

## Prevalence of Non-Alcoholic Fatty Liver Disease in Hypothyroid Subjects.

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### Abstract:

**Background:** Thyroid hormones are associated with the digestion of lipids, insulin obstruction and bodyweight control. There is uncertain proof on the significant part of hypothyroidism in non-alcoholic liver fat sickness (NAFLD). motivation behind examination is to decide pervasiveness of NAFLD in hypothyroidism. Thyroid hormones are involved in lipid metabolism, insulin resistance and regulation of bodyweight. There are inconclusive data regarding substantial involvement of hypothyroidism in non-alcoholic fatty liver disease (NAFLD). The aim of this study is to evaluate the prevalence of NAFLD in hypothyroidism.

### Objectives:

- Association of non-alcoholic fatty liver disease (NAFLD) with overt hypothyroid and subclinical hypothyroid subjects.
- To correlate anthropometric measures, lipid profile and fasting blood glucose with NAFLD

**Methodology:** Study will be carried out in AVBRH, Sawangi (Meghe) associated to DattaMeghe institute of Medical sciences, Wardha, and it will be an Observational Cross-sectional study.

Patients' height, weight, blood pressure, circumference of hip, circumference of waist, such as blood sugar levels at fasting, serum levels of triglycerides, serum high density lipoprotein (HDL), SGOT, SGPT, albumin levels and platelet counts are considered to ascertain the

patient into one of the phenotypes of obesity and estimate the NAFLD score using above parameters and correlate it with USG findings and predict the correlation between scoring and radiological findings .

**Expected results:** Number of NAFLD cases will be found higher in hypothyroid subjects.

**Keywords:** Non-alcoholic fatty liver disease, hypothyroidism, overt hypothyroidism, subclinical hypothyroidism.

## INTRODUCTION:

In recent decades, the commonness of non-alcoholic liver fat infection (NAFLD) has developed significantly and has become the world's driving reason for liver sickness, which can be incompletely because of the developing predominance of weight <sup>(1)</sup>. Without extreme liquor admission, NAFLD is a constant liver illness known as hepatic fat gathering, and insulin obstruction (IR) yet in addition hereditary inclination assume a vital part of pathogenesis <sup>(1)</sup>. NAFLD can be part into 2 primary histological classes, to be specific non-alcoholic fatty liver & non-alcoholic steatohepatitis, which is reformist subtype of the NAFLD and could additionally prompt cirrhosis of liver&carcinoma of hepatocellular type<sup>(2)</sup> NAFLD has been viewed as connected with an expanding number of sicknesses, for example, type 2 diabetes, cardiovascular infection, persistent kidney illness and disease<sup>(3,4,5)</sup>. In recent years, NAFLD prevention and care have been the subject of medical studies, &it is valuable to interpret the risk factors for NAFLD in order to create successful NAFLD preventive strategies.

Hypothyroidism is a typical endocrine framework issue which affects long lasting wellbeing. Numerous specialists have played the physiological part of the thyroid organ truly, not just as a result of the thyroid hormones' basic function in the cell digestion and homeostasis of energy. <sup>(6)</sup> But likewise, in light of the more significant reality that different problems are related with thyroid dysfunction <sup>(7)</sup>. Hypothyroidism can be separated to the hypothyroidism at subclinical and plain hypothyroidism. Subclinical hypothyroidism is known to be a condition with a level of expanded thyroid-invigorating hormone (TSH) over as far as possible, a degree of typical serum free thyroxine (fT4) and no clear clinical indication. Plain hypothyroidism is portrayed as a condition with an expanded degree of TSH and the lower level of fT4, and apparent clinical side effects can go with it. Numerous examinations have exhibited that coronary problems and mortality are connected with both obvious hypothyroidism and subclinical hypothyroidism. Other writing has additionally discovered that different sicknesses, for example, constant kidney illness, dementia, and breaks, can be connected with either clear hypothyroidism or subclinical hypothyroidism <sup>(8,9,10)</sup>. Past examinations have exhibited that hypothyroidism may assume a significant function in NAFLD pathogenesis. Hypothyroidism is notable to be related with raised measures of the LDL-cholesterol and fatty oils optional to a decrease in capacity of the LDL receptors and fatty substance rich lipoprotein freedom. <sup>(11,12)</sup> The state of steatosis, a part of non-alcoholic greasy liver infection (NAFLD) or non-alcoholic steatohepatitis, is the sign of extreme fatty substance collection in the liver. A few reports show that the predominance of

