A Study on Gamma Glutamyl Transferase and Amylase Levels in Chronic Alcoholics with Hepatitis

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Aim of the study **-** The aim of the present project is to assess the effects of chronic alcoholism on liver and pancreatic tissue and to differentiate nonalcoholic hepatitis by estimating serum levels of gamma glutamyl transferase (GGT) and Amylase in addition to regular biochemical investigations like serum bilirubin, Alanine transaminase (ALT) and alkaline phosphatase (ALP) levels in about 40 cases of adult jaundice patients admitted in S.V.S Hospital, Mahabubnagar.

Abstract- To evaluate the diagnostic importance of the serum gamma glutamyl transferase (GGT)(E.C : 2.3.2.2) and amylase(E.C : 3.2.1.1) to assess the effects of chromic alcoholism on liver and pancreatic tissue and to differentiate alcoholic hepatitis from nonalcoholic hepatitis by estimating serum levels of GGT and amylase in addition to regular biochemical investigations like serum bilirubin, alanine transaminase (ALT)(E.C: 2.6.1.2) and alkaline phosphatase (ALP)(E.C: 3.1.3.1) levels in about 40 cases of adult jaundice patients admitted in S.V.S Hospital.

Estimation of GGT in all cases of Hepatitis, to exclude the underlying damage caused by chronic alcoholism which is widely prevalent in all segments of population. Elevated blood levels of the liver enzyme GGT indicate heavy alcohol use and liver injury. GGT is the best indicator of excessive alcoholic consumption; GGT is often abnormal in alcoholics even with normal LFT or with normal liver histology. So it's more useful index of occult alcoholism.

An increased level of serum amylase in alcoholics is due to two types of effects of alcohol on pancreas. i) Direct toxic effects of alcohol on acinar cells of pancreas.

ii) By alcohol induced oxidant stress and damage to pancreatic acinar cells.

The rise of these two enzymes was noted particularly in patients who consume unrefined alcoholic beverages frequently in this region belong to the age group of 42 ± 9. Cases of alcoholic hepatitis and alcohol related damage to pancreas are also observed with increased levels of amylase.

So it is advisable to estimate GGT activity in all cases of hepatitis to exclude the underlying damage caused by chronic alcoholism, which is widely prevalent in all segments of population.

Index Terms- Gamma Glutamyl Transferase, Amylase, Chronic alcoholism.

I. INTRODUCTION

Alcoholism is an illness characterized by significant impairment that is directly associated with persistent and excessive use of alcohol. Impairment may involve physiological, psychological or social dysfunction. [1, 2, 3]

The word alcohol comes from Arabic "ALKOHL" which means "the essence" before recorded history; human beings discovered that grape juice, when exposed to naturally occurring yeasts, becomes wine (Fermentation). Later wine and other alcoholic beverages have become an integral part of many cultures, meals, celebrations and religious ceremonies.

Unfortunately alcoholic beverages have also contributed to a considerable portion of human misery. Data from the national center for health statistics indicate that excessive alcohol consumption causes more than 100000 deaths per year in the United States alone, primarily through cirrhosis of the liver, drunk driving and alcohol related homicide and suicide. According to THE COLUMBIA UNIVERSITY COLLEGE OF PHYSICIANS AND SURGEONS COMPLETE HOME MEDICAL GUIDE, alcohol use is involved in half of all murders, accidental deaths, and suicides, half of all crimes, and almost half of all fatal automobile accidents.

Prolonged abuse of alcohol caused both physical and mental conditions and there are also various social implications from associated behaviors of the users. Although cirrhosis of the liver is the best known complication, there are numerous effects to the digestive system pancreas, nerves, and heart [6, 7, and 8]. Alcoholism can be difficult to diagnose because of secrecy and the tendency towards denial of a serious problem. In some cases alcoholism may actually be a symptom of an underlying condition such as depression or schizophrenia. [10, 11]

The reality is that alcohol is often abused because it initially offers a very tantalizing promise, with mild intoxication. Many people become more relaxed, they feel more carefree, any preexisting problems tend to evade into the background. Alcohol can be used to enhance good mood or change a bad mood. At first alcohol allows the drinker to feel quite pleasant, with no emotional costs? As an individual's drinking progresses, however, it takes more and more alcohol to achieve the same high. It ultimately leads to the development of alcohol related disorders and medical complications. They include liver disease such as hepatitis and cirrhosis, [4, and 5] (Liver disease specifically caused by alcohol is called "alcoholic liver disease")

Acute/Chronic pancreatitis, high blood pressure and bleeding of the esophageal lining can result from prolonged use.

