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Study of the Association between Hypothyroidism and Non-Alcoholic Fatty Liver Disease

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ABSTRACT

Aim: The aim of the present study was to investigate the association between hypothyroidism and non-alcoholic fatty liver disease (NAFLD).

Methods: In a prospective observational study, the hypothyroidism patients were evaluated for NAFLD using ultrasonography. The participant's characteristics such as age, gender, thyroid profile, history of diabetes, hypertension, ischemic heart disease (IHD) were recorded using a data gathering form.

Results: A total of 51 participants were included in this study. From 51 participants, 47 (92.18%) individuals were females whereas 4 (7.82%) individuals were males. Out of 51 participants 27 individuals had NAFLD. There was statistically significant difference in FT 4 levels with the participants with NAFLD.

Conclusion: Results from this study suggested that low FT4 concentration is associated with increased risk of NAFLD.

Keywords: Hypothyroidism, NAFLD, ultrasonography, FT4.

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INTRODUCTION:

The thyroid gland is a source of fundamentally two different types of hormones. The thyroid follicle produces the two iodothyronine hormone, thyroxine (T4) and 3,5,3'-triidothyronine (T3). These hormones are essential for the growth of the cells, development of the cells and play an important role in energy metabolism. The thyroid also contains a para follicular cell (C-cells) that produces calcitonin. Serum concentration of thyroid hormones are precisely regulated by the pituitary hormone "Thyrotropin" (thyroid stimulating hormone, TSH) [1]. Thyroid hormones affect the role of almost every organ system. In a child, thyroid hormone is critical for normal growth and development. The major role of thyroid hormone in an adult is to maintain metabolic stability. Thyroid hormones play an important role in thermogenesis and influence all major metabolic pathways such as protein, carbohydrate and lipid metabolism [2]. Hypothyroidism or underactive thyroid is defined as the clinical and biochemical syndrome resulting from decreased thyroid hormone production [3]. Hypothyroidism can cause a number of symptoms, like weight gain, weakness, joints pain, constipation, depression, and hair loss. Occasionally there may be swelling of the front part of the neck due to goiter [4]. Untreated hypothyroidism during pregnancy can lead to delays in growth and intellectual development in the baby or congenital iodine deficiency syndrome [5]. Subclinical hypothyroidism is a milder form of hypothyroidism characterized by an elevated serum TSH level, but with a normal serum free thyroxine level [6,7]. This milder form of hypothyroidism is most commonly caused by Hashimoto's thyroiditis [8]. In adults it is diagnosed when TSH levels are greater than 5mIU/L and less than 10mIU/L [9]. The presentation of subclinical hypothyroidism is variable and classic signs and symptoms of hypothyroidism may not be observed [6]. Non-alcoholic fatty liver disease (NAFLD) is the most common chronic liver condition all over the world [10-13]. NAFLD develops in the absence of excessive alcohol consumption and ranging from the simple steatosis to NASH, even to fibrosis and cirrhosis that can possibly progress to liver failure or hepatocellular carcinoma [14,15]. Moreover, accumulating evidence has shown that NAFLD, either independently or in combination with other metabolic risk factors, is associated with extra hepatic complications such as cardiovascular disease, T2DM, CKD, malignancy, and all-cause mortality [16-19]. Despite

improved understanding and treatment of its risk factors (e.g., diabetes and dyslipidemia), prevalence of NAFLD has rapidly increased [20]. NAFLD has no definitive biochemical markers or peculiar clinical signs. A simple and effective screening approach for NAFLD should include inquiry into other common causes of fatty liver (alcohol, drugs, hepatitis C virus–related chronic hepatitis, hemochromatosis), an ultrasound scan of the liver and assessment of serum transaminase levels. All over the world, hypothyroidism is one of the most common disease. Thyroid hormones play a fundamental role in the lipid metabolism. Results of some of the reviewed studies showed that hypothyroidism play an important role in the development of NAFLD. This may lead us to find out the association between hypothyroidism and NAFLD. It is remains unclear that whether the hypothyroidism is the risk factor for the progression of NAFLD, or if it, then to what extent hypothyroidism affects the NAFLD. Studies confined to euthyroid subjects have been inconsistent as well, reporting that free T4 (FT3) alone (12), TSH alone (13), both (5), or neither of them (14) are linked with NAFLD. These discrepancies are mainly due to small sizes and cross-sectional design of previous studies. Hypothyroidism is a modifiable risk factor and can easily be treated with thyroid replacement therapy. In this study, we will rule out that whether the hypothyroidism is a risk factor for the progression of non-alcoholic fatty liver disease or not.

