



Research Article

COMPARATIVE STUDY OF HEPATIC CHANGES IN PATIENTS OF METABOLIC SYNDROME AND CHRONIC ALCOHOLISM

Mahesh Gupta¹

¹Department Of Medicine, NIMS Medical College, JAIPUR

Correspondence should be addressed to **Mahesh Gupta**

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ABSTRACT

Aims and Objective: Comparative study of hepatic changes in patients of metabolic syndrome and chronic alcoholism.

Material and Method: The material of the study included 30 metabolic syndrome patients and 30 chronic alcoholics selected from the medicine outdoor clinic (including diabetic clinic) and medicine indoor wards as well as from GI clinic of Postgraduate Department of Medicine, S.N. Medical College and Hospital Agra .

Results: Most metabolic syndrome patients (60%) as well as chronic alcoholics (50%) were asymptomatic. Anorexia and fatigue/ malaise was present in 13.3% and 40% respectively in metabolic syndrome patients as compared to anorexia (30%) and fatigue / malaise (50%) in chronic alcoholics. Nausea / vomiting and right upper abdominal quadrant pain was present in 10% metabolic syndrome patients as compared Nausea / vomiting (40%) and Right upper abdominal quadrant pain(26.6%) in chronic alcoholics.

Hepatomegaly and icterus was present in 23.3% and 10% respectively in metabolic syndrome patients as compared hepatomegaly (80%) and icterus (60%) in chronic alcoholics. Ascites and upper GI bleeding was present in 13.3% and 6.7% metabolic syndrome patients respectively as compared to ascites (50%) and upper GI bleeding (9%) in chronic alcoholics.

Mean AST and ALT levels were 65.56 ± 67.22 and 84.9 ± 91.9 U/L respectively in metabolic syndrome patients. AST/ALT ranged from 0.91 to 1.85 with mean of 0.98 ± 0.26 while in chronic alcoholics mean AST and ALT levels were 98.4 and 48.2 .AST and ALT levels were statistically significant (p value <0.05) in chronic alcoholics and the AST/ ALT was 2.04. Gamma glutamyl transferase enzyme level was elevated in most (80%) chronic alcoholics while was near normal in metabolic syndrome patients.

On ultrasonography most of chronic alcoholics (93.3%) had abnormal findings like fatty liver (80%), cirrhosis (13.3%) as compared to metabolic syndrome patients having NAFLD (33.3%), and cirrhosis (6.67%).

On Histological examination metabolic syndrome patients had NAFLD in 33.3%, NASH in 41.6% and cirrhosis in 8.3% as compared to chronic alcoholic patients having fatty liver in 35.7%, alcoholic hepatitis in 49.9% and cirrhosis in 14.3%.

Conclusions:

- Symptoms like anorexia, fatigue/malaise, nausea/vomiting, right upper abdominal pain and signs like hepatomegaly, icterus, Splenomegaly, ascites, UGI bleeding were compared and statistically significant (p value <0.05) Symptomatology and signs were found in chronic alcoholics as compared to metabolic syndrome patients.
- Statistically significant (p value <0.05) deranged liver function tests were found in chronic alcoholics as compared to metabolic syndrome patients.

- c. On Hepatic Ultrasonography statistically significant (p value <0.05%) hepatic changes in the form of fatty liver, cirrhosis were observed in 93.4% patients of chronic alcoholics as compared to metabolic syndrome patients (60%).
- d. Patients with hepatomegaly, abnormal liver function tests and abnormal ultrasonographic findings were observed as high risk cases. Histopathological assessment of high risk patients revealed significant changes in the form of NAFLD (33.3%), NASH (41.6%) and cirrhosis (8.3%) in metabolic syndrome patients as compared to chronic alcoholics in the form of alcoholic fatty liver (35.7%), alcoholic hepatitis (49.9%) and cirrhosis (14.3%).
- e. Statistically positive correlation of high risk group patients has shown abnormal ultrasonographic finding, abnormal liver function tests and the histopathological changes in the patients of both the groups. Though statistically (p value <0.05) significant changes were seen in chronic alcoholics as compared to metabolic syndrome patients.

