. Puukka K et al. (2007)[21] found that serum GGT is an enzyme having special relation with alcoholic liver diseases and is widely used clinical marker of alcohol abuse.A systematic review also showed that alcoholic liver diseases patients were 1.26-times more likely to be vitamin D deficient. Interestingly, these differences were higher in Western populations than in Eastern populations.[110] Fisher L et al. (2007)[22] reported that patients with alcoholic liver diseases showed a marked reduction in serum 25(OH) D3 levels compared with controls. In another study Konijn AM. (1994)[23] found that there were highly significant positive correlations between Ferritin and GGT in both men and women. The acute phase response that occurs during inflammation or infection produces a decrease in serum iron as well as an increase in serum ferritin.

A correlation coefficient was also observed between Vitamin D and Ferritin along with GGT in patients suffering from Alcoholic liver diseases as shown in table no.-1. An inverse correlation between serum Vitamin D concentration and Ferritin along with GGT were recorded. These results were in close agreement with the findings of Fisher L et al. (2007)[22] who observed an inverse correlation of Ferritin and GGT. In the present study, the correlation coefficients were found to be ($r = -0.014$; $r = -0.155$) with ferritin and GGT respectively by keeping a unit score of Vitamin D. The correlation coefficients were found to be statistically significant for magnesium and ferritin ($p < 0.01$) and highly significant for GGT as shown by p value ($p < 0.0001$; table no.-1,2)

These results were in close agreement with the findings of Rogers JT et al. (2007)[20], who observed an inverse correlation between Vit.D levels and ferritin, GGT.[24] Our findings are also in confirmation with the study of Malham et al., who found a similar correlation.[25]

Table – 1: Correlation Coefficient Between Vitamin D And Ggt, Ferritin With Alcoholic Liver Disease Cases

Characteristic	Control Healthy subjects (Mean±S.D) (n=50)			Alcoholic liver disease (Mean±S.D) (n=50)		
	Male (n=31)	Female (n=19)	P- values	Male (n=48)	Female (n= 2)	P- values
Ferritin (ng/ml)	152.58 ± 25.24	160.26 ± 21.24	0.273	340.75 ± 21.50	359.0 ± 11.31	0.241
Vitamin D (ng/ml)	38.45 ±4.10	38.52 ± 4.69	0.95	22.54 ± 4.04	21.0 ± 8.48	0.611
GGT (IU/L)	21.19 ± 5.65	20.10 ± 4.71	0.48	223.33 ± 12.65	235.0 ± 12.72	0.20

Table – 2: Clinical And Biochemical Characteristics, Adjusted For Age And Sex, In Healthy Control Subjects With Alcoholic Liver Disease

S. No.	Correlations	r-value	P value	Inference
1.	GGT v/s Vit. D	-0.155	<0.001	HS*
2.	Vit. D v/s Ferritin	-0.014	<0.01	S*
3.	Ferritin v/s GGT	0.89	<0.001	HS*

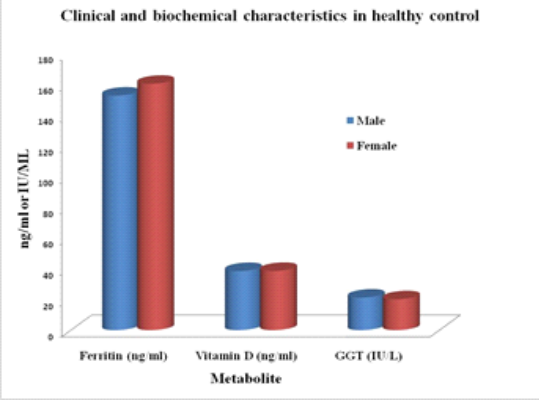

Figure:1 Clinical and biochemical characteristics, adjusted for age and sex, in healthy control subjects with Alcoholic liver disease

CONCLUSIONS

In conclusion, this study indicates that, Serum ferritin is more frequently elevated in abusing patients with alcoholic liver disease than in patients with other chronic liver diseases such as autoimmune liver diseases and hepatitis C. Because serum ferritin decreases rapidly during abstinence, the measurement of ferritin for the detection of haemochromatosis in patients abusing alcohol should be postponed until the patients are abstaining. Most of the patients with increased serum ferritin have normal transferrin saturation values which can be used to separate them from haemochromatosis.

Vitamin D is becoming increasingly accepted as an important physiological regulator outside of its classical role in skeletal homeostasis. A growing body of evidence connects vitamin D with hepatic disease. This review summarises the role of vitamin D in liver homeostasis and disease and discusses the therapeutic potential of vitamin D-based treatments to protect against hepatic disease progression and to improve response to treatment.

Alcohol liver desease (ALD) is a condition that affects only a small percentage of heavy drinkers. The diagnosis of ALD can be challenging and is based on a combination of clinical and laboratory findings in addition to the essential role of communication with the patient to assess the amount and duration of alcohol intake. Clinical findings may be minimal or absent in early ALD characterized only by hepatic steatosis, whereas in cirrhosis there will be typical signs and symptoms of cirrhosis and portal hypertension. Laboratory studies characteristic of ALD include elevated transaminase levels with AST greater than ALT but also increased, GGT, and IgA to IgG ratio. GGT acts as a marker for diagnosis of Alcohol liver desease.

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