Research Article / *Araştırma Makalesi*

Ege Journal of Medicine / *Ege Tıp Dergisi* 2022; 61 (3): 476-483

Work-related factors affecting the thyroid hormone levels among workers in different sectors

Farklı sektörlerde çalışanlarda tiroit hormon düzeylerini etkileyen işle ilgili faktörler

Seher Kurtul[1] Meral Türk[2]

[1] University of Health Sciences, Bozyaka Training and Research Hospital, Department of Occupational Disease, Izmir, Turkiye

[2] Ege University Medical Faculty, Department of Occupational Disease, Izmir, Turkiye

ABSTRACT

Aim: This study purposed to evaluate thyroid hormone levels and work-related factors in workers.

Materials and Methods: This retrospective study was perfomed at 475 workers who applied to the outpatient clinic of occupational diseases between November 2015-February 2020. Sociodemographic variables, work-related factors and laboratory records were retrospectively evaluated. Student's t-test was performed to compare mean values. Multiple linear regression analysis was used, including independent variables that were found to be statistically significantly related in binary analysis of thyroid-stimulating hormone (TSH) value.

Results: Of the 475 participants, 433 (91.2%) were male and 173 (36.4%) worked night shifts, 293 (61.7%) were exposed to silica dust, 23 (4.8%) to plastic fumes, and 80 (16.8%) to solvent. Study participants who were over 40 years of age, night shift workers, and workers with exposure to silica dust had significantly lower TSH values (p=0.026, p=0.023, p=0.002, respectively); male workers, workers under 40 years of age, and workers with body mass index (BMI) <25 had significantly higher free T4 levels (p=0.017, p=0.042, p=0.026, respectively). In the regression analysis, it was observed that there was a significant relationship BMI, silica dust exposure, night shift work and low TSH level (p=0.033, p=0.028, p=0.045).

Conclusion: It was found that night shift work and exposure to silica dust were associated with decreased TSH levels in workers. Silica dust exposure and night shift work are among the preventable risk factors. For this reason, the workplace environment should be reorganized, periodic health examinations should be carried out, and workers should be ensured to comply with occupational health and safety rules.

Keywords: Thyroid hormones, silica, workplace.

ÖZ

Amaç: *Meslek hastalıkları polikliniğine başvuranlarda tiroid hormon düzeyleri ile işle ilişkili faktörlerin değerlendirilmesi amaçlanmıştır.*

Corresponding author: Seher Kurtul

University of Health Sciences, Bozyaka Training and Research Hospital, Department of Occupational Disease, Izmir, Turkiye

E-mail: *seherkurtul79@gmail.com*

Application date: 29.03.2022 Accepted: 18.07.2022

Gereç ve Yöntem: *Çalışmaya üniversite hastanesi meslek hastalıkları polikliniğine Kasım 2015-Şubat 2020 tarihleri arasında başvuran 475 çalışan dahil edildi. Çalışanların verilerine; meslek hastalıkları poliklinik muayene formları ve laboratuvar kayıtları retrospektif olarak incelenerek ulaşıldı. Ortalama değerleri karşılaştırmak için Student t testi kullanıldı. İkili analizlerde tiroid stimulan hormon (TSH) değeri ile istatiksel olarak anlamlı ilişkili saptanan bağımsız değişkenler için çoklu lineer regresyon analizi yapıldı.*

Bulgular: *475 çalışanın 433'ü (%91,2) erkek ve 173'ü (%36,4) gece vardiyasında çalışıyordu. İşyerinde 293'ü (%61,7) silika tozuna, 23'ü (%4,8) plastik dumana ve 80'i (%16,8) solvente maruz kaldığını ifade etti. 40 yaş üzeri olanlarda (p=0.026), gece vardiyalı çalışanlarda (p=0.023), silika tozuna maruz kalanlarda (p=0.002) daha düşük TSH değerleri; erkek çalışanlarda (p=0.017), 40 yaş altı olanlarda (p=0.042), vücut kitle indeksi (VKİ) 25'den küçük olanlarda (p=0.026) serbest T4 düzeyleri daha yüksek olarak bulundu. Regresyon analizinde VKİ, silika tozu maruziyeti, gece vardiyası çalışması ile azalmış TSH düzeyi arasında anlamlı bir ilişki olduğu görüldü (sırasıyla p=0.033, p=0.028, p=0.045).*

