Cumhuriyet Medical Journal, 44(4): 412-415, 2022
DOI: http://dx.doi.org/10.7197/cmj.1088088

Cumhuriyet Medical Journal

| cmj.cumhuriyet.edu.tr | Founded: 2004 Available online, ISSN:1305-0028 Publisher: Sivas Cumhuriyet Üniversitesi

Thyroid Nodule Prevalence in Non-Alcoholic Fatty Liver

Zeynep Ergenc[1,a], Hasan Ergenc[1,b*], Özlem Karaca Ocak[2,c], Feyzi Gökosmanoğlu[3,d]

1 Department of Internal Medicine, Ayancık Government Hospital, Sinop, Turkey, 2 Department of General Surgeon, Medicana International Hospital, Samsun, Turkey, 3 Department of Endocrinology and Metabolic Diseases, Biruni University Faculty of Medicine, İstanbul, Turkey

**Corresponding author*

Research Article

History

Received: 18/03/2022
Accepted: 29/12/2022

ABSTRACT

Objectives: This study aimed to investigate the effects of non-alcoholic fatty liver disease on thyroid nodule prevalence

Methods: A total of 384 patients who were followed up with Grade 2-3 Non-Alcoholic Fatty Liver diagnosis were investigated for the presence of multinodular and/or nodular goiter. Demographic characteristics, biochemical data, and abdominal and thyroid ultrasonography reports of the patients were collected from patient files and electronic records.

Results: The ALT (cut-off level 10-40 U/L), GGT (cut-level 0 - 65 U / L), triglyceride (0-150 mg/dL), homeostasis model assessment of insulin resistance (HOMA-IR index value < 2.71), and TSH (cut-off level 0.45-4.12 mU / L), which are biochemical and metabolic parameters examined in our study, increased at statistically significant levels as the fat increased in the liver. A total of 45.8% (176/384) of the patients had Grade-2 Non-Alcoholic Fatty Liver Disease, and 54.1% (208/384) had Grade-3 Non-Alcoholic Fatty Liver Disease. As fat increased in the Non-Alcoholic Fatty Liver Disease, the prevalence of nodules increased at statistically significant levels (p=0.001).

Conclusion: Our study found that the frequency of thyroid nodules, disruption of the parenchymal structure, and metabolic and biochemical disruption are parallel in non-Alcoholic fatty liver patients.

Keywords: Non-Alcoholic Fatty Liver, thyroid nodule, parenchymal structure

Alkolsüz Yağlı Karaciğerde Tiroid Nodülü Prevalansı

Süreç

Geliş: 18/03/2022
Kabul: 29/12/2022

ÖZ

Amaç: Bu çalışmada, alkole bağlı olmayan yağlı karaciğer hastalığının tiroid nodülü prevalansı üzerine etkilerinin değerlendirilmesi amaçlandı.

Materyal metod: Alkolsüz yağlı karaciğer evre 2-3 tanısı ile izlenen toplam 384 hasta multinodüler ve/veya nodüler guatr varlığı açısından geriye dönük olarak incelendi. Hastaların demografik özellikleri, biyokimyasal verileri, abdominal ve tiroid ultrasonografi raporları hasta dosyalarından ve elektronik kayıtlardan elde edildi.

Bulgular: Çalışmamızda incelenen biyokimyasal ve metabolik parametrelerden ALT (10-40 U/L), GGT (0 - 65 U/L), trigliserit (0-150 mg/dL), TSH (0.45-4.12 mU/L) ve homeostaz modeli insülin direnci değerlendirmesi (HOMA-IR indeks değeri) karaciğerde yağlanma arttıkça istatistiksel olarak anlamlı düzeylerde artış gösterdi. Hastaların toplam %45,8'inde (176/384) Evre 2 alkolsüz yağlı karaciğer hastalığı, %54,1'inde (208/384) Evre 3 alkolsüz yağlı karaciğer hastalığı vardı. Alkolsüz yağlı karaciğer hastalığında yağlanma arttıkça nodül prevalansı istatistiksel olarak anlamlı düzeylerde artığı görüldü (p=0,001).

Sonuç: Çalışmamızda alkolik olmayan yağlı karaciğer hastalarında tiroid nodül sıklığı, parankimal yapının bozulması, metabolik ve biyokimyasal bozulmanın paralel olduğu saptandı. Alkolik olmayan yağlı karaciğer hastalarında hematolojik, biyokimyasal ve endokrinolojik parametre değişikliklerinin yanı sıra tiroid nodü prevelansının da değerlendirilmesi gerekmektedir.

