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ABOUT

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Original Article

Depression Paradox in Cardiovascular Outcomes of Adult Patients with Obstructive Sleep Apnea: Insights from 2 Million Nationwide Hospitalizations

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Rupak Desai and Sashwath Srikanth share equal contributions to the manuscript.

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Abstract

OBJECTIVE: Depression is a frequent comorbidity in obstructive sleep apnea (OSA) patients. There is a scarcity of data on the impact of depression on the outcomes of OSA.

MATERIAL AND METHODS: Using the National Inpatient Sample (2018), we identified hospitalizations in the US with OSA. Following propensity-score matching, the two cohorts of OSA with depression (OSA+D+) vs. without depression (OSA+D-) were compared for demographic and comorbidities profiles differences. Multivariable regression analyses were performed to assess the odds of events with depression versus those without.

RESULTS: Of 2,169.730 hospitalizations in patients with OSA, 20.1% had comorbid depression. Matched cohorts included 846,150 admissions in both groups: OSA+D+ and OSA+D-. Both cohorts predominantly comprised Caucasians, the elderly (median age, 64 vs. 65 years), and females (55.5% vs. 55.2%). OSA+D+ cohort had a higher prevalence of hypertension, diabetes, hyperlipidemia, congestive heart failure, anemia, smoking, substance abuse, prior myocardial infarction (MI), transient ischemic attack (TIA), TIA/stroke, and venous thromboembolism than the OSA+D- group (all $P < 0.001$). Paradoxically, there was decreased risk of all-cause mortality [odds ratios (OR): 0.79, 95% confidence interval (CI): 0.73-0.86], major adverse cardiac and cerebrovascular events (OR: 0.83, 95% CI: 0.80-0.87), acute MI (OR: 0.80, 95% CI: 0.76-0.85), dysrhythmia/atrial fibrillation (OR: 0.81, 95% CI: 0.79-0.83), and cardiac arrest including ventricular fibrillation (OR: 0.65, 95% CI: 0.73-0.82) in the OSA+D+ cohort ($P < 0.001$).

CONCLUSION: OSA+D+ patients had better in-hospital outcomes as compared to OSA+D- despite having a higher burden of comorbidities. Additional research is warranted to validate this paradoxical effect of depression in OSA.

KEYWORDS: Obstructive sleep apnea, sleep-disordered breathing, depression, mortality myocardial infarction, cardiac arrest, stroke

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INTRODUCTION

A cause-and-effect relationship has not been determined between depression and obstructive sleep apnea (OSA). However, OSA patients have a higher prevalence of depression, ranging from 5% to 63%.[1] Prospective studies have shown that the development of depression in OSA patients is twice as likely as when compared with the general population.[2] The pathophysiology of OSA consists of sleep fragmentation and nocturnal intermittent hypoxemia, which results in excessive daytime sleepiness (EDS).[1,2] Studies so far have shown, OSA patients with EDS are more likely to

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have depression than those without EDS.[2] Additionally, elevated proinflammatory markers such as tumor necrosis factor-alpha and interleukin-6 are associated with daytime sleepiness and are elevated in both OSA and depression.[1] The same inflammatory markers are also observed as higher in cardiovascular disease, thus forming a positive association between OSA, depression, and cardiovascular disease prevalence.[1,3]

To understand the impact of OSA on depression, studies have been conducted on the treatment of OSA in patients with comorbid depression. Long-term studies noted improvement in depression among OSA patients treated with continuous positive airway pressure therapy. Lack of improvement in depression treatment was noted for OSA patients who had persistent EDS despite therapy.[4] In the acute setting, while the impact of OSA with comorbid depression on cardiovascular outcomes remains a chronic process, it remains understudied. We have conducted this nationwide analysis to study the effect of concurrent depression on in-hospital cardiovascular outcomes in patients with OSA.

MATERIAL AND METHODS

We conducted this study focusing on hospitalizations with medial conditions with underlying OSA using the National Inpatient Sample (NIS) for the year 2018. The NIS is the largest all-payer dataset in the United States (US), and discharge records comprise demographics of patients, hospital characteristics, several diagnoses, procedures, and comorbidities coded with pertinent International Classification of Diseases Clinical Modification, 10th Revision (ICD-10, CM). NIS datasets are issued by the Agency of Healthcare Research and Quality under the Healthcare Cost and Utilization Project. The results from the weighted survey analysis of the NIS datasets are representative of the US population.

The study included inpatient encounters involving patients with OSA and comorbid depression who were hospitalized in 2018. We used ICD-10-CM codes to identify OSA and depression patients. Trends studied in these patients included patient demographics, types of admission, primary expected payer [Medicare, Medicaid, private including Health Maintenance Organizations (HMO)], and location/teaching status of hospitals (rural, urban non-teaching, urban teaching) (Tables 1, 2).

Main Points

- Obstructive sleep apnea (OSA) patients have a higher prevalence of depression; data is scarce on the impact of depression on the outcomes of OSA.
- The two cohorts of OSA with (OSA+D+) vs. without depression (OSA+D-) were compared for demographic and comorbidities profile differences using the National Inpatient Sample (2018).
- Patients with OSA with depression had better in-hospital outcomes compared to OSA+D- despite having a higher burden of comorbidities.
- Compared to the OSA group, patients in the OSA and depression group have lower levels of serotonin and catecholamines, which could explain the more severe adverse cardiovascular outcomes.

Primary outcomes were identified as all-cause in-hospital mortality and major adverse cardiovascular complications, while secondary outcomes were described in terms of disposition status (routine to home, transfer to a short-term hospital or skilled nursing facility). All the primary and secondary outcomes of these inpatients with OSA, with comorbid depression, were compared to those without depression.

Ethics committee approval was not obtained as data was obtained from a publicly available data set. Informed consent was not obtained as data was obtained from a publicly available data set.

Statistical Analysis

We used Pearson's chi-square test and Mann-Whitney U test to compare the categorical and continuous variables between the two cohorts. Propensity score matching (1:1) was performed adjusting for age, sex, and race using a caliper width of 0.01 to obtain two cohorts of OSA+D+ vs. OSA+D-. Hospitalized patients with comorbid depression were compared with those without depression in terms of demographics, and comorbidities, and primary and secondary outcomes.

Adjusted odds ratios (aOR) with a 95% confidence interval (CI), were used to analyze the outcomes. The multivariable analysis, controlling for confounders (sociodemographic characteristics and preexisting cardiac and extra-cardiac comorbidities), was performed with a two-tailed adjusted $P < 0.05$ considered statistically significant. Complex sample modules in Statistical Package for the Social Sciences v25 (IBM Corp, Armonk, NY, USA) were used to perform statistical analysis on weighted data.

RESULTS

Of the 2,169.730 hospitalizations in patients with OSA, 435.185 (20.1%) had comorbid depression, and 1,734.545 (79.9%) had no depression. The propensity-score matched cohorts included 846.150 admissions in both groups, namely OSA+D+ and OSA+D-. Both cohorts predominantly comprised whites, the elderly (median age, 64 vs. 65 years), and females (55.5% vs. 55.2%). OSA-D+ had 4,559 (10.8%), and OSA-D- had 47,090 (11.1%) black patients. The Hispanic population consisted of 24,100 (5.7%) of the OSA+D+ cohort and 22,815 (5.4%) of the OSA+D- cohort. Both groups primarily had Medicare-enrolled patients, 25,165 (59.5%) in the OSA-D vs. 26,678 (63.1%) in OSA+D+. Medicare is a federal health insurance program for people aged 65 and older, people with certain disabilities, and people with end-stage renal disease, whereas private insurance, including HMO requires a referral from one's health provider to see a specialist. Private insurance beneficiaries formed the next largest group after Medicare beneficiaries, with 111.445 (26.4%) in OSA+D- vs. 94680 (22.4%) in OSA+D+.

Median household income was higher across all quartile groups except the 76-100 national quartile range for patient ZIP code in OSA+D+ patients (19.6% vs. 18.7%). The OSA+D+ cohort had significantly higher rates (all $P < 0.001$) of comorbidities such as hypertension (68.6% vs. 64.6%); diabetes (48.4% vs. 47.4%); hyperlipidemia (59.2% vs. 53.5%); congestive heart failure (21.7% vs. 20.6%); peripheral vascular disease (6.7% vs. 6.3%); anemia (22.4% vs. 19.7%); smoking (44.6% vs. 41.8%);

Table 1. Baseline characteristics of study population with osa with vs. without comorbid depression from NIS (2018)*

Variable		No depression (n = 423.075)	Depression (n = 423.075)	*P* value
Age (years) at admission, median (IQR)		65	64	<0.001
Sex	Male	44.8% (n = 189.420)	44.5% (n = 188.310)	0.015
	Female	55.2% (n = 233.655)	55.5% (n = 234.765)	
Race	White	81.1%	81%	<0.001
	Black	11.1%	10.8%	
	Hispanic	5.4%	5.7%	
	Asian or Pacific Islander	0.6%	0.6%	
	Native American	0.5%	0.6%	
	Others	1.2%	1.3%	
Primary expected payer	Medicare	59.5%	63.1%	<0.001
	Medicaid	9.8%	10.6%	
	Private including HMO	26.4%	22.4%	
	Self-pay/no charges/others	4.2%	3.9%	
Median household income national quartile for patient ZIP code#	0-25th	26.8%	27.2%	<0.001
	26-50th	27.9%	28.2%	
	51-75th	25.8%	25.9%	
	76-100th	19.5%	18.7%	
Comorbidities^				
Hypertension		64.6%	68.6%	<0.001
Diabetes mellitus		47.4%	48.4%	<0.001
Hyperlipidemia		53.5%	59.2%	<0.001
Smoking		41.8%	44.6%	<0.001
Obesity		49.8%	49.6%	0.029
Chronic kidney disease		23.8%	23.8%	0.475
Deficiency anemias		19.7%	22.4%	<0.001
Alcohol abuse		2.4%	3.8%	<0.001
Rheumatoid arthritis/collagen vascular disease		4.9%	5.9%	<0.001
Coagulopathy		6%	5.9%	0.142
Congestive heart failure		20.6%	21.7%	<0.001
Valvular heart disease		5.4%	5.5%	0.070
Pulmonary circulation disease		1.2%	1.1%	<0.001
Peripheral vascular disease		6.3%	6.7%	<0.001
Drug abuse		2.7%	3.9%	<0.001
Prior myocardial infarction		8.8%	9.9%	<0.001
Prior TIA/stroke		8%	9.5%	<0.001
Prior history of VTE		8.4%	9.5%	<0.001

*NIS: National Inpatient Sample, HCUP: Healthcare Cost and Utilization Project. 2012. Agency for Healthcare Research and Quality, Rockville, MD. https://www.ahrq.gov/data/hcup/index.html

#: Represents a quartile classification of the estimated median household income of residents within the patient's zip code, https://hcup-us.ahrq.gov/db/vars/zipinc_qrtl/nisnote.jsp

^Elixhauser comorbidity software downloadable from https://hcup-us.ahrq.gov/toolssoftware/comorbidity/comorbidity.jsp

$P < 0.05$ indicates statistical significance.

OSA: obstructive sleep apnea, HFpEF: heart failure with preserved ejection fraction, HMO: health maintenance organization, TIA: transient ischemic attacks, VTE: venous thromboembolic events, AMI: acute myocardial infarction, IQR: interquartile range

Table 2. Odds of in-hospital outcomes with vs. without depression in patients with OSA

	Odds ratio	95% CI [LL-UL]	*P*	% of outcomes in D-	% of outcomes in D+
All-cause mortality	0.79	0.73-0.86	<0.001	1.7	1.4
MACCE-all-cause mortality, AMI, cardiac arrest, stroke	0.83	0.80-0.87	<0.001	8.4	7.1
AMI	0.80	0.76-0.85	<0.001	4.4	3.6
Dysrhythmia	0.81	0.79-0.83	<0.001	30.8	26.8
AF	0.811	0.789-0.833		27.2	23.4
Cardiac arrest including VF	0.73	0.65-0.82	<0.001	1	0.7
Stroke	0.94	0.88-1.01	0.086	2.3	2.1

OSA: obstructive sleep apnea, CI: confidence interval, AMI: acute myocardial infarction, AF: atrial fibrillation, VF: ventricular fibrillation

substance abuse (3.9% vs. 2.7%), prior MI (9.9 vs. 8.8%), prior transient ischemic attacks/stroke (9.5% vs. 8%), alcohol abuse (3.8% vs. 2.4%), rheumatoid arthritis/ collagen vascular disease (5.9% vs. 4.9%), and venous thromboembolism (9.5% vs. 8.4%) compared to the OSA+D- group.

Conversely, the OSA+D- cohort had slightly higher rates (all $P < 0.001$) of comorbidities such as pulmonary circulation disease (1.2% vs. 1.1%). Comorbidities such as valvular heart disease and chronic kidney disease did not have a significant difference between the subgroups ($P > 0.05$). Paradoxically, there was decreased all-cause mortality (OR: 0.79, 95% CI: 0.73-0.86), major adverse cardiac and cerebrovascular events (OR: 0.83, 95% CI: 0.80-0.87), acute MI (OR: 0.80, 95% CI: 0.76-0.85), dysrhythmia/atrial fibrillation (OR: 0.81, 95% CI: 0.79-0.83), and cardiac arrest, including ventricular fibrillation (OR: 0.65, 95% CI: 0.73-0.82) in the OSA+D+ cohort during hospitalization (all $P < 0.001$). Secondary outcomes, which included patients' disposition as routine discharges or to another healthcare or nursing facility, length of hospital stay, and cost of hospitalization, did not differ between the two cohorts.

DISCUSSION

Approximately 20% of the total population is affected by OSA.[1] Epidemiological studies estimate an up to 18% prevalence of depression in OSA populations.[2]

To date, this is the first and largest study to explore the effect of comorbid depression on cardiovascular outcomes in patients with OSA. Interestingly, we found that patients with OSA and depression had better cardiovascular outcomes despite having a higher burden of cardiovascular comorbidities. There are considerable data to suggest higher serotonin levels in the body are associated with angiographically significant coronary artery disease and adverse cardiac events. When compared to controls, individuals with coronary artery disease or myocardial infarction had higher levels of serotonin.[5] Low serotonin levels have been linked to major depression.[6,7] Studies have demonstrated increased mortality in patients with increased catecholamine levels.[8] Multiple studies have shown that patients with depression have lower levels of serotonin and catecholamines.[9,10] Compared to the OSA group, patients in the OSA and depression group have lower levels of serotonin and catecholamines, which could explain the worse cardiovascular outcomes; however, it remains unclear how antidepressant medication would modify this effect.

We do not know if the patients were on anti-depressants (selective serotonin reuptake inhibitors, etc.) and for how long, which is one of the study's limitations. However, a large prospective study with 51,547 participants conducted by Thornicroft et al.[11] showed that only about 22% of patients with major depressive disorder in high-income countries received minimally adequate treatment. According to this data, although patients in our study were on treatment, it is unlikely that the levels of catecholamines and serotonin are adequately elevated. A conclusive explanation for this paradoxical effect of co-morbid depression requires additional research.

Although the largest inpatient sample enabled us to achieve nationwide estimates using weighted discharge records, there are a few limitations of this study that should also be considered while drawing any firm conclusions. These include over or under-coding errors due to the administrative nature of data collection, a lack of a longitudinal/follow-up information in retrospective databases, lack of medication data, lack of data around compliance with OSA therapy, and lack of the reasoning behind the studied hospital admissions or laboratory parameters.

CONCLUSION

In this population-based analysis, OSA patients with depression had better in-hospital outcomes despite having a higher burden of cardiovascular comorbidities. There could be a association between serotonin levels and cardiovascular outcomes in OSA patients with comorbid depression. However, additional research is warranted to confirm the paradoxical association between co-morbid depression and OSA and to understand the role of antidepressant medication.

Ethics

Ethics Committee Approval: Ethics committee approval was not obtained as data was obtained from a publicly available data set.

Informed Consent: Informed consent was not obtained as data was obtained from a publicly available data set.

Footnotes

Authorship Contributions

Concept: R.D., S.S., S.C., Design: R.D., S.S., S.C., Data Collection or Processing: R.D., Z.G., W.S., Analysis or Interpretation: R.D., B.R., S.C., S.S., Z.G., W.S., Literature Search: R.D., B.R., S.C., S.S., Z.G., W.S., A.R., Writing: R.D., B.R., S.S., Z.G., W.S., A.R., A.J.

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Original Article

Medical Students' Tobacco Consumption Status and Experiences with Smoke-free Law Violations in Enclosed Spaces in Türkiye and Northern Cyprus

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Abstract

OBJECTIVE: This study aimed to determine the frequency of tobacco smoking among medical students and assess their exposure to violations of smoke-free laws in enclosed spaces 30 days before the study. It also identifies key locations where such infractions occur and explores associated factors.

MATERIAL AND METHODS: A descriptive study was conducted using a questionnaire-based survey among students from two public and two private medical faculties in Türkiye and Northern Cyprus in 2023. Of the invited students, 628 responded. Data were analyzed using IBM Statistical Package for the Social Sciences statistics for Windows, version 23.0. Descriptive statistics included frequencies, percentages, means±standard deviations, and medians (interquartile ranges). Relationships between categorical variables were assessed using chi-squared and Fisher's exact tests, with significance set at $P < 0.05$. Binary logistic regression analysis of predictors of exposure to smoke-free violations was conducted. Ethical approval was obtained from each university.