Sonuç: *Meslek hastalıkları polikliniğine başvuran çalışanlarda gece vardiyalı çalışma ve silika tozuna maruziyetin azalmış TSH seviyeleri ile ilişkili olduğu bulundu. Silika tozu maruziyeti ve gece vardiyalı çalışma önlenebilir risk faktörleri arasında yer almaktadır. Bu nedenle çalışma ortamı yeniden düzenlenmeli, periyodik sağlık muayeneleri yapılmalı, çalışanların iş sağlığı ve güvenliği kurallarına uymaları sağlanmalıdır.*

Anahtar Sözcükler: *Tiroid hormonları, silika, işyeri.*

INTRODUCTION

Thyroid hormones are the regulators of the organism and play a significant role in the maintenance of normal physiological processes. The thyroid hormones thyroxine (T4) and triiodothyronine (T3) are released by the thyroid gland. The synthesis and excretion of thyroid hormone are organized by thyroid-stimulating hormone (TSH) produced from the anterior pituitary gland, while the production and secretion of TSH are regulated by hypothalamic thyrotropin-releasing hormone (TRH). Genetic factors are responsible for up to 65% of interpersonal diversity in TSH and thyroid hormone levels, however several other factors can also affect thyroid function. These factors include demographic determinants (age and gender), internal determinants (microbiota, stress), drug use, and various environmental factors (1). TSH release demonstrates a daily rhythm according to the sleep-wake cycle and sleeping schedule. Today, due to the increasing competitive economic environment, globalization, and the increasing demand for labor, a necessity for 24-hour work has arisen, and the emergence of shift work systems (2). Night shifts, which comprises a portion of shift work, causes mainly physiological, psychological, and sociologic problems in workers. The circadian rhythm, which controls the daily sleep-wake cycle in the human body, is controlled by the biological clock set according to the 24-hour period. Numerous studies have shown that TSH secretion has a circadian rhythm and also effects the secretion of free T4 (fT4) (3). A slow increase in plasma TSH levels is observed in the evening hours, which peaks at the start of sleep, decreases during sleep, and stays at low levels during the day; disruption of this cycle is a significant problem in night shift workers (4). Several literatures have shown that night shift work may induce illnesses such as cardiovascular diseases, sleep disorders, peptic ulcer, and breast cancer in women (5). The effect of night shift work on health is believed to be primary related to its interaction with circadian rhythms. Light exposure and sleep deprivation during the night are thought to disrupt this physiological rhythm.

Occupational exposure to silica dust has been strongly associated with autoimmune diseases. Workers exposed to silica dust were shown to have significantly higher mean serum T3, free T3 (fT3) and fT4, and lower mean T4 levels than controls, and a strong association was found between exposure time and thyroid hormone levels (6).

Endocrine disrupting chemicals such as bisphenol A, polybrominated diphenyl ethers and phthalates are generally used for plastic additives. The detrimental effects of these

substances on thyroid physiology and thyroid hormone metabolism have been demonstrated in both experimental and clinical studies (7). Furthermore, the effects of industrial solvents on adrenal, thyroid, and parathyroid glands have been shown in studies conducted in humans and experimental animals. In animal experiments, inhalation of methanol, toluene, and mixtures of both were observed to cause mild and rarely moderate shrinkage in thyroid follicles in females, while thyroid follicular cell hyperplasia was observed after exposure to ethyl benzene (8, 9).

Work-related factors can affect with the hypothalamic pituitary thyroid axis at various levels and through different mechanisms of action (10). There are a few number of literatures investigating the influence of work-related factors on thyroid hormone levels in several countries. This study purposed to assess the relationship between thyroid hormone levels and sociodemographic variables and work-related factors in workers.

MATERIALS and METHODS

Study procedure

In this cross-sectional study, a study sample of 566 workers who applied to the outpatient clinic of occupational diseases of a university hospital between November 2015-February 2020 was included. No sample selection was made in the study. Among the study participants, 91 individuals with a diagnosis of any thyroid disorder before starting employment, diabetes, liver disease, kidney failure, heart failure, coagulopathy, and other severe chronic diseases, and chronic drug use were excluded from the study. Workers who do not have the specified chronic diseases and who have a total of at least one year of work were included in the study. This study was confirmed by the ethics committee of Ege University Medical Faculty (2020, No: 20-12T/37).