Anahtar sözcükler: Alkolsüz yağlı karaciğer, tiroid nodülü, parankimal yapı

[a] *drzeyneperturk@gmail.com* *https://orcid.org/0000-0001-7598-4508*
[b] *dr.hasanergenc@hotmail.com* *https://orcid.org/0000-0003-0519-0264*
[c] *karacaocakozlem@gmail.com* *https://orcid.org/0000-0003-3637-4074*
[d] *gokosmanoglu@gmail.com* *https://orcid.org/0000-0002-6432-8668*

How to Cite: Ergenc Z, Ergenc H, Karaca Ocak Ö, Gökosmanoğlu F (2022) Thyroid Nodule Prevalence in Non-Alcoholic Fatty Liver, Cumhuriyet Medical Journal, December 2022, 44 (4): 412-415

Introduction

With increased incidence in recent years, thyroid nodules have become a common thyroid disease detected by ultrasound in 20-67% of individuals [1]. The developments in diagnostic tools such as High-Resolution Ultrasonography, Computed Tomography, and Magnetic Resonance Imaging may explain this increasing trend partially [2]. There are very few studies in the literature showing the association between Non-Alcoholic Fatty Liver, Metabolic Syndrome, and Nodular Thyroid Disease.

Due to the increasing incidence in thyroid nodules, the risk factors related to nodules should be investigated further. It was shown in some studies that thyroid nodule is related closely to larger waist circumference, higher triglyceride levels, and insulin resistance [3-4]. The metabolic mechanisms facilitating the development of thyroid nodules are complex, and the studies conducted in this regards are few in number. The purpose of this study was to investigate the effects of Non-Alcoholic Fatty Liver Disease on thyroid nodule prevalence.

Materials and Methods

The present study investigated the presence of multinodular and/or nodular goiter in 384 patients who were followed-up with Grade 2-3 Non-Alcoholic Fatty Liver diagnosis in our Endocrinology and General Surgery Clinic between 2015 and 2021. Exclusion criteria were alcohol use, history of hepatitis, pregnancy, being below the age of 18, and having malignity. Demographic characteristics, biochemical data, and abdominal and thyroid ultrasonography reports of the patients were collected from patient files and electronic records. The serum fasting blood glucose, insulin, triglyceride, ALT, GGT, and TSH levels of the patients were measured at the biochemistry laboratory of our hospital. By using the fasting glucose and insulin measurements, the homeostasis model assessment of insulin resistance was measured with the following formula: [fasting plasma glucose level (mg/dL) × fasting serum insulin level (µU/mL)] / 405.

The thyroid nodules and parenchyma of all patients were evaluated by the same radiologist in the radiology clinic of our hospital by using the same Ultrasonography (US) device and by the same endocrinologist in the same US device (The *Philips* Affinity 70 *Ultrasound*; Philips North America Corporation 3000 Minuteman Road M/S 109 Andover, MA 01810, USA).

Statistical Analyses

The IBM SPSS Statistics 22.0 (IBM Co., Armonk, NY, USA) Program was used for statistical analyses when the findings of the study were evaluated. When the study data were evaluated, the suitability of the parameters to normal distribution was evaluated with the Shapiro Wilks Test. When evaluating the study data, descriptive statistical methods (i.e. Mean, Standard Deviation, frequency) were used. The One-Way Anova Test was used in the comparison of the quantitative data for the parameters that were distributed normally. The Pearson Correlation Analysis was used to examine the relations between the parameters that fit normal distribution; and the significance level was taken as $p<0.05$.

This study was conducted in accordance with the ethical rules with the approval of Medicana International Samsun Hospital clinical research ethics committee (decision no 7125, 16.04.2021).

Results

A total of 384 patients (280 women and 104 men) were included in the study. The mean age of the patients was 54±12.5 (18-75). The ALT (cut-off level 10-40 U/L), GGT (cut-level 0 - 65 U / L), triglyceride (0-150 mg/dL), homeostasis model assessment of insulin resistance (HOMA-IR index value < 2.71) and TSH (cut-off level 0.45-4.12 mU / L), which are biochemical and metabolic parameters examined in our study, increased at statistically significant levels as the fat increased in the liver. Demographic characteristics and biochemical data of the cases are given in Table 1.

