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A Cross- sectional Study On Relationship Between AST/ALT Ratio and Metabolic Syndrome at a Tertiary Care Centre in Tamilnadu

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#### ABSTRACT

**Introduction:**The metabolic syndrome is a combination of insulin resistance, visceral adiposity, dyslipidemia and hypertension, which are interrelated. One important use of metabolic syndrome is clinical assessment of patients, in identifying patients with high risk of Non-Alcoholic Fatty Liver Disease(NAFLD)Type 2 Diabetes Mellitus(T2DM) or Cardiovascular Disease(CVD)

**Materials & Methods:** This is a cross- sectional study conducted among 150 patients admitted in a tertiary care centre in Chengalpattu district. All the study participants underwent clinical examinations, anthropometric measurements and laboratory investigations to be diagnosed a metabolic syndrome as per NCEP: ATP III criteria.

**Results:** The prevalence of Metabolic syndrome was found to be 26%. Only educational status had association (p value <0.001) with Liver enzymes in our study. Metabolic syndrome had significant association with AST/ ALT ratio with p value of 0.001.

**Conclusion:**Our study had Liver enzymes strongly correlated with Metabolic syndrome. Since NAFLD is more prevalent in Metabolic syndrome patients, these liver enzymes play a major role in identifying patients with NAFLD which is early predictor of cardiovascular diseases.

Key words: Metabolic Syndrome, Liver enzymes, NAFLD, AST/ ALT ratio

## **INTRODUCTION**

Some patients were found to have a cluster of several metabolic disorders as early as 1923, including hypertension, hyperglycemia, and hyperuricemia.Reaven took over five decades to coin the term "syndrome X" to describe a group of abnormalities regarding metabolism that include intolerance to glucose, elevated blood pressure, increased very-low-density lipoproteins and triglycerides, and decreased high-density lipoprotein cholesterol, with resistance to insulin as the root cause of pathophysiologic problem.

Various organizations have offered alternative definitions and terminologies in recent years.

Metabolic Syndrome is described by the World Health Organization as glucose intolerance, impaired glucose tolerance (IGT) or diabetes mellitus (DM), and/or insulin resistance, in combination with following two or more of the components: Raised arterial (>140/90 1. pressure mm Hg) 2. High plasma triglycerides ( $\geq 150 \text{ mg/dl}$ ) and/or low HDL-C levels (<35 mg/dl in men and <39 mg/dl women). in 3. Central obesity, defined as a waist/hip ratio (WHR) > 0.9 in men and > 0.85 in women, as well body >30mass index (BMI) kg/m2. as a 4. Microalbuminuria: urine albumin excretion rate  $\geq 20 \ \mu g/min$  or albumin/creatine ratio > 30g/mg.

National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) defined Metabolic Syndrome as if the person has three or more of the following criteria:

- 1. Abdominal obesity: WC  $\geq 102$  cm in men and  $\geq 88$  cm in women
- 2. Hypertriglyceridemia: ≥150 mg/dl (1.695 mmol/l)
- 3. Low HDL-C: <40 mg/dl in men and <50 mg/dl in women
- 4. High blood pressure (BP): >130/85 mmHg
- 5.Elevated fasting level of glucose: more than 110 mg/dL (1)

One important use of metabolic syndrome is clinical assessment of patients, in identifying patients with high risk of Type 2 Diabetes Mellitus(T2DM) or Cardiovascular Disease(CVD). However, the metabolic syndrome should not be considered only in identifying patients with high risk, as other established risk assessment methods also play a major role in identifying the risk. For example, history of T2DM running in the families which is a important triggering factor is not considered in above definitions.

This syndrome is a combination of resistance to insulin, visceral adiposity, dyslipidaemia and hypertension, which are interrelated. This idea provides insight to the underlying mechanism of metabolic syndrome. While considering the pathophysiology, each factor of the patients involved are given importance, but are not adequate for the definition of the syndrome. For example, people with individual risk factors such as elevated blood pressure alone or elevated lipids alone are at risk of developing cardiovascular disease, but it is only few when compared to people satisfying numerous criteria.

Role of endothelium is to find out and provide solution to any stimuli which can be physiological or pathological. They release vasoactive molecules such as NO, prostacyclin, and endothelins. Endothelium will express cell adhering molecules which will modulate attachment with white blood cells such as leucocytes and monocytes. Disturbances are noted in homeostasis and inflammatory processes. Regulation of vascular smooth muscle response is also done by endothelium. It plays a role in atherosclerosis.Normal endothelium protects against these processes and disrupted endothelium is a key factor in the etiology of atherosclerotic lesions. (2)

Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are two liver enzymes routinely utilized in blood tests to assess liver function. Elevated ALT and AST levels are indicative of liver injury. Recent research has linked increased serum aminotransferase levels to a variety of medical disorders, including dementia, stroke, colorectal adenoma, frailty, disability, sarcopenia, metabolic syndrome (MS), and liver injury. Elevated liver enzymes can be used as a surrogate sign for nonalcoholic fatty liver disease (NAFLD), which is defined as liver fat accumulation. A comparable prevalence pattern has been described in NAFLD and MS (3).