KEYWORDS: Metabolic Syndrome, Chronic Alcoholic

INTRODUCTION

The metabolic syndrome is a constellation of clinical and metabolic abnormalities including abdominal obesity, hypertension, dyslipidemia and impaired fasting glucose/or impaired glucose tolerance. All these manifestations are surrogate marker of insulin resistance which is the crux abnormality associated with metabolic syndrome.

As diabetes manifests its complications through glucotoxicity, similarly metabolic syndrome mediate their toxic effects via the free fatty acids on various tissues of the body including liver and muscle. Therefore, the accumulation of excessive fat in the liver is a manifestation of lipotoxicity to the liver. Initially this is characterized by only steatosis, but later on free fatty acids induce inflammatory reactions called as steatohepatitis.

The long-term consequences of non-alcoholic steatohepatitis (NASH) include cirrhosis of the liver and hepatocellular carcinoma.

Patients with simple steatosis have a relatively benign liver disease with a risk of developing clinical evidence of cirrhosis. Over 15-20 years in the order of 1-2 Patients with NASH and fibrosis can progress to cirrhosis, defined histologically or clinically with the risk varying from 0% at 5 years to 12% over 8 years. Once cirrhosis develops, patients are at higher risk of developing hepatic decompensation and of dying from liver related cause including hepatocellular carcinoma.

Therefore, NASH has to be identified early in the disease course and requires appropriate therapy to prevent long-term undesirable consequences.

Alcohol, a drug is consumed at some time by up to 80% of population. At low doses alcohol can have some beneficial

effects such as decreased rates of Myocardial infarction, stroke, gall stones & possibly vascular & Alzheimer’s dementias. However, the consumption of more than two standard drinks per day increases the risk for health problems in many organ systems.

Chronic and excessive alcohol ingestion (more than 10 years) is one of the major causes of liver disease. Quantity and duration of alcohol intake are the most important risk factors involved in the development of alcoholic liver disease.

In general the time it takes to develop liver disease is directly related to the amount of alcohol consumed .The threshold for developing alcohol liver disease in men is an intake of more than 60 to 80 gm/day of alcohol for 10 years, while women are at increased risk of developing similar degrees of liver injury by consuming 20 – 40 gm/day. Ingestion of 160 gm/day is associated with 25 fold increased risk of developing alcoholic cirrhosis.

Alcohol impair gluconeogenesis in liver resulting in a fall in the amount of glucose produced from glycogen, increased lactate production and decreased oxidation of fatty acids. This contributes an increase in fat accumulation in liver cells. In healthy individuals these changes are reversible, but with repeated exposure to Alcohol more severe changes in liver occur, including alcohol induced Hepatitis, perivenular sclerosis and cirrhosis, with the later observed in an estimated 15% of alcoholics.

No study showing comparative study of hepatic changes in the patients of metabolic syndrome and chronic alcoholism done until today so I have chosen this study for comparative study.

Table 1: Age and sex distribution of all subjects

Age of study group (years)	METABOLIC SYDNROME (N = 30)				CHRONIC ALCOHOLICS (N = 30)			
	Male (N = 12)	Female (N = 18)	Total (N = 30)	%	Male (N = 27)	Female (N = 3)	Total (N = 30)	%
30-39	2	2	4	13.3	5	0	5	16.6
40-49	2	10	12	40	9	1	10	33.3
50-59	6	5	11	36.7	5	2	7	23.3
>60	2	1	3	10	8	0	8	26.6

AIMS & OBJECTIVES

- i. To compare the clinical symptoms and signs in the patients of metabolic syndrome and chronic alcoholism.
- ii. To compare the derangement in liver function tests, ultrasonographic findings as well as histopathological findings in the patients of metabolic syndrome and chronic alcoholism.
- iii. To determine the high risk patients who have potentiality for NAFLD as well as NASH in metabolic syndrome and Alcoholic fatty liver and alcoholic hepatitis as well as alcoholic cirrhosis in chronic alcoholism.