RESULTS: Most participants were female (56.4%), with a mean age of 21.5±2.37 years. Nearly one in five students was a current tobacco user (19.9%). Smokers had higher exposure to passive smoking than non-smokers (92.0% vs. 82.5%, $P = 0.009$). Encountering tobacco industry-branded vehicles was associated with higher exposure (92.3% vs. 83.7%, $P = 0.03$). Exposure to violations of the antismoking ban in enclosed spaces was significantly higher among students who smoked with higher frequency (odds ratio: 2.418, 95% confidence interval: 1.172 to 4.990, $P = 0.017$).

CONCLUSION: This study underscores the need for strict tobacco control among medical students, with an emphasis on advocacy and interdisciplinary collaboration to combat the tobacco industry's influence.

KEYWORDS: Tobacco consumption, medical student, smoke-free law, violation

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INTRODUCTION

Tobacco consumption and exposure to passive tobacco smoke are major tobacco-related public health challenges faced globally.[1,2] According to estimates by the World Health Organization (WHO), tobacco consumption, including exposure to tobacco smoke, results in approximately 8 million deaths annually.[1,3] Strong and persistent tobacco control strategies are needed to overcome these challenges with the help of health professionals, including medical doctors.[4,5] In this regard, medical schools are crucial in tobacco control strategies. Medical schools should educate students about the tobacco control roles they will play throughout their careers. Physicians' expected tasks in tobacco control are to protect their patients from the dangers of active and passive smoking, to help them quit tobacco, and to advocate for comprehensive smoke-free legislation.[5]

Implementing comprehensive smoke-free legislation to create 100% smoke-free indoor public spaces is an effective strategy to mitigate environmental tobacco exposure. Research has demonstrated the success of such legislation; reductions in second-hand smoke exposure were associated with decreased incidences of heart attacks, strokes, and respiratory diseases, increased cessation rates among smokers, and protection of vulnerable populations such as children and pregnant women from the harmful effects of tobacco smoke.[6-9]

Article 8 of the WHO's Framework Convention on Tobacco Control mandates that countries implement effective legislation to prevent individuals from exposure to tobacco smoke in enclosed indoor spaces.[10] In compliance with this directive, the Turkish Parliament enacted an amendment that prohibited smoking in all enclosed public spaces across Türkiye, starting in July 2009.[11] A similar legislation also applied to Northern Cyprus. Although the legislation initially saw successful implementation, the effectiveness of enforcement diminished over time.[12] A study employing a direct observation method to evaluate violations in hospitality venues in Türkiye revealed that non-compliance with indoor smoke-free law was 49.0% in 2013 and 29.7% in 2014. Moreover, establishments previously fined were more likely to violate the law, indicating significant weaknesses in enforcement activities. Additionally, the Global Adult Tobacco Survey (GATS) conducted in 2016 determined that 12.7% of adults aged 15 years and older were exposed to tobacco smoke in restaurants, whereas 28.0% were exposed in cafes, coffee shops, or tea houses.[13]

Main Points

- **Prevalence of tobacco use:** Approximately 20% of medical students are current tobacco users, indicating a significant level of tobacco consumption within this population.
- **Exposure to smoke-free violations:** Most students experienced passive smoke exposure, primarily in cafes, highlighting a common breach of smoke-free legislation.
- **Impact of smoking on violations:** Smokers face higher rates of exposure to smoke-free law violations than non-smokers, suggesting that smoking status influences exposure levels.
- **Perception of anti-tobacco laws:** Students who view anti-tobacco laws as ineffective are more likely to experience smoke-free law violations, underscoring the need for improved legislation and enforcement.
- **Need for targeted interventions:** The findings emphasize the necessity for enhanced enforcement of smoke-free policies and targeted public health interventions to reduce tobacco use and associated violations.

Evidence from research shows that tobacco consumption is high among medical students.[14,15] Additionally, tobacco smoke exposure exposes medical students to the same risks as other community members. Such unwanted consequences may be caused by the lack of awareness among medical students and the weak enforcement of indoor smoking prohibition in Northern Cyprus and Türkiye.

The objective of this study was to ascertain the tobacco smoking frequency among medical students and quantify the proportion of students affected by infractions of smoke-free legislation in enclosed spaces within the preceding 30 days (prior to the study). Furthermore, this research aims to identify the predominant locations where smoke-free policy violations occur and to elucidate the factors associated with exposure to these violations among medical student populations.

MATERIAL AND METHODS

Study Design and Population

In this descriptive study, a questionnaire-based survey was carried out among students in four medical schools in Türkiye and Northern Cyprus in 2023. Two of the medical schools, Marmara University and Hacettepe University, were public academic institutions located in Türkiye, and the other two, Near East University and Girne University, were private academic institutions in Northern Cyprus.

All students registered in the four medical schools were invited to participate in the study, and 628 students voluntarily replied to the questionnaire.

Data were collected through an online self-administered questionnaire using Google Forms. The questionnaire was developed after an extensive review of relevant data sources, including the GATS and other comparable studies on smoking behavior. The questions were adapted and tailored to explore sociodemographic variables, smoking status, and exposure to smoke-free violations in enclosed spaces, ensuring they aligned with the objectives of the study.

The tobacco consumption status of the students was one of the main variables used in this study to assess the general student profile. The outcome variable of the study was exposure to smoke-free violations in enclosed spaces within the last 30 days. Having been exposed to tobacco smoke in a cafe, taxi, or public transport, the room where the student stayed, or common spaces at school or in a dormitory were identified as being exposed to a violation. The independent variables were sociodemographic characteristics and smoking status.

Statistical Analysis

Data obtained from each school were collected and converted to International Business Machines Corporations, Statistical Package for the Social Sciences (IBM SPSS) file. IBM SPSS statistics version 23.0 was used for data analysis. Descriptive data were summarized as frequencies, percentages, means±standard deviations, and medians (interquartile ranges). Chi-squared and Fisher's exact tests were used to explore the relationship between the categorical variables. Statistical significance was set as $P < 0.05$.

Binary logistic regression was performed to analyze the relationship between exposure to smoke-free violations and predictor variables. Hosmer-Lemeshow test was used to measure the model's predictive accuracy in the binary logistic regression model.

Ethical Issues

Participation in the study was entirely voluntary, and informed consent was obtained from all participants prior to their involvement. The purpose of the study, procedures, and benefits were explained to the students through an introductory section of the online questionnaire. The participants were informed that they could withdraw from the study at any time without any consequences. No personally identifiable information was collected to ensure the confidentiality and anonymity of the responses. Data was securely stored and used only for research.

The study was approved by the ethical review boards of each of the four participating institutions as follows: Marmara University in İstanbul (approval no: 09.2023.524, date: 7th of April 2023), Hacettepe University in Ankara (approval no: 2023/09-53, date: 23rd of May 2023), Near East University in Northern Cyprus (approval no: 2023/113-1722, date: 27th of April 2023), and Girne University in Northern Cyprus (approval no: 02, date: 22nd of August 2023).

RESULTS

As shown in Table 1, the students' characteristics according to their medical training were collected. Most students were enrolled in the English program of the faculty (n = 379, 60.3%), and 56 students were from various international backgrounds (8.9%). The data indicate that first-year students exhibited the highest participation frequency among all participants (n = 169, 26.9%), as illustrated in Table 1.

As highlighted in Table 2, the sociodemographic features and health status of the students were assessed. The majority of students were female (n = 355, 56.4%). The mean age of the students was 21.5±2.37 years. Only three students were married (0.5%). Most students stated that their economic situation was sustainable (n = 494, 78.5%). The most frequently stated place of residence was "in the dormitory, with friends (n = 215, 34.2%)" and "at home, with friends (n = 94, 15.0%). Most students perceived their health as "healthy" (80.8%, n = 508). Twenty-seven percent of the students had a diagnosed disease (n = 170), and 19.7% of them were taking prescribed medication (n = 124).

Tobacco consumption by students and their relatives or friends, as well as exposure to smoke-free law violations, were analyzed, as shown in Table 3, where about one out of five students is a current tobacco user (n = 125, 19.9%). The quit frequency was 12.7% (n = 80). The frequency of tobacco consumption was highest among the best friends of the students (n = 223, 35.8%) compared with the other categories. Ninety-nine students (48.3%) stated that they started smoking because of curiosity. The mean age at which students started smoking was 18.05±2.58 years. The students' fathers' smoking status was higher than the mothers' smoking status (30.5% vs. 19.1%).

As shown in Figure 1, the frequency of passive smoke exposure among students in the last 30 days prior to their study in the selected venues is highlighted. The most common place where the students were exposed to a smoke-free violation in the last 30 days was "cafes" (n = 509, 80.9%). Other venues where passive smoking exposure was significant included taxis, public transport, places of residence, and common areas used by students.

As supported by Table 4, the univariate analysis of exposure to violations of the smoke-free law within the last 30 days according to selected characteristics was performed. Students who smoked were more exposed to passive smoking than nonsmokers (92.0% vs. 82.5%, $P = 0.009$). Students who perceived themselves as healthy were less exposed to passive smoking than those who were hesitant about their health and perceived themselves as unhealthy (82.9% vs. 90.9, $P = 0.02$).

As shown in Table 5, the results of a univariate analysis examining the exposure of students to violations of smoke-

Table 1. Students' characteristics according to their medical education

	Number	Percentage
University		
Marmara University	281	44.7
Hacettepe University	185	29.4
Near East University	110	17.5
Girne University	53	8.4
Program language		
English	379	60.3
Turkish	250	39.7
International students		
No	573	91.1
Yes	56	8.9
Academic year		
1	169	26.9
2	118	18.8
3	107	17.0
4	73	11.6
5	81	12.9
6	81	12.9
Total	**629**	**100.0**

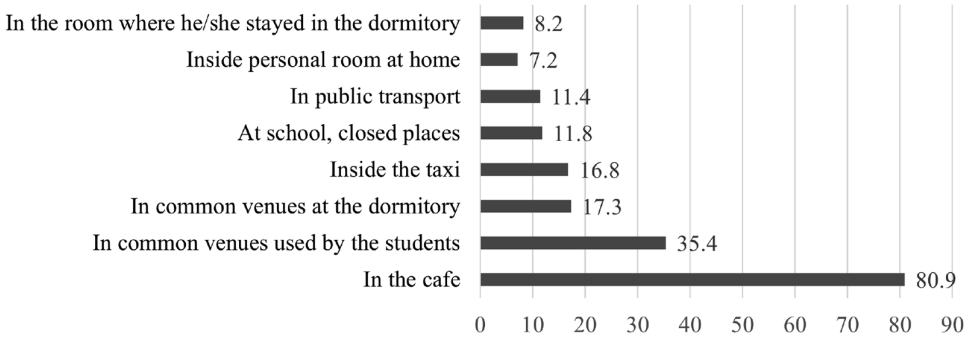

Figure 1. Frequency of passive smoke exposure of the students in the last 30 days prior to the study in selected venues (n = 629)

Table 2. Sociodemographic features and health status of the students

Feature	Number	Percentage
Sex (n = 629)		
Female	355	56.4
Male	274	43.6
Age (n = 628)		
Mean±SD	21.52±2.37	
Median	21	
Min-max	16-35	
Marital status (n = 629)		
Not married	626	99.5
Married	3	0.5
Economic sustainability (n = 629)		
Yes	494	78.5
I could not decide	92	14.6
No	43	6.8
Place of residence (n = 628)		
In a dormitory with friends	215	34.2
At home, with family	182	29.0
At home with friends	94	15.0
At home, alone	93	14.8
In the dormitory alone	38	6.1
At home, with siblings or cousins	6	1.0
Perceived health status (n = 629)		
Healthy	508	80.8
I could not decide	83	13.2
Unhealthy	38	6.0
Disease diagnosed by doctor (n = 629)		
No	459	73.0
Yes (top 3 diseases)*	170	27.0
Respiratory system diseases	*27*	*15.0*
Mental health diseases	*21*	*12.4*
Endocrinology/metabolic diseases	*17*	*10.0*
Take medication prescribed by a doctor (n = 629)		
No	505	80.3
Yes	124	19.7

*Percentages were calculated for more than 170 students.
SD: standard deviation, Min-max: minimum-maximum

free laws within the past 30 days, stratified by the extent of tobacco industry interference, were analyzed. Students who encountered tobacco industry-branded vehicles were exposed to passive smoking at a higher rate than the others (92.3% vs. 83.7, P = 0.03). Students who found national anti-tobacco control legislation successful were less exposed to passive smoking than the others (72.9% vs. 87.0%, P = 0.004). Students who found the country succesful in preventing passive smoking were less exposed to passive smoking than the others (74.2% vs. 88.9%, P < 0.001).

Table 6 shows the infractions of anti-tobacco legislation pertaining to passive smoking within indoor environments, stratified by selected characteristics. Exposure to violations of the anti-smoking ban in enclosed spaces was statistically significantly higher among students who smoked with higher frequency (OR=2.418, 95% CI: 1.172 to 4.990, P = 0.02), compared with their respective reference categories.

DISCUSSION

Medical students are expected to be role models as they are defined as "the five-star doctor" by the WHO.[16] Their role as "care giver," "decision maker," "communicator," "community leader," and "manager" gives them significant responsibility in leading both individuals and the community in tobacco control.[16] They are expected to be role models for the community. Nevertheless, our data show that 19.9% of students are current tobacco users, and 12.7% have quit smoking. In addition to traditional cigarettes, they use other tobacco products, including water pipes and e-cigarettes, etc. (Table 3). Different frequencies have been reported in other studies. For example, tobacco use among medical students in the Western Balkan region was reported to have a higher frequency.[15] Smoking prevalence in Malaysian medical students was reported to be lower than that of Balkan students.[17]

Medical students reported having diagnosed diseases (27.0%), with respiratory system diseases, mental health disorders, and endocrinology/metabolic diseases ranking among the top three (Table 2). Tobacco consumption is closely related to a variety of diseases. The WHO calls for the use of these reasons to convince smokers to quit.[18] Awareness among medical students should be improved in this regard.

The status of tobacco smoking is very closely linked to tobacco industry interference. The recent Global Tobacco Industry Interference Index was published in 2023, and Türkiye's rank was 72 out of a total of 90 countries.[19] As lower scores represent better rankings, it seems that Türkiye should improve its capacity to combat the tobacco industry. Full implementation of the current anti-tobacco legislation in Türkiye is believed to be a good step toward improving the situation of the country.[11] Nevertheless, this study revealed the interference of the industry, as 23.1% of the students stated their exposure to tobacco industry sponsorship, and 19.3% of them emphasized that they had encountered tobacco industry-branded vehicles in the last 30 days prior to the study (Table 5). Tobacco control is a health promotion intervention, and legislation plays an important role. In this regard, primordial prevention strategies are necessary. The WHO already recommends tobacco control measures, such as laws, regulations, administrative decisions, enforcement measures, and population-based interventions.[20]

While a significant number of students were exposed to passive smoking in various ways in the last 30 days prior to the study, being a smoker was associated with higher exposure (Table 6). The tactics of the tobacco industry may have influenced these results and should therefore be thwarted. The tobacco industry has employed approximately seven tactics consistently for many years.[21,22]

Table 3. Tobacco consumption-related characteristics of the students

Feature	Number	Percentage
Tobacco consumption status of students (n=629)		
Current users	125	19.9
Cigarette*	112	89.6
Waterpipe*	21	16.8
E-cigarettes*	17	13.6
Use of more than one tobacco product*	23	18.4
Quit	80	12.7
Cigarette**	68	85.0
Waterpipe**	31	38.8
E-cigarettes**	21	26.2
Heated, not burned tobacco	7	8.8
Never used	424	67.4
Reason for starting smoking (n=205)* **		
Curiosity	99	48.3
Wannabe smoker, peer influence	71	34.6
More than one reason (curiosity, peer influence, etc.)	21	10.2
Stress, unhappiness	9	4.4
No specific reason	1	0.4
Shifting from one tobacco product to another	1	0.4
Age at which smoking started (n=205)* **		
Mean±SD	18.05±2.58	
Median	18	
Min-max	10-30	
Consumption of tobacco by relatives/friends of students** (n=629)**		
Mother	120	19.1
Father	192	30.5
Siblings	123	19.6
Best friend	223	35.8
Partner	89	19.1
The friend whom he/she lives with	159	25.3

*Percentages are calculated for 125 current smokers. More than one option was mentioned by the students.
**Percentages are calculated for over 80 quitters; more than one option is mentioned by the students.
***Percentages are calculated over 205 students; more than one option is mentioned by the students.
****Percentages were calculated for 629 students; more than one option is mentioned by the students.
SD: standard deviation, Min-max: minimum-maximum

Table 4. Exposure violate smoke-free law within the last 30 days according to selected characteristics of the students (%)

Characteristics	Exposure to violations of smoke-free law within the last 30 days*			*P*
	Yes	No	Total	
Sex (n = 629)				
Male	85.8	14.2	43.6	0.41
Female	83.4	16.6	56.4	
Age group in years (n = 627)				
16-24	84.1	15.9	91.5	0.38
25 years	88.7	11.3	8.5	
Faculty (n = 629)				
Marmara University	82.9	17.1	44.7	0.26
Hacettepe University	85.9	14.1	29.4	
Near East University	81.8	18.2	17.5	
Girne University	92.5	7.5	8.4	
Academic level (n = 629)				
Pre-clinic	86.0	14.0	62.6	0.15
Clinic	81.7	18.3	37.4	
Sustainability based on economic status (n = 537)**				
Yes	83.4	16.6	92.0	0.10
No	93.0	7.0	8.0	
Disease diagnosed by a doctor (n = 629)				
Yes	87.6	12.4	27.0	0.17
No	83.7	16.8	73.0	
Perception of health (n = 629)				
Healthy	82.9	17.1	80.8	**0.03**
Hesitant and not healthy	90.9	9.1	19.2	
Tobacco consumption status (current) (n = 629)				
Yes	92.0	8.0	19.9	**0.009**
No	82.5	17.5	80.1	

*Passive smoking exposure in the café; OR inside the taxi; OR on public transport; OR in the room where the student stayed in the dormitory; OR in common places at school; OR in common venues at the dormitory
**Students who did not select this category were excluded.