NAFLD development is multifaceted, with dietary variables, insulin resistance (IR), inflammation, adipocytokines, lipotoxicity, and a genetic predisposition all potentially contributing. Elevated Alanine aminotransferase (ALT) levels have been linked to an increased risk of MetS, diabetes, and cardiovascular disease, as well as being a predictor of nonalcoholic steatosis. Adipose tissue contributes significantly to the low-grade inflammation associated with NAFLD. ALT is intimately linked to fat accumulation in the liver and is thought to be a sensitive sign of liver damage. It has been linked to obesity and numerous MetS-related conditions, including dyslipidemia. Its rise has also been linked to an increased risk of MetS, diabetes, and cardiovascular disease. Children with elevated hepatic transaminases as surrogates of NAFLD have a greater prevalence of prediabetes and type 2 diabetes mellitus compared to those with normal transaminases. AST and Gamma Glutamate Transferase (GGT) have yet to be independently tested as screening measures for NAFLD in children. Higher AST and GGT levels, when combined with greater ALT, are related with poorer histology. However, high AST or GGT in the setting of normal ALT(4)

Normal functioning of liver is responsible for metabolism of glucose and fatty acids. Homeostasis of liver glucose will affect insulin sensitivity. But peripheral resistance to insulin and increased breakdown of lipids will lead to accumulation of fat in liver (hepatic steatosis).When deposition of fat occurs in organs sensitive to insulin like liver and muscle, there is fall of adipokines and rise of free fatty acids and cytokines causing inflammation. These alterations can contribute to peripheral insulin resistance, early atherogenesis, poor glucose metabolism, and Metabolic Syndrome. (5)

Inflammatory adipokines, endothelial dysfunction, and greater plasma levels of nonesterified fatty acids (NEFA) may all affect the development of NAFLD(6).

Increasing physical activity levels was connected with decreased insulin resistance and transaminases, despite no correlation with waist-hip ratio, indicating that regular physical activity had a direct effect in reducing nonalcoholic fatty liver disease(7).

Normally, when blood glucose levels rise after eating, pancreatic  $\beta$  cells produce insulin. Insulin, together with glucose, increases glucose uptake from circulation into cells for glycolysis or storage as glycogen in the liver, muscle, or adipose tissues. This leads to the inhibition of hepatic gluconeogenesis. All of these physiological systems work together to reduce blood glucose levels to within the typical basal range. GLUT4 (Glucose transporter 4) is a key glucose transporter found mostly in muscle and adipose tissue. Insulin stimulates the mobilization of GLUT4 from the cytosol to the cell membrane, allowing glucose to be transported from outside to inside the cell. This is the rate-limiting step for glucose absorption and muscle glycogen synthesis.

Amount of time spent in sedentary activities showed strong connection with metabolic risk irrespective of metabolic activity. Lethargic behavior becomes more prevalent as people get older (8). Elder persons have a greater risk of obtaining metabolic syndrome because of the lazy lifestyle associated with age(9).

Hypoxia in adipose tissue is related with increased inflammatory gene expression and decreased adiponectin expression, leading to local and systemic inflammation. Insulin sensitivity and glucose intolerance are among the responses to adipose tissue hypoxia because adiponectin is related with proper glucose and lipid metabolism. Obesity has also been linked to an increase in leptin expression, which is most likely due to adipose tissue hypoxia. This is essential because leptin expression influences insulin resistance. Furthermore, ghrelin control in obese individuals is disrupted, and serum ghrelin suppression in response to stomach fullness is hindered, resulting in a failure to suppress the continuous desire to eat, exacerbating the situation(10).

One among the risk factors involving fasting glucose and insulin is ALT. Factors unaffected by ALT are two -hour post glucose challenge and HbA1c.Early stages of metabolic syndrome may be contributed by ALT Long time increase in blood glucose cannot be done by ALT. It is because of lack of effect on Hb1Ac. An high ALT level may be a cause of dyslipidemia, which includes a drop in HDL-C and an increase in LDL-C. ALT has no effect on triglyceride levels.The differences between ALT and AST could be due to their respective locations in the human body. AST is found in the liver and numerous types of organs, whereas ALT resides mostly in the liver (11).As a result, the purpose of this study was to determine the prevalence of metabolic syndrome as well as the relationship between the AST/ALT ratio and metabolic syndrome.