Alcoholic is at high risk for a heart attack or stroke, depression, insomnia and even suicide are more prevalent at this stage. [12, 13]

A condition known as wernicke – korsakoff syndrome, which involves memory loss, indicates that the individual has sustained brain damage from drinking. An alcoholic at this stage experiences seizures or delirium tremors (DTS). This condition is due to Trans ketolase enzyme defect and thiamine deficiency induced by malnutrition associated with chronic alcoholism.

II. REVIEW OF LITERATURE

Hepatitis

Hepatitis implies injury to liver, characterized by presence of inflammatory cells in the liver tissue. The condition can be self limiting, healing on its own or can progress to scarring of the liver. Hepatitis is acute when it lasts less than 6 months and chronic when it persists longer.

Causes [2]:-

1. **acute hepatitis :-**
   - viral hepatitis:- hepatitis A to E
   - Non viral hepatitis:-toxoplasmosis, leptospira, Q fever, rocky mountain spotted fever.
   - Alcohol
   - Toxins: Ammonia toxin in mushrooms, CCl_4, Asafetida.
   - Ischemic hepatitis : (circulatory insufficiency)
   - Pregnancy:
   - Auto immune conditions:

Eg: Systemic Lupus Erythematus (SLE)

   - Metabolic diseases:- Eg: Wilson's disease
2. **Chronic hepatitis:-**
   - Viral hepatitis B with or without hepatitis D, C.
   - Auto immune: Autoimmune hepatitis
   - Alcohol
   - Drugs: Methyl dopa, Nitrifurantoin, Isonizide.
   - Genetic: Wilson's disease, alfa-1 antitrypsin deficiency
   - Primary biliary cirrhosis and primary sclerosing cholongitis occasionally mimic chronic hepatitis.

Signs and symptoms:-

Acute hepatitis:-

Symptoms include muscle and joint aches, fever, nausea or vomiting, diarrhea and headache. They are very much common for viral hepatitis. Loss of appetite is common in all types of hepatitis. Along with these symptoms dark urine, yellowing of the eyes and skin (jaundice) and abdominal discomfort are common. Physical findings are usually minimal apart from jaundice (33%) and tender hepatomegaly (10%) there can be occasional lymphadenopathy (5%) or spleenomegaly (5%).

Chronic hepatitis:-

Symptoms are abdominal fullness from enlarged liver or spleen, low grade fever and fluid retention (ascites). Extensive damage and scarring of liver i.e., cirrhosis leads to weight loss, easy bruising and bleeding tendencies. Acne, abnormal menstruation, lung scarring, inflammation of the thyroid gland and kidneys may be present in women with autoimmune hepatitis [4].

Types of hepatitis:-

1. Viral hepatitis:- Most cases of acute hepatitis are due to viral infections.

- Hepatitis A
- Hepatitis B
- Hepatitis C
- Hepatitis B with D
- Hepatitis E
- Hepatitis F
- Hepatitis G or GBV-C

In addition to the hepatitis viruses, other viruses can also cause hepatitis, including Cytogalovirus, Epstein Barr virus, Yellow fever virus etc. [3].

2. Alcoholic hepatitis:-

Ethanol mostly in alcoholic beverages is a significant cause of hepatitis. Patients who drink alcohol to excess are also more often than others found to be have hepatitis C and alcohol consumption accelerates the development of cirrhosis in western countries.

3. Drug induced hepatitis:-

A large number of drugs can cause hepatitis[5]. The ant diabetic drug Troglitazone was withdrawn in 2000 for causing hepatitis. Other drugs associated with hepatitis are-

- Allopurinol
- Amitriptylin (antidepressant)
- Amidarone (antiarrhythmic)
- Azathiopurin
- Halothane (a specific type of anesthetic gas)
- Hormonal contraceptives
- Isoniazide, riflapcin and pyrazyanide etc.

