NONALCOHOLIC FATTY LIVER DISEASE IN TYPE 2 DIABETES MELLITUS WITH OBESITY

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ABSTRACT

Recent times overweight and obesity have reached epidemic levels in India. Nonalcoholic fatty liver disease (NAFLD) is significant lipid deposition in hepatocytes of liver without history of excessive alcohol consumption. Type 2 Diabetes Mellitus (T2DM) is the commonest cause of NAFLD. Patients may have varying combination of obesity, diabetes, hyperlipidemia, hypertension and impaired fibrinolysis. This study was done to find out the prevalence of NAFLD in T2DM with obesity and find out the correlation of biochemical risk factors and liver enzymes with ultrasound findings. Our study showed 55% prevalence of NAFLD in obese T2DM patients. The Risk of developing NAFLD is increased with poor glycemic control, hypercholesterolemia and hypertriglyceridemia which is evident with increasing liver enzymes. The incidence of NAFLD can be brought under control with good glycemic control and periodic evaluation of liver enzymes.

Keywords:- Nonalcoholic fatty liver disease, type 2 Diabetes mellitus, Obesity

INTRODUCTION

India is the seventh-largest and second-most populous country in the world. Easy access to calorie-dense food and a sedentary lifestyle together with the modern epidemics of type 2 diabetes mellitus (T2DM) and obesity have catapulted nonalcoholic fatty liver disease (NAFLD) into a substantial public health problem in India as in other parts of the world. NAFLD includes non-alcoholic fatty liver (NAFL) and non-alcoholic steatohepatitis (NASH). The prevalence of NAFLD is underestimated as most of the patients with NAFLD are asymptomatic.

The prevalence of NAFLD in type 2 diabetes mellitus ranges from 34 - 94% around the Globe . Studies revealed that among NASH patients, 30–40% have advanced liver fibrosis at the time of presentation, while 10–15% have established cirrhosis. The rapidly growing incidence of NAFLD is causing an increase in non-communicable diseases (NCDs), such as cardiovascular disease, cancer, diabetes, and, obesity . Hence, T2DM is an important determinant of both the presence and severity of NAFLD. The mortality rate of diabetic patients due to cirrhosis is more than twice the general population and patients with both NASH and T2DM have a poorer prognosis in terms of higher rates of cirrhosis and mortality.

Overweight and obesity have reached epidemic levels in India [1]. Non-alcoholic fatty liver disease (NAFLD) is significant lipid deposition in hepatocytes of liver without history of excessive alcohol consumption [2] . Most people with NAFLD presents with simple steatosis and may proceed to steatohepatitis, fibrosis,

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cirrhosis and liver failure [3]. Type 2 Diabetes Mellitus (T2DM) is the commonest cause of NAFLD and the varying presentation is due to insulin resistance [4]. Patients may have varying combination of obesity, diabetes, hyperlipidemia, hypertension and impaired fibrinolysis [5]. NAFLD is the most common cause for elevated transaminase levels [6]. Studies have shown improvement in liver parameters after treatment with insulin sensitizing agents like thiazolidinedione group of drugs [7]. This study was done to show the prevalence of NAFLD and association of liver enzymes with diabetes risk factors.

Our study aim is to find out the change in liver enzymes in obese T2DM patients and its correlation with NAFLD and to find out the association of biochemical risk factors such as poor glycemic control and dyslipidemia for NAFLD in obese T2DM patients.

MATERIAL AND METHODS

Our study is conducted at the Biochemistry and Microbiology of Sri Lakshmi Narayana Institute of Medical Sciences,Pondicherry. After obtaining institutional ethics committee approval study was done Cross sectional study Sample size: 100 (50 males and 50 females)

Inclusion criteria: Established cases of T2DM patients (35-80 years) without complications on treatment with sulphonylureas/ biguanides or both. Nonalcoholic with body mass index (BMI)>25 BMI, Fasting blood sugar, blood pressure, Liver enzymes Aspartate transaminase (AST), Alanine transaminase (ALT), Gamma glutamyl transferse (GGT), Alkaline phosphatase (ALKP), Total cholesterol, Triglycerides, High density lipoprotein (HDL), Urea, Creatinine levels are measured in fully automated analyzers. Statistical analysis was done with Microsoft excel software system.

RESULTS

The mean age of our study group is 53.87 years and the mean BMI is 2 28.28 kgm

Table 1: Correlation of Elevated Liver Enzymes with Ultrasound Findings

ENZYMES	USG ABDOMEN		TOTAL (%)	P value
	NORMAL (%)	FATTY LIVER (%)		
AST NORMAL	45	24	69	P< 0.0005*
ELEVATED	-	31	31	
ALT NORMAL	37	14	51	P< 0.0005*
ELEVATED	8	41	49	
GGT NORMAL	43	19	62	P< 0.0005*
ELEVATED	2	36	38	
ALKP NORMAL	41	18	59	P< 0.0005*
ELEVATED	4	37	41	

Table 2: Correlation of Biochemical Risk Factors with Ultrasound Findings

BIOCHEMICAL RISK FACTORS	USG ABDOMEN		TOTAL (%)	P value
	NORMAL (%)	FATTY LIVER (%)		
FASTING BLOOD SUGAR CONTROLLED	36	10	46	P< 0.0005*
POORLY CONTROLLED	9	45	54	
TOTAL CHOLESTEROL NORMAL	19	8	27	P< 0.002*
ELEVATED	26	47	73	
TRIGLYCERIDES	34	11	45	P< 0.0005*
NORMAL ELEVATED	11	44	55	
HDL	45	31	76	P< 0.0005*
NORMAL LOW	-	24	24	