Table 2: Prevalence of symptomatology and signs of hepatic involvement in the study group

	Symptoms	Metabolic Syndrome Patients (n = 30)		Chronic Alcoholics (n = 30)	
		No.	%	No.	%
1.	Anorexia	4	13.3	10	30
2.	Fatigue/malaise	12	40	15	50
3.	Nausea & Vomiting	3	10	12	40
4.	Right upper quadrant discomfort	3	10	8	26.6
5.	Hepatomegaly	7	23.3	24	80
6.	Icterus	3	10	18	60
7.	Splenomegaly	4	13.3	9	30
	• Mild	2	6.6	5	16.6
	• Moderate	1	3.3	3	10
	• Huge	1	3.3	1	3.3
8.	Ascites	4	13.3	15	50
9.	UGI bleeding	2	6.7	3	9.0

MATERIAL & METHODS

The study was carried out in the Post-graduate Department of Medicine, S.N. Medical College, Agra in the period of March 2010 to Feb., 2011.

The material of the study included 30 metabolic syndrome patients and 30 chronic alcoholics selected from the medicine outdoor clinic (including diabetic clinic) and medicine indoor wards as well as from GI clinic.

Inclusion criteria for metabolic syndrome

According to the National Cholesterol Education Programme Adult Treatment Panel III (ATP III) metabolic syndrome was diagnosed in the patients who have at least three of the following criteria.

Elevated waist circumference

- i. **Men:** equal to or greater than 40 inches (102 cm) (90 cm for Indian).
- ii. **Women:** equal to or greater than 35 inches (88 cm) (80 cm for Indians).

Elevated Triglycerides

- i. Equal to or greater than 150 mg/dl

Reduced HDL (gold) cholesterol

- i. **Men-** less than 40 mg/dl
- ii. **Women-** less than 50 mg/dl

Elevated blood pressure

- i. Equal to or greater than 130/85 mmHg

Elevated fasting glucose

- ii. Equal to or greater than 100 mg/dl

INCLUSION CRITERIA FOR CHRONIC ALCOHOLISM

History of chronic alcohol intake should be present –

In case of men: Intake of more than 60 to 80 gm/day of alcohol intake at least for 10 years.

In case of women: Intake of more than 20 to 40 gm/day of alcohol intake at least for 10 years.

EXCLUSION CRITERIA

- 1. Chronic liver disease due to other causes i.e. hepatitis B, hepatitis C, drug induced and autoimmune disease,
- 2. Decompensated cirrhosis (child pugh-3),
- 3. Patient with overt cardiac dysfunction, recent stroke and pregnancy
- 4. Patients on Hepatotoxic drugs
- 5. Patients with history suggestive of inflammatory bowel disease, jejunioileal bypass, total parental nutrition were also excluded from this study.

The enrolled patients were subjected to a protocol which included detailed history regarding mode of onset, presentation, duration of illness, personal antecedents including history of alcohol intake. The subjects were subjected to thorough general physical examination.

All patients selected were subjected to following laboratory investigations.

- i. Complete haemogram
- ii. Blood sugar (fasting and post prandial)
- iii. Renal function test
- iv. Urine routine and microscopic examination
- v. Liver function tests (Serum bilirubin, SGOT/SGPT, PT, S. proteins)
- vi. Lipid profile
- vii. Electrolyte (Na⁺, K⁺, iCa⁺⁺)
- viii. USG abdomen especially for size, shape and echo texture of liver to diagnose NAFLD & NASH in metabolic syndrome and fatty liver, alcoholic hepatitis, alcoholic cirrhosis and to exclude other causes of chronic liver disease.

Patients those with abnormal liver function tests were subjected to further investigations.