Table 1. Demographic Characteristics of Patients

Parameters		Fatty Liver Grade-2	Fatty Liver Grade-3	P value
ender (Female/Male)	280/104			
Age	54±12.5			
ALT. U/L		57±11.8	62±14.2	0.012
GGT. U/L		89±13.2	107±18.6	0.001
Triglyceride. mg/dL		210±16.8	275±15.6	0.001
HOMA-IR		3.2±1.5	4.4±1.9	0.011
TSH. mU / L		3.5±1.7	4.3±1.9	0.046

ALT; Alanine Aminotransferase, GGT; Gamma-Glutamyl Transferase, HOMA-IR; Homeostasis Model Assessment of Insulin Resistance, TSH; Thyroid Stimulating Hormone

A total of 45.8% (176/384) of the patients had Grade-2 Non-Alcoholic Fatty Liver Disease, and 54.1% (208/384) had Grade-3 Non-Alcoholic Fatty Liver Disease. Among the Non-Alcoholic Fatty Liver Grade-2 cases, 48.8% (86/176) were Thyroid Paranoid Grade-2 Echogenic (Multiple Hypo-Echoic Areas), 51.1% (90/176) were Thyroid Parenchyma Grade-3 Echogenic (Moderate-level Hypo-Echogenicity); and among the Fatty Liver Grade-3 cases, 37.5% (78/208) were Thyroid Parenchyma Grade-3 Echogenic, 62.5% (130/208) were Thyroid Parenchyma Grade-4 Echogenic (common, significant hypo-echogenicity). As the grade increased in Non-Alcoholic Fatty Liver Disease, thyroid tissue parenchyma increased at statistically significant levels (p=0.021).

Among the Non-Alcoholic Fatty Liver Grade-2 cases, it was found that 68.1% (120/176) had thyroid nodules, and among the Fatty Liver Grade-3 cases, 84.1% (175/208) had thyroid nodules. As fat increased in the Non-Alcoholic Fatty Liver Disease, the prevalence of nodules increased at statistically significant levels (p=0.001) as seen in Table 2.

Table 2. Changes in thyroid nodule and thyroid tissues in fatty liver cases

Parameters	Thyroid nodule	Thyroid parenchyma Grade-2 echogenic	Thyroid parenchyma Grade-3 echogenic	Thyroid parenchyma Grade-4 echogenic
Fatty Liver Grade-2 (n=176)	%68.1 (120/176)	%48.8 (86/176)	%51.1 (90/176)	
Fatty Liver Grade-3 (n=208)	%84.1 (175/208)		%37.5 (78/208)	%62.5 (130/208)
P value	0.001*			

*As the grade increases in fatty liver, so does the nodule frequency at statically significant levels.

Discussion

Thyroid nodules are structurally different lesions in the thyroid gland and are also separated from the parenchyma [5]. We found in our study that thyroid nodule frequency was increased in fatty liver cases. We also showed that the fat levels increased parallel to thyroid parenchyma echogenicity in Fatty Liver. Fatty Liver and thyroid prevalence was 2.69 times higher in women.

Thyroid nodule is a clinically common disease, and its prevalence has increased significantly in recent years. The prevalence of thyroid nodules was reported to be approximately 8% [6], and increased to 25% in 2013 [7-8], 19-67% were documented with High-Resolution Ultrasound, and 20-76% were shown in autopsies [9 9-10]. In our study, we detected 68.1% (120/176) thyroid nodules in Non-Alcoholic Fatty Liver Grade-2 Cases with High-Resolution US; and 84.1% (175/208) thyroid nodules were detected in Fatty Liver Grade-3 Cases. The prevalence of nodules increases at significant levels as the grade increases in the Non-Alcoholic Fatty Liver Disease.

There are very few data on Non-Alcoholic Fatty Liver with thyroid nodule in the literature. It was shown in a recent study that thyroid nodules had increased prevalence in female patients diagnosed with Non-Alcoholic Fatty Liver Disease, and another study showed that there was 43% increase in men [11-12]. In the present study, we detected that the prevalence of thyroid nodules increased at significant levels in male and female patients with Non-Alcoholic Fatty Liver Disease. For this reason, the data obtained in this study showed that the metabolic disorder in nonalcoholic fatty liver has a potential role in the thyroid nodule pathogenesis, which expands our current understanding on the relation between Non-Alcoholic Fatty Liver Disease and thyroid nodule.

There are thyroid parenchymal inflammation, parenchymal fat infiltration, and ultrasonographic echogenic changes in Non-Alcoholic Fatty Liver [13-14]. The studies conducted on this subject are inadequate in the literature [15-16]. In our study, it was found that thyroid tissue parenchyma ultrasonographic echogenicity increased in parallel to the increase in fat in the Non-Alcoholic Fatty Liver Disease. No published studies were detected investigating its role in thyroid nodule pathogenesis in fatty liver to date. We believe that thyroid parenchymal fat and parenchymal fat infiltration develop in fatty liver with a mechanism similar to liver parenchymal fat.

Recent comprehensive studies identified metabolic disorders and the roles of thyroid hormones in Non-Alcoholic Fatty Liver Disease. Studies especially focused on direct effects of thyroid hormones on hepatic lipid metabolism [17-18]. We showed in this study that as fat increased in the

Non-Alcoholic Fatty Liver Disease, metabolic parameters deteriorated, the prevalence of thyroid nodule increased, and thyroid parenchymal structure deteriorated. When considered in this context, studies conducted so far have reported that the liver is affected over the thyroid. We showed in our study that the interaction between the liver and the thyroid is a bilateral interaction.