MATERIALS AND METHODS:

This prospective observational study was conducted at Shri Mahant Indiresh Hospital, Patel Nagar, Dehradun. From February 2019 to July 2019, patients coming to the medicine OPD department with the complaints of thyroid dysfunction (hypothyroidism) were enrolled in this study. The Protocol of the study was approved by Institutional Ethics Committee and a written informed consent form was obtained from all the patients. In this study, all male and female patients with hypothyroidism were included. Patients with other metabolic syndrome and pediatric groups were excluded. Alcoholic patients were also excluded. Initially demographic information was collected from all the individuals. 4 clinical and biochemical parameters that are FT3, FT4, serum TSH and ultrasonography were evaluated and assessed in the central laboratory of the Shri Mahant Indiresh Hospital. Data was analyzed by Statistical Package for Social Sciences (SPSS) version 20. Statistical analysis was performed by using Unpaired T test for analysis of change in FT3, FT4, serum TSH and ultrasonography. All p value less than 0.05 were considered as statistically significant. The strength of the association between FT3, FT4, TSH and ultrasonography were calculated by using Karl Pearson correlation coefficient (r).

RESULTS:

According to the data collected in the study, among 51 patients, 4 patients were males and 47 patients were females accounting for 92.16% and 7.84% respectively. Out of 51 patients, 17 (33%) patients were in the age group of 41-50 years, 14 (27%) patients were in the age group of 18-30 years, 13 (26%) patients were in the age group of 31-40 years, 6 (12%) patients were in the age group of 51-60 and only 1 (2%) patient was in the age group of more than 60 years. 15 patients were from the urban areas, whereas, 36 patients were from the rural areas. 45 patients were complaining of generalized weakness, 42 patients were complaining of weight gain, 32 patients were complaining of joints pain, 12 patients were complaining of constipation, 16 patients were complaining of swelling over the body and 10 patients were complaining of hair loss.

Out of 51 patients, 27 patients were suffering from NAFLD and 24 patients were without NAFLD. Out of 27 patients, 23 patients were found with grade I fatty liver, 3 patients were found with grade II fatty liver and only 1 patient was found with grade III fatty liver.

Association between thyroid dysfunction and NAFLD: T test was performed to check the accuracy of the data. Total 6 parameters were taken in the test and total 51 patients were investigated in this procedure. Statics of results are shown in the table no 1 and table no 2.

Table No 1. Statistics using Student T-test

	N	Mean	Std. Deviation	Std. Error Mean
Age	51	39.24	10.792	1.511
Gender	51	1.92	.272	.038
FT3	51	4.7871	1.47901	.20710
FT4	51	14.7853	5.33802	.74747
TSH	51	14.2778	31.14473	4.36114
USG	51	1.63	.692	.097

Table No 2. Statistics using 2 tailed Student T-test

	Test Value = 0					
	t	df	Sig. (2-tailed)	Mean Difference	nfidence Interval of the Difference	
					Lower	Upper
Age	25.964	50	.000	39.235	36.20	42.27
Gender	50.540	50	.000	1.922	1.85	2.00
FT3	23.114	50	.000	4.78706	4.3711	5.2030
FT4	19.780	50	.000	14.78529	13.2840	16.2866
TSH	3.274	50	.002	14.27784	5.5182	23.0374
USG	16.803	50	.000	1.627	1.43	1.82

Correlation: To find out the strength of the association of FT3, FT4 and TSH with the ultrasonography, Karl Pearson's correlation was studied at the base line. A significant association of FT4 with ultrasonography was found. But no significant association was found with FT3 and TSH level as shown in table no 3.

Table No. 3. Correlation between thyroid functions and USG

		FT3	FT4	TSH	USG
FT3	Pearson Correlation	1	.230	-.291*	-.062
	Sig. (2-tailed)		.105	.038	.668
	N	51	51	51	51
FT4	Pearson Correlation	.230	1	-.403**	.334*
	Sig. (2-tailed)	.105		.003	.017
	N	51	51	51	51
TSH	Pearson Correlation	-.291*	-.403**	1	-.083
	Sig. (2-tailed)	.038	.003		.564
	N	51	51	51	51
USG	Pearson Correlation	-.062	.334*	-.083	1
	Sig. (2-tailed)	.668	.017	.564	
	N	51	51	51	51

*. Correlation is significant at the 0.05 level (2-tailed). **. Correlation is significant at the 0.01 level (2-tailed).

DISCUSSION:

Hypothyroidism is a metabolic disorder in which the thyroid gland can't produce the required amount of thyroid hormones (FT3 & FT4) which can be lead to the malfunctioning of the metabolism of the human body. This metabolic disorder causes decreased absorption of the carbohydrate, protein and lipid from the synthesis site that is hepatocytic cells. The inability of the lipid utilization causes storage of the lipid content in the hepatocytes that causes progression of NAFLD. In this study the relation of the Hypothyroidism was checked with the NAFLD. The patients of Hypothyroidism were investigated and diagnosed pathologically for the amount of serum TSH, FT4 and FT3 hormones in their body. And they were also tested for NAFLD by ultrasonography. The results showed that 51 patients were suffering from Hypothyroidism out of which 27 patients were also suffering from NAFLD. Results indicate that there is an association of NAFLD with the Hypothyroidism which may due to the malfunctioning of the metabolism caused by hyper production of serum TSH and insufficient amount of FT4 and FT3 hormones in the body. So it is important to control the level of FT3 and FT4 hormones in the body to prevent the risk of NAFLD. And in the patients that are suffering from both Hypothyroidism and NAFLD, they should be first prioritized for the control of Hypothyroidism, that will support the proper function of the metabolic reactions leading to good health of the liver and reduction in the amount of fat in the hepatocytes. So control of Hypothyroidism is necessary for it. Hypothyroidism can be easily treated with the help of thyroid replacement therapy (LEVOTHYROXINE). There is no effective drug is yet discovered for the treatment of NAFLD but liver has regeneration ability, so maintaining good level of thyroid hormones by thyroid replacement therapy with good diet and proper exercise can help in NAFLD.