1. Investigations to rule out other causes responsible for abnormal LFT.
 - a. Serological markers for HBV, HCV
 - b. Autoimmune marker
2. The selected patients were subjected for liver biopsy to find out histopathological changes in NAFLD and NASH in metabolic syndrome and alcoholic fatty liver, alcoholic hepatitis and alcoholic cirrhosis in chronic alcoholics and to exclude other causes of chronic liver diseases.

Most metabolic syndrome patients (60%) as well as chronic alcoholics (50%) were asymptomatic. Anorexia was present in 13.3% metabolic syndrome patients as compared 30% chronic alcoholics, fatigue and malaise was present in 40% metabolic syndrome patients as compared 50% chronic alcoholics.

Nausea and vomiting was present in 10% metabolic syndrome patients as compared to 40% chronic alcoholics. Right upper abdominal quadrant pain was present in 10% metabolic syndrome patients as compared to 26.6% of chronic alcoholics.

Hepatomegaly was present in 23.3% metabolic syndrome patients as compared to 80% chronic alcoholics; While Icterus was present in 10% metabolic syndrome patients as compared to 60% chronic alcoholics.

Ascites and upper GI bleeding was present in 13.3% and 6.7% metabolic syndrome patients respectively as compared to ascites (50%) and upper GI bleeding (9%) in chronic alcoholics.

Mean AST and ALT levels were 65.56 ± 67.22 and 84.9 ± 91.9 U/L respectively in metabolic syndrome patients. AST/ALT ranged from 0.91 to 1.85 with mean of 0.98 ± 0.26 while in chronic alcoholics mean AST and ALT levels were 98.4 and 48.2. AST and ALT levels were statistically significant ($p < 0.05$) in chronic alcoholics and the AST/ALT was 2.04. Gamma glutamyl transferase enzyme level was elevated in most (80%) chronic alcoholics while was near normal in metabolic syndrome patients. The levels of enzyme were statistically significant ($p < 0.05$) in chronic alcoholics.

On ultrasonography most of chronic alcoholics (93.3%) had abnormal findings like fatty liver (80%), cirrhosis (13.3%) as compared to metabolic syndrome patients having NAFLD (33.3%), and cirrhosis (6.67%). On statistical analysis chronic alcoholic patients had significant ($p < 0.05$) ultrasonographic findings as compared to metabolic syndrome patients.

On Histological examination metabolic syndrome patients had NAFLD in 33.3%, NASH in 41.6% and cirrhosis in 8.3% as compared to chronic alcoholic patients having fatty liver in 35.7%, alcoholic hepatitis in 49.9% and cirrhosis in 14.3%.

Table 3: Abnormal liver function tests in the study group

Abnormal LFTs		Metabolic Syndrome Patients (n = 30)		Chronic Alcoholic patient (n = 30)	
		No.	%	No.	%
1.	Serum bilirubin	8	26.7	12	40.0
2.	AST	12	40.0	15	50.0
3.	ALT	14	46.7	13	43.3
4.	Mean AST / ALT Ratio	0.98		2.04	
5.	Gama Glutamyl Transferase Level	3	10	24	80
6.	S.alkaline phosphatase	12	40.0	14	46.7
7.	Prothrombin time	8	26.7	10	30.0
8.	S. albumin	5	16.6	15	50.0

RESULTS

The majority of patients were of age group 40 – 60 years.

Table 4: Hepatic ultrasonographic changes in the study group

USG Abdomen		Metabolic Syndrome Patients (n = 30)		Chronic Alcoholic patient (n = 30)	
		No.	%	No.	%
1.	Normal	18	60	2	6.6
2.	Increased hepatic echogenicity	10	33.3	24	80
3.	Coarse echo texture of liver	2	6.67	4	13.3

DISCUSSION

The present study was undertaken to compare the hepatic changes in the patients of metabolic syndrome and chronic alcoholics due to lack of study in this field.