Table 5. Incidence of exposure to violations of smoke-free legislation within the past 30 days stratified by tobacco industry interference and students' perceptions of legislative efficacy (%)

Characteristics	Exposure to violations of smoke-free law within the last 30 days*			*P*
	Yes	No	Total	
Encounter with tobacco industry sponsorship (n=542)**				
Yes	86.4	13.6	23.1	0.63
No	84.7	15.3	76.9	
Encounter with tobacco industry-branded vehicles (n=540)**				
Yes	92.3	7.7	19.3	**0.03**
No	83.7	16.3	80.7	
Finding national tobacco control legislation successful (in general) (n = 528)**				
Yes	72.9	27.1	11.2	**0.004**
No	87.0	13.0	88.8	
Finding country succesful in preventing passive smoking (n = 534)**				
Yes	74.2	25.8	29.0	**<0.001**
No	88.9	11.1	71.0	

*Passive smoking exposure in the café; OR inside the taxi; OR on public transport; OR in the room where the student stayed in the dormitory; OR in common places at school; OR in common venues at the dormitory
**Students who do not understand this category are excluded.

Table 6. Logistic regression model of exposure to violations of antismoking bans in enclosed spaces in association with selected characteristics

Characteristics	OR	95% CI	*P*
Perception of health			
Healthy (reference)	1.00		
Hesitant and not healthy	1.970	0.981-3.953	0.06
Tobacco consumption status (current)			
No (reference)	1.00		
Yes	2.418	1.172-4.990	**0.02**

*Model is adjusted for age, sex, perceived health status, and current tobacco use.
OR: odds ratio, CI: confidence interval

This study has some strengths. First, research data were obtained from four medical faculties. Second, the findings of this study cover an updated and wide range of tobacco control behaviors.

However, this study has a number of limitations. First, the results cannot be generalized to the general population because of limited participation. Second, a deep dive into the novel tobacco product consumption profiles could not be achieved due to the descriptive cross-sectional study design and self-reporting data. Third, the research data were self-reported by the students and were not a result of observed behaviors.

CONCLUSION

This study provides critical insights into tobacco consumption and smoke-free law violations among medical students in Türkiye and Northern Cyprus. With a significant proportion of students being current tobacco users and experiencing frequent exposure to smoke-free law violations, especially in cafes, the findings highlight a pressing public health issue. The study revealed that higher exposure to violations was associated with frequent smoking and skepticism regarding the effectiveness of anti-tobacco legislation. These results underscore the need for enhanced enforcement of smoke-free policies and targeted interventions to reduce tobacco use and its impact on public health among medical students. Moreover, advocacy work is crucial for reminding medical students of their role in tobacco control. As tobacco control is an interdisciplinary approach, all stakeholders should play their role. The fight against the tobacco industry should be a common goal for all stakeholders.

Ethics

Ethics Committee Approval: The study was approved by the ethical review boards of each of the four participating institutions as follows: Marmara University in İstanbul (approval no: 09.2023.524, date: 7th of April 2023), Hacettepe University in Ankara (approval no: 2023/09-53, date: 23rd of May 2023), Near East University in Northern Cyprus (approval no: 2023/113-1722, date: 27th of April 2023), and Girne University in Northern Cyprus (approval no: 02, date: 22nd of August 2023). Additionally, official permissions from the faculty administrations were secured prior to distributing the survey to ensure compliance with institutional guidelines and regulations regarding research involving human subjects.

Informed Consent: Participation in the study was entirely voluntary, and informed consent was obtained from all participants prior to their involvement in the research. The purpose of the study, procedures, and benefits were explained to the students through an introductory section of the online questionnaire. The participants were informed that they could withdraw from the study at any time without any consequences. No personally identifiable information was collected to ensure confidentiality and anonymity of the responses. Data was securely stored and only used for research purposes.

Presented in: The findings of the study were presented at the 9th ENSP-ECTC Conference between 22 and 24 October, 2024 in Athens.

Footnotes

Authorship Contributions

Surgical and Medical Practices - Concept – Design - Data Collection or Processing - Analysis or Interpretation – Literature Search - Writing: All authors contributed equally to all contribution sections.

Conflict of Interest: No conflict of interest was declared by the authors.

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Original Article

Third-hand Smoking Beliefs in Patients with Cancer

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Abstract

OBJECTIVE: Exposure to third-hand smoke (THS) represents an important health concern in many indoor environments. This study was conducted to test the beliefs of cancer patients about THS and to examine associations with effective factors.

MATERIAL AND METHODS: This cross-sectional study included 119 patients who were being treated for cancer in the oncology clinic of a University Hospital. The data were collected using a face-to-face questionnaire. This study consisted of the introductory characteristic form and the "Turkish Form of the Beliefs About Third-hand Smoke Scale".

RESULTS: The mean age was 58.52±14.01, with 73% of the participants being female, and 58% reported not smoking. They had a moderate Third-hand Smoke Scale (3.53±0.45). The impact of THS on health was 3.92±0.48 and Persistence in the Environment was 3.21±0.57. Education, smoking, and having cancer relatives were significantly associated with the THS scale scores.

CONCLUSION: None of the participants had previously heard of the concept of THS. Beliefs about the harms of THS exposure were moderate. They believed that THS has a more harmful impact on health than its persistence in the environment. Graduate degrees, smoking, and those with cancer relatives believed the harms of third-hand exposure more than the others.

KEYWORDS: Belief, cancer, patient, third-hand smoke

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INTRODUCTION

There is no safe dose of exposure to the smoke and residues produced by the consumption of cigarettes or tobacco products. Therefore, 1.3 million people worldwide are exposed to passive smoking.[1] One of the less well-known forms of passive exposure is third-hand smoke (THS) exposure. THS is a new concept in the field of tobacco control. The term refers to residual tobacco smoke contamination that remains on the surface and in dust, carpets, upholstery, and clothing long after the cigarette or other tobacco products have been extinguished.[2] This residue can react with common indoor pollutants to create a toxic mix of compounds that pose a health risk, especially to children and infants who are in contact with contaminated surfaces or who breathe in the particles that become airborne.[2,3]

The term "the four Rs" is often used to describe the characteristics of THS. Residual refers to residue left on surfaces, such as walls, furniture, and clothing, after tobacco smoke has cleared. The term reactive indicates that the chemicals in tobacco can react with other substances, such as cleaning products or pollutants in the air, creating new toxic compounds that can be harmful to health. Remains highlight that THS can persist in the environment for long periods, even after the cessation of active smoking, and can accumulate in indoor environments like homes and cars. Risks emphasize that THS poses health risks to non-smokers, especially children and infants, who may come into contact with contaminated surfaces or breathe in airborne particles.[3] THS can be harmful to health and has been associated with respiratory infections, such as asthma and bronchitis, as well as with an increased risk of cancer and many other health problems. THS has been described in relation to cancer in previous studies, and it has been shown that THS contains many carcinogenic substances.[3,4] THS undergoes long-lasting chemical transformations with ozone gases[4,5] and nitrous

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acidmajority set in cars[6] and homes[7] producing secondary immensely carcinogenic pollutants, such as formaldehyde[3] and the tobacco-specific nitrosamines 4-(methylnitrosamino)-4-(3-pyridyl)butanal(NNA) and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK).[6,8] THS exposure occurs through dermal absorption, ingestion, and inhalation. Nicotine in cigarettes often reacts with ozone, nitrous acid, and formaldehyde to form carcinogens and isis re-dispersed as vapor or adsorbed on dust, thereby returning to an inhalable aerosol form to form THS exposure. Traditional cleaning methods are not effective in eliminating THS exposure. In contrast, the ability of THS compounds to strongly adsorb on surfaces and penetrate materials is an important factor in their survival in the environment. Vacuuming and wiping strategies can also cause THS particles to transform. THS compounds released on any surface may be resuspended in aerosol form, increasing the risk of inhalation exposure.[9] In fact, a study reported that THS compounds remained in the tissue of clothing for more than 19 months.[10] As an important pollutant and carcinogen source in the environment for a long time, THS is harmful to human health and can affect the healthy functioning of vital biological processes, as well as organ systems.[11,12] It is a huge public health problem that affects many patient groups. To the best of our knowledge, few studies have described the knowledge and beliefs of patients with cancer related to THS, and no study has been conducted in Türkiye on this issue. This is the first and only study in which patients with cancer were asked about their knowledge of THS. After briefly explaining THS to the participants, they were asked if they believe THS is harmful to their health. Based on these findings, the aim was to test the beliefs of cancer patients about THS and examine the relationships between effective factors.

MATERIAL AND METHODS

Procedure and Participants

The study was an observational-descriptive study conducted to test the beliefs and behaviors of patients with cancer about THS. Informed consent forms, permission from the hospital management, and ethics committee approval (decision no: 55, date: 30.06.2022) from the Atatürk University Clinical Research Ethics Committee were obtained.

The study population consisted of 119 patients with cancer who were being treated in an oncology unit at a university hospital (in a province of Türkiye) and who completed a brief anonymous questionnaire. The inclusion criteria for this study were patients with cancer, treatment in the hospital where conducted research, not have to be psychiatric diagnosis. Participants had not heard of THS before the survey, so it was explained that THS refers to residual tobacco smoke pollutants that linger on surfaces, fabrics, and in dust after cigarette smoking.

Main Points

- Smoking is the leading cause of death worldwide.
- Third-hand smoke (THS) is a relatively new phenomenon in the public health field.
- Third-hand tobacco smoke is composed of residual tobacco smoke gases and particles that settle on surfaces and dust.
- Exposure to THS poses significant health risks for nonsmokers as well as for smokers.

This study utilized a sociodemographic characteristics form, comprising questions about age, sex, marital status, education, presence of chronic illness, smoking habits, smoking at home or work, having a smoking household, treatment period, and having relatives with cancer. To measure patients' beliefs about THS, the Beliefs About Third-hand Smoke Scale (BATHS) was utilized. The BATHS was developed by Haardörfer et al.[13] (2017) and was adapted by Odacı and Kitis[14] (2021) to assess BATHS. The Likert scale is a 5-point Likert scale ranging from "1 = Strongly disagree to 5 = Strongly agree". The scale consists of nine items and two factors, namely "Persistence of THS in the Environment" and "Impact of THS on Health". The highest and lowest scores obtained from the scale are 5 and 1, respectively. The score was obtained by dividing the total score of the scale by the number of items. As the score approaches 5, the individual believes in the effects of THS on the environment and health, and as it approaches 1, the individual does not believe in the effects of THS on the environment and health. The original scale had excellent overall reliability (Cronbach's alpha = 0.91) and strong reliability in the subscales (Cronbach's alpha = 0.88 for both factors). The internal consistency of the nine items formed by Odacı and Kitis[14] was 0.83. In our study, the value was 0.72. The internal consistency was 0.78 for impact on health and 0.63 for persistence in the environment. After obtaining informed consent, the data were collected face-to-face by the researcher.

Statistical Analysis

The data were analyzed using the Statistical Package for the Social Sciences 20.0 package program. Kolmogorov-Smirnov test and comparative analysis were used for data with normal distribution. The binary categorical variables (such as gender) and BATHS means were compared using the independent t-test, and variables with more than two groups were compared using the one-way ANOVA test.

RESULTS

The mean age was 58.52±14.01 in the study. 61.3% of the participants were female, 83.2% were primary school graduates, 14.3% were smoking at least a packet of cigarettes a day, and 78.2% had relatives with cancer. Table 1 shows the participants' demographic characteristics.

The highest frequency of the scale items was "Breathing air in a room today where people smoked yesterday can harm the health of adults (82.4%)" and "Breathing air in a room today where people smoked yesterday can harm the health of infants (81.5%)" (Figure 1).

The total score of BATHS was 3.53±0.45, the impact of THS on health was 3.92±0.48, and the persistence of THS in the environment was 3.21±0.57. A statistically significant difference was found between education ($P = 0.022$), smoking ($P = 0.027$), having relatives with cancer ($P = 0.036$), and BATHS. The mean score was higher among university graduates, smokers, and those with relatives with cancer. Further details are presented in Table 2. In our study, it was found that 82.4% of the participants

Table 1. Findings on the introductory characteristics

		n	%
Age	**Mean±SD**		
	58.52±14.01		
Gender	Female	73	61.3
	Male	46	38.7
Marital status	Married	111	93.3
	Single	8	6.7
Education	Primary school	99	83.2
	Secondary school	8	6.7
	University	12	10.1
Chronic illness	Yes	50	42.0
	No	69	58.0
Smoking	No	69	58.0
	Yes, but you should quit	33	27.7
	At least one packet in a day and more	17	14.3
Smoking at home or in the car	Yes	55	46.2
	No	64	53.8
Smoking household	Yes	61	52.1
	No	58	47.9
Treatment period	4-7 days	19	16.0
	1-8 months	44	37.0
	1-10 years	56	47.0
Having a cancer relative	Yes	93	78.2
	No	26	21.8
Total		**119**	**100.0**

SD: standard deviation

stated that "Breathing air in a room where smoking took place yesterday may harm the health of adults" and 72.3% stated that "Particles in a room where smoking took place yesterday may cause cancer" (Figure 1).

DISCUSSION

This study is important to raise awareness about THS. One of the most important aspects of this study was to be related to patients with cancer. The total score of BATHS was 3.53±0.45, the impact of THS on health was 3.92±0.48, and the persistence of THS in the environment was 3.21±0.57. The mean BATHS score was higher among university graduates, smokers, and those with cancer. Eight out of ten people were of the opinion that "breathing air in a room where people had smoked the day before could harm the health of adults" and "breathing air in a room where people had smoked the day before could harm the health of babies".

This study assessed the beliefs of Turkish patients with cancer about THS. Three different studies have been conducted on healthy individuals in Türkiye regarding the validity and reliability of the BATHS.[14-16] Our study was the first to investigate the presence of THS in patients with cancer. Cronbach's alpha values were in line with those of studies in the literature. The Cronbach's alpha coefficient for BATHS ranged from 0.63 to 0.78. Internal consistency was 0.78 for the impact on health and 0.63 for persistence in the environment. The total BATHS score of the study group was found as 3.53±0.45, the effect of THS on health was 3.92±0.48, and the persistence in the Environment was 3.21±0.57. In a study on the perceived THS exposure of pregnant women, the mean BATHS score was 3.79±0.859.[17] All participants in our study reported that they had never heard of THS before, which was an important finding for us. Exposure to firsthand and secondhand cigarettes is an active situation that has been tried to be prevented by several legal prohibitions, as well as individual measures, such as opening the windows while smoking, smoking in other rooms, operating the fans, or waiting for the smoke to disperse to reduce the harmful effects of smoking on others.

