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Thyroid function disorders associate with non alcoholic fatty liver in malwa region

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Introduction

Fat accumulation in the liver in persons even with less consumption of alcohol in a chronic state is known as Non-Alcoholic Fatty Liver disease NAFLD. The key factors in the pathogenesis are predisposition genetically based and also insulin resistance. The spectrum of NAFLD is depicted in Figure 1. Metabolic Syndrome is major and important for runner of NAFLD. The increased obesity prevalence and change in food habits, binge eating practice has led to increase in incidence of NAFLD worldwide[1]. Liver cirrhosis without any identifiable cause is called as Cryptogenic cirrhosis. The thyroid hormones regulate lipid metabolism in the liver via thyroid hormone receptor-beta, and they can decrease cholesterol and triglyceride levels. The thyroid gland is significantly involved in energy homeostasis, lipid and carbohydrate metabolism, regulation of body weight and adipogenesis. Subclinical and overt hypothyroidism has been associated with metabolic syndrome, cardiovascular mortality and disturbance in lipid metabolism[2]. Hypothyroidism is an endocrine as well as autoimmune disorder. It is caused by decrease in thyroid function. The patient of hypothyroidism is obese. There may have diabetes, hypercholesterolemia, and may present with weight gain, puffy face, hoarse and croaky voice, non-pitting edema in legs, loss of outer third of eyebrow, dry skin and bradycardia[3]. There is also delayed relaxation of ankle jerk and hypertension. Laboratory finding of hypothyroidism.

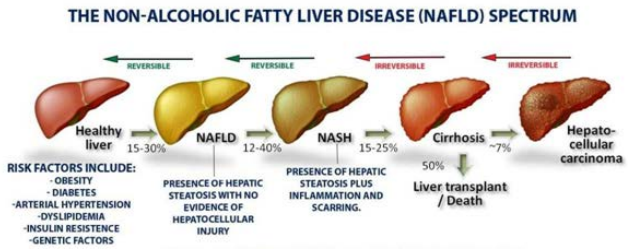
It is well known that thyroid hormones have a significant effect on hepatic lipid metabolism[4]. Hypothyroidism induced NAFLD has generally been attributed to interruptions in thyroid hormone signals, leading to reduced utilization of lipids by the live[5].Indeed, subclinical hypothyroidism, even in the upper range of normal serum thyroid stimulating hormone (TSH) concentrations, has been found to be associated with NAFLD in a dose-dependent way[6] .Found that subclinical hypothyroidism and low normal thyroid function are independent predictors of non-alcoholic steatohepatitis (NASH) and advanced fibrosis[7]

Aims

To investigate the Association and Impact of Thyroid function on Non-Alcoholic Fatty liver disease.

Background

NAFLD is excessive fat build-up in the liver with insulin resistance due to causes other than alcohol use. In 1952, Samuel Zelman, first acknowledged a case of obesity related non-alcoholic fatty liver.



Non-Alcoholic Fatty Liver Disease – Spectrum

The body mass index (BMI) ,Prevalence and Severity of NAFLD are directly correlated. The prevalence of NAFLD increases to 57.5% to 74% in obese persons and 90% in morbidly obese persons[8]. In India prevalence of NAFLD is around 9% to 32% of general population.

Natural History

Simple steatosis is nearly ninety percent of population and approximately 20% to 30% patients have Steatohepatitis[9]. Around forty percentage of this population develop fibrosis, cirrhosis and eventually land up in end stage liver disease.

Metabolic Syndrome

Metabolic syndrome is independent predictor of fibrosis.70-90% of patients with NAFLD have metabolic syndrome. Insulin resistance is a key mediator between NAFLD and metabolic syndrome[10]

Dietary factors

Diet containing high cholesterol and saturated fats, high fructose intake, low carbohydrates increases the risk of NAFLD. Caffiene may be protective in some patients.

Genetic Factors

Patatin –like phospholipase domain- containing 3 (PNPLA3). PNPLA3 lysophosphatidic acid acyltransferase[11] activity could also contribute to altered plasma triacylglycerol composition and concentration.

Etiopathogenesis of nafld/nash

Initially there is steatosis which later may progress on to inflammation and fibrosis and finally to cirrhosis and end stage liver disease. NASH may be considered as a two hit process, first hit is accumulation of the fat and the second hit is hepatocellular injury in the fatty liver.

Nafld and cardiovascular diseases

Non alcoholic fatty liver disease is associated with increased risk and morbidity for cardiovascular diseases and risk further increases in Type 2 diabetes mellitus. In addition patients with non alcoholic steatohepatitis have further increased risk of cardiovascular diseases

Material and Methods

100 cases

Source of data-The data collected by the principle investigator from patients with NAFLD either in OPD or Wards in SAIMS Hospital.

Inclusion criteria- Patients with NAFLD, both male and female more than or equal to 18 years.

Exclusion criteria- Patients on glucocorticoid therapy.Cushing's disease**.**Underlying chronic liver disease (Hep A-E infections)**.** Alcohol intake more than 20g/day.

Methodology- Ultrasonogram of abdomen was done, patients with fatty liver were selected.