In this study we found that out of 30 metabolic syndrome patients, 12 (40%) were male and 18 (60%) female. Male

to female ratio was 2:3 providing that disease was more dominant in females. In study of Ludwig J. et al (1988) metabolic syndrome was more in middle aged obese women as compared to men. Most of patients of metabolic syndrome were belonging to age group 40 – 59 years in my study. Mean age of patients with metabolic syndrome

in a study by Bacon and colleagues was 47 and similarly Ludwig j. et al (1988) also noted mean age of 54 years.

In chronic alcoholics 27 patients were male and 3 were females. Most of patients were belonging to age group 40 – 60 years. Mean age of chronic alcoholics in study by Sarmistha biswas, sujat Paul et al (1999) was 51 years and most of patients(47 out of 50) were male.

Most metabolic syndrome patients (60%) were asymptomatic. Study of angulo P et al gastroenterology hepatology 2002; 17(suppl) also observed that 45 -100% patients of metabolic syndrome have no symptoms or signs of liver disease at time of diagnosis. When symptoms occur they were non-specific like persistent, fatigue/ malaise (40%). Loss of appetite (13.3%), Right upper quadrant discomfort (10%), Mofrad p.s., Sanyal aj et al. medsoape general medicine 2003; 5(2) reported above symptoms in about 40 – 60% of patients.

In chronic alcoholics 50% patients were asymptomatic. Symptoms were present like anorexia (30%), fatigue and malaise (50%), nausea and vomiting (40%), right upper quadrant pain (26.6%) in chronic alcoholics. Symptomatology was more eminent in chronic alcoholics than the patients of metabolic syndrome. Study of Abus Sayeed, M.D. Shahrar Mahbub,2003 reported fatigue and malaise in 34%, Anorexia in 40%, Nausea and vomiting in 20% chronic alcoholics.

Hepatomegaly was present in 23.3% metabolic syndrome patients as compared to 80% chronic alcoholics.

Advanced disease was presented with ascites (13.3%), icterus (10%), UGI bleeding (6.7%) in metabolic syndrome patients. Study from Patel, lee JG. Medicine journal 2001; 2:8 reported ascites in (0-3%), jaundice in (0-5%), and G.I bleeding in (0-3%) metabolic syndrome patients.

While in chronic alcoholics ascites in 15 (50%), Icterus in 18 (60%) and UGI bleeding in 3 (9.1%) were present. These findings were more eminent in chronic alcoholic patients. Study from Mendohal cl alcoholic hepatitis clin gastro enterol 1981, 10; 417 – 41 reported, hepatomegaly in 86.71, Icterus in 60.1%, Ascites in 57.1% chronic alcoholics.

Liver functions tests were more deranged in chronic alcoholics. Mean alkaline phosphate level was 158.73 ± 73.31 which was not significant (p value > 0.05) in metabolic syndrome while in case of chronic alcoholics this level was 580.00 ± 74.3 which was statistically significant (p value < 0.05). In metabolic syndrome patients mean SGPT (ALT) was 84.9 ± 91.04 and mean SGOT (AST) level was 65.56 ± 67.22 which were statistically insignificant (p value < 0.05) . Amaraparkar DN. et al. Acta Med Scand (suppl) 1985; 703:103-110 observed that mean AST & ALT level were 40.2 ± 17.1 U/L and 44.4 ± 21.7 U/L respectively in metabolic syndrome patients.

While in chronic alcoholics the mean SGPT (ALT) level was 58.01 and SGOT (AST) level was 90.42 which were statistically significant (p value < 0.05).In chronic alcoholics AST level was more elevated than ALT. Mendohal cl; alcoholic hepatitis clin. Gastroenterol 1981; 10: 417 – 41 reported mean AST level 84 ± 99 and mean ALT level 56 ± 57 .

Gamma glutamyl transferase was elevated only in 10% metabolic syndrome patients which was statistically insignificant (p value>0.05) while in chronic alcoholic patients it was significantly (p value<0.05) elevated in most (80%) patients.