Fig 1:RESULTS OF ULTRASONOGRAPHY OF ABDOMEN

- NORMAL
- MODERATE FATTY LIVER
- MODERATE FATTY LIVER WITH HEPATOMEGALY
- MILD FATTY LIVER
- MILD FATTY LIVER WITH HEPATOMEGALY
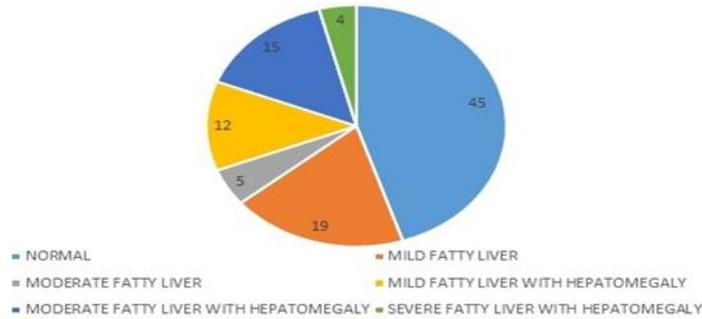- SEVERE FATTY LIVER WITH HEPATOMEGALY

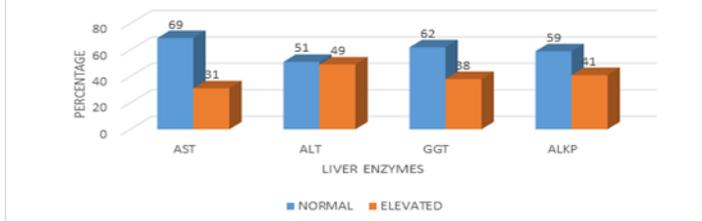Fig 2: NORMAL AND ABNORMAL FREQUENCY OF MARKERS OF LIVER ENZYMES FOR NAFLD
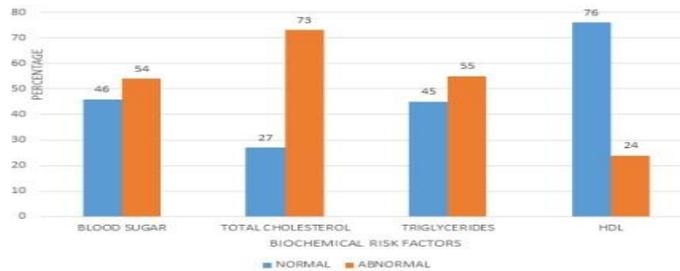

Fig 3:NORMAL AND ABNORMAL FREQUENCY OF BIOCHEMICAL RISK FACTORS FOR NAFLD

DISCUSSION

The public health implications of the emerging pandemic of obesity are dire in light of the growing list of associated metabolic consequences. Recent year's obesity has been implicated in the development of NAFLD. In this study ultrasound findings shows 55% prevalence of NAFLD in the study population which is also supported by the elevated liver enzymes (Table 1). Elevated liver enzymes indicate presence of hepatocyte injury. The mechanism of cell injury may be due to the excess of free fatty acids found in insulin resistant state. Other mechanisms may be cell membrane disruption, mitochondrial dysfunction and defect in regulation of metabolism [8].

In the globe, the prevalence of NAFLD has increased significantly with the increased rate of obesity and metabolic syndrome. In Western countries, the prevalence of NAFLD varies from 15% to 40%, whereas in Asian countries the prevalence varies from 9% to 40%. As per our knowledge, this study first reported the prevalence of NFALD by using the CAP technique for detection from India. The prevalence of NAFLD in Type 2 diabetes mellitus in our study is 57%, among them 37.3% developed mild to moderate steatosis and 26.6% developed severe steatosis.

Worldwide, the risk of NAFLD is increased at an alarming rate with both diabetes and pre-diabetes individuals. The prevalence of NAFLD in T2DM patients is highly variable in our country, ranging from 45.0% to 72.0% as per the report from different parts of the country. Our study revealed that approximately 26% of patients with NAFLD will develop into NASH, increasing the risk of liver advanced fibrosis or cirrhosis. Hence, it is indicated that the presence of diabetes

enormously drives NAFLD progression to NASH and cirrhosis.

Other potential explanation may be due to oxidant stress from reactive lipid peroxidation and increase in proinflammatory cytokines [9]. Poor glycemic control is a major biochemical risk factor for NAFLD. Abnormalities of triglyceride storage and lipolysis in insulin sensitive tissues (liver) are early markers of insulin resistance and are detected earlier than fasting hyperglycemia [9-10]. This study reveals that poor glycemic control, hypercholesterolemia, hypertriglyceridemia, low HDL levels are important biochemical risk factors for development of NAFLD in obese T2diabetics (Table 2)

Conclusion

NAFLD is one of the common liver disorders which is highly prevalent in obese and diabetic individuals. Patients with NAFLD are characterized by elevated circulating concentration of liver enzymes like AST, ALT, GGT and ALKP. So by periodic evaluation of liver enzymes along with other biochemical risk markers can predict the development of NAFLD in obese type 2 diabetic individuals. Our results support the implication of type 2 diabetes as toxic state forhepatic system and highlights the already strong rationale for aggressive intervention on obesity and type 2 diabetes at population level. The prevalence of NAFLD is high in the eastern region of India, need for early diagnosis and treatment of NAFLD in T2DM. The use of TE with other serum markers can be helpful for the diagnosis of advanced fibrosis. Our study showed a higher prevalence of NAFLD among patients with Type 2 diabetes mellitus stressing the need for preventive strategies.

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