hypothyroidism in NAFLD patients is 15.2% to 36.3%, recommending that hypothyroidism is a successive attendant problem of NAFLD and might be connected with NAFLD movement. There is an assortment of observational investigations at present that have dissected the relationship among NAFLD and hypothyroidism. Numerous investigations have shown a potential relationship among NAFLD and hypothyroidism.<sup>(13,14,15)</sup>, however many Study results have additionally indicated that there was no relationship<sup>(16)</sup>. The connection among hypothyroidism and the chance of NAFLD remains, anyway in uncertainty up until now. Hence, the relationship among hypothyroidism and NAFLD weakness should be guaranteed by a meta-investigation.

### **STUDY DESIGN:**

This will be Observational Cross-sectional Study with Control Group and will include normal weight cases and control cases.

### **SELECTION OF SUBJECTS:**

- All cases will be selected from the university students, staff, and patients attending OPD and Inpatients admitted for accelerated Hypertension and uncontrolled Diabetes mellitus matching up with research criteria.
- All subjects' demographic records (information comprised of sex, age, race, educational, occupation and postal address) and information about physical activity, history of past illness, smoking, alcohol consumption, hypertension, diabetes mellitus and medication status will be collected.
- Age: above 18 years to 70 years

### **CONTROLS:**

Age and sex matched non obese healthy persons will be taken as control.

### **EXCLUSION CRITERIA:**

- Etiology of hepatic steatosis other than NAFLD will be excluded, history of alcohol abuse

### **METHODS**

#### **ANTHROPOMETRIC MEASUREMENTS: -**

Anthropometric features including weight, height, BMI, waist circumference (WC).

**WEIGHT:** Weight in kilograms will be recorded with a static patient on measuring scale without foot wear and with light clothing using portable weight scale and measuring inflexible bars with high accuracy.

**HEIGHT:** Measured in centimeters with, the subject stands in an erect posture, without foot wear and with the head placed back to a vertical scale so that the bony orbit and top of the external auditory meatus are in a line. (Frankfurt's plane).

**BLOOD PRESSURE:** We will measure blood pressure by auscultatory method using stethoscope and sphygmomanometer, which consists of Riva-Rocci cuffs positioned around the upper arm at height the same as the heart, connected to the mercury manometer, which

measures the height of a column of mercury providing an absolute result

### **WAIST CIRCUMFERENCE:**

The WHO stepwise convention for estimating midsection circuit teaches that the estimation be made at the rough center - point between the edge of the last rib obvious and the highest point of the iliac peak.<sup>(15)</sup>

According to Modified NCEP ATPIII normal reference of waist circumference for Asian population is <90 cms for males & <80 cms for females. Circumference of waist of > 90 cms for males and of >80 cms for females is considered as abnormal with normal metabolic syndrome.

### **Investigations:**

#### **BIOCHEMICAL PARAMETER ESTIMATION:**

- Fasting blood sugar.
- Serum triglyceride
- Serum HDL
- SGPT/SGOT
- Albumin
- Platelet count

### **VARIABLE AND MEASUREMENT**

- BMI:  $\text{weight}/(\text{height})^2$  expressed in  $\text{Kg}/\text{Mtr}^2$ .
- Weight
- Height
- Blood pressure
- Waist circumference

### **NAFLD BY USG:**

#### **Ultrasonography for NAFLD:**

All patients will undergo Ultrasound (USG) of the midsection to recognize greasy changes in the liver, performed by a single experienced radiologist.