#### METHODOLOGY

The current study is a cross-sectional study conducted on patients admitted to the general ward of a tertiary medical center in Chengalpattu. The study had a total of 150 participants. The sample size was determined using the method n = Z2pq/d2.

The study included patients above the age of 18 years and study participants who are willing to participate in the study. The study excluded subjects who are critically ill, pregnant and lactating mothers. Informed consent was obtained before start of the study from all the study participants. The study population was selected by Simple Random sampling method. Every 3<sup>rd</sup> patient admitted in the general ward was included in the study. Data was collected using a questionnaire consisting of Sociodemographic details, personal details of the study participants. The questionnaire was validated by using a pilot study among 10% of the study population.

Informed consent was obtained before the start of the study. Body weight was determined using an electronic weighing machine. The study participants were advised to wear clothes which were light weight. Shoes and socks were advised to be taken off. Height was calculated using a measuring tape which is non extendable. The participants were advised to stand and keep feet Body mass was calculated together. index (BMI) using the formula BMI= Weight(kilogram)/Height<sup>2</sup>(meter). Blood pressure was measured using mercurv sphygmomanometer. Venous blood was collected by venipuncture after a fast of 12 hours to measure Fasting Blood sugar, Triglycerides, High Density Lipoprotein(HDL), Aspartate Aminotransferase(AST) and Alanine aminotransferase(ALT). The analysis of various serum samples was done using an automated clinical chemistry analyser, Beckman DXC 800. The

ALT/ AST ratio was calculated using the Liver enzymes. ALT/ AST ratio value of 0.6 to 1 was considered normal, <0.6 was considered as low and >1 is considered as high.

## **Operational definition:**

We used National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III) for the diagnosis of Metabolic Syndrome among the study participants. The NCEP ATP III defines Metabolic Syndrome as having three or more of the following criteria: 1) Abdominal obesity: waist circumference  $\geq 102$  cm in males and  $\geq 88$  cm in women; 2) Hypertriglyceridemia:  $\geq 150 \text{ mg/dl}$  (1.695 mmol/l); 3) Low HDL-C: <40 mg/dl in men and <50 mg/dl in women; 4) High blood pressure (BP):  $\geq 130/85 \text{ mmHg}$ ; 5) High fasting glucose:  $\geq 110 \text{ mg/dl}$ .

Ethical clearance was obtained from the Institutional Human Ethics Committee for student research (IHEC-I/2032/23 dated 11.07.2023). Data collected was entered in MS excel sheet and analysed using SPSS software version 26. Quantitative data is expressed in mean and standard deviation. Prevalence of Metabolic Syndrome was calculated by using the formula number of study participants having Metabolic Syndrome per total number of study participants multiplied by 100. Prevalence of metabolic syndrome is expressed in percentage. The qualitative data will be presented as frequency and percentage. Chi-square is used to find the association between dependent and independent variables.

#### RESULTS

As shown in Table 1 majority of the study participants 48(32%) belonged to 20- 30 years of age. There were more males 79(52.7%) in our study than the females. Majority 132(88%) of the study participants belonged to Hindu religion. Among our study participants 125(83.3%) of the them have been graduates. In our study 115(76.7%) of the study participants were married. Among the personal characteristics of the study participants 131(87.3%) of them were non-smokers and 123(82%) of them were non- alcoholic as shown in Table 2. Among our study participants 49(32.7%) of them were having a BMI of above 30 as shown in Table 2.

Parameter		No.of Patients	%
	20 - 30	48	32
	31 - 40	30       48         40       20         50       31         60       28         23       23         e       79         ale       71         du       132	13.3
Age	41 - 50	31	20.7
	51-60	28	18.7
	>60	23	15.3
Sex	Male	79	52.7
Sex	Female	71	47.3
Religion	Hindu	132	88
Kengion	Christian	9	6

 Table 1: Demographic Characteristics of Study participants

	Muslim	9	6
	Illiterate	5	3.3
		2.7	
Education		9	6
	Graduate	125	83.3
	Post Graduate	7	4.7
	Married	115	76.7
Marital Status	Illiterate5Middle School4High School9Graduate125Post Graduate7Married115Unmarried30	20	
	Divorced	5	3.3

**Table 2: Personal Characteristics of study participants** 

Parameter		No.of Patients	%
	Yes	19	12.7
Smoking	No	131	87.3
Alashal	Yes	27	18
Alcohol	No	123	82
	<19	2	1.3
DMI	19 – 25	57	38
BMI	26-30	42	28
	>30	49	32.7

All the demographic characteristics, personal characteristics was compared with the liver enzymes of the study participants. Among all the demographic characteristics by using chi square test, only education and ALT had statistically significant association 0.026(<0.05) while none of the personal characteristics were significantly associated with the liver enzymes as shown in Table 3.