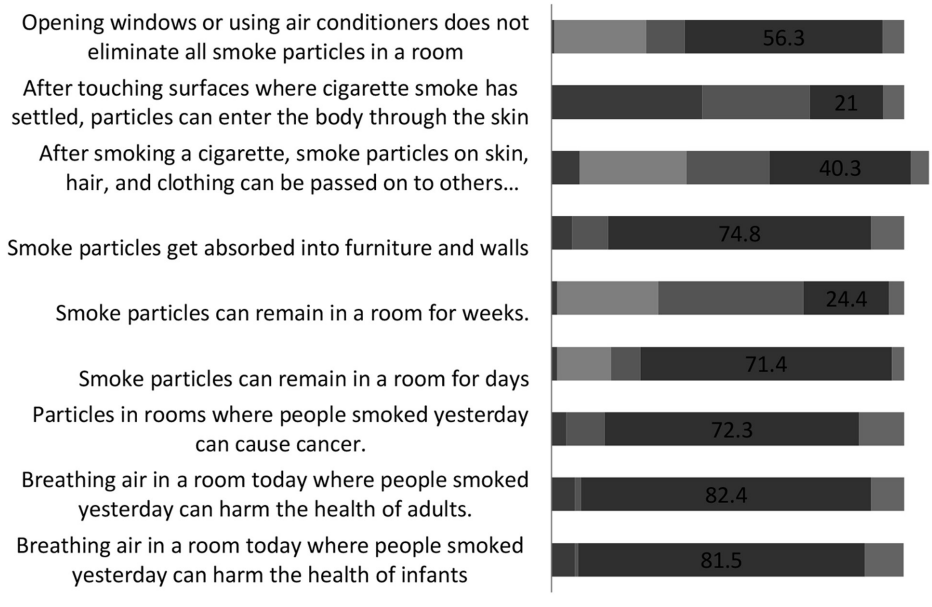

Figure 1. The items and answers of the BATHS scale

BATHS: Beliefs About Third-hand Smoke Scale

Table 2. Findings on comparison of introductory characteristics and BATHS

	BATHS total score	Impact on health	Persistence in the environment
Age			
r	-0.027	-0.083	0.015
P	0.770	0.037	0.871
	Mean±SD	**Mean±SD**	**Mean±SD**
Gender			
Female	3.51±0.52	3.89±0.56	3.21±0.65
Male	3.56±0.30	3.98±0.34	3.22±0.43
	t: -0.596	t: -1.072	t: -0.113
	P = 0.506	*P* = 0.236	*P* = 0.902
Marital status			
Married	3.52±0.44	3.91±0.49	3.21±0.57
Single	3.65±0.48	4.06±0.34	3.32±0.67
	t: -0.769	t: -0.800	t: -0.536
	P = 0.443	*P* = 0.425	*P* = 0.593
Education			
Primary school	3.49±0.45	3.90±0.51	3.17±0.57
Secondary school	3.45±0.37	3.90±0.32	3.10±0.53
University graduate	**3.87±0.38**	4.12±0.34	**3.66±0.47**
	F: 3.925	F: 1.076	**F: 4.270**
	P* = 0.022	*P* = 0.344	***P* = 0.016***
Chronic illness			
Yes	3.52±0.50	3.90±0.53	3.21±0.57
No	3.54±0.41	3.94±0.15	3.22±0.58
	t: 0.289	t: 0.540	t: 0.040
	P = 0.773	*P* = 0.590	*P* = 0.968
Smoking			
No	3.48±0.46	3.88±0.55	3.17±0.57
Used to but quit	3.48±0.39	3.90±0.36	3.14±0.53
Yes (at least a pk and more daily)	**3.80±0.42**	4.16±0.36	3.51±0.60
	F: 3.712	F: 2.341	F: 2.739
	P* = 0.027	*P* = 0.101	*P* = 0.069
Smoking at home or in the car			
Yes	3.60±0.44	3.95±0.45	3.32±0.59
No	3.47±0.45	3.90±0.51	3.13±0.56
	t: -1.532	t: -0.535	t: -1.787
	P = 0.594	*P* = 0.594	*P* = 0.077
Smoking household			
Yes	3.57±0.53	3.92±0.41	3.28±0.66
No	3.49±0.35	3.93±0.55	3.15±0.47
	t: -0.966	t: -0.147	t: -1.256
	P = 0.330	*P* = 0.883	*P* = 0.207
Treatment period			
4-7 days	3.46±0.49	3.77±0.61	3.22±0.63
1-8 months	3.45±0.38	3.89±0.43	3.10±0.46
1-10 years	3.61±0.47	4.00±0.47	3.31±0.63
	F: 1.912	F: 1.700	F: 1.645
	P = 0.152	*P* = 0.187	*P* = 0.198
Having a cancer relative			
Yes	3.49±0.47	4.07±0.39	3.34±0.44
No	**3.67±0.33**	3.88±0.50	3.18±0.60
	t: -1.766	t: -1.764	t: -1.273
	P* = 0.036	*P* = 0.047	*P* = 0.205
Total BATHS score	3.53±0.45		
Mean score of impact on health subscale	3.92±0.48		
Mean score of impact on health subscale	3.21±0.57		

r: Spearman's correlation analyses, t: independent t-test, F: one-way ANOVA test, *$P < 0.05$ statistical significance.
BATHS: Beliefs About Third-hand Smoke Scale, SD: standard deviation

While this is the case, THS continues to remain in an environment a hidden danger.[2] It is also an important source of carcinogens. Therefore, it is important to be aware of THS. Similar to our findings, Darlow et al.[18] reported that two-thirds of the participants had never heard of THS before. The findings of this study and ours show that even health professionals are not yet entirely aware of THS. There is awareness of THS even in non-cancer populations. The literature has shown that the percentage of parents who believed that THS is harmful ranged from 42.4% to 91%.[19]

In this study, 53.8% of the participants reported that they did not smoke at home or in the car. There are countries with a low prevalence of indoor smoking bans, such as the United States (50.0%), Kuwait (2.0%), and China (35.2%), compared with countries with a high prevalence of indoor smoking bans, such as Italy (61%), Poland (66%), Canada (67.8%), and Australia (66.2%).[13,20-24] In our study, we did not detect any difference between the smoking ban at home and the BATHS. Contrary to this, Haardörfer et al.[13] (2017) found positive associations between THS beliefs and levels of home smoking bans. Shehab and Ziyab[23] (2022), on the other hand, reported that the effects of THS exposure on health and permanence in the environment scores were higher in those with a strict smoking ban at home. Winickoff et al.[2] (2009) found that beliefs about the health effects of THS were associated with smoking bans at home. The reason our study revealed a different result from the literature may be because the concept of THS has not been heard yet. This indicates the importance of awareness of this issue.

We found that 51.3% of the participants smoked at home. A statistically significant intergroup difference was observed between smoking status and BATHS. Our findings support those of previous studies. Similar studies have reported higher awareness of THS among non-smokers.[17,22,23] A study conducted in Spain reported that smoking was not associated with THS.[24]

In our study, a statistically significant difference was found between education and BATHS. The mean BATHS scores of university graduates were significantly higher than those of the other students. This demonstrated that BATHS could be increased through education and training activities. Among the studies in the literature, some have reported that higher education levels increase awareness of THS and that there is a significant relationship between them.[17,22] However, a study conducted in Spain explained that there was no relationship between education levels and THS.[25]

In this study, we did not find any significant relationship between income level, gender, age, smoking at home, and THS beliefs. However, Xie et al.[22] (2021) reported that there was a significant difference between BATHS exposure, harm to health, and persistence in the environment due to a higher income level. Darlow et al.[18] (2017) reported that having a female gender made it easier to discuss the effects of THS exposure with others. On the other hand, Xie et al.[22] (2021) explained that being male created a significant difference in THS beliefs. However, the findings are similar findings to our study results.

In a study about THS exposure in pregnant women, no difference was found between income level, age, smoking in the home, and THS.[17] In another study conducted with medical school students, no statistically significant difference was determined according to gender, place of residence, family income level, and tobacco use status.[26]

In our study, participants with relatives with cancer had higher BATHS scores than those without. This was evidence that diseases are also effective against beliefs. To our knowledge, our study is the first and only study to determine the THS beliefs of patients with cancer. Therefore, we could not find any studies that can compare our findings.

The limitation of this study is that it included patients with cancer in only one medical oncology clinic in a province.

CONCLUSION

As conclusion; we evaluated the beliefs of cancer patients about THS. Participants expressed concern about the harmful effects of THS on the environment and health. Furthermore, the belief that "smoking is harmful to health" was higher than "it is persistent in the environment". Education was an effective factor in the respondents' beliefs. University graduates expressed greater belief in the harmful effects of THS and its persistence on the environment than others. Smokers and those who have relatives with cancer believe more strongly in the harmful effects of THS. This study provides information about factors that influence beliefs about exposure to passive tobacco smoking. The most important outcome of the current study was improving tobacco control efforts. Educational and informational practices were recommended to recognize exposure to THS as a potential carcinogen and public health challenge. Future studies should try to determine the knowledge and beliefs of different samples about THS.

Ethics

Ethics Committee Approval: The study was approved by the Atatürk University Clinical Research Ethics Committee (decision no: 55, date: 30.06.2022).

Informed Consent: Consent form was filled out by all participants.

Aknowledgements

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Footnotes

Authorship Contributions

Surgical and Medical Practices - Concept – Design - Data Collection or Processing - Analysis or Interpretation – Literature Search - Writing: All authors contributed equally to all contribution sections.

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Original Article

The Relationship Between Gender and Women's Tobacco Use: An Ecological Analysis with Country-level Data

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Abstract

OBJECTIVE: Health and well-being are profoundly influenced by gender and its dimensions. This study explores the intricate relationship between gender roles and tobacco use.

MATERIAL AND METHODS: The study investigates correlations between the Gender Development Index (GDI), the Global Gender Gap Index (GGGI), and its sub-indicators—critical markers of gender equality—and tobacco prevalence and tobacco-related mortality. Statistical analyses, conducted using the Statistical Package for Social Science and Microsoft Excel, involve Spearman correlation analysis for continuous numerical data and the Kruskal-Wallis H test for differences between means.

RESULTS: As per the GDI, a decrease in gender inequality correlates with an increase in tobacco prevalence among women. The highest prevalence of tobacco use in women is found in countries within GDI group 1, with the lowest observed in group 5, characterized by pronounced gender inequality. A moderate positive correlation is identified between the prevalence of tobacco use in women and the GDI, GGGI, and the education sub-component of GGGI. Similarly, a moderate positive relationship is observed between tobacco-related mortality in women and the education subcomponent of GGGI. Education exhibits the highest correlation with both tobacco prevalence and tobacco-related mortality in women.

CONCLUSION: The increased prevalence of tobacco use among women in countries with high education and socioeconomic status suggests the early stages of the tobacco epidemic. Smoking cessation remains a persistent challenge, especially for women. The study emphasizes the imperative for tailored gender-specific policies, highlighting the integration of gender considerations into health promotion and public health initiatives.

KEYWORDS: Tobacco use, gender equity, health policy

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INTRODUCTION

Tobacco use, prevalent both in our country and worldwide, stands as the leading preventable behavioral factor contributing to mortality. Smoking causes substantial health issues for both genders; however, women exhibit a heightened susceptibility to numerous diseases associated with smoking.[1,2]

Although tobacco use is currently more prevalent among men, there is a narrowing gender gap. While tobacco use among women is generally on the decline, the rate of decrease is considerably slower than among men and is even increasing in some regions. According to the Lopez Curve, depicting the four stages of the tobacco epidemic, women's tobacco use emerged later than that of men. A noticeable gap of 30-40 years is observed when assessing the highest tobacco use and mortality rates related to tobacco with women lagging behind. As women's tobacco use began later, the anticipated rise in female deaths is expected to occur later than males. This underscores the concerning reality for public health regarding the projected increases in female smoking prevalence.[1,3,4]

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Gender is a pivotal factor influencing health outcomes, demanding due consideration in tobacco control initiatives. It shapes susceptibility to various health conditions and access to healthcare throughout individuals' lives. Existing literature reveals a connection between gender roles and health behaviors, notably in terms of tobacco use. The empowerment of women has coincided with heightened industry activities targeting this demographic, resulting in an increase in smoking prevalence among women. Concepts such as "freedom," "economic independence," "equality with men," and "strength equal to men" have been emphasized, contributing to the rise in women's initiation of smoking.[1,5,6]

As women assumed more prominent roles in society, they became the primary focus of the tobacco industry. For instance, in 1968, Philip Morris tapped into the burgeoning women's movement with messages of 'freedom, independence, and power' through the introduction of 'Virginia Slims' cigarettes. This marked the first instance of a cigarette marketed exclusively for women, featuring a 'taller, slimmer, and more feminine' design. Concurrently, there was a rapid increase in smoking initiation among young girls aged 14-17, and 'Virginia Slims' emerged as one of the most popular brands among women.[7,8] To address women's concerns about smoking-related health risks, the tobacco industry has introduced nicotine-reduced, thin, filtered, and flavored cigarettes. These cigarettes are specially packaged in colorful and pictorial designs aimed at women. Over the years, the tobacco industry has actively supported women's organizations, ethnic minority groups with broad societal impact, sponsored sports organizations, and provided gift vouchers and tickets for events like concerts. Throughout these activities and advertisements, the image of thin, beautiful women is prominently featured, associating tobacco use with the independence and success of the modern, strong woman. This narrative has also found support in films, television programs, and plays. As access to traditional advertising has become increasingly restricted, there has been a shift toward product placement in art and cinema, as well as increased exposure through online advertising and promotion on social media. This evolution makes it more challenging to counteract the influence of advertising in tobacco control efforts.[1,6]

Main Points

- As the Gender Development Index, the Global Gender Gap Index, and their sub-components, education and women's political participation increase, tobacco product usage in women also appears to increase.
- Education is the parameter that shows the highest correlation with tobacco usage frequency and tobacco-related mortality in women.
- In countries with low gender inequality, tobacco usage and tobacco-related mortality are higher among women.
- The high prevalence of tobacco usage among women in countries with high education and socio-economic status indicates that the tobacco epidemic is in its early stages for women.
- Public health interventions and campaigns promoting health should consider gender-specific policies to address tobacco usage among women.

It is important to understand the gender-based reasons for smoking and to take into account gender roles in developing intervention plans, aiming to create women-specific and women-centered approaches.[9,10] Gender inequality indicators are important parameters because they encompass most of the welfare indicators and illustrate the role of women in society. However, there is no gold standard criterion for evaluating gender inequality.[11] In our study, we examined the relationships between the Gender Development Index (GDI) and the Global Gender Gap Index (GGGI), which are indicators of gender equality, along with the subheadings of the GGGI related to the economy, education, health, and politics, as well as the frequency of tobacco use and tobacco-related mortality.

MATERIAL AND METHODS

Data Sources and Data Collection

In the data collection phase, the most recent versions of the examined reports have been included. Information regarding the data obtained from the reports is presented below. Data from 144 countries in the GGGI and 147 countries in the GDI, along with data on the frequency of tobacco use and tobacco-related mortality, have been evaluated (Supplementary Table 1). The research ethics committee approval was received from Hacettepe University Non-interventional Clinical Research Ethics Committee (approval number: 2021/19-12, date: 16.11.2021). The study used publicly available country data, but did not use individual data. Therefore, informed consent was not required.

Dependent Variables

Tobacco use frequency: Data on total tobacco use frequency (current smoking) and gender-specific tobacco use frequency were obtained using the World Health Organization (WHO) Global Tobacco Epidemic 2021 Report attachments.[12] In the research, "current smoker" refers to individuals who have used more than 100 tobacco products in their lifetime and have used them in the last 28 days.

Tobacco-related mortality data: Obtained through the Tobacco Atlas, a resource sponsored by the American Cancer Society that conducts tobacco control studies to provide effective solutions in combating tobacco and explores the harmful aspects, nature, and impact of tobacco.[13]

Gender-specific tobacco use frequency rate (GSR): Calculated by researchers by dividing the frequency of tobacco use among women by the frequency of tobacco use among men.

Gender-specific tobacco-related mortality rate (GMR): Calculated by researchers by dividing the mortality related to tobacco use among women by the mortality related to tobacco use among men.

Independent Variables

Gender Development Index: The GDI found in the United Nations Development Programme's Human Development Report is not specifically a measure of gender inequality but rather an evaluation of the Human Development Index's components—life expectancy, education, and income—based

on gender. Countries are categorized into five groups according to their GDI levels. As the GDI value increases, inequality between genders decreases. GDI assesses gender inequality with the parameters listed below:[11,14]

- Gender-specific life expectancy at birth,

- Expected years of schooling,

- Average years of education for females and males aged 25 and above,

- Gender-specific estimated earned income.

Global Gender Gap Index: The study utilizes the GGGI from the Global Gender Gap Report. This index, designed by the World Economic Forum, is a four-dimensional measure to assess gender equality. The GGGI is constructed by examining data on education, political empowerment, economic gains, and opportunity equality. As the index value increases, gender inequality decreases. The indicators include the following dimensions:

- Economic gains and opportunity equality: Assessed through factors such as salary, high-skilled employment, duration of maternity leave, percentage of women in managerial positions, government-provided child support, wage equality between men and women, levels of male and female unemployment, economic activities, and equal pay for equal work.

- Education: Evaluated through literacy rates, enrollment rates for primary, secondary, and tertiary education, average years of education, and access to basic and advanced education, with a gender-specific perspective.

- Political empowerment: Assessed based on the representation of women in decision-making structures, including the number of female ministers, the percentage of women in parliament, the number of women in high-status legislative and administrative positions, and the number of years a woman has served as the head of state.

- Health and survival: Evaluated through gender-specific life expectancy, the effectiveness of government efforts to reduce poverty and inequality, adolescent fertility rate, the percentage of births attended by educated health personnel, and maternal and infant mortality rates.[15]

Statistical Analysis

For data entry and analysis in the study, the Statistical Package for the Social Sciences 24.0 and Microsoft Excel were used. A map was created using Microsoft Excel to visualize gender-specific tobacco use frequency based on the GGGI of countries.

In the analyses, descriptive statistics such as percentage, mean, standard deviation, median, quartiles, minimum-maximum values, were used or reported. The relationships between continuous numerical data were evaluated using the Spearman correlation test. According to the correlation coefficient (r), relationships were considered negligibly weak between 0-0.19, weak between 0.20-0.39, moderate between 0.40-0.69, strong between 0.70-0.89, and very strong between 0.90-1.00.[16] To assess differences between means, the non-parametric Kruskal-Wallis H test was employed. In cases where the results were significant in the Kruskal-Wallis H test, pairwise comparisons were conducted using the Mann-Whitney U test to identify which groups differed. The significance level in the study was set at $P < 0.05$.

RESULTS

The frequency of tobacco product use is an average of 28.6±13.2% in males and 9.3±9.9% in females, with median values of 26.7% and 4.8%, respectively. The GSR has a mean value of 0.3±0.3, indicating that for every 1 woman, approximately 3.3 men use tobacco products. Tobacco-related mortality is 14.9±7.3% for males and 7.1±4.6% for females, with median values of 15.6% and 6.3%, respectively. The GMR has a mean value of 0.5±0.3, signifying that for every 5 females, 10 males die due to tobacco use.