**Diagnosis of NAFLD:** Diagnosis made by the appearance of an ultrasonographic pattern persistent with increase echogenicity i.e. high ultrasonographic contrast among hepatic and renal parenchyma.

Standard Ultrasonographic grading of NAFLD is classified into 3 grades.

### **Sample size:**

$$\text{Sample size} = \frac{Z_{1-\alpha/2}^2 p (1-p)}{d^2}$$

### **Reference Study:**

$$p = \text{Prevalence of hypothyroidism} = 15\% = 0.15 \quad (17)$$

$$d = \text{Desired error of margin} = 5\% = 0.06$$

$$n = \frac{1.96^2 * 0.15 * (1-0.15)}{0.06^2}$$

$$n = 136.05 = 140 \text{ patients needed in the study}$$

$$\text{Sample Size} = 140$$

## DISCUSSION:

In our study, 100 non-obese hypothyroid patients were included and USG was done on every patient to detect presence of NAFLD and USG grading of NAFLD was done. These hypothyroid patients were divided in two groups, basing on their treatment status, of which 50 were in treated group and 50 were in untreated group. The results were compared with 100 age, sex and BMI matched non-obese euthyroid control population. In treated group, maximum number of patients 27 (54%) belonged to age group of 40-59 years and in untreated group also maximum number of patients 28 (56%) belonged to age

group of 40-59 years. Among all hypothyroid cases, 68 (68%) were male and 32 (32%) were female. In treated group, 28 (56%) were male and 22 (44%) were female, whereas in the untreated group 40 (80%) were male and 10 (20%) were female. In a study by Liangpunsakul and Chalasani (2003), the association between thyroid dysfunction and NAFLD have been characterised by relatively small sample and gender imbalance showing female preponderance<sup>12</sup>. Mean age of male patients was 45.58 yrs. and female was 45.09 yrs. which was fairly correlated. Out of 100 hypothyroid patients, 30 patients had NAFLD of which 20 were in untreated group and 10 in treated group. Study by Marco Bertolotti, Amedeo Leonardo et al demonstrated that prevalence of NAFLD increases with age<sup>13</sup>, but in our study majority of NAFLD cases i.e. 56.6% were found in the age group 40-59 yrs.,  $P=1.563$  which is statistically insignificant. In our study, out of 30 NAFLD cases, 19 (63.3%) were male and 11 (36.7%) were female. From 19 male NAFLD cases, majority cases i.e. 8 cases (42.1%) were having NAFLD USG grade-II and out of 11 female NAFLD cases, 5 (45.4%) were having NAFLD USG grade-II.  $P=0.063$ , which was statistically insignificant showing no significant relationship between gender & USG grading of NAFLD. So far as age is concerned, majority NAFLD cases i.e. 17 (56.7%) were of age group 40-59 yrs. and no NAFLD case was detected above 60 yrs. of age. In the study group, 77 cases were having  $TSH \geq 4.1$  mIU/L, from which 27 (35%) had NAFLD and rest 23 cases were having  $TSH < 4.1$  mIU/L, of which 3 (13%) had NAFLD.  $P=0.0163$ , which is statistically significant, shows increased value of TSH is associated with increased prevalence of NAFLD. In a study by Loria Paola et al regarding endocrine and liver interaction, the role of endocrine pathway in NASH showed that increase in TSH value increases the risk of developing NAFLD<sup>14</sup>. Among 100 hypothyroid cases, 71 had FT4 between 0.7 to 1.8 ng/dL, of which 7 (9.8%) had NAFLD and rest 29 had FT4,  $< 0.7$  ng/dL, of which 23 (79.3%) had NAFLD.  $P=0.0238$ , which is statistically significant and shows decreased value of FT4 is associated with more prevalence of NAFLD. Study by Loria Paola et al demonstrated decrease in FT4 increases the risk of developing NAFLD<sup>14</sup>. Among total 30 cases of NAFLD, 20 were detected in untreated hypothyroid cases and 10 were detected in treated hypothyroid cases.  $P=0.0034$ , which was statistically significant, showing more prevalence of NAFLD in untreated hypothyroid patients than treated hypothyroid patients.