 Table 3: Demographic details, personal characteristics and metabolic syndrome of study participants in association with Liver enzymes (AST, ALT)

Parameter	AST	P-Value	ALT	P-Value
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		<46 U/L n(%)	>46 U/L n(%)		<49 U/L n(%)	>49 U/L n(%)	
	20 - 30	45(31.7)	3(37.5)		45(32.8)	3(23.1)	
	31-40	20(14.1)	0(0)		18(13.1)	2(15.4)	
Age	41 - 50	31(21.8)	0(0)	0.281	29(21.2)	2(15.4)	0.074
	51 - 60	25(17.6)	3(37.5)		22(16.1)	6(46.2)	
	>60	21(14.8)	2(25)		23(16.8)	0(0)	
Sex	Male	74(52.1)	5(62.5)	- 0.567	71(51.8)	8(61.5)	0.502
Sex	Female	68(47.9)	3(37.5)	- 0.307	66(48.2)	5(38.5)	- 0.503
	Hindu	125(88)	7(87.5)		120(87.6)	87.6) 12(92.3)	
Religion	Christian	9(6.3)	0(0)	0.576	9(6.6)	0(0)	0.621
	Muslim	8(5.6)	1(12.5)		8(5.8)	1(7.7)	
	Illiterate	5(3.5)	0(0)		4(2.9)	1(7.7)	
	Middle School	4(2.8)	0(0)		2(1.5)	2(15.4)	
Education	High School	9(6.3)	0(0)	0.793	9(6.6)	0(0)	0.026*
	Graduate	117(82.4)	8(100)		115(83.9)	10(76.9)	
	Post Graduate	7(4.9)	0(0)		7(5.1)	0(0)	
	Married	108(76.1)	7(87.5)		103(75.2)	12(92.3)	
Marital Status	Unmarried	29(20.4)	1(12.5)	0.723	29(21.2)	1(7.7)	0.367
	Divorced	5(3.5)	0(0)		5(3.6)	0(0)	
Smolting	Yes	18(12.7)	1(12.5)	0.000	18(13.1)	1(7.7)	0.572
Smoking	No	124(87.3)	7(87.5)	- 0.988	23(16.8)         0(0)           71(51.8)         8(61.5)           66(48.2)         5(38.5)           120(87.6)         12(92.3)           9(6.6)         0(0)           8(5.8)         1(7.7)           4(2.9)         1(7.7)           2(1.5)         2(15.4)           9(6.6)         0(0)           115(83.9)         10(76.9)           7(5.1)         0(0)           103(75.2)         12(92.3)           29(21.2)         1(7.7)           5(3.6)         0(0)           18(13.1)         1(7.7)           119(86.9)         12(92.3)           24(17.5)         3(23.1)	12(92.3)	- 0.573
Alashal	Yes	24(16.9)	3(37.5)	0.140	24(17.5)	3(23.1)	0.610
Alcohol	No	118(83.1)	5(62.5)	- 0.140	113(82.5)	10(76.9)	- 0.618

	<19	2(1.4)	0(0)		2(1.5)	0(0)	
	19 – 25	54(38)	2(25)		53(38.7)	3(23.1)	
BMI	26-30	43(30.3)	1(12.5)	0.302	40(29.2)	4(30.8)	0.601
	>30	43(30.5)	5(62.5)		42(30.7)	6(46.2)	
	No	106(74.6)	5(62.5)		104(74.8)	7(63.6)	

\*p value=<0.05

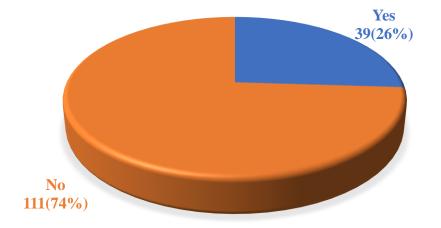
The AST/ ALT ratio was compared with all the demographic characteristics, personal characteristics and metabolic syndrome status of the study participants. As seen in Table 4 Age had statistically significant association with AST/ ALT ratio and the metabolic status of the study participants was also statistically significant with AST/ ALT ratio

# Table 4- Demographic details, personal characteristics and metabolic syndrome of study participants in association with AST/ ALT ratio

