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ORIGINAL ARTICLE

Association of nonalcoholic fatty liver disease with thyroid functions.

Mumtaz Ali Memon[1], Ramesh Kumar Suthar[2], Kavita Bai[3]

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ABSTRACT… Objective: To assess thyroid functions in individuals having non-alcoholic fatty liver disease. **Study Design:** Cross Sectional, Comparative Study. **Setting:** Indus Medical College Hospital, Tando Muhammad Khan. **Period:** March 2018 to August 2018. **Material & Methods:** All diagnosed cases of non-alcoholic fatty liver disease (NAFLD) ≥ 18 years of age, of either gender enrolled via OPD. Age and gender matched healthy controls also included for comparison. Thyroid stimulating hormone (TSH) and thyroid hormones (T3 and T4) levels were measured in study participants by cobas e411(Roche). Data analyzed on SPSS version 18.0. The p value<0.05 was taken statistically significant. **Results:** When TSH of NAFLD patients were compared with that of healthy controls; highly significant difference found amongst both groups with (p value <0.01). Out of 83 NAFLD patients, 36.8% were euthyroid, 53.0% were subclinically hypothyroid and 10.8% were hypothyroid. While in healthy controls (n=47); 45 (97.9%) were euthyroid and only one found with subclinical hypothyroidism. When thyroid status compared among the patient suffering from NAFLD and healthy controls, (p-value <0.01). **Conclusion:** It is concluded that that there is substantial difference of TSH in the NAFLD group besides control healthy population.

Key words: NAFLD, Thyroid Functions.

INTRODUCTION

Nonalcoholic fatty liver disease (NAFLD) epitomizes an extensive medical continuum oscillating from the fatty liver towards non-alcoholic steatohepatitis (NASH) that might further progress towards fibrotic changes in hepatic parenchyma, cirrhosis as well as also the hepatocellular carcinoma. Thyroid hormones play an important role the origination and development of NAFLD and NASH.[1] NAFLD distresses up to 1/3rd of the individuals at global level and may meet expanded cardio metabolic hazard with resulting adverse cardiovascular results independent of traditional cardiovascular danger elements and the metabolic syndrome. It is portrayed generally by insulin resistance and is unequivocally linked obesity and type two diabetes.[2] Nonalcoholic fatty liver disease (NAFLD), being well recognized health issue globally, might be allied with decreased thyroid levels.[3,4]

Prevalence of NAFLD has been observed as augmenting globally with overall prevalence of 25 percent in last two decades. It's frequency has been observed as expanding to peak in Pakistan. In general, NAFLD is not considered as a grave ill health, although, if this stayed un-recognized and unmanaged then this might lead to complications, i.e., hepatic cirrhosis.[5] In Pakistan, overall prevalence of NAFLD is 47 percent and out of that 35.3 percent prevalence has been observed in Sindhi individuals.[6] Recently the relationship between obvious or subclinical hypothyroidism and NAFLD has been talked and is thought debatable.[7,21] For hepatic lipid and glucose metabolism, thyroid hormones have a vital role. NAFLD is one of the frequent and possibly grim illness of present-day world, shares frequent clinical manifestations with hypothyroidism, such as insulin resistance, obesity, and disturbed lipid profile.[8]

1. MBBS, M.Phil (Physiology), Professor Physiology, Indus Medical College Tando Muhammad Khan.
2. MBBS, M.D (General Medicine) Associate Professor Medicine, Indus Medical College Tando Muhammad Khan.
3. MBBS, M.Phil (Physiology), Assistant Professor Physiology, Indus Medical College Tando Muhammad Khan.