Other toxins that cause hepatitis:-

- Amatoxin containing mushrooms
- White phosphorus an industrial toxin
- Paracetamol
- Carbon tetrachloride
- Cylindrospermosin, a toxin from cyanobacteriom

4. Metabolic disorders:-

Some metabolic disorders cause different forms of hepatitis. Hemochromatosis and Wilson's disease (copper accumulation) can cause liver inflammation and necrosis.

5. Obstructive :-

Obstructive jaundice of long lasting leads to destruction and inflammation of liver tissue.

6. Autoimmune:-

It has an incidence of 1 or 2 per 100000 per year. It affects women more often than men (8:1).Anomalous presentation of human leukocyte antigen (HLA) class on the surface of hepatocytes possibly due to genetic predisposition or acute liver infection causes a cell mediated immune response against the body's own liver resulting in autoimmune hepatitis.

7. **Alfa 1 antitrypsin deficiency**:-

In sever cases of Alfa 1 antitrypsin deficiency (AIAD), the accumulated protein in the endoplasmic reticulum causes liver cell damage and inflammation.

8. Non alcoholic steatohepatitis:-

Which resembles alcoholic hepatitis on liver biopsy, but occurs in patients who have no known history of alcohol abuse. NASH is more common in women and the most common cause is obesity or the metabolic syndrome. A related but less serious condition is called fatty liver. This occurs in up to 80 % of all clinically obese people. NASH is becoming recognized as the most important cause of liver disease second only to hepatitis C, in numbers of patients going on to cirrhosis.

9. Ischemic hepatitis:-

It is caused by decreased circulation to the liver cells. Usually this is due to decreased blood pressure leading to the equivalent term shock liver. Blood testing of person with ischemic hepatitis will show very high levels of transaminase enzymes (AST & ALT).which may exceed 1000 U/L. it is rare that liver function will be affected by ischemic hepatitis.

III. MATERIALS AND METHODS

The present study was done by taking blood sample from 58 patients who are admitted in S.V.S Hospital. All are male patients belonging to same age group. From all of them clinical data regarding to diet, weight, vitamin deficiency symptoms jaundice, ascites, pain and swelling in abdomen if any are collected.

Among the 58 patients, 38 patients showing abnormal LFT are grouped as hepatitis group/test group. Again in these 38 patients, 20 had history of chronic alcoholism, and they were consuming strong alcoholic beverages like whisky and brandy. And the remaining 18 are non alcoholics.

Remaining 20 patients admitted with various other complaints, where LFT also done and found to be normal are included as control group and control subjects had no history of alcoholism.

In all those 58 patients following biochemical investigations are done to asses the effect of alcohol on liver and pancreas and its contribution for causing hepatitis.

- Total Bilirubin (T.B)
- Direct Bilirubin (D.B)
- Alkaline phosphatase (ALP)
- Alanine transaminase (ALT)
- Gamma glutamyl tranferase (GGT)
- Amylase

All of these are estimated by using semi automated clinical chemistry analyzer, 3000 EVOLUTION.

IV. RESULTS

In all 58 patients included in the study, serum levels of Total Bilirubin, Direct Bilirubin, Alkaline phosphatase (ALP), Alanine- transaminase (ALT), Gamma glutamyl transferase (GGT) and Amylase levels are estimated. Based on the results and patients history of alcoholism, they are grouped as follows.

Group I: Non alcoholics with normal LFT.(20 cases).

Group II A: Hepatitis Patients with no history of alcoholism (20 cases).

Group II B: Hepatitis patients with the history of alcoholism (18 cases).

- Group I, subjects had shown all parameters with in the normal limit, hence they are treated as control group.
- Group II A, patients are non alcoholics and they had shown increased Total Bilirubin, Direct Bilirubin, Alkaline phosphatase (ALP), Alanine transaminase (ALT) values but no increase in GGT and amylase levels.
- Group II B, patients are alcoholics with increased Total Bilirubin, Direct Bilirubin, Alkaline phosphatase (ALP), Alanine transaminase (ALT), GGT and Amylase levels.

Statistical analysis was done by comparing the values of group II A and group II B with group I, and the results are presented in the table number I and II respectively.

