



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

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ABSTRACT

Aims and Objectives- Study of hepatic changes in patients of metabolic syndrome and chronic alcoholism. **Materials and Methods -** 30 metabolic syndrome patients and 30 chronic alcoholic patients were selected from the Postgraduate Department of Medicine, SN Medical College Agra. **Results-** Most of metabolic syndrome patients (60%) as well as chronic alcoholics (50%) were asymptomatic. Anorexia and fatigue was present in 13.3% and 40% respectively in metabolic syndrome patients as compared to anorexia (30%) and malaise (50%) in chronic alcoholics. Nausea / vomiting and right upper abdominal quadrant pain was present in 10% metabolic syndrome patients as compared to 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 to 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:** 1. Symptoms like anorexia, fatigue/malaise, nausea/vomiting, right upper abdominal pain and signs like hepatomegaly, icterus, splenomegaly, ascitis, 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. 2. Statistically significant (p value < 0.05%) deranged liver function tests were found in chronic alcoholics as compared to metabolic syndrome patients. 3. 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%). 4. 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 (40%) and cirrhosis (14.3%). 5. 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 groups. Though statistically (p value <0.05) significant changes were seen in chronic alcoholics as compared to metabolic syndrome patients.

KEYWORDS: Metabolic syndrome, chronic alcoholism, hepatomegaly.

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 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

issues of the body including liver and muscle. Therefore, the accumulation of extensive 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 causes 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 consumed by up to 80% population. At low doses, alcohol can have some beneficial effects such as decreased rates of myocardial infarction, stroke, gallstones & possibly vascular & Alzheimer 's dementia. However, the consumption 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 g / day of alcohol for 10 years while women are at increased risk of developing similar degrees of liver injury by consuming 20 - 40 g /day. Ingestion of 160 g / day is associated with 25 fold increased risk of developing alcoholic cirrhosis.

Alcohol impairs 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.

AIMS AND OBJECTIVES

1. To compare the clinical symptoms and signs in the patients of metabolic syndrome and chronic alcoholism.

2. To compare the derangement in liver function tests, ultrasonographic findings as well as histopathological findings in the patients of metabolic syndrome and chronic alcoholism.
3. 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.

MATERIAL AND METHODS

The study was carried out in the Postgraduate Department of Medicine, SN 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 alcoholic 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

Men -equal to or greater than 40 inches (102 cm) (90 cm for Indians).

Women- equal or greater than 35 inches (88 cm) (80 cm for Indians).

Elevated Triglycerides

Equal to or greater than 150 mg / dl

Reduced HDL (gold) cholesterol

Men -less than 40 mg / dl

Women -less than 50 mg / dl

Elevated blood pressure

Equal to or greater than 130 / 85 mmHg

Elevated fasting glucose:

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 like 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.

- Complete haemogram.
- Blood sugar (fasting and post prandial).
- Renal function test.
- Urine routine and microscopic examination.
- Liver function tests (Serum bilirubin, SGOT / SGPT, PT, S. proteins).

- Lipid profile.
- Electrolyte (Na, K, iCa⁺⁺)
- 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.
 - Serological markers for HBV, HCV.
 - 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.

RESULTS AND DISCUSSION

Table 1: Age and sex distribution of all subjects.

Age of study group In Years	Metabolic syndrome (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

Aforesaid table clearly depicting that chronic alcoholism is predominant in male as compared to metabolic syndrome, where female preponderance has been observed. Similarly, Ludwig J. et al (1988) metabolic syndrome was more in middle aged obese women as compared to men. Most of the patients of metabolic syndrome were belonging to age group 40-59 years in

the study. Mean age of patients with metabolic syndrome in a study by Bacon & colleagues was 47 and similarly, Ludwig J. et al (1988) also noted mean age of 54 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.

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

Symptoms		Metabolic syndrome Patients (N=30)		Chronic alcoholic (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

Various signs and symptoms are comparable in both the groups but alcoholic patients relatively had more early symptomatology as compared to metabolic syndrome. Similar observations has also been noted in the study of

Mofrad p.s., Sanyal aj et al medscape general medicine 2003; 5(2) reported above symptoms in about 40-60% of patients. Study of Abus Sayeed, M.D. Shahriar Mahbub, 2003 reported the same.

Table 3: Abnormal liver function tests on the study group.

Abnormal LFT's		Metabolic syndrome patients (n=30)		Chronic alcoholic patients (n=30)	
		No.	%	No.	%
1	Serum bilirubin	8	26.7	12	40
2	AST	12	40.0	15	50
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	Serum 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

LFT abnormality and its severity were statistically significant ($p < 0.05$) in alcoholic group as compared to metabolic syndrome group. Similar study performed by Amaraparker DN. et al. Acta Med Scand (suppl) 1985;

703: 103-110 observed that mean AST and ALT level were 40.2 ± 17.1 U/L and 44.4 ± 21.7 U/L respectively in metabolic syndrome patients.

Table 4: Hepatic Ultrasonography changes in the study group.

USG ABDOMEN		Metabolic syndrome patients (n=30)		Chronic alcoholic patients (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

Ultrasound clearly showing abnormal USG findings more in patients of chronic alcoholic as compared to metabolic syndrome which is statistically significant. 40% patients of metabolic syndrome had ultrasonographic abnormality out of which 33.3% had increased hepatic echogenicity, 6.67% coarse echotexture 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 echotexture of liver. Sh Saverymuttu 1986 citedly 305 –related articles observed 94% abnormal USG findings in alcoholic liver disease patients.

Table 5: Histopathological Findings Observed in The Study Group Who Have Abnormal LFT Or Ultrasonographic Findings.

HISTOPATHOLOGICAL GRADING		METABOLIC SYNDROME PETIENTS (N=12)		CHRONIC ALCOHOLIC (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

Aforesaid table depicting 14 patients in chronic alcoholic group vs 12 patients in metabolic group and none of the patients having normal histopathology. While in chronic alcoholics, 35.7% had fatty liver diseases, 49.9% had alcoholic hepatitis and 14.3% hhad 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).

Table 6: Histological Findings Observed In High Risk Group Patients (Having Hepatomegaly, Abnormal LFT's, Abnormal Ultrasonography Finding 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%)

Aforesaid table clearly depicting more histological findings in form of fatty liver, alcoholic hepatitis & cirrhosis compared to metabolic syndrome. Statistically significant association observed in chronic alcoholic patients having alcoholic steatohepatitis.

CONCLUSION

1. 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.
2. Statistically significant (p value < 0.05) deranged liver function tests were found in chronic alcoholics as compared to metabolic syndrome patients.
3. 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)%.
4. 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%).
5. 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.

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