According to the GDI, as gender inequality decreases, the frequency of tobacco use among women increases. Women's tobacco use frequency is higher in countries belonging to group 1 compared to other groups. It is the lowest in the countries in group 5 where gender inequality is most pronounced, and the difference between groups is statistically significant ($P < 0.001$, Table 1).

According to the GDI, in evaluating the frequency of tobacco use among men, it is observed that countries in group 5 have a lower frequency of tobacco use compared to other groups, and the difference between groups is statistically significant ($P = 0.030$, Table 1).

In Figure 1, the GGGI ranges from red to green, with the index value increasing as gender inequality decreases. The size of the circles in the visualization represents the frequency of tobacco use, with larger circles indicating higher tobacco use frequency. In European countries where the GGGI is high, the frequency of tobacco use is higher among women, while a similar pattern is not observed in men. In Europe and America, countries with higher GGGI, indicating less gender inequality, have a higher rate of tobacco use by gender compared to other countries (Figure 1).

In countries belonging to group 1, where gender inequality is the least pronounced, 10 men smoke for every 4 women, while in group 2, approximately 10 men smoke for every 3 women. In groups 3, 4, and 5, approximately 10 men smoke for every 1 woman. It is observed that women in countries belonging to group 1 and group 2 use more tobacco compared to those in other groups, and the difference between groups is statistically significant ($P < 0.001$, Table 1). According to the GDI, in group 5 countries, tobacco-related mortality is the lowest for both genders, and the difference between groups has been found to be statistically significant ($P < 0.001$, Table 2).

When evaluating the rate of tobacco-related mortality according to gender, there is no statistically significant difference between groups ($P = 0.401$, Table 2).

There is a moderately positive relationship between the frequency of tobacco use in women and the GDI (r=0.439; $P < 0.001$,

Table 1. Assessment of tobacco use frequency according to GDI

GDI group****	Tobacco use prevalence in women			*P* value
	Median	Q1-Q3	Min-max	
1	10.6	4.0-20.1	0.4-39.3	
2	6.5	2.6-20.4	0.3-35.8	
3	2.8	1.0-6.0	0.1-29.6	***P* < 0.001***
4	2.2	0.7-5.3	0.3-19.0	
5	1.6	0.6-2.7	0.1-28.2	
GDI group	**Tobacco use prevalence in men**			***P* value**
	Median	**Q1-Q3**	**Min-max**	
1	30.0	17.1-40.4	8.4-56.9	
2	25.3	18.7-33.3	12.8-51.4	
3	26.7	18.7-44.5	15.1-72.6	**0.030****
4	32.6	16.9-44.3	5.1-45.8	
5	19.2	13.3-26.6	6.4-57.1	
GDI group	**GSR**			***P* value**
	Median	**Q1-Q3**	**Min-max**	
1	0.4	0.1-0.8	0-0.9	
2	0.3	0.1-0.8	0-1.1	
3	0.1	0.1-0.2	0-0.7	***P* < 0.001*****
4	0.1	0.1-0.2	0-0.4	
5	0.1	0-0.2	0-0.7	

*The difference is due to groups 1 and 3, groups 1 and 4, groups 1 and 5, and groups 2 and 5.
**The difference is due to the contrast between groups 1 and 5.
***The difference is attributed to groups 1 and 3, groups 1 and 4, groups 1 and 5, and groups 2 and 5.
****The number of countries in group 1 according to the GDI is 56, in group 2 it is 32, in group 3 it is 19, in group 4 it is 9, and in group 5 it is 31.
GDI: Gender Development Index, GSR: gender-specific tobacco use frequency rate, Min-max: minimum-maximum

Table 3). In men, a weak positive relationship is observed between the frequency of tobacco use and the GDI (r=0.187; $P = 0.023$, Table 3).

In women, there is a moderately positive relationship between the frequency of tobacco use and the GDI (r=0.439, $P < 0.001$) and the GGGI (r=0.512, $P < 0.001$); a weak positive relationship with the economic component of GGGI (r=0.241, $P = 0.004$); a moderately positive relationship with the education component of GGGI (r=0.580, $P < 0.001$); and a weak positive relationship with the political component of GGGI (r=0.350, $P < 0.001$). As the GDI and GGGI indices increase, gender inequality decreases, and the frequency of tobacco use increases among women. The highest correlation is found with the GGGI subheading of education. There is no correlation between the health subcomponent of GGGI and tobacco use in women (Table 3).

For the rate of tobacco use by gender, there is a moderately positive relationship with the GDI (r=0.421, $P < 0.001$), a moderately positive relationship with the GGGI (r=0.591, $P < 0.001$), a weak positive relationship with the economic component of GGGI (r=0.286, $P = 0.001$), a moderately positive relationship with the education component of GGGI (r=0.577, $P < 0.001$), and a moderately positive relationship with the political component of GGGI (r=0.468, $P < 0.001$). The variables showing the highest correlation with the rate of tobacco use by gender are the GGGI and its subcomponent, education (Table 3).

There is a weak positive relationship between tobacco-related mortality and the GDI for both women (r=0.290, $P < 0.001$) and men (r=0.349, $P < 0.001$) (Table 3).

For women, there is a weak positive relationship between tobacco-related mortality and the GGGI (r=0.265, $P < 0.001$), a moderate positive relationship with the education component of GGGI (r=0.459, $P < 0.001$), and a very weak positive relationship with the political component (r=0.177, $P = 0.034$). The subcomponent with the highest correlation is education. As education increases, tobacco use increases in women (Table 3). There is a positive low-level statistically significant relationship between the political subcomponent of GGGI and tobacco-related mortality rates by gender (r=0.164, $P = 0.049$, Table 3).

DISCUSSION

Tobacco use frequency and tobacco-related mortality are higher in men than in women. On average, 10 men smoke for every 3

Table 2. Evaluation of tobacco-related mortality according to the GDI

GDI group***	Mortality related to tobacco in women			*P* value
	Median	Q1-Q3	Min-max	
1	7.6	4.9-11.1	1.0-20.8	
2	8.1	4.0-10.4	1.6-22.4	
3	6.0	2.5-11.0	1.6-14.1	***P* < 0.001***
4	7.6	2.9-8.7	1.2-9.7	
5	2.7	1.9-6.1	0.5-15.8	
GDI group	**Mortality related to tobacco in men**			***P* value**
	Median	**Q1-Q3**	**Min-max**	
1	18.9	11.4-22.3	3.8-29.2	
2	15.1	9.1-21.4	4.7-29.1	
3	13.0	6.1-21.4	3.9-29.8	***P* < 0.001****
4	20.0	6.7-25.2	4.0-26.1	
5	6.4	5.0-13.0	1.8-23.1	
GDI group	**GMR**			***P* value**
	Median	**Q1-Q3**	**Min-max**	
1	0.4	0.3-0.6	0-2.4	
2	0.5	0.4-0.7	0.2-1.26.1	
3	0.4	0.4-0.6	0.3-0.9	0.401
4	0.4	0.3-0.5	0.3-0.6	
5	0.4	0.3-0.5	0.3-0.8	

*The difference stems from group 1 and 5, group 2 and 5, group 3 and 5, group 4 and 5.
**The difference arises from group 1 and 5, group 2 and 5, group 4 and 5.
***The number of countries in group 1 according to the GDI is 56, in group 2 it is 32, in group 3 it is 19, in group 4 it is 9, and in group 5 it is 31.
GDI: Gender Development Index, GMR: gender-specific tobacco-related mortality rate, Min-max: minimum-maximum

Table 3. Correlation analysis of tobacco use frequency and tobacco-related mortality with GDI, GGGI and GGGI subcomponents

Indicators	Tobacco use prevalence in women		Tobacco use prevalence in men		GSR	
	Correlation coefficient	*P* value	Correlation coefficient	*P* value	Correlation coefficient	*P* value
GDI	**0.439**	**<0.001**	**0.187**	**0.023**	**0.421**	**<0.001**
GGGI	**0.512**	**<0.001**	-0.034	0.688	**0.591**	**<0.001**
GGGI - Economy	**0.241**	**0.004**	-0.016	0.851	**0.286**	**0.001**
GGGI - Education	**0.580**	**<0.001**	**0.210**	**0.012**	**0.577**	**<0.001**
GGGI - Health	0.061	0.466	0.035	0.676	0.012	0.885
GGGI - Politics	**0.350**	**<0.001**	-0.160	0.055	**0.468**	**<0.001**
Indicators	**Mortality related to tobacco in women**		**Mortality related to tobacco in men**		**GMR**	
	Correlation coefficient	***P* value**	**Correlation coefficient**	***P* value**	**Correlation coefficient**	***P* value**
CDGE	**0.290**	**<0.001**	**0.349**	**<0.001**	0.005	0.954
GGGI	**0.265**	**0.001**	0.209	0.012	0.154	0.065
GGGI - Economy	0.111	0.186	0.128	0.125	-0.007	0.935
GGGI - Education	**0.459**	**<0.001**	**0.451**	**<0.001**	0.144	0.085
GGGI - Health	**-0.177**	**0.034**	-0.075	0.373	-0.110	0.188
GGGI - Politics	**0.177**	**0.034**	0.076	0.362	**0.164**	**0.049**

GGGI: Global Gender Gap Index, GDI: Gender Development Index, GMR: gender-specific tobacco-related mortality rate, GSR: gender-specific tobacco use frequency rate

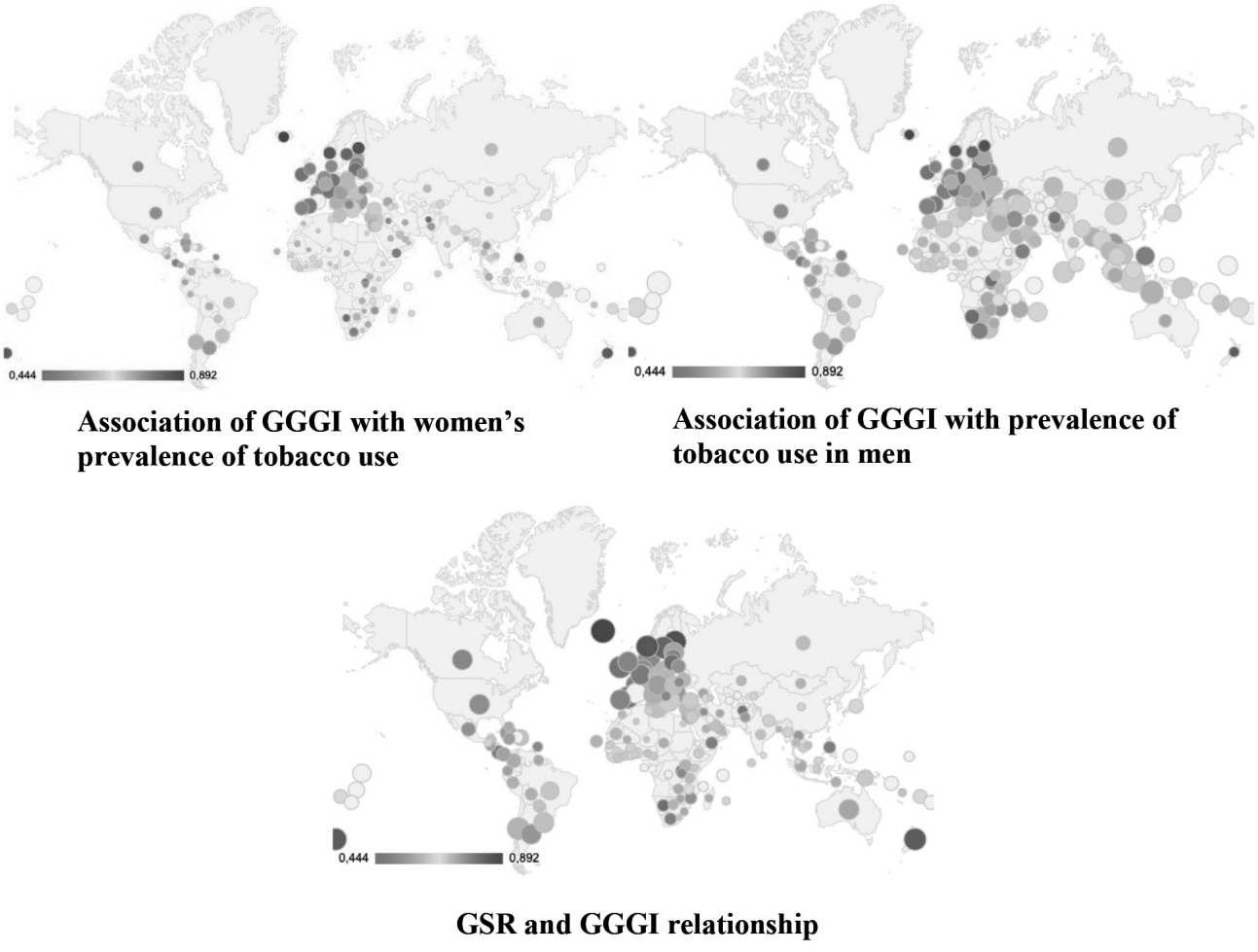

Figure 1. Tobacco use prevalence in relation to the GGGI

GGGI: Global Gender Gap Index, GSR: gender-specific tobacco use frequency rate

women, while 10 men lose their lives due to smoking for every 5 women. According to the WHO, the prevalence of tobacco use is 22.3% overall, with 36.7% in men and 7.8% in women among adults aged 30 and older. Tobacco is attributable to 12% of all deaths among adults aged 30 and older, corresponding to 7% for women and 16% for men.[1,2,17]

In our study, countries with a high GDI observe, tobacco use is higher among women. In GDI group 1 countries, four women smoke for every 10 men, while in group 5 countries, one woman smokes for every 10 men (Table 1). According to the GGGI, women living in countries with more gender equality, higher educational levels, better economic conditions, and greater female political participation generally exhibit higher tobacco use. In men, tobacco use shows a low correlation with the education subcomponent of both GDI and GGGI, while in women, it demonstrates a moderate correlation (Tables 1, 3). Highly educated young women with a high socioeconomic status are the initial group of women who start smoking.[3] At the beginning of the 20th century, consistent and powerful gender-based messages and advertisements by the tobacco industry led to the widespread adoption of smoking among women in middle and high-income countries. Consequently, tobacco product usage increased primarily among women in Western societies. While global male smoking rates have peaked, it is anticipated that female usage, particularly in low and middle-income countries, will rise in the 21st century as the tobacco industry continues to create markets, especially in these regions.[9] An analysis of the relationship between educational status and smoking was conducted in a study encompassing 12 European countries, including Denmark, Germany, the Netherlands, Switzerland, Portugal, Spain, and Italy. In most countries, smoking prevalence was found to be higher among individuals with lower educational levels. However, in Northern European countries such as the United Kingdom, Norway, and Sweden, higher-educated women exhibited a higher prevalence of smoking.[18]

During the first stage of the smoking epidemic, the prevalence of smoking is low in both genders. In the second stage, smoking frequency rapidly increases among men, while the increase in women occurs approximately twenty years later. In the third stage, smoking prevalence peaks among men and begins to decline. Following a delay of several decades, it also starts to decline in women. In the fourth stage, smoking prevalence continues to decrease and gradually reaches a stable minimum level. Due to the higher education levels of early adopters, the epidemic starts earlier among those with higher education than among those with lower education. According to the smoking epidemic

model, smoking prevalence increases among highly educated men and women in the early stages of the epidemic, followed by a decrease in smoking among highly educated individuals, while smoking prevalence increases among men and women with lower education.[19] During the smoking epidemic, there is a shift from a positive relationship to a negative relationship between socioeconomic status and smoking prevalence.[18] In the later stages of the epidemic, although smoking prevalence generally decreases among women in high-income countries, it declines unevenly. It is anticipated that women in developed countries who experience social exclusion, poor economic status, a history of violence, psychiatric disorders, and substance use will continue smoking.[20,21]

According to our study's data, in countries with high GDI and GGGI indicating lower gender inequality, higher education levels, and increased education and political participation among women, there is a higher prevalence of tobacco use. This suggests a rising trend in the smoking epidemic among women. The reflection of these parameters may vary in each society, with tobacco use potentially higher among women with low socioeconomic status in developed Western societies that are in the third to fourth stages of the epidemic, while in some societies in the early stages of the epidemic, tobacco use may be higher among women with high socioeconomic status.

In our study, tobacco-related mortality is higher among women in GDI groups 1, 2, and 4, compared to women in other groups, but overall, these mortality rates are still significantly lower than those of men. Additionally, as GDI, GGGI (and its sub-component, education), and women's political participation increase, tobacco-related mortality also increases (Tables 2, 3). When assessed temporally, it is observed that women start smoking after men. In a study evaluating a cohort of individuals aged 50-85 between 1950 and 2015, it was found that since 1980, overall smoking-attributable death rates have generally decreased, with a declining trend in men and an overall increasing trend in women.[22] In a study analyzing data on tobacco-attributed mortality from the WHO covering 63 countries, a decrease in smoking-related deaths was observed in men in most countries. However, among women residing in high-income countries, increases in the impact of tobacco on life expectancy were observed.[23] As education levels increase, tobacco-related mortality unexpectedly also increases in men. However, this counterintuitive trend should be carefully studied for potential confounding factors. In France, since the 1970s, there has been a dramatic increase in the prevalence of smoking among women and a decrease in smoking prevalence among men. However, gender inequality in the burden of tobacco-related diseases has been steadily increasing. Between 2002 and 2014, the incidence and death rates of lung cancer in women increased by approximately 70%, while the incidence of lung cancer in men remained stable, with a 15% decrease in mortality rates.[24] Over the years, the number of men dying from smoking has decreased, while the number of women continues to rise.[4,25]

There are several limitations to this study. The data were collected during the pandemic period, which may have influenced the findings either positively or negatively. Conducting similar studies in the post-pandemic period would be valuable for assessing the impact of the pandemic more clearly. Additionally, cultural norms are an important factor influencing smoking behavior. However, as this study is ecological and does not include country-specific data, the effect of cultural norms on smoking could not be evaluated. Similarly, because country-level data were not analyzed, cross-country comparisons were not made. Future studies, especially those in Türkiye, should include trend analyses by gender and take cultural norms into account to inform the development of gender-specific policies.