- When group IIA is compared with group I, Total bilirubin, Direct bilirubin, Alkaline phosphatase (ALP), Alanine transaminase (ALT) levels are increased, and they are statistically significant, ("p" value = <0.01). But there is no significant increase in GGT and Amylase levels.("p" value = 0.9 and 0.8 respectively).
- When group II B is compared with group I, all parameters are increased including GGT and Amylase. And they are statistically significant, ("p" value = <0.01).

Statistical analysis was also done by Comparing group II A with group II B to know the significance of GGT and Amylase to distinguish alcoholic hepatitis from non alcoholic hepatitis, and results are presented in table number III. Both these biochemical parameters had shown significance. ("p" value = <0.01).

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TABLE – I SUMMARY OF RESULTS WITH GROUP I AND GROUP IIA

BIOCHEMICAL PARAMETERS	VALUES OF	(GROUP- I)	(GROUP- II A)
Total bilirubin (mg/dl)	Mean	0.8	4.4
Normal value: Up to1.0mg/dl	S.D	0.15	1.9
	SED	0.4	
	t- value	9	
	"p" value	< 0.001	
Direct bilirubin (mg/dl)	Mean	0.3	2.1
Normal value: Up to 0.2 mg/dl	S.D	0.1	1.0
	SED	0.2	
	t- value	9	
	"p" value	< 0.001	
Alkaline phosphatase (U/L)	Mean	157.4	212.4
Normal value: In adults = 60-170 U/L In children = 151 to 471 U/L	S.D	15.16	57.9
	SED	13	
	t- value	4.2	
	"p" value	<0.01	
Alanine transaminase (U/L)	Mean	35.5	70.8
Normal value: Up to 49 U/L.	S.D	8.7	59.7
	SED	4.6	
	t- value	7.6	
	"p" value	< 0.01	
Gamma glutamyl transferase (U/L)	Mean	35.7	40
Normal value; In males =10-50U/L In females=07-35U/L.	S.D	7.42	13.8
	SED	3.5	
	t- value	1.2	
	"p" value	<0.8	
Amylase (U/L)	Mean	50.4	49.4
Normal values: Up to 85U/L.	S.D	12.8	18
	SED	5.0	
	t- value	0.2	
	"p" value	<0.8	

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TABLE II - SUMMARY OF RESULTS WITH GROUP I AND GROUP IIB

BIOCHEMICAL PARAMETERS	VALUES OF	NON ALCOHOLIC PATIENTS WITH NORMAL L.F.T. (GROUP- I)	ALCOHOLIC HEPATITIS (GROUP- II B)

Total bilirubin (mg/dl)	Mean	0.8	5.1
Normal value: Up to1.0mg/dl	S.D	0.15	3.7
	SED	0.7	
	t- value	6.1	
	"p" value	< 0.001	
Direct bilirubin (mg/dl)	Mean	0.3	2.1
Normal value: Up to 0.2 mg/dl	S.D	0.1	1.0
	SED	0.2	
	t- value	10.43	
	"p" value	< 0.001	
Alkaline phosphatase (U/L)	Mean	157.4	220.5
Normal value: In adults = 60-170 U/L In children = 151 to 471 U/L	S.D	15.16	121.9
	SED	27.48	
	t- value	2.3	
	"p" value	<0.02	
Alanine transaminase (U/L)	Mean	35.5	100.4
Normal value: Up to 49 U/L.	S.D	8.7	67.2
	SED	15.1	
	t- value	4.2	
	"p" value	< 0.01	
Gamma glutamyl transferase (U/L)	Mean	35.7	113.8
Normal value; In males =10-50U/L In females=07-35U/L.	S.D	7.42	28.1
	SED	6.5	
	t- value	12.0	
	"p" value	<0.001	
Amylase (U/L)	Mean	50.4	331.5
Normal values: Up to 85U/L.	S.D	12.8	235.5
	SED	52.7	
	t- value	5.3	
	"p" value	<0.001	

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TABLE III
SUMMARY OF RESULTS WITH GROUP II AAND GROUP II B

BIOCHEMICAL PARAMETERS	VALUES OF	(GROUP II A)	(GROUP II B)
Total bilirubin (mg/dl)	Mean	4.4	5.1
Normal value: Up to1.0mg/dl	S.D	1.9	3.7
	SED	0.9	
	t- value	0.7	
	"p" value	0.4	
Direct bilirubin (mg/dl)	Mean	2.1	2.7
Normal value: Up to 0.2 mg/dl	S.D	1.0	2.1
	SED	0.5	
	t- value	1.1	
	"p" value	0.2	