Correspondence Address:
Dr. Kavita Bai
Department of Physiology
Indus Medical College Tando Muhammad Khan.
baidrkavita@gmail.com

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NAFLD was defined by ultrasonography recognizing of hepatic steatosis in the nonexistence of further identified liver disorders. Aspartate aminotransferase to platelet ratio index (APRI), and FIB-4 score are useful tools to determine existence and severity of hepatic fibrosis in subjects of NAFLD.[9] NAFLD may be associated with altered thyroid functions. As transformed thyroid functions in NAFLD individuals change thyroid hormone signaling in the liver and this may alter lipid metabolism in hepatic tissue and that might progress to cardiovascular dysfunctions. Present study was designed to determine thyroid functions among NAFLD patients in Outpatient Department of IMCH, TMK.

MATERIAL & METHODS

This cross sectional comparative study was conducted in Physiology Department in collaboration with Department of Medicine, Indus Medical College Hospital, Tando Muhammad Khan from 07 March 2018 to 08 August 2018 approved from ethical committee was acquired (REC/IMC/2018-2019). Sampling technique was non probability purposive sampling. All diagnosed cases of NAFLD who were ≥ 18 years of age, irrespective of gender were enrolled for this study. All the data including history, test results incorporated in specially designed pro-forma after informed consent.

The volunteers recruited in the study were total 130 (n=130); i.e., 83 diagnosed cases of NAFLD and for comparison 47 healthy controls. Thyroid stimulating hormone (TSH) and thyroid hormones (T3 and T4) were measured on cobas e411 by Roche. The patients having previously diagnosed other endocrinal dysfunction, autoimmune condition, wilson's disease, α-1-antitrypsin-linked hepatic illnesses, diabetes mellitus, individuals taking lipid lowering or thyroid level altering drugs, pregnant women and with previous diagnosis of thyroid disease, consuming alcohol, having viral hepatitis of either etiology or having metabolic hepatic disorder were excluded from the study. Thorough history of all such patients with complete physical and relevant clinical examination was performed, ultrasonography of abdomen, liver function tests, thyroid function test and hepatic viral profile were taken from all participants. Individuals having TSH levels 0.3 to 4.9μU/ml and T4 levels 4.8 to 11.7μg/d were considered euthyroid. They were considered sub-clinically hypothyroid, if their TSH levels are greater than 4.9μU/ml and the T4 levels from 4.8 to 11.7μg/dl). Those having TSH >4.94μU/ml and T4 <4.87μg/dl were considered as clinically hypothyroid. If TSH was lesser than 0.3μU/ml and T4 in the range of 4.8 to11.7μg/dl were considered sub-clinically hyperthyroid and if T4 levels are also augmented than 11.7 then they were considered as clinically hyperthyroid.

The data analyzed on SPSS version 18.0. The p value<0.05 was taken statistically significant.

RESULT

Total 130 (n=130) individuals participated in the study; mean age ±SD was 39.76±6.45 years. Mean± SD of TSH, T3 and T4 among study population (n=130) were 3.73±2.77 μU/ml, 3.64±1.30μg/dl and 5.69±0.84 μg/dl respectively. Out of 130(n=130), 83(63.8%) were cases of NAFLD. (Table-I)

Out of 83 patients (n=83) of NAFLD, 11(84.6%) were suffering from NASH (Figure-2). Over all among study population (n=130), 76(58.46%) were euthyroid and 45(34.62%) were subclinical hypothyroid while 09(0.6.92%) were clinically hypothyroid. (Figure-1).

Mean of the TSH, T3 and T4 were compared among NAFLD patients (n=83) and non- NAFLD (N=47) by applying independent test. When mean±SD levels of TSH of NAFLD patients (5.18μU/ml ±2.3) were compared with that of healthy controls (1.15μU/ml ±1.1), there were highly significant difference between both groups with p value <0.01 (Table-II). When mean±SD levels of T3 of NAFLD patients (3.34μg/dl ±1.3) were compared with that of healthy controls (4.15μg/dl ±1.0), there were significant difference between both groups with p value =0.01 (table No. 2) Instead, when mean±SD levels of T4 among the NAFLD patients were compared with that of healthy controls, there were no significant

difference between both groups with p value =0.613. (Table-II)