CONCLUSION:

Results from the study suggested that the lower concentration of the FT4 in the body have significant role in progression of the NAFLD. To treat NAFLD it is required to first control hypothyroidism with the significant use of Thyroid replacement therapy. It is also suggested that the control balanced diet and exercise is required to get rid from NAFLD.

REFERENCES:

1. Sharma KK, Sharma HL. Principles of pharmacology, Paras medical publisher Hyderabad, 2nd Edition, 2011; 610-11.
2. Okita M, Hayashi M, Sasagawa T, Takagi K, Suzuki K, Kinoyama S. Effect of a moderately energy-restricted diet on obese patients with fatty liver. Nutrition. 2001; 17(7–8):542–7.
3. Roberts CG, Ladenson PW. Hypothyroidism. Lancet- a Medical Journal, 2004; 363(9411); 793–803.
4. Hypothyroidism. National Institute of Diabetes and Digestive and Kidney Diseases. March 2013. Archived from the original on 5 March 2016. Retrieved 5 March 2016.
5. Preedy, Victor. Comprehensive Handbook of Iodine Nutritional, Biochemical, Pathological and Therapeutic Aspects. Burlington: Elsevier. 2009. p. 616.
6. Bona G, Prodam F, Monzani A. Subclinical hypothyroidism in children: natural history and when to treat. Journal of Clinical Research in Pediatric Endocrinology (Review). 2013;5 Suppl 1 (4): 23–8. [PMID 23154159].
7. Fatourechi V. Subclinical hypothyroidism: an update for primary care physicians. Mayo Clinic Proceedings (Review). 2009;84 (1): 65–71. [PMID 19121255]
8. Baumgartner C, Blum MR, Rodondi N. Subclinical hypothyroidism: summary of evidence in 2014. Swiss Medical Weekly (Review). 144. [PMID 25536449]
9. Dons, Robert F, Frank HW. Endocrine and metabolic disorders clinical lab testing manual (4th ed.). Boca Raton: CRC Press.2009.
10. Vernon G, Baranova A, Younossi ZM. Systematic review: the epidemiology and natural history of non-alcoholic fatty liver disease and non-alcoholic steatohepatitis in adults. Aliment of Pharmacology and Therapeutics. 2011; 34:274–285.
11. Milic S, Stimac D. Nonalcoholic fatty liver disease/steatohepatitis: epidemiology, pathogenesis, clinical presentation and treatment. Digestive Disease (Basel, Switzerland). 2012; 30:158–162.
12. Loomba R, Sanyal AJ. The global NAFLD epidemic. Nature Reveiws Gastroenterology and Hepatology. 2013; 10:686–690.
13. Nascimbeni F, Pais R, Bellentani S. From NAFLD in clinical practice to answers from guidelines. Journal of Hepatology. 2013; 59:859–71.
14. Bugianesi E, Leone N, Vanni E, et al. Expanding the natural history of nonalcoholic steatohepatitis: from cryptogenic cirrhosis to hepatocellular carcinoma. Gastroenterology. 2002; v 123:134–140.
15. Neuschwander-Tetri BA, Caldwell SH. Nonalcoholic steatohepatitis: summary of an AASLD Single Topic Conference. Hepatology (Baltimore, MD). 2003; 37:1202–1219.
16. Armstrong MJ, Adams LA, Canbay A, Syn WK. "Extrahepatic complications of nonalcoholic fatty liver disease". Journal of Hepatology. 2014; 59; 1174–97.
17. Mazo DF, Lima VM, Stefano JT, Rabelo F, Faintuch J, Oliveira CP. Gluco-lipidic indices in treated hypothyroidism associated with non-alcoholic fatty liver disease. Arquivos de Gastroenterologia (Archives of Gastroenterology). 2011; 48:186–189.
18. Grattagliano I, Vendemiale G, Caraceni P, Domenicali M, Nardo B, Cavallari A, et al. Starvation impairs antioxidant defense in fatty livers of rats fed a choline-deficient diet. Journal of Nutrition. 2000; 130(9):2131–6.
19. James OF, Day CP. Non-alcoholic steatohepatitis (NASH): a disease of emerging identity and importance. Journal of Hepatology. 1998; 29(3):495–501.
20. Armstrong MJ, Houlihan DD, Bentham L, et al. Presence and severity of non-alcoholic fatty liver disease in a large prospective primary care cohort. Journal of Hepatology. 2012; 56; 234–40.