CONCLUSION

This study underscores the complex relationship between gender equality, socio-economic factors, and tobacco use, particularly among women. The findings reveal that higher education levels and women's political participation are associated with increased tobacco use and tobacco-related mortality. Countries with less gender inequality show higher prevalence rates among women, suggesting the early stages of a tobacco epidemic in these populations. Education stands out as the strongest correlate of tobacco use and its health consequences, highlighting the dual impact of socio-economic development. As smoking rates among men decline globally, the predicted rise in female smoking, especially in low- and middle-income countries, requires urgent attention. To combat this growing challenge, public health policies must adopt gender-sensitive approaches that account for cultural and demographic differences. Tailored, evidence-based prevention strategies and research with gender-segregated data are essential to effectively address tobacco use and its consequences among women, ensuring equitable and impactful health interventions.

Ethics

Ethics Committee Approval: The research ethics committee approval was received from Hacettepe University Non-interventional Clinical Research Ethics Committee (approval number: 2021/19-12, date: 16.11.2021).

Informed Consent: The study used publicly available country data, but did not use individual data. Therefore, informed consent was not required.

Footnotes

Authorship Contributions

Concept: H.E.E., T.Ç., L.H.Ö., Design: T.Ç., L.H.Ö., Data Collection or Processing: T.Ç., Analysis or Interpretation: H.E.E., Literature Search: H.E.E., T.Ç., L.H.Ö., Writing: H.E.E., T.Ç., L.H.Ö.

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Original Article

Moving Toward a Smoke-free Campus: A Survey of Students' Knowledge, Behavior, and Opinions

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Abstract

OBJECTIVE: This study examines the tobacco and product use status of university students, their awareness of smoke-free campuses, and the relationship between tobacco use awareness and tobacco use status.

MATERIAL AND METHODS: Data were collected using a questionnaire for students (n = 15.515) who continued their education at a state university. The questionnaire consisted of three sections: sociodemographic, tobacco and product use behaviors, and a Smoke-free Campus Awareness Scale (SCAS). The chi-square test was used for categorical variables, and the Kruskal-Wallis test was used for continuous variables.

RESULTS: 28.5% of the university students were active smokers, and 48.7% were exposed to passive smoking on campus. When the SCAS scores were compared according to the smoking status of the students, never smokers (median: 44.0, Q1=36.0-Q3=48.0), active smokers (median: 27.0, Q1=20.0-Q3=36.0), and recent quitters (median: 33.0-Q1=11.0-Q3=43.0) ($P < 0.001$). SCAS scores were compared according to gender; the median score of female students (Q1=31.0-Q3=46.0) was statistically higher than that of male students (Q1=19.0-Q3=44.0). Non-smokers were found to be statistically more uncomfortable with being exposed to secondhand smoke on campus than smokers ($P < 0.001$).

CONCLUSION: Most students were unaware of the smoke-free campus policy but were aware that passive smoking is an important public health problem. The fact that male students and smokers oppose implementation requires investigation of the reasons for these attitudes in future studies, and monitoring tobacco use trends after implementation is important to effectively evaluate smoke-free campus implementation.

KEYWORDS: Cigarette smoking, students, university tobacco policies, smoke-free policy, tobacco control

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INTRODUCTION

The use of tobacco and other tobacco products is a source of many diseases, especially cancer, and it ranks first among the preventable risk factors.[1] Approximately eight million people die worldwide every year because of diseases associated with the use of tobacco and related products.[2] Studies have shown that the annual damage caused by cigarette consumption to the economy of the United States is approximately 600 billion dollars.[3] Effective methods should be used to combat addiction, which has serious health and economic effects. In this context, the World Health Organization (WHO) proposed the Framework Convention on Tobacco Control (FCTC) in 2003 as a guide for countries to combat the harmful health effects of tobacco and tobacco products.[2] In this context, serious steps have been taken in our country since 2008 in line with the FCTC recommendations, and the success achieved has been shown as an example for other countries by WHO.[4]

Tobacco and tobacco products are not only harmful to consumers. It also harms the health of other people who share the same environment as those who use these products. Exposure to smoke and thus carcinogenic substances due to the use of these products by others even though they do not use these products themselves is called second-hand smoke and is a serious health problem in terms of public health.[5]

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Tobacco manufacturers use marketing methods to gain new customers and replace the addicts they have lost due to anti-tobacco campaigns initiated under the leadership of the WHO and receiving great support worldwide. In this context, university students have significant potential. Because they become lifelong users when they become addicted, the tobacco industry employs special marketing techniques for young people.[6]

According to researchers conducting in recent years, cigarette packet sales have been increasing in Türkiye. The prevalence of smoking among university students in Türkiye varies between 20% and 48%.[7] In this context, the Ministry of Health presented a Smoke-Free Air Space 'DHS' campaign to the public in 2008 with the priority of protecting and treating public health.[8] Smoke-free areas offer cleaner, healthier areas to employees and those who use them, increase employee success, reduce diseases, increase work efficiency, and reduce the risk of fire.[1]

This study aimed to (1) determine university students' tobacco and tobacco product use status, (2) determine university students' thoughts and awareness about smoke-free campuses, and (3) examine the relationship between smoke-free campus awareness and tobacco and tobacco product use status. In this study, data on a smoke-free campus at our university will be obtained and used in the strategies developed in line with the data obtained.

MATERIAL AND METHODS

Study Design

This was a cross-sectional epidemiological study.

Population and Sample

The study population includes undergraduate students (n = 15,515) who study at faculties, colleges, and vocational schools on the central campus of Kırşehir Ahi Evran University. Sampling was performed in this study. Epi Info 7.2.5. software was used for sample calculation. In the sample of the study, the prevalence was calculated as 28.8%, the margin of error was 5%, the pattern effect was 2%, and the confidence level was 95% and 630 people.[9] The number of samples to be taken was determined by the stratified sampling method according to the class sizes of the faculties, colleges, and vocational schools. At the end of the study, 703 questionnaires were collected, and when blank and incorrectly filled out questionnaires were excluded from the study, a total of 688 questionnaires were collected (Figure 1).

Main Points

- Only one-fifth of the students were aware of the smoke-free campus initiative.
- The majority of students recognized that passive smoking is a significant public health issue.
- Male students and those who smoke opposed the smoke-free campus initiative.
- Attitudes toward tobacco use should be assessed not only before the implementation of the smoke-free campus policy and should be monitored over time.
- Gathering this information is crucial for planning measures to prevent students from smoking.

Data Collection Tool

A questionnaire consisting of 34 questions was used as the data collection tool. The questionnaire consisted of three parts. The first part consists of questions examining the sociodemographic characteristics created by the literature review. In the second part, questions are given about tobacco and tobacco product usage status and the characteristics of students who use tobacco and tobacco products.[7,10] In the third part, the Smoke-free Campus Awareness Scale (SCAS) was used.

SCAS; Dereli et al.[11] 2023 in Türkiye. The SCAS was determined to be valid and reliable and can measure the opinions and awareness of individuals about smoke-free campus application and smoking in campus areas. The SCAS is a one-dimensional scale consisting of 11 items scored on a 5-point Likert (Strongly Disagree, Disagree, Neutral, Agree, Agree, Strongly Agree). A minimum of 11 and a maximum of 55 points were obtained from the scale, and as the score increased, the level of smokeless campus awareness of individuals increases.

Data Collection

Prior to the study, class availability lists for faculties, colleges, and vocational schools were obtained. The data were collected from the 1st, 2nd, 3rd, and 4th grades (including 5th and 6th grades for the faculty of medicine) according to the number determined by the stratified sampling method according to class availability using the Google online survey method. Before the questionnaires were collected, the purpose of the study and what they would do were explained to the students, after which their consent was obtained.

Ethical Permission

This study was approved by the Kırşehir Ahi Evran University Health Sciences Scientific Research Ethics Committee (decision no: 2024-06/34, date: 05.03.2024), and necessary permissions were obtained from Kırşehir Ahi Evran University.

Statistical Analysis

Descriptive statistics are presented as the number of units (n), percentage (%), median (M), and interquartile range (Q_1-Q_3). The normality of continuous variables was tested using the Kolmogorov-Smirnov test ($P < 0.001$). The dependent variables of the study were the students' scores on the smoke-free campus scale; the independent variables were sociodemographic characteristics, smoking status, smoking status of the people around them, and opinions and knowledge about the smoke-free airspace. The Mann-Whitney U test and Kruskal-Wallis test were used for comparisons between groups. Pearson's chi-square test was used to determine differences between the variables. The data were evaluated using the IBM Statistical Package for the Social Sciences Statistics standard concurrent user, version 26 (IBM SPSS Corp.; Armonk, NY, USA) statistical package program. The statistical significance level was set as $P < 0.05$.

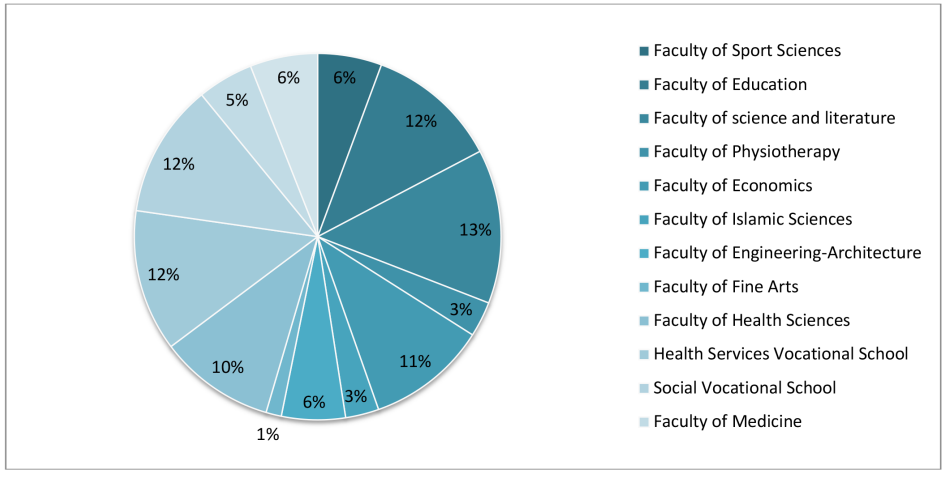

Figure 1. Faculties and number of students from which data will be collected

RESULTS

The median age of the students who participated in the study was calculated as 21.0 (Q_1=20.0-Q_3=22.0). Of the students, 64.4% (n = 443) were female, 34.7% (n = 239) were studying in their second year, and 68.9% (n = 474) were living in dormitories. The perceived income status of 73.1% (n = 503) of the students was moderate, and 12.8% (n = 88) had a chronic disease diagnosed by a doctor (Table 1). The median score of the SCAS administered to the students was found to be 40.0 (Q_1=24.0, Q_3=45.0). In the scale items, 59.6% of the students 'agree' or 'strongly agree' with the item 'Smoke-free campus should be implemented in every university'. 33.0% of the students 'agree' or 'strongly agree' with the item 'It will be easy to adapt to the smoke-free campus application'. 39.2% of the participants stated that the smoke-free campus implementation would increase the rate of smoking cessation (Figure 2).

When the smoking status of university students was analyzed, 28.5% (n = 196) were active smokers and 4.5% (n = 31) had quit smoking within the last 6 months. 31.7% (n = 218) of the students stated that most of their close friends smoked, and 23.3% (n = 160) stated that half of their close friends smoked. In addition, 11.5% (n = 79) of the participants stated that both of their parents smoked (Table 2). It was found that 6.8% (n = 47) of the participating students used e-cigarettes, 6.4% (n = 44) used hookah, and 4.5% (n = 31) used other tobacco products.

Among the participants, 27.4% (n = 188) indicated that they had tried e-cigarettes but did not continue their use. Among non-smokers, 2.6% (n = 12) stated that they used e-cigarettes every day, while 16.9% (n = 78) stated that they tried and did not continue. Among smokers, 15.4% (n = 35) also used e-cigarettes every day, and 44.9% (n = 102) tried e-cigarettes. Among smokers, 16.0% (n = 110) stated that they wanted to quit smoking, whereas 10.8% (n = 74) were undecided. It was found that 23.7% (n = 163) of the students who smoked had tried to quit smoking at least once.

The opinions and knowledge of the students regarding smokeless campus applications and passive exposure are presented in Table 3. It was determined that only 17.3% (n = 119) of the participants had heard of the smoke-free campus application before. Moreover, 83.7% (n = 576) of the participants stated that passive smoking was a very serious problem, and 48.7% (n = 335) stated that they were exposed to passive smoking on campus. Among the students studying at the central campus, 35.6% (n = 245) believed that smoking should be banned in the indoor and outdoor areas of the campus, and 45.9% (n = 316) believed that smoking should be banned only in indoor areas.

Table 1. Distribution of sociodemographic characteristics of the students

Variables		Number (n)	Percentage (%)
Gender			
	Female	443	64.4
	Male	245	35.6
Class			
	1st grade	204	29.6
	2nd grade	239	34.7
	3rd grade	147	21.4
	4th grade	62	9.0
	5th grade	19	2.8
	6th grade	17	2.5
Accommodation			
	With family	115	16.7
	The dormitory	474	68.9
	Home/apartment alone	44	6.4
	Homes or apartments with flatmates	55	8.0
Perceived income			
	Good	102	14.8
	Medium	503	73.1
	Poor	83	12.1
Chronic disease diagnosed by a physician			
	No	600	87.2
	Yes	88	12.8

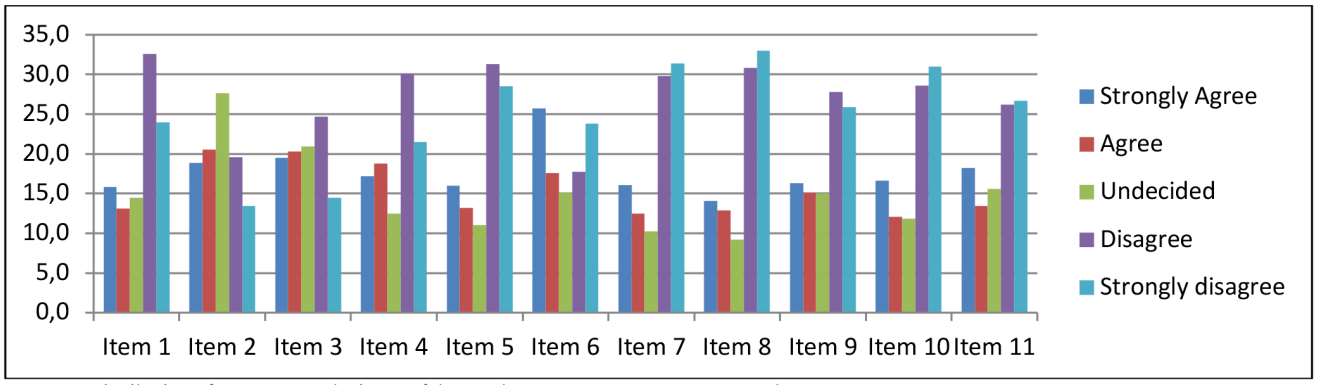

Figure 2. Distribution of responses to the items of the Smoke-free Campus Awareness Scale

Item 1: Trainings and activities related to a smoke-free campus should be held at the university. Item 2: It will be easy to adapt to the smoke-free campus application. Item 3: Smoke-free campus application increases smoking cessation rates. Item 4: Smoking in universities encourages smoking. Item 5: Smoke-free areas should be increased on smoke-free campuses. Item 6: I do not go out to smoke alone between classes and work on campus. Item 7: Passive smoking decreases with the implementation of smoke-free campus. Item 8: Smoke-free airspace should be increased. Item 9: Smoke-free airspace are a factor that can help quit smoking. Item 10: Smoke-free campuses should be implemented in every university. Item 11: Smoke-free airspace should be implemented in both open and closed areas

Table 2. Smoking status of participants and their environment

Variables	Number (n)	Percentage (%)
Smoking status of the mother and father		
None of them use it.	319	46.4
Only one of them uses it.	290	42.1
They are both using	79	11.5
Smoking status of friends		
None of them use it.	88	12.8
Very few people use it.	222	32.3
Half of the people use it.	160	23.2
Most use	218	31.7
Smoking status		
Never used	435	63.2
Former user	26	3.8
New user	31	4.5
Active user	196	28.5
*The place most commonly used by smokers		
Off campus	40	17.7
Equal amounts of on-campus and off-campus	161	71.2
In the campus	26	11.1

*Active and new quitters have answered

Furthermore, 70.2% (n = 483) of the students agreed that the consumption of tobacco and tobacco products in front of doors and windows could be harmful to people inside buildings.