The association between thyroid dysfunction and NAFLD was defined in a study by Liangpunsakul and Chalasani (2003)<sup>(18)</sup> by a comparatively small sample and a gender

difference indicating female preponderance. The mean male patient age was 45.58 years. The female was 45.09 years of age. And was associated equally. Among the hundred hypothyroid patients, thirty had non-alcoholic fatty liver disease, twenty of whom were in the untreated group and ten of whom were in the treated group.

Study by Marco Bertolotti, Amedeo Lonardo et al.<sup>(19)</sup> NAFLD inescapability has been accepted to augment with age, 13 anyway a large portion of the NAFLD cases for instance 56.6 percent, were arranged in the age range 40-59 years,  $P=1.563$ , which is quantifiably unimportant in our model. In this model, 19 (63.3 percent) out of 30 NAFLD cases were male and 11 (36.7 percent) were female. The vast majority of 19 male NAFLD cases for instance 8 cases (42.1 percent) had NAFLD USG grade-II and 5 (45.4 percent) of 11 female NAFLD cases had NAFLD USG grade-II.  $P=$  of 0.063, This was for the most part low and shown no basic relationship between NAFLD's sex and USG evaluating. Taking everything into account, the greater part of NAFLD cases were 40-59 years of age, for instance 17 (56.7 percent). Furthermore, no example of NAFLD more than 60 years has been represented. About age. In the investigation people, 77 cases had  $TSH > 4.1$  mIU/L, of which 27 (35%) had NAFLD, and 23 cases had  $TSH < 4.1$  mIU/L, of which 3 (13%) had NAFLD.  $P=0.0163$ , which is quantifiably colossal, Increased TSH regard is connected with extended NAFLD regularity.

The capacity of the endocrine pathway in NASH in an examination by Loria Paola et al on endocrine and liver alliance found that extended TSH criticalness raises the threat of making NAFLD. 14 Of 100 hypothyroid cases, 71 had FT4 some place in the scope of 0.7 and 1.8 ng/dL, of which 7 (9.8 percent) had NAFLD, and 29 had  $FT4 < 0.7$  ng/dL, of which 23 (79.3 percent) had NAFLD.  $P=0.0238$ , which is quantifiably significant and exhibits a diminished FT4 regard is related with higher NAFLD inescapability. The Study by Loria Paola et al displayed decrease in FT4 constructs the peril of making NAFLD. 14 Among full scale 30 examples of NAFLD, 20 were distinguished in untreated hypothyroid cases and 10 were perceived in treated hypothyroid cases.  $P=0.0034$ , which was quantifiably colossal, showing more inescapability of NAFLD in untreated hypothyroid patients than treated hypothyroid patients.<sup>(20)</sup> Studies on non-alcoholic fatty liver disease were reported by Raja et. al.<sup>(21)</sup>, Srata et. al.<sup>(22)</sup> and Bagga et. al.<sup>(23)</sup>. Jose et. al. reported the profile of thyroid dysfunctions among the female population in a rural community of Wardha district<sup>(24)</sup>. Wagh et. al. assessed the relationship between hypothyroidism and body mass index in women<sup>(25)</sup>. Few of the related studies on thyroidism were reviewed<sup>(26-28)</sup>.

## CONCLUSION:

Prevalence of NAFLD in non-obese hypothyroid patients is higher in comparison to non-obese euthyroid controls, and the incidence is also high in untreated hypothyroid patients in comparison to treated hypothyroid patients.

Contrasted with non-stout euthyroid controls, the event of NAFLD in non-hefty hypothyroid patients is more noteworthy and the recurrence is likewise higher in untreated hypothyroid patients contrasted with treated hypothyroid patients.

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