Data collection

Study data were collected from outpatient clinic examination forms and laboratory records and retrospectively examined. Sociodemographic variables of the workers consisted of gender, age, education status, body mass index (BMI), smoking and alcohol consumption; work-related factors included sector, employment status, history of night shift work, exposure to silica dust, plastic fume exposure, solvent exposure, total years of night shift work, and total years of silica dust exposure. Venous blood samples were taken from all applicants (8 hours fasting) and thyroid hormone analyzes were performed using enzymatic methods (Roche Diagnostics, Mannheim, Germany). Normal ranges measured in venous blood were considered 0.27–4.2 mIU/L for TSH and 0.89–1.76 ng/dL for fT4. Participants were questioned in regards to smoking and alcohol consumption in the last six-month period. Those who break smoking more than six months ago and never smoked were considered as the non-smoker group. Participants who worked regular night shifts in the last year or longer were considered regular night shift workers. In addition, participants who were exposed to silica dust, plastic fumes, and solvent in the last year in workplace according to detailed work history were considered exposed workers.

Statistical analysis

Measurement variables were written as mean ± standard deviation (SD), median (min-max) values, while categorical data were written in number-% tables. Student's t-test was performed to compare mean values between two groups. Multiple linear regression analysis was performed, including independent variables that were found to be statistically significantly related in binary analysis of TSH value. In the regression analysis, the enter method was used, in which each variable was added to the model at the same time. Models were created in the direction of hypotheses according to variable groups. SPSS 22.0 was used for the analysis of all data. The value of $p<0.05$ was accepted statistically significant.

RESULTS

Among the 475 workers from different sectors who applied to the outpatient clinic, 433 (91.2%) were male. The socio-demographic variables of the workers and their work-related factors are shown in (Table-1).

When the demographic variables and work-related factors of the workers were assessed in terms of mean TSH levels, workers who were over 40 years of age, night shift workers, and workers with exposure to silica dust had significantly lower TSH values ($p=0.026$, $p=0.023$, $p=0.002$, respectively). When demographic and work-related factors were evaluated in terms of mean fT4 levels, male workers, workers under 40 years of age, and workers with BMI <25 had significantly higher fT4

levels (p=0.017, p=0.042, p=0.026, respectively) (Table-2).

The results of the multiple linear regression analysis, in which the independent variables found to be statistically significantly related in the binary analyzes of the TSH value in the participants were included, are presented in Table-3 with two different models. In the regression analysis, it was found that there was a strong relationship between BMI, silica dust exposure, night shift work and low TSH level (p=0.033, p=0.028, p=0.045 respectively). According to the R^2 values, it was found that night shift work and silica dust exposure explained 2.5% of the low TSH.

Table-1. Distribution of sociodemographic and work-related factors.

Parameter	
Gender (n,%)	
Male	433 (91.2)
Female	42 (8.8)
Age (n,%)	
≤40 years	269 (56.6)
>40 years	206 (43.4)
Education Level (n,%)	
Primary	264 (55.6)
Middle	164 (34.5)
University	47 (9.9)
BMI (n,%)	
<25	141 (29.7)
≥25	334 (70.3)
Smoking (n,%)	
Yes	350 (73.7)
No	175 (26.3)
Alcohol Use (n,%)	
Yes	77 (16.2)
No	398 (83.8)
Sector (n,%)	
Agriculture	29 (6.1)
Industry	349 (73.5)
Service	97 (20.4)
Employment Status (n,%)	
Blue collar	412 (86.7)
White collar	63 (13.3)
Night Shift Work (n,%)	
Yes	173 (36.4)
No	302 (63.6)
Silica Dust Exposure (n,%)	
Yes	293 (61.7)
No	182 (38.3)
Plastic Fumes Exposure (n,%)	
Yes	23 (4.8)
No	452 (95.2)
Solvent Exposure (n,%)	
Yes	80 (16.8)
No	395 (83.2)
Total years of night shift work years, Median(min-max)	10.00 (1-27)
Total years of exposure to silica dust years, Median(min-max)	9 (1-28)

BMI: Body mass index.