Thyroid status compared in NAFLD patients (n=83) and non-NAFLD controls (n=47), (Pearson chi-square value 47.1, DF=2 and p value was <0.01). In NAFLD patients, 44 (53.0%) were sub-clinically hypothyroid. (Shown in Table-III)

In the NAFLD group (n=83), frequency (%) of NASH was 9(10.84%) in hypothyroids. (Figure-3)

	Mean± Std. Deviation	N (%)
Age(years)	39.7±6.4	--
TSH(μU/ml)	3.7±2.7	--
T3(μg/dl)	3.6±1.3	--
T4(μg/dl)	5.6±0.8	--
NAFLD (No)	--	47(36.2%)
NAFLD (Yes)	--	83(63.8%)

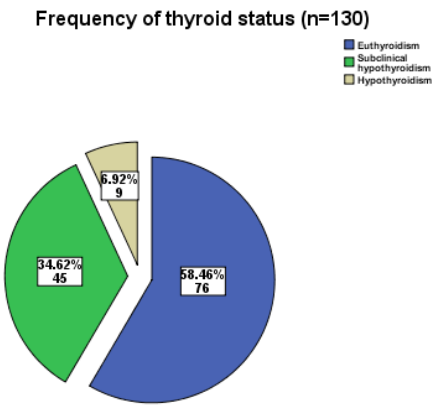

Figure-1. Frequency of thyroid functions in study population. (n=130)

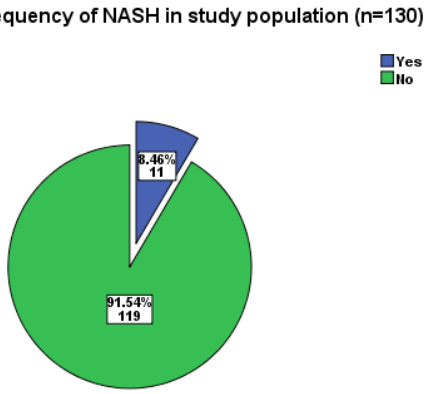

Figure-2. Frequency of NASH in study population. (n=130)

Table-I. Descriptive statistics of study population. (n= 130)

	NAFLD	N	Mean	SD	P-Value
TSH (μU/ml)	yes	83	5.1894	2.33446	0.00**
	no	47	1.1594	1.12917	
T3 (μg/dl)	yes	83	3.3493	1.32581	0.01**
	no	47	4.1536	1.08989	
T4 (μg/dl)	yes	83	5.6707	.83409	0.613
	no	47	5.7496	.88389	

Table-II. TSH, T3 and T4 among NAFLD patients (n=83) and controls. (n=47) **highly significant

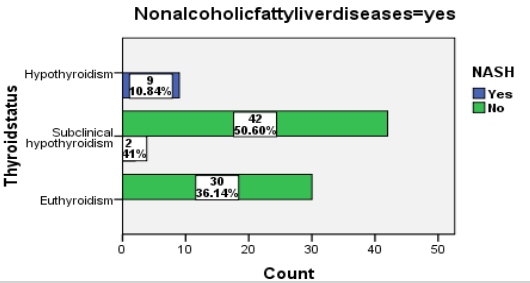

Figure-3. Frequency of NASH in NAFLD patients in association with thyroid status. (n=83)

			Thyroid Status			Total
			Euthyroidism	Subclinical Hypothyroidism	Hypothyroidism	
Nonalcoholic fatty liver disease (NAFLD)	yes	Frequency	30	44	9	83
		%	36.1%	53.0%	10.8%	100.0%
	No	Frequency	46	1	0	47
		%	97.9%	2.1%	.0%	100.0%
Total		Frequency	76	45	9	130
		%	58.5%	34.6%	6.9%	100.0%

Table-III. Thyroid status among NAFLD (n=83) and controls. (n=47) Pearson Chi-Square value 47.100a DF=2 and p value<0.01