The median score of the SCAS administered to the students was calculated as 40.0 (Q_1=24.0, Q_3=45.0). The distribution of responses to the SCAS items is presented in Table 4. A statistically significant difference was found between the groups according to the students' smoking status ($P < 0.001$). This difference was due to the difference between never smokers (median: 44.0, Q_1=36.0-Q_3=48.0), active smokers (median: 27.0, Q_1=20.0-Q_3=36.0), recent quitters (median: 33.0, Q_1=11.0-Q_3=43.0), and never smokers (median: 44.0, Q_1=36.0-Q_3=48.0) ($P < 0.001$, $P < 0.001$ respectively). In addition, when the SCAS score was compared by gender, the median score of female students was 42.0 (Q_1=31.0-Q_3=46.0), while the median score of male students was 33.0 (Q_1=19.0-Q_3=44.0).

The smoking rate of male students was higher than that of female students ($P < 0.001$). The smoking rate of students living with their parents or in dormitories was lower than that of students living alone or in a flat/apartment with a flatmate ($P < 0.001$). Students with poor perceived income status had a higher smoking rate ($P = 0.005$). No statistically significant difference was found according to education level or presence of chronic disease. The smoking status of both parents was found to be higher among students who smoked ($P < 0.001$). The smoking rate of university students increased significantly as the smoking rate of their friends increased ($P < 0.001$). Non-smokers were more likely to be disturbed by passive exposure on campus ($P < 0.001$) (Table 4).

DISCUSSION

In this study, it was determined that one-third of the university students were active smokers; the majority of the students knew that passive cigarette exposure is a serious problem, and half of them were exposed to passive cigarette smoke on campus. Only 17.3% of the students had heard about smoke-free campus practices before and scored high on the SCAS.

According to the WHO 'Türkiye Health Survey 2019' report, 27.2% of individuals over the age of 15 use tobacco products every day and 3.4% use tobacco products occasionally.[12] In studies conducted on university students, 35% of students were found to smoke in a study conducted in İzmir.[13] In another study conducted in Çukurova, 52.1% of students reported using tobacco or tobacco products.[14] In a study conducted with university students in the Eastern Black Sea region, 31.3%

Table 3. Distribution of participants' opinions about smoke-free campuses

Variables	Number (n)	Percentage (%)
I feel uncomfortable being exposed to secondhand smoke on campus		
No	190	27.6
Yes	335	48.7
No answer	163	23.7
Have you heard about the smoke-free campus application?		
No	545	79.2
Yes	119	17.3
No answer	24	3.5
Your thoughts about the risks of the passive inhalation of cigarette smoke to human health		
Very serious, lethal	161	23.4
Very serious disease	415	60.4
It is not a very serious air risk	73	10.6
Not a serious risk at all, no harm done	14	2.0
No answer	25	3.6
Information on smoking bans in indoor public spaces and workplaces		
A lot of reading	280	40.7
He could hear a little	318	46.2
I didn't hear much	52	7.6
Heard nothing	16	2.3
No answer	22	3.2
Should smoking be banned in open areas at universities?		
It should be banned at all levels.	245	35.6
It should be limited to indoor areas only.	316	45.9
It should only be allowed in indoor areas and in canteens and cafes.	59	8.6
It should be free in all areas.	46	6.7
No answer	22	3.2
Consuming tobacco and tobacco products in front of doors and windows is harmful to people inside buildings.		
Strongly agree	323	46.9
Agree	160	23.3
Undecided	97	14.1
Disagree	45	6.5
Strongly disagree	38	5.5
No answer	25	3.7

were found to be smokers.[15] In another study conducted in the Central Anatolia region, 29.57% of university students were reported to be smokers.[16] Although smoking among university students in Italy was found to be 19%, the rate was found to be 14.7% in a study conducted in Portugal.[17,18] According to the WHO 2020 tobacco report, the WHO European region had a prevalence of 27.4%.[1] Compared with European countries, the rate of smoking is higher among university students in our country.

Studies conducted in recent years have revealed that smoking rates are higher in men than in women. According to the 2016 report of the 'Global Adult Tobacco Survey', while the smoking rate in men was 44.1%, this rate was 19.2% in women.[19] Studies conducted on university students in Niğde, Adana, and İstanbul provinces reported that smoking was more common among male students.[10,14,20] In this study, we found that the prevalence of smoking was higher among male students, which is consistent with the literature. The reasons for this may include the fact that social attitudes in Türkiye do not approve of women smoking, and women tend to consult more sources of information about their health.

In a study covering 15 low- and middle-income countries, it was reported that the rate of e-cigarette use was below 10% in most countries except Romania (4.4%) and Russia (3.5%), whereas the rate of 'never use' was below 10% and the rate of 'current use' was approximately 1%.[21] In a study conducted in an adolescent group, the rate of e-cigarette use was found to be 1.02%, while in a study conducted on university students in İstanbul, this rate was found to be 8.5%.[10,22] In another study conducted in Adana, 0.92% of e-cigarette users were found, and in another study conducted in İzmir, 19.1% e-cigarette users were found.[13,14] In a study conducted on only medical faculty students from the same university, the rate was found to be 4.6%.[23] This wide range in e-cigarette use may be related to socioeconomic factors. It is seen that e-cigarette use is higher in regions with higher economic levels. It is believed that this may be due to the widespread belief that e-cigarettes are 'smoking cessation' and 'less harmful'.

The prevalence of smoking was higher among individuals living alone or with a flatmate in a flat or apartment than among those living with family or in dormitories. A study conducted by Ulukoca et al.[24] reported that people living with friends were more likely to smoke. In another study conducted in Kars province, the risk of smoking increased 1.67-fold in those living at home with friends.[25] The fact that living with family or in a dormitory environment is more controlled may be a factor that prevents individuals from starting smoking. In addition, smoking is expected to be more prevalent among individuals who live with their friends, which is an important factor in smoking initiation.

According to the study results, smoking was found to be higher among individuals with poor and moderate perceived incomes. Studies conducted in Qatar and Jordan have reported that higher income levels increase the risk of smoking.[26,27] These differences at the international level may be due to differences in the cultural and traditional structures of the countries. In another study of university students in Türkiye, no relationship was found between perceived income level and smoking.[13,28] In another study, it was reported that there was a relationship between smoking and family income.[29] In Türkiye, low incomes may increase the risk of smoking by affecting family education and close friends.

Table 4. Comparison of smoking status with other variables

Variables	Smoker		Non-smoker		
	Number (n)	Percentage (%)	Number (n)	Percentage (%)	*P*
Gender					
Female	83	18.7	360	81.3	0.001
Male	113	46.1	132	53.9	
Class					
1st grade	54	26.5	150	73.5	
2nd grade	67	28.0	172	72.0	0.727
3rd grade	47	32.0	100	68.0	
4/5/6th grade	28	28.6	70	71.4	
Accommodation					
With family	33	28.7	82	71.3	
The dormitory	117	24.7	357	75.3	0.001
Home/apartment alone	20	45.5	24	54.5	
Homes or apartments with flatmates	26	47.3	29	52.7	
Perceived income					
Good	33	32.4	69	67.6	
Medium	128	25.4	375	74.6	0.005
Poor	35	42.2	48	57.8	
Chronic disease diagnosed by a physician					
No	170	28.3	430	71.7	0.814
Yes	26	29.5	62	70.5	
Smoking status of the mother and father					
None of them use	79	24.8	240	75.2	
Only one of them uses	80	27.6	210	72.4	0.001
They both use	37	46.8	42	53.2	
Smoking status of friends					
None of them use it.	2	2.3	86	97.7	
Very few people use it.	23	10.4	199	89.6	0.001
Half of the people use it.	45	28.1	115	71.9	
Most use	126	57.8	92	42.2	
I feel uncomfortable being exposed to secondhand smoke on campus.					
No	159	83.7	31	16.3	0.001
Yes	31	9.3	304	90.7	
Have you heard about the smoke-free campus application?					
No	161	29.5	384	70.5	0.833
Yes	34	28.6	85	71.4	

Of the students who smoked cigarettes, 11.0% stated that they smoked more cigarettes inside the campus, and 71.2% stated that they smoked equally inside and outside the campus. A study comparing before and after the smoke-free university campus implementation found that the prevalence of smoking on campus statistically decreased significantly.[30] These findings suggest that smoke-free campuses are expected to decrease smoking rates among students. Most students (79.2%) who participated in the study were not aware of the smoke-free campus application. A study conducted by Acımış et al.[28] reported that only 2.7% of university students were aware of smoke-free campus practice. These data demonstrate that students did not sufficiently comprehend the smokeless campus application. Increasing awareness of smoke-free campus practices, announcing successful examples in other universities, and encouraging students to gain awareness and advocate in universities where such practices do not exist may encourage students to advocate.

Almost all non-smoking students stated that they felt uncomfortable about being exposed to secondhand smoke on campus. Studies conducted in Italy and Serbia found that most participants had been exposed to passive smoking within the last week.[18,31] In a study conducted on the adolescent population in Türkiye, >80% of adolescents were passive smokers.[32] The majority of participants believed that passive exposure would cause diseases on human health, and more than half of them believed that smoke-free campuses would reduce passive exposure. As a result, it is clear that the belief in the necessity of protection from passive exposure is widespread, and smoke-free campus practices should be implemented not only in closed areas but also in open areas.

In this study, 35.6% of the participants supported the prohibition of smoking in open areas on university campuses, but almost all of those who provided this support were non-smokers. A study conducted in Europe reported that the majority of students and employees supported smoke-free campus practices, but former and current smokers opposed bans in open areas, despite supporting tobacco-free practices.[33] The median score of the SCAS was 40.0. This value is close to the maximum score, indicating that most students believe that smoke-free campus implementation will reduce passive exposure, encourage smoking cessation, and support its implementation. In a study involving five universities in the United States, 77.5% of the participants stated that they supported the implementation of smoke-free campuses. In this study, passive exposure decreased from 41.2% to 32.8% after the smoke-free campus implementation, and smoking decreased from 13.0% before implementation to 10.3%.[34] In another study conducted in Türkiye, half of the students stated that they would definitely support a smoke-free campus.[29]

This study is limited in generalizability because it covers only students at one university. Although the findings may be informative for other universities, the results are more reflective of the university where the study was conducted. Second, the study was based on questionnaire responses, which may have led to biases, such as a lack of compliance and misinterpretation of the question. Third, due to the total number of students at the university, the population could not be reached; thus, data were collected using the stratified sampling method. Therefore, there is a potential bias. These problems are mostly valid for the survey results and are difficult to control. The limitations of the study should be taken into consideration when reviewing the results.

Despite these limitations, students' tobacco use habits and risk perceptions, as well as their awareness of and support for smoke-free campus implementation, were evaluated. This will help guide future efforts to prevent and reduce tobacco use by students. Baseline data reflecting the prevalence and causes of tobacco use can be used to plan and evaluate future prevention and cessation strategies.

CONCLUSION

In our study aimed to evaluate students' knowledge and attitudes toward the concept of a smoke-free campus, it was observed that only one-fifth of the students had heard of the smoke-free campus application, and the majority of them knew that passive smoking is an important public health problem. For this reason, it is believed that students will be supported in future smoke-free campus applications. It was understood that most students did not know about the smoke-free campus application, but they were aware of the importance of preventing passive smoking, the indoor bans implemented for this purpose, and the prevention of use near doors and windows. Male students opposed the smoke-free campus application. The reasons for these should be investigated in future studies. Tobacco use and opinions should not only be evaluated before implementation of the smokeless campus, but also trends should be monitored after implementation. This is of great importance in the evaluation of smokeless campus implementation. Accessing this information may help plan measures to prevent students from starting to smoke.

Ethics

Ethics Committee Approval: This study was approved by the Kırşehir Ahi Evran University Health Sciences Scientific Research Ethics Committee (decision no: 2024-06/34, date: 05.03.2024), and necessary permissions were obtained from Kırşehir Ahi Evran University.

Informed Consent: Consent form were filled out by all participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Ü.T.B., H.İ., Concept: Ü.T.B., H.İ., Design: Ü.T.B., Data Collection or Processing: Ü.T.B., H.İ., Analysis or Interpretation: Ü.T.B., Literature Search: Ü.T.B., H.İ., Writing: Ü.T.B., H.İ.

Conflict of Interest: No conflict of interest was declared by the authors.

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Original Article

Evaluation of Risk Factors Causing Diagnostic Delay in Non-steroidal Anti-inflammatory Drug-exacerbated Respiratory Disease

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Abstract

OBJECTIVE: Non-steroidal anti-inflammatory drug (NSAID)-exacerbated respiratory disease (N-ERD) can be difficult to diagnose due to the heterogeneity of phenotypes and a lack of validated *in vitro* tests. This study aimed to provide a better understanding of the course of N-ERD disease, analyze whether there was a delay in clinical diagnosis, and explore the factors that might cause diagnostic delay.

MATERIAL AND METHODS: This observational, cross-sectional, study included patients aged over 18. The time taken by clinicians to diagnose N-ERD was recorded as the clinician diagnosis time, while the time taken by patients to complete the N-ERD triad was recorded as the actual diagnosis time. A difference of six months or longer between actual diagnosis and clinician diagnosis times was accepted as diagnostic delay. Statistical analyses were performed to ascertain the parameters that could cause this delay.

RESULTS: The study included a total of 107 patients diagnosed with N-ERD. The patients had been diagnosed with chronic rhinosinusitis with nasal polyps, asthma, and NSAID hypersensitivity for an average duration of 14.9±9.6, 14.3±9.9, and 11.7±9.3 years, respectively. Thirty-nine (36.4%) of the patients had a delayed diagnosis. The mean delay in the diagnosis of N-ERD was 7.4±6.6 (2.0-12.0) years. Delayed diagnosis showed a correlation with thyroid dysfunction ($P = 0.021$), while it did not have a significant relationship with the remaining factors.

CONCLUSION: The results of this study have indicated delays in diagnosing N-ERD patients and emphasized the need for adequately recognizing the disease to initiate timely, appropriate treatment.

KEYWORDS: Non-steroidal anti-inflammatory drug-exacerbated respiratory disease, nasal polyp, asthma, aspirin, non-steroidal anti-inflammatory drug hypersensitivity

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INTRODUCTION

Non-steroidal anti-inflammatory drug (NSAID)-exacerbated respiratory disease (N-ERD) is a chronic eosinophilic inflammatory disorder of the respiratory tract that occurs in patients with asthma, chronic rhinosinusitis, and/or nasal polyps (CRSwNP), whose symptoms are exacerbated by NSAIDs.[1] The prevalence of N-ERD increases as the severity of respiratory disease increases, reaching 14.9% in patients with severe asthma and 24% in those admitted to the intensive care unit due to asthma exacerbations.[2] Severe asthma is twice as common in individuals with N-ERD compared to the general asthma population. Asthma symptoms can be severe, and treatment is difficult. Aspirin therapy after desensitization (ATAD) and biological therapy are successfully used in many patients.[3] Upper respiratory tract symptoms are also severe, in addition to lower respiratory tract symptoms. The treatment of CRSwNP is difficult due to the high likelihood of NP being resistant to treatment and their common recurrence.[4-8] In a previous study, 80% of patients with

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NP who had N-ERD required revision surgery because ATAD had not been applied.[8]

In most patients with N-ERD, asthma symptoms emerge one to five years after upper respiratory tract symptoms, while NSAID hypersensitivity develops years later.[9,10] Relying solely on anamnesis may not be sufficient to diagnose N-ERD, and the gold standard diagnostic test is the aspirin provocation test.[11,12] The early diagnosis of N-ERD is essential for the successful management of the disease and allows patients' timely access to appropriate treatment. However, N-ERD often cannot be diagnosed early due to its variable clinical symptoms, a lack of validated *in vitro* tests and biomarkers, the long disease course, and low clinical suspicion. There is insufficient data in the literature regarding the extent and implications of diagnostic delays in N-ERD. Enhancing our understanding of N-ERD will facilitate early diagnosis and prompt the timely initiation of successful treatment.

This study aimed to provide a better understanding of the course of N-ERD, analyze whether there was a delay in clinical diagnosis, and explore the factors that might cause diagnostic delay.

MATERIAL AND METHODS

This observational, cross-sectional study was conducted at the Hacettepe University Faculty of Medicine, Adult Allergy and Immunology Clinic. It included patients aged 18 and older who were diagnosed with N-ERD from January 1, 2010, through December 27, 2023. Patients with asthma and recurrent nasal polyposis were diagnosed with N-ERD based on their history of multiple respiratory reactions occurring within 1-2 hours after NSAID intake, or positive results from an aspirin provocation test.[1] The patients' demographic characteristics, comorbidities, smoking status, medications used for N-ERD treatment, the use of biological therapy and ATAD, nasal polypectomy history, pulmonary function test parameters [forced expiratory volume in 1 (FEV1) second, forced vital capacity (FVC), and FEV1/FVC ratio] obtained at the time of clinician diagnosis, asthma control test (ACT) scores obtained at the time of clinician diagnosis, serum eosinophil count, serum total immunoglobulin (Ig) E level, skin prick test results, and food allergy history were recorded.

ACT is a test used to evaluate control of asthma symptoms. An ACT score below 20 points is a sign of uncontrolled asthma, while a score of 20-25 points indicates well-controlled asthma.[13]

The mean and median values of the time from the first symptom onset to the diagnosis of N-ERD, as well as the diagnosis times of asthma, CRSwNP, and NSAID hypersensitivity, were recorded. The mean and median values of the diagnosis times of asthma + CRSwNP, asthma + NSAID hypersensitivity, and CRSwNP + NSAID hypersensitivity were also calculated.