Table-2. Comparison of demographic and work-related factors according to serum TSH and fT4 levels.

Parameter	TSH (µUI/mL) (mean±SD)	P value	fT4 (ng/dL) (mean±SD)	P value
Gender				
Male	1.62±0.81	0.431	1.23±0.16	0.017
Female	1.72±0.80		1.16±0.16	
Age				
≤40 years	1.70±0.87	0.026	1.24±0.16	0.042
>40 years	1.53±0.72		1.20±0.16	
Education level				
Primary	1.67±0.91	0.123	1.22±0.17	0.468
Middle school	1.53±0.59		1.23±0.15	
University	1.76±0.91		1.25±0.18	
BMI				
<25	1.56±0.79	0.214	1.25±0.17	0.026
≥25	1.66±0.82		1.21±016	
Smoking				
Yes	1.62±0.80	0.675	1.23±0.84	0.445
No	1.65±0.84		1.21±0.18	
Alcohol use				
Yes	1.55±0.70	0.301	1.22±0.17	0.663
No	1.64±0.83		1.23±0.16	
Sector				
Agriculture	1.71±0.94	0.606	1.26±0.17	0.475
Industry	1.60±0.81		1.22±0.16	
Service	1.68±0.80		1.22±0.16	
Employment status				
Blue collar	1.63±0.81	0.907	1.23±0.169	0.820
White collar	1.62±0.82		1.22±0.15	
Night shift work				
Yes	1.52±0.75	0.023	1.22±0.13	0.44
No	1.69±0.84		1.23±0.17	
Exposure to Silica Dust				
Yes	1.56±0.79	0.022	1.22±0.16	0.946
No	1.74±0.84		1.23±0.17	
Plastic Fumes Exposure				
Yes	1.69±0.65	0.652	1.23±0.18	0.919
No	1.62±0.82		1.22±0.16	
Solvent Exposure				
Yes	1.72±0.89	0.278	1.22±0.18	0.740
No	1.61±0.80		1.23±0.16	

TSH: Thyroid-stimulating hormone, fT4: free T4, BMI: Body mass index

Table-3. Multiple linear regression analysis of the variables that were significant with the mean TSH value.

		Model 1			Model 2		
		B	Beta	P	B	Beta	P
Individual factors							
Gender		-0,005	-0,058	0,217	-,006	-0,002	0,960
Age		-0,124	-0,052	0,270	-,006	-0,068	0,153
BMI		0,015	0,095	0,045	,016	0,100	**0,033**
Work-related factors							
Silica dust exposure					0,154	0,111	**0,028**
Night shift work					0,132	0,094	0,045
The explanatory and significant levels of the models	aR^2	0,007			**0,025**		
	P	0,098			**0,006**		

BMI: Body mass index

DISCUSSION

This study indicate that night shift work and exposure to silica dust are associated with TSH levels in workers who applied to our outpatient clinic of occupational diseases. Lower mean serum TSH levels were observed in night shift workers and workers who were exposed to silica dust. Studies have shown that night shift work often causes a disruption between the person's biological clock and the actual time of the day (11). Serum TSH concentrations are used as a specific and sensitive measure for early diagnosis of endocrine disturbances. Since TSH is regulated by both sleep and circadian rhythms, sleep deprivation causes TSH to nearly double the normal level at night. This elevated TSH level persists during the day due to the hormone's long half-life (12).

Studies investigating the influences of night shift work on TSH levels report varying results. Coherent with the results of our study, Korompeli et al (13). and Marlmberg et al (14). found a decrease in serum TSH levels in nurses that worked shifts and physicians who worked night shifts. Night shift work has been considered a stress factor for the human body, as changes in the sleep-wake cycle can influence human biological functions, physical-psychological status, and life quality (15). This decrease in TSH levels is thought to be a likely result of stress-induced inhibition at the hypothalamic level. One cross-sectional study on male workers who worked night shifts demonstrated that they had significantly higher TSH levels compared to daytime workers (16). Despite the reason for this effect is not completely understood, it is thought that changes in sleep schedule, sleeping times, and sleep quality, primarily caused by night shifts, can change the body's normal circadian rhythm and cause to circadian rhythm pathology for TSH secretion (17). Eating at night can affect hormone levels such as TSH, insulin, and glucagon. Working night shifts can cause to irregular eating habits and eating at night, resulting in an increase in TSH levels (18).