DISCUSSION

Currently, NAFLD is incredibly common and its association with thyroid physiology is the topic of focus for discussion.[10] The aim of current research was to make a widespread appraisal of the connection joining NAFLD and thyroid functions. In present study mean age of study population was 39.76±6.45 years, that is younger age group and revealed increased occurrences of NAFLD(n=83). According to a study by Frith et al.[19] NAFLD is essentially a illness of middle and old age. In this study mean of the TSH, T3 and T4 were compared among NAFLD patients (n=83) and non- NAFLD (N=47) by applying independent t-test. Mean levels of TSH of NAFALD patients were higher than that of healthy controls, (p value <0.01). These findings are similar to that of Zhang J and et al[11] and Bilgin H;[12] Findings of the study by Biligan observed that the ratio of free T3 to free T4 was greater in the individuals having BMI>30 and had NAFLD, signifying advanced transformation from free T4 to free T3 because of enhanced activity of enzyme de-iodinase as a compensatory means for fat amassing to expand energy utilization. Having NAFLD in obesity bears hazardous influence on physiology of thyroid as well as it is also linked with augmented insulin resistance.[12]

NAFLD poses increased oxidative stress that leads to loss of anti-oxidant capability of liver cells including damage of liver tissue. NAFLD induced oxidative stress build up steatosis of hepatic tissue by means of augmented lipid peroxidation as well as transported cytokines might lead to dysfunction of cell organelle, mitochondria.[12,13] The liver exploit the thyroid hormones and also controls their endocrine impacts on body systems. So, hepatic tissue alterations could influence metabolism of thyroidal hormones. Oxidative stress plays pivotal role in the worsening of hepatic dysfunctions.[14]

In this study out of 83 NAFLD patients, 30(36.8%) were euthyroid, 44 (53.0%) were subclinically hypothyroid and 9(10.8%) were hypothyroid. While in healthy control group not suffering from NAFLD, out of 47 individuals 45(97.9%) were euthyroid and only one found with subclinical hypothyroidism. The meta-analysis by He W, An X, Li L, et al.[15] offers strong epidemiological suggestions for the linkage amongst hypothyroidism and NAFLD.

In present study, in the NAFLD group, (n=83) frequency (%) of NASH were 9(10.84%), 42(50.60%) and 30(36.14%) in hypothyroid, subclinical hypothyroid and euthyroid groups respectively. Hypothyroidism was more common among patients with NAFLD (21percent vs. 9.5 percent and p value<0.01) matched to controls, and was augmented in NASH individuals than NAFLD individuals without NASH (25% vs. 12.8% with p value=0.03).[16]

Obese individuals with NAFLD and subclinical hypothyroidism had a more hostile cardiovascular hazard contour.[17] Tao et al.[18] suggested connection of thyroid profile with NAFLD among the people with normal thyroid functions. Though, Tahara K. revealed the augmented occurrences of NAFLD in the patients having previously diagnosed subclinical hypothyroidism. Amplified levels of TSH in euthyroid range is also a self-sufficient risk for developing NAFLD as well as might have impact over progression to hepatic fibrosis, even with a normal levels of free tetra-iodo thyronine.[20] Lugari S et al.[21] in their review, upkeep a substantial affiliation of primary hypothyroid condition with probability of progressing towards development of fatty hepatic condition among the non-alcoholics. Decreased thyroid functions and NAFLD together has been found allied with augmented danger of death related to cardiovascular diseases.[22] This way, this correlation might contribute to development of cardiovascular diseases and increase the disease burden. Keeping in mind, this association, in future further studies are needed to find out underlying mechanisms.

CONCLUSION

It is concluded that that there is substantial difference of TSH in the non-alcoholic fatty liver disease group besides control healthy population.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

No.	Author(s) Full Name	Contribution to the paper	Author(s) Signature
1	Mumtaz Ali Memon	Concept and critical revision.	
2	Ramesh Kumar Suthar	Critical revision, data collection and finalizing of article.	
3	Kavita Bai	Statistical analysis.	