40% patients of metabolic syndrome had ultrasonographic abnormality out of which 33.3% had increased hepatic echogenicity, 6.67 have coarse echo texture of liver as compared to chronic alcoholic patients 93.3% patients had ultrasonographic abnormality out of which 80% had increased hepatic echogenicity, 13.3% had coarse echo texture of liver. Sh Saverymuttu 1986 cited by 305-related articles observed 94% abnormal USG findings in alcoholic liver disease patients.

Liver biopsy has been done in high risk cases having hepatomegaly, abnormal USG findings, abnormal LFT's. Metabolic syndrome patients 33.3%had NAFLD, 41.6% had NASH, and 8.5% had cirrhosis study by Diehl am et al gastroenterology 1988; 95:1056-62 observed around 80%changes on liver biopsy in metabolic syndrome patients.

While in chronic alcoholics 35.7% had fatty liver disease, 49.9% had alcoholic hepatitis and 14.3% had cirrhosis. Study done by Bravo AA, Seth sg, and Chopra s .liver biopsy .n Engl j med .Feb. 15 2001; 344(7):495-500. Observed hepatic changes on liver biopsy in all his alcoholic patients (9 out of 9) and Ballard et al. (1961) also observed changes in all his patients (5 out of 5).

Biopsy of these patients was shown more hepatic changes in chronic alcoholics as compared to metabolic syndrome patients.

Table 5: Histopathological changes in the study group who have abnormal lft's or ultrasonographic findings

Histopathological grading		Metabolic Syndrome Patients (n = 12)		Chronic Alcoholics (n = 14)	
		No.	%	No.	%
1.	Normal	2	16.6	0	0
2.	I	4	33.3	5	35.7
3.	II	3	25	4	28.5
4.	III	2	16.6	3	21.4
5.	IV	1	8.3	2	14.3

CONCLUSIONS

- i. Most metabolic syndrome patients (60%) and chronic alcoholics (50%) were asymptomatic. Symptoms like anorexia, fatigue/malaise, nausea/vomiting, right upper abdominal pain and signs like hepatomegaly, icterus, Splenomegaly, ascites, UGI bleeding were compared and statistically significant (p value<0.05) Symptomatology and signs were found in chronic alcoholics as compared to metabolic syndrome patients. Hence it appears from this study that

- alcoholics have earlier signs and symptoms as compared to metabolic syndrome patients
- ii. Statistically significant (p value <0.05) deranged liver function tests were found in chronic alcoholics as compared to metabolic syndrome patients.
- iii. On Hepatic Ultrasonography statistically significant (p value <0.05%) hepatic changes in the form of fatty liver, cirrhosis were observed in 93.4% patients of chronic alcoholics as compared to metabolic syndrome patients (60%).
- iv. Patients with hepatomegaly, abnormal liver function tests and abnormal ultrasonographic findings were observed as high risk cases. Histopathological assessment of high risk patients revealed significant changes in the form of

NAFLD (33.3%), NASH (41.6%) and cirrhosis (8.3%) in metabolic syndrome patients as compared to chronic alcoholics in the form of alcoholic fatty liver (35.7%), alcoholic hepatitis (49.9%) and cirrhosis (14.3%).

- V. Statistically positive correlation of high risk group patients has shown abnormal ultrasonographic finding, abnormal liver function tests and the histopathological changes in the patients of both the groups .Though statistically (p value <0.05) significant changes were seen in chronic alcoholics as compared to metabolic syndrome patients. Hence it is concluded from the aforesaid study that a larger study with more number of patients may be needful for more fruitful conclusions.

Table 6: Histological Diagnosis in high risk group patients (having Hepatomegaly, abnormal LFT's, Abnormal Ultrasonographic Findings along with abnormal histopathological findings)

	Metabolic Syndrome			Chronic Alcoholic Patients		
	NAFLD	NASH	Cirrhosis	Fatty Liver	Alcoholic Hepatitis	Cirrhosis
	4(33.3%)	5(41.6%)	1(8.3%)	5(35.7%)	7(49.9%)	2(14.3%)

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