Conclusion

It was found in the present study that the frequency of thyroid nodules, disruption of the parenchymal structure, and metabolic and biochemical disruption are parallel in Non-Alcoholic Fatty Liver patients. This increase might have a prognostic importance in terms of possible risk increases for hypothyroidism, which might lead to a vicious cycle in Non-Alcoholic Fatty Liver patients. In this respect, a holistic approach is inevitable for the diagnosis and successful treatment of patients.

References

1. Gharib H, et al. Task Force on Thyroid Nodules. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and EuropeanThyroid Association Medical Guidelines for Clinical Practice for the Diagnosis and Management of Thyroid Nodules. Endocr Pract. 2010 16:1-43.
2. Davies L, Welch HG. Increasing incidence of thyroid cancer in the United States, 1973-2002. JAMA. 2006;295(18):2164-7.
3. Yin J, Wang C, Shao Q, Qu D, Song Z, Shan P, Zhang T, Xu J, Liang Q, Zhang S, Huang J. Relationship between the Prevalence of Thyroid Nodules and Metabolic Syndrome in the Iodine-Adequate Area of Hangzhou, China: A Cross-Sectional and Cohort Study. Int J Endocrinol. 2014;2014:675-796.
4. Arduc A, et al. Higher body mass index and larger waist circumference may be predictors of thyroid carcinoma in patients with Hürthle-cell lesion/neoplasm fine-needle aspiration diagnosis. Clin Endocrinol (Oxf). 2015;83(3):405-11.
5. Polyzos SA, Kita M, Avramidis A. Thyroid nodules - stepwise diagnosis and management. Hormones (Athens). 2007;6(2):101-19.
6. Hu F, Teng X, Teng W, Guan H, Yang F, Gao T, Wang W, Shi X, Tong Y. A comparative epidemic study of goiter and thyroid nodules in areas with different iodine intake. *Chinese Journal Of Endemiology.* 2002;21:464–467.
7. Men X. The Research of The Prevalence of Thyroid Nodule in Physical Examination Population. *China Practical Medical.* 2013;33: 103–104.
8. Liu Y, Lin Z, Sheng C, Zhu Y, Huang Y, Zhong N, Jia Z, Qu S. The prevalence of thyroid nodules in northwest China and its correlation with metabolic parameters and uric acid. Oncotarget. 2017;8(25):41555-41562.
9. Zhao W, et al. Prevalence of goiter and thyroid nodules before and after implementation of the universal salt iodization program in mainland China from 1985 to 2014: a systematic review and meta-analysis. PLoS One. 2014;9(10):109-549.
10. Oertel JE, Klınck GH. Structural changes ın the thyroıd glands of healthy young men. Med Ann Dist Columbia. 1965 Feb;34:75-7. PMID: 14272722.
11. Ding X, et al. Gender Disparity in the Relationship between Prevalence of Thyroid Nodules and Metabolic Syndrome Components: The SHDC-CDPC Community-Based Study. Mediators Inflamm. 2017;2017:848-1049.
12. Chen Y, et al. The Association of Thyroid Nodules with Metabolic Status: A Cross-Sectional SPECT-China Study. Int J Endocrinol. 2018;2018:685-3617.
13. Rezzónico JN, Rezzónico M, Pusiol E, Pitoia F, Niepomniszcze H. Increased prevalence of insulin resistance in patients with differentiated thyroid carcinoma. Metab Syndr Relat Disord. 2009;7(4):375-80.
14. He W, An X, Li L, Shao X, Li Q, Yao Q, Zhang JA. Relationship between Hypothyroidism and Non-Alcoholic Fatty Liver Disease: A Systematic Review and Meta-analysis. Front Endocrinol (Lausanne). 2017;8:335.
15. Geach T. Thyroid function: Poor thyroid function linked to NAFLD. Nat Rev Endocrinol. 2016;12(8):434.
16. Nakade Y, Yoneda M. Relationship between Non-alcoholic Fatty Liver Disease and Thyroid Dysfunction. Intern Med. 2016;55(15):1941-1942.
17. Martínez-Sánchez N, et al. Hypothalamic AMPK-ER Stress-JNK1 Axis Mediates the Central Actions of Thyroid Hormones on Energy Balance. Cell Metab. 2017 5;26(1):212-229
18. Sinha RA, Singh BK, Yen PM. Direct effects of thyroid hormones on hepatic lipid metabolism. Nat Rev Endocrinol. 2018;14(5):259-269.