		AST/ ALT	' ratio		P value
Parameters		Low (<0.6) n(%)	Normal (0.6 to 1) n(%)	High (>1) n(%)	_
	20 - 30	20(28.2)	24(34.3)	4(44.4)	0.036*
	31-40	8(11.3)	12(17.1)	0(0)	
Age	41 - 50	14(19.7)	17(24.3)	0(0)	
	51 - 60	14(19.7)	13(18.6)	1(11.1)	
	>60	15(21.1)	4(5.7)	4(44.4)	
Sex	Male	40(56.3)	36(51.4)	3(33.3)	0.411
Sex	Female	31(43.7)	34(48.6)	6(66.7)	
	Hindu	62(87.3)	62(88.6)	8(88.9)	0.213
Religion	Christian	7(9.9)	2(2.9)	0(0)	
	Muslim	2(2.8)	6(8.6)	1(11.1)	
Education	Illiterate	2(2.8)	1(1.4)	2(22.2)	0.102
	Middle School	2(2.8)	2(2.9)	0(0)	

	High School	5(7)	4(0)	0(0)	
	Graduate	60(84.5)	58(82.9)	7(77.8)	
	Post Graduate	2(2.8)	5(7.1)	0(0)	
	Married	55(77.5)	53(75.7)	7(77.8)	0.656
Marital Status	Unmarried	15(21.1)	13(18.6)	2(22.2)	
	Divorced	1(1.4)	4(5.7)	0(0)	
~	Yes	12(16.9)	7(10)	0(0)	0.234
Smoking	No	59(83.1)	63(90)	9(100)	
Alcohol	Yes	14(19.7)	11(15.7)	2(22.2)	
AICOHOI	No	57(80.3)	59(84.3)	7(77.8)	
	<19	0(0)	2(2.9)	0(0)	0.307
DMI	19 – 25	31(43.7)	22(31.4)	3(33.3)	
BMI	26-30	21(29.6)	22(31.4)	1(11.1)	
	>30	19(26.8)	24(34.3)	5(55.6)	
Metabolic	Yes	10(14.1)	28(40)	1(11.1)	0.001*
Syndrome	No	61(85.9)	42(60)	8(88.9)	

As shown in Figure 1 among the study participants only 39 of the study participants was positive for metabolic syndrome according to CEP ATP III criteria. So, the prevalence of metabolic syndrome among our study participants was found to be 26%.



#### Figure 1: Prevalence of Metabolic Syndrome

#### DISCUSSION

The aim of the present study is to find the prevalence of metabolic syndrome and to find the association between Metabolic syndrome and Liver enzymes (AST, ALT). In our study majority (45.3%) of the study population were in the age group of 20- 40 years whereas a study done by Apurva Sawant et. al had majority (52.20) of the study participants 41- 60 years of age group. (12). In our study majority (52.7%) of the study population were males which is similar to study done by Sundara Kumar et. al which has a male population of 52.5%(13). Our study had majority of them being a graduate (83.3%) while a study done by Karl Krupp et. al had most (57.3%) of them uneducated and had a prevalence of metabolic syndrome of 47%. So, education might play a major role in prevalence of metabolic syndrome (14). In our study majority (88%) of them are Hindus which is similar to the study did by Sundara Kumar et. al which had majority (62.3%) of them being Hindus. (13).

Our study had majority of the study participants being Non –smokers and non alcoholics and both the personal habits had no association with the Liver enzymes while a study done by Hae Ran Kim et al also had majority of the study participants being smokers and alcoholics and both the personal habit had association with metabolic syndrome (3).

In our study the prevalence of metabolic syndrome was found to be 26% while a study done by Deepa et al found the prevalence of metabolic syndrome to be 11.2% and another study done by Ramachandran el al found the prevalence of metabolic syndrome to be 41.1%. (15)(16). Another study did by Rajarshi Banerjee et. al had a prevalence of 44.6%(17).

In our study metabolic syndrome was significantly associated with AST/ ALT ratio with a p value of 0.001which is similar to the study did by Lidan Chen et.al also had significant association between metabolic syndrome and AST/ALT ratio with p value of <0.001(18). **CONCLUSION** 

This study showed high prevalence of metabolic syndrome. Primary level of prevention in the form of information regarding preventive aspects of metabolic syndrome should be provided to the general population. Our study had Liver enzymes strongly correlated with Metabolic syndrome. Since NAFLD is more prevalent in Metabolic syndrome patients, these liver enzymes play a major role in identifying patients with NAFLD which is early predictor of cardiovascular diseases.

FINANCIAL SUPPORT Nil CONFLICT OF INTEREST Nil

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