Alkaline phosphatase (U/L)	Mean	212.4	220.5
Normal value: In adults = 60-170 U/L In children = 151 to 471 U/L	S.D	57.9	121.9
	SED	31.48	
	t- value	0.25	
	"p" value	0.8	
Alanine transaminase (U/L)	Mean	70.8	100.4
Normal value: Up to 49 U/L.	S.D	59.7	67.2
	SED	20.6	
	t- value	1.4	
	"p" value	0.1	
Gamma glutamyl transferase (U/L)	Mean	40	113.8
Normal value; In males =10-50U/L In females=07-35U/L.	S.D	13.8	28.1
	SED	7.3	
	t- value	10.1	
	"p" value	< 0.001	
Amylase (U/L)	Mean	49.4	331.7
Normal values: Up to 85U/L.	S.D	18	235.5
	SED	55.5	
	t- value	5.0	
	"p" value	< 0.001	

V. DISCUSSION

Laboratory investigations may help for the diagnosis of alcoholism and alcohol related diseases, like alcoholic hepatitis and alcoholic pancreatitis.

In the present study serum GGT and Amylase levels are taken as diagnostic markers of alcoholism and alcohol related diseases like alcoholic hepatitis and alcoholic pancreatitis. These parameters are estimated along with normal LFT (Total bilirubin, Direct bilirubin, Alkaline phosphatase (ALP), Alanine transaminase (ALT) in all subjects included in the study.

According to the results, it is found that in both types of hepatitis (alcoholic and non alcoholic), increased levels of Total bilirubin, Direct bilirubin, Alkaline phosphatase (ALP), Alanine transaminase (ALT) are observed, in addition to this an increase in serum GGT and Amylase levels is observed in alcoholic hepatitis cases.

Increased synthesis of GGT in the liver of Alcohol consuming persons, leads to the elevated levels of GGT in their serum. That is commonly noted in patients with the alcoholic liver disease. Elevated blood levels of the liver enzyme Gamma Glutamyl transferase (GGT) indicate heavy alcohol use and liver injury. This test has greater sensitivity but less specificity than AST or ALT tests. Of the three enzymes, GGT is the best indicator of excessive alcohol consumption; GGT is often abnormal in alcoholics even with normal LFT or with normal histology. So it is more useful index of occult alcoholism, but it is less sensitive as GGT is present in many organs and because some drugs can raise GGT levels, so high GGT levels are not necessarily an indicator of alcohol abuse. In the present study increased GGT levels are observed in 4 cases of non alcoholics, indicating the less specificity of GGT.

Increased levels of serum Amylase in alcoholics is due to 2 types of effects of alcohol on pancreas.

1) Direct toxic effects of alcohol on acinar cells of pancreas
2) By alcohol induced oxidant stress and damage to pancreatic acinar cells.

However, recent studies indicate that up to one-third of patients with alcoholic pancreatitis may fail to show any significant rise in amylase levels.But, as this study was done in patients belonging to rural areas, who consume un refined alcoholic beverages and such consumption is very frequent on daily basis in this region, and was done in patients belonging to the age group of 42±9 (Alcoholic pancreatitis usually occurs in men in their forties) in almost all cases of alcoholic hepatitis, alcohol related damage to pancreas is also observed with increased levels of amylase.

Normally in acute pancreatitis amylase levels may increases 3-6 times than its normal value. In this study among the 20 cases (hepatitis patients with the history of alcoholism) such type of increase is observed in 8 cases, in remaining 12 cases mild increase is observed. It is due to the alcohol related damage to the pancreas.

VI. CONCLUSION

From this study it can be concluded that serum GGT activity is an indicator of hepatic damage in cases of hepatitis with the history of alcoholism. Most of the cases included in the study have elevated serum amylase also, indicating pancreatic damage by alcohol. It is advisable to estimate gamma glutamyl tranferase activity in all cases of hepatitis to exclude the

underlying damage caused by chronic alcoholism, which is widely prevalent in all segments of population.

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