Various composites such as asbestos, silica, nanoparticles and silicone cause major biological changes including immune hyperactivation, production of reactive oxygen species, and tissue damage (19). Beshir et al. found that occupational exposure to silica dust may affect thyroid hormone activity through autoimmune mechanisms, regardless of clinical features (6). Although these autoimmune diseases occur predominantly in women, autoimmunity due to occupational exposure to silica is mostly recognized in men. There is a relationship between silica exposure and autoimmune disease and autoantibodies, and silica-induced autoantibody production can occur even without severe lung damage (20). Many studies demonstrating the development of autoimmune diseases and autoantibody production in patients exposed to silicone implants have reported a possible relationship between silicone exposure and autoimmune diseases (21, 22). Improvement of clinical symptoms after implant removal supports this association between silicone and autoimmunity (19).

In a study that compared workers who developed silicosis and those who did not develop silicosis among ceramic workers who were exposed to silica dust, it was found that the silicosis cases had significantly lower fT3 and fT4 levels compared to the control group. TSH levels were lower among silicosis cases. This finding

suggests that mechanisms such as thyroid transcription factor-1(TTF-1), increased surfactant protein SP-A expression occurring in silicosiswith lung fibrosis and idiopathic pulmonary fibrosis may be responsible for the decrease in serum thyroid hormone (23). In our study, it was found that TSH levels were significantly lower in workers who were exposed to silica dust, while both groups had the same levels of fT4. There was no correlation between total years of silica dust exposure and fT4 and TSH levels. It was thought that decrease in TSH due to exposure to silica dust may play a role in increased expression of TTF-1 and SP-A in workers diagnosed with silicosis.

Our study had some limitations. Workers from different sectors referred to the outpatient clinic of occupational disease may work in different shift schedules and may also be exposed to other risk factors in the workplace that affect thyroid function. Workplace exposure and occupational histories were evaluated based on the self-reports of the workers. Occupational exposures were at different levels and not homogeneous among the workers as they worked in different workplaces. In addition, the number of female workers working in shifts and exposed to silica dust was much less than men due to the prominence of the industrial sector, so a meaningful comparison could not be made between men and women. Blood samples were taken at various times of the day. Therefore, homogeneity may not be achieved in thyroid hormone levels that are secreted rhythmically during the day.

CONCLUSION

We observed that night shift work and exposure to silica dust were associated with decreased TSH levels in workers admitted to the outpatient clinic of occupational diseases.

Considering the high number of night shift workers and workers exposed to silica dust, this is a major occupational health problem. However, silica dust exposure and night shift work are among the preventable risk factors. For this reason, the workplace environment should be reorganized, periodic health examinations should be carried out, and workers should be ensured to comply with occupational health and safety rules. The association of silica dust exposure and night shift work with TSH levels needs to be evaluated in future research.

Conflict of interest: The authors declare that they have no conflict of interest associated with this publication and they will not provide access to the study data. All authors contributed equally to the conception and design of the research, to the analysis of the data, and to the writing of the final version of the manuscript.