Parameters like fasting sugar, blood pressure, waist circumference, HDL, triglyceride, albumin, platelet count were studied. Clinical hypothyroidism is defined on the basis of the criteria of thyroid abnormalities as defined by the Dutch National Healthcare Consensus Committee.

Subclinical hypothyroidism: it is indicated by increased serum TSH in the presence of a normal serum FT4

level. Clinical hypothyroidism: it is indicated by increased serum TSH with decreased serum FT4 level, at which stage most patients have symptoms and benefit from treatment.

Result

Table: 1. Showing the age wise distribution of the study population.

Age in years	No of patients	Percentage
< 30	9	9%
31-40	30	30%
41-50	43	43%
> 50	18	18%

Maximum distribution of patients was among the age group of 41 to 50 years, nearly 43% of the total study population.30 people were among the age group of 31 to 40 years.18% were above 50 years of age, whereas 9% population were less than 30 years.

Table: 2: Showing the classification of patients based on their BMI.

Body mass index	No of patients	Percentage
18.5-25	15	15%
25-30	53	53%
30-35	26	26%
35-40	6	6%

Classifying the study population based on BMI has showed that nearly 53% of people are overweight, whereas 26% population belong to Class I Obesity, 6% of total population belong to class II obesity. Waist circumference is one of the components of Metabolic syndrome.67% of the total study population had higher waist circumference, showing the important relationship between metabolic syndrome and Non alcoholic Fatty liver disease patients. High fasting blood sugar constitutes a major component of Metabolic Syndrome. Nearly 56 % of the study population had increased fasting blood sugar, indicating their vulnerability for development of Metabolic syndrome, in turn fatty liver development.

Table: 3: Shows the grading of Fatty liver of study population based on Ultrasonogram.

Usg abdomen	No of patients	Percentage
GRADE I FATTY LIVER	48	48%
GRADE II FATTY LIVER	35	35%
GRADE III FATTY LIVER	17	17%

Majority of the population had grade-I fatty liver(48%). Among the remaining 52 members, 17 had grade III fatty liver (17%).

Table 4: Serum T3 levels according to Fibroscan Grading.

FIBROSCAN	SERUM T3 LEVELS	
	MEAN	SD
2TO7	1.21	0.51
7.5 TO 10	1.18	0.54
10 TO 14	0.87	0.77
14 OR HIGHER	0.1	0.08
ANOVA	P VALUE -SIGNIFICANT	

When liver stiffness increases elasticity is lost, the readings of transient elastography also increases. T3 levels became low when fibrosis was severe as indicated by fibroscan.

Table: 5. Comparison of Hypothyroidism and USG Grading

USG ABDOMEN	HYPOTHYROIDISM		
	OVERT	SUBCLINICAL	Euthyroid
FATTY LIVERGRADE I	1	6	41
FATTY LIVERGRADE II	14	11	10
FATTY LIVERGRADE III	9	5	3
P VALUE - 0.001KRUSKAL WALLIS TEST			SIGNIFICANT

48 people had Grade I fatty liver, out of which 41 had normal thyroid function, 6 are subclinical, one had overt hypothyroidism.35 people had Grade II fatty liver, of which 14 are overt hypothyroid, 11 have subclinical hypothyroidism.17 people had Grade III fatty liver of which 9 had overt hypothyroidism, 5 had subclinincal hypothyroidism.

Out of 24 male with Metabolic Syndrome, 7 were overt hypothyroid, 9 had subclinical hypothyroidism, 8 had normal thyroid function.36 female had Mtabolic Syndrome, of which 12 were overt hypothyroid, 11 had subclinical hypothyroidism, 13 had normal thyroid function.

Discussion

Hundred patients who are Non alcoholic with fatty liver was chosen based on the inclusion and exclusion criteria mentioned above. Variables such as Blood pressure, HDL, Triglycerides, Fasting blood sugar, waist circumference, albumin, platelet count, AST/ALT ratio were studied. Fibrosis in these patients were analysed and graded by ultrasonogram, NAFLD**.** Of the 100 patients included in our study with NAFLD, 48 patients had grade I fatty liver, 35 patients had grade II fatty liver, 17 patients had grade III fatty liver, according to ultrasonogram findings. While 43 patients had NAFLD Fibrosis score less than -1.455, 26 patients had score in the range of -1.455 to 0.675, 31 people had score greater than 0.675. Thyroid function tests was carried out in these patients to assess the association of it with fatty liver. Nearly 46% had hypothyroidism, none had hyperthyroidism,54 had normal thyroid function. So hypothyroidism was significantly associated with the fatty liver.24 people had overt hypothyroidism, 22 people had subclinical hypothyroidism.

Conclusion

46% of the study population had hypothyroidism, among them 24% had overt hypothyroidism, 22% had subclinical hypothyroidism. The results clearly shows that **hypothyroidism** is an independent risk factor for NAFLD. So Thyroid function should be evaluated for all patients with NAFLD. Thyroxine should be started at the earliest to avoid the risk of acquiring NAFLD and also to prevent dreadly complications. Non invasive imaging techniques and scoring systems help us in early diagnosis of NAFLD. Proper education of the symptoms and seriousness of complications like cirrhosis, hepatocellular carcinoma that can develop will increase the quality of life and decrease the morbidity and mortality.

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