The suspected diagnosis was defined as when the patient exhibited two components of the N-ERD triad (asthma and CRSwNP, asthma and NSAID hypersensitivity; or CRSwNP and NSAID hypersensitivity). The time of clinician diagnosis was defined as the date when the triad (asthma, CRSwNP, NSAID hypersensitivity) was complete and the clinician officially diagnosed N-ERD. The actual diagnosis time was defined as the date when the patient completed the triad. The diagnostic latency period was defined as the time interval between the actual diagnosis and the clinician diagnosis. If the duration between the actual diagnosis time and the time of receiving the N-ERD diagnosis exceeds 6 months, this is defined as diagnostic delay. In other words, a diagnostic latency period of more than 6 months, was defined as diagnostic delay (Figure 1). The patients were divided into two groups according to whether they had a diagnostic delay. Statistical analyses were performed to determine the parameters that potentially caused this delay.

The study was approved by the Ethics Committee of Hacettepe University Hospital (approval number: 24/239, date: 02.04.2024). The recommendations of the World Medical Association Declaration of Helsinki were followed.

Statistical Analysis

IBM Statistical Package for Social Sciences v. 11.5 was used for the statistical analysis of the data. The results were presented with cross-tabulations and evaluated with the Pearson chi-square analysis. For 2x2 tables that had more than 25% of cells with expected values below 5, Fisher's exact test was employed. To determine the statistical analysis method to be used for the comparison of laboratory values according to the diagnostic delay status, the Kolmogorov-Smirnov and Shapiro-Wilks tests

Main Points

- High prevalence of diagnostic delay: The study found that 36.4% of patients with non-steroidal anti-inflammatory drug (NSAID)-exacerbated respiratory disease (N-ERD) experienced a significant diagnostic delay, averaging seven years. This delay was observed more frequently in female patients.
- Lack of association with common risk factors: No significant relationship was detected between the delay in N-ERD diagnosis and factors such as age, sex, allergy status, smoking, comorbidities, or total IgE and eosinophil levels. However, thyroid dysfunction was more prevalent among patients with delayed diagnosis.
- Chronic rhinosinusitis as the initial symptom: Most patients first developed chronic rhinosinusitis, followed by asthma and finally NSAID hypersensitivity, indicating a progression of symptoms over time.
- The need for early diagnosis and intervention: The study emphasizes the importance of early diagnosis of N-ERD to allow timely initiation of treatment. Delays in diagnosing NSAID hypersensitivity can result in more severe disease progression and complications, such as increased asthma exacerbations and frequent nasal polyp recurrence.
- Raising awareness among non-allergist physicians: The delay in diagnosis may be attributed to low awareness of N-ERD among non-allergist physicians and the lack of routine aspirin challenge testing. The study calls for improved awareness and the availability of standardized diagnostic protocols to facilitate early identification and management of N-ERD.

were applied to the dataset to investigate the normality of the data distribution. Additionally, the homogeneity of variances was examined with the Levene test. Since the data did not meet the parametric distribution assumptions, the Mann-Whitney U test was used. Within the scope of the analysis, results with a *P* value of <0.05 were considered statistically significant.

RESULTS

A total of 107 patients diagnosed with N-ERD were included in the study. The mean age of the patients was 45.84±12.1 [interquartile range (IQR): 20-70] years, and 38 (35.5%) of the patients were male. The mean serum eosinophil count at the time of clinician diagnosis was 514.4±401.8 (IQR: 215.0-700.0) cells/mm^3, and total IgE was 210.8±268.7 (IQR: 61.0-238.0) UI/mL. The mean ACT score was 19.5±5 (IQR: 15.3-24.0). Nasal polypectomy operations had been performed three or more times in 46 (43.0%) patients; 16 times in one (0.93%) patient; 11 times in two (1.8%) patients; and 10 times in four (3.7%) patients. Of the patients, 19 (17.8%) were sensitized to house dust mite, and 15 (14%) to pollen. Twenty (19.4%) patients were active smokers. The general characteristics of the patients are presented in Table 1 according to the presence of diagnostic delay.

Forty-seven (43.9%), patients with a strong clinical history of N-ERD were diagnosed solely based on their clinical history, without the need for an aspirin challenge test. Sixty (56.1%) patients underwent aspirin challenge testing, which confirmed the diagnosis of N-ERD. Thirty-nine (36.4%) patients had a delayed diagnosis. The mean diagnostic delay time for N-ERD was 7.4±6.6 (IQR: 2.0-12.0) years. The delay in diagnosis was not related to age (*P* = 0.514), sex (*P* = 0.878), allergy status (*P* = 0.137), smoking status (*P* = 0.148), eosinophil count at the time of clinician diagnosis (*P* = 0.316), total IgE (*P* = 0.919), and ACT score (*P* = 0.147). In addition, thyroid dysfunction was observed more frequently in the group with diagnostic delay (*P* = 0.021) (Table 1). Thyroid dysfunction was observed in 10 (9.35%) of the subjects. Among these, 7 (17.95%) were in the group with diagnostic delay, 6 (85.7%) were diagnosed with Hashimoto's thyroiditis, 5 (71.4%) presented with hypothyroidism, and 1 (14.3%) with hyperthyroidism. The patients had been diagnosed with CRSwNP, asthma, and NSAID hypersensitivity for an average duration of 14.9±9.6, 14.3±9.9, and 11.7±9.3 years, respectively. In the group without diagnostic delay, the mean duration of NSAID hypersensitivity was 9.6±8.4 (IQR: 3.0-15.0) years, and the mean duration of NSAID hypersensitivity + asthma was 9.1±7.4 (IQR: 3.0-14.0) years. According to the paired evaluation, the time since diagnosis was 12.9±9.3 (IQR: 5.0-20.0) years for the patients with asthma + CRSwNP, 10.3±7.8 (IQR: 4.0-15.0) years for those with asthma + NSAID hypersensitivity, and 10.6±7.9 (IQR: 4.0-16.0) years for those with CRSwNP + NSAID hypersensitivity (Table 2). N-ERD developed 2.9±5.0 years on average (IQR: 0.0-27.0) after the diagnosis of asthma and CRSwNP, and there was no significant difference between the groups with and without delay in diagnosis (*P* = 0.06).

At the time of inclusion into the study, the mean time elapsed since the clinician's N-ERD diagnosis was 7.1±6.9 (IQR: 1.0-10.0) years. If there had not been a diagnostic delay, the disease would have been diagnosed on average 9.8±7.8 (IQR: 3.0-15.0) years earlier. The mean time from the onset of symptoms for the first component of the N-ERD triad to the N-ERD diagnosis was 9.7±8.9 years (IQR: 2.0-15.7), and the mean time to actual diagnosis was 7.0±7.9 (IQR: 2.0-9.9) years (Table 3).

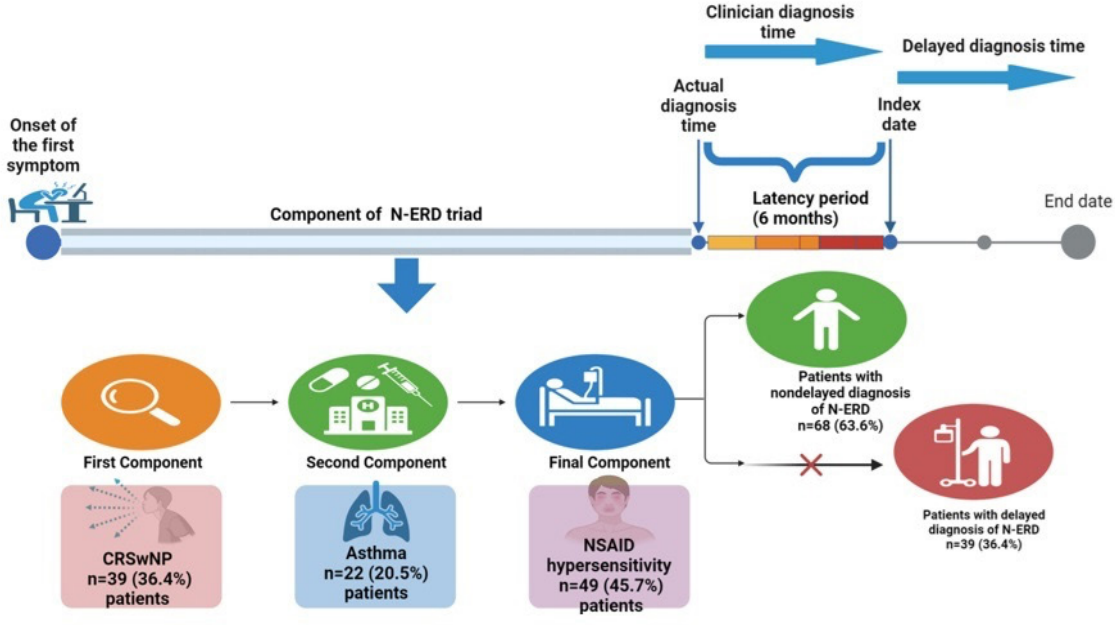

Figure 1. Visual summary

NSAID: non-steroidal anti-inflammatory drug, CRSwNP: chronic rhinosinusitis with nasal polyps, N-ERD: non-steroidal anti-inflammatory drug-exacerbated respiratory disease

Table 1. Characteristics of the patients according to the presence of a delay in N-ERD diagnosis

	Total (n = 107)	Diagnostic delay		
		Present (n = 39)	Absent (n = 68)	*P*
Age (year), mean±SD (median; IQR)	45.84±12.1 (46.0; 36.0-46.0)	48.5±11.7 (50.0; 40.0-57.0)	44.3±12.4 (42.0; 33.3-53.0)	0.070
Sex, n (%)				0.950
Female	69 (64.5)	25 (36.2)	44 (63.8)	
Male	38 (35.5)	14 (36.9)	24 (63.1)	
Comorbidity, n (%)				
Hypertension				0.814
Absent	89 (83.2)	32 (36.0)	57 (64.0)	
Present	18 (16.8)	7 (38.9)	11 (61.1)	
Diabetes mellitus				0.484
Absent	99 (92.5)	37 (37.3)	62 (62.7)	
Present	8 (7.5)	2 (25.0)	6 (75.0)	
Thyroid dysfunction				0.021*
Absent	97 (90.7)	32 (33.0)	65 (67.0)	
Present	10 (9.3)	7 (70.0)	3 (30.0)	
Coronary artery disease				0.463
Absent	103 (96.3)	37 (35.9)	66 (64.1)	
Present	4 (3.7)	2 (50.0)	2 (50.0)	
Malignancy				0381
Absent	101 (94.4)	36 (35.7)	65 (64.3)	
Present	6 (5.6)	3 (50.0)	3 (50.0)	
Smoking tobacco use, n (%)				0.168
Current	20 (19.4)	4 (20.0)	16 (80.0)	
Never	60 (58.3)	26 (43.3)	34 (56.7)	
Former	23 (22.3)	8 (34.8)	15 (65.2)	
Asthma inhaler treatment, n (%)				
ICS	21 (19.6)	6 (28.6)	15 (71.4)	-†
SABA	3 (2.8)	1 (33.3)	2 (66.7)	
ICS + LABA	63 (58.9)	26 (41.3)	37 (58.7)	
ICS + LABA + LAMA	9 (8.4)	2 (22.2)	7 (77.8)	
ICS + LABA + SABA	11 (10.3)	4 (36.3)	7 (63.7)	
ATAD, n (%)	54 (50.5)	18 (33.3)	36 (66.7)	
Absent	53 (49.5)	21 (39.6)	32 (60.4)	-†
100 mg	4 (3.7)	2 (50.0)	2 (50.0)	
300 mg	45 (42.1)	18 (40.0)	27 (60.0)	
500 mg	1 (0.9)	0 (0.0)	1 (100.0)	
600 mg	3 (2.8)	1 (33.3)	2 (66.7)	
Biological therapy, n (%)				0.915
Absent	82 (76.6)	29 (35.4)	53 (64.6)	
Mepolizumab	15 (14.0)	6 (40.0)	9 (60.0)	
Omalizumab	10 (9.3)	4 (40.0)	6 (60.0)	
Nasal polyp operation, n (%)				0.292
None	19 (17.8)	4 (21.0)	15 (79.0)	

Table 1. Continued

	Total (n = 107)	Diagnostic delay		
		Present (n = 39)	Absent (n = 68)	*P*
<3	42 (39.3)	16 (38.1)	26 (61.9)	
≥3	46 (43.0)	19 (41.3)	27 (58.7)	
Food allergy, n (%)				
Present	17 (15.9)	5 (29.4)	12 (70.6)	0.511
Absent	90 (84.1)	34 (37.8)	56 (62.2)	
Pollen allergy, n (%)				
Present	15 (14.0)	8 (53.3)	7 (46.7)	0.143
Absent	92 (86.0)	31 (33.7)	61 (66.3)	
House dust mite allergy, n (%)				
Present	19 (17.8)	4 (21.1)	15 (78.9)	0.124
Absent	88 (82.2)	35 (39.7)	53 (60.3)	
PFT				
FEV1, mean±SD (median; IQR)	82.1±17.0 (84.0; 74.5-95.5)	79.7±15.6 (82.0; 66.0-90.0)	83.5±17.7 (84.0; 75.0-98.0)	0.317
ACT, mean±SD (median; IQR)	19.5±5 (22.0; 15.3-24.0)	20.6±4.8 (22.0; 17.5-24.3)	18.8±5.0 (20.0; 14.0-22.0)	0.051
Serum total IgE level (UI/mL), mean±SD (median; IQR)	210.8±268.7 (113.0; 61.0-238.0)	204.0±205.2 (169.0; 66.5-260.5)	215.0±302.9 (102.0; 61.0-231.8)	0.513
Serum eosinophil count (cells/mm³), mean±SD (median; IQR)	514.4±401.8 (400.0; 215.0-700.0)	468.2±310.8 (400.0; 300.0-600.0)	541.7±447.0 (450.0; 200.0-700.0)	0.711

*$P < 0.05$; †statistical value could not be calculated because the number of cells with expected values below 5 was more than 25%.

SD: standard deviation, IQR: interquartile range, ICS: inhaler corticosteroid, LABA: long-acting ß2-agonist, LAMA: long-acting muscarinic antagonist, SABA: short-acting ß2 agonist, ATAD: aspirin therapy after desensitization, PFT: pulmonary function test, FEV1: forced expiratory volume in one second, FVC: forced vital capacity, ACT: asthma control test, IgE: immunoglobulin E

Table 2. Relationship between the time since disease diagnosis and delay in N-ERD diagnosis

Time since diagnosis (year), mean±SD (median; IQR)	Total (n = 107)	Diagnostic delay	
		Present (n = 39)	Absent (n = 68)
Asthma	14.3±9.9 (13.0; 7.0-22.0)	16.1±7.9 (15.0; 10.0-22.0)	13.3±10.8 (9.5; 4.3-22.0)
NSAID hypersensitivity	11.7±9.3 (10.0; 5.0-16.0)	15.4±9.7 (16.0; 8.0-20.0)	9.6±8.4 (8.5; 3.0-15.0)
CRSwNP	14.9±9.6 (15.0; 7.0-22.0)	17.4±8.4 (18.0; 10.0-22.0)	13.5±9.9 (11.5; 6.0-20.0)
Asthma + NSAID hypersensitivity (suspected diagnosis)	10.3±7.8 (9.0; 4.0-15.0)	13.5±7.4 (14.0; 7.0-18.0)	8.5±7.4 (6.5; 3.0-13.0)
Asthma + CRSwNP (suspected diagnosis)	12.9±9.3 (11.0; 5.0-20.0)	14.9±7.9 (14.0; 9.0-22.0)	11.6±9.7 (9.0; 3.0-20.0)
NSAID hypersensitivity + CRSwNP (suspected diagnosis)	10.6±7.9 (9.0; 4.0-16.0)	13.9±8.1 (14.0; 7.0-20.0)	8.7±7.2 (8.0; 3.0-14.5)

SD: standard deviation, IQR: interquartile range, NSAID: non-steroidal anti-inflammatory drug, CRSwNP: chronic rhinosinusitis with nasal polyps, N-ERD: non-steroidal anti-inflammatory drug-exacerbated respiratory disease

Table 3. Time from symptom onset to the diagnosis of N-ERD and actual and N-ERD diagnosis times according to the presence of diagnostic delay

	Total (n = 107)	Diagnostic delay	
		Present (n = 39)	Absent (n = 68)
Time since actual diagnosis (year)	9.8±7.8 (9.0; 3.0-15.0)	12.6±7.9 (11.0; 5.0-18.0)	8.2±7.3 (6.0; 3.0-11.0)
Time since N-ERD diagnosis (year)	7.1±6.9 (4.0; 1.0-10.0)	5.2±5.7 (3.0; 1.0-9.0)	8.1±7.3 (6.0; 3.0-11.0)
Time from symptom onset to actual diagnosis (year)	7.0±7.9 (5.0; 2.0-9.9)	6.5±7.8 (5.0; 3.0-7.0)	7.3±8.1 (5.0; 1.3-10.0)
Time from symptom onset to N-ERD clinician diagnosis (year)	9.7±8.9 (8.0; 2.0-15.7)	13.8±8.9 (12.0; 7.0-18.0)	7.3±8.0 (5.0; 1.3-10.0)

Data presented as mean±standard deviation (median; interquartile range).
N-ERD: non-steroidal anti-inflammatory drug-exacerbated respiratory disease