References

1. Leko MB, Gunjaca I, Pleic N, Zemunik T. Environmental Factors Affecting Thyroid-Stimulating Hormone and Thyroid Hormone Levels. Int. J. Mol. Sci. 2021; 22: 6521.
2. Costa G. Shift work and health: current problems and preventive actions. Saf Health Work. 2010; 1 (2): 112-23.
3. Liyanage YSH, Siriwardhana ID, Dissanayake M, Dayanath BKPT. Study on diurnal variation in TSH and freeT4 levels of healthy adults. Sri Lanka Journal of Diabetes Endocrinology and Metabolism.2018; 8 (1): 8-16.
4. Roelfsema F, Veldhuis JD. Thyrotropin Secretion Patterns in Health and Disease. Endocr Rev.2013; 34: 619-57.
5. Moon SH, Lee BJ, Kim SJ. et al. Relationship between thyroid stimulating hormone and night shift work. Ann of Occup and Environ Med.2016; 28: 53.
6. Ahmed SB, Aziz HM, Elserougy SM. Effect of Occupational Exposure to Silica Dust on the Thyroid Gland in Ceramic Workers. Central European Journal of Occupational and Environmental Medicine. 2007; 13 (1): 33-42.
7. Duntas LH. The thyroid under threat in a world of plastics. Facta Universitatis Series: Medicine and Biology Vol. 2017; 19 (2): 47-50.
8. Poon R, Chu I, Bjarnason S, Potvin M, Vincent R, Miller RB, et al. Inhalation toxicity study of methanol, toluene and methanol/toluene mixtures in rats: effects of 28-days exposure. Toxicol Ind Health. 1994; 10 (3): 231-45.
9. National Toxicology Program. NTP Toxicology and Carcinogenesis Studies of Ethylbenzene (CAS No. 100-41-4) in F344/N Rats and B6C3F1 Mice (Inhalation Studies). Natl Toxicol Program Tech Rep Ser. 1999; 466: 1-231.

10. Saad-Hussein A, Hamdy H, Aziz HM, Mahdy-Abdallah H. Thyroid functions in paints production workers and the mechanism of oxidative-antioxidants status. Toxicol Ind Health.2011; 27 (3): 257-63.
11. Copertaro A, Bracci M. Working against the biological clock: a review for the Occupational Physician. Industrial Health. 2019; 57: 557-69.
12. Allan JS, Czeisler CA: Persistence of the circadian thyrotropin rhythm under constant conditions and afterlight-induced shifts of circadian phase. J Clin Endocrinol Metab.1994; 79 (2): 508-12.
13. Korompeli A, Sourtzi P, Tzavara C, Velonakis E. Rotating shift-related changes in hormone levels in intensive care unitnurses. J Adv Nurs. 2009; 65 (6): 1274-82.
14. Malmberg B, Persson R, Jönsson BA, Erfurth EM, Flisberg P, Ranklev E, Orbaek P. Physiological restitution after night-call duty in anaesthesiologists: impact on metabolic factors. Acta Anaesthesiol. Scand. 2007; 51: 823–30.
15. Leso V, Vetrani I, Sicignano A, Romano R, Ivo Iavicoli I. The Impact of Shift-Work and Night Shift-Work on Thyroid: A Systematic Review. Int. J. Environ. Res. Public Health. 2020; 17 (5): 1527.
16. Hye-a Hwang, Young-jee Jeon. Relationship between Shift Work and Subclinical Hypothyroidism. Korean J Fam Pract 2020;10(1):3-8.
17. Parker DC, Rossman LG, Pekary AE, Hershman JM. Effectof 64-hour sleep deprivation on the circadian wave form of thyrotropin (TSH): Furtherevidence of sleep-related inhibition of TSH release. J Clin Endocrinol Metab. 1987;64:157-61.
18. Holmbäck U, Forslund A, Lowden A, Forslund J, Akerstedt T, Lennernäs M, et al. Endocrine responses to nocturnal eating–possible implications for night work. Eur J Nutr. 2003; 42: 75–83.
19. Speck-Hernandez CA, Montoya-Ortiz G. Silicon, a Possible Link between Environmental Exposure and Autoimmune Diseases: The Case of Rheumatoid Arthritis. Arthritis. 2012; 2012: 604187.
20. Mayeux JM, Escalante GM, Christy JM, Pawar RD, Kono DH and Pollard KM. Silicosis and Silica-Induced Autoimmunity in the Diversity Outbred Mouse. Front. Immunol. 2018; 9: 874.
21. Muzaffar AR, Rohrich RJ. The silicone gel-filled breast implant controversy: an update. Plast Reconstr Surg. 2002; 109 (2): 742-7; quiz 748.
22. Bar-Meir E, Teuber SS, Lin HC, Alosacie I, Goddard G, Terybery J, et al. Multiple autoantibodies in patients with silicone breast implants. J Autoimmun. 1995; 8 (2): 267-77.
23. Karataş M. Silikozis tanılı seramik işçilerinde kan tiroid hormon düzeyinin değerlendirilmesi. Journal of Harran University Medical Faculty. 2019; 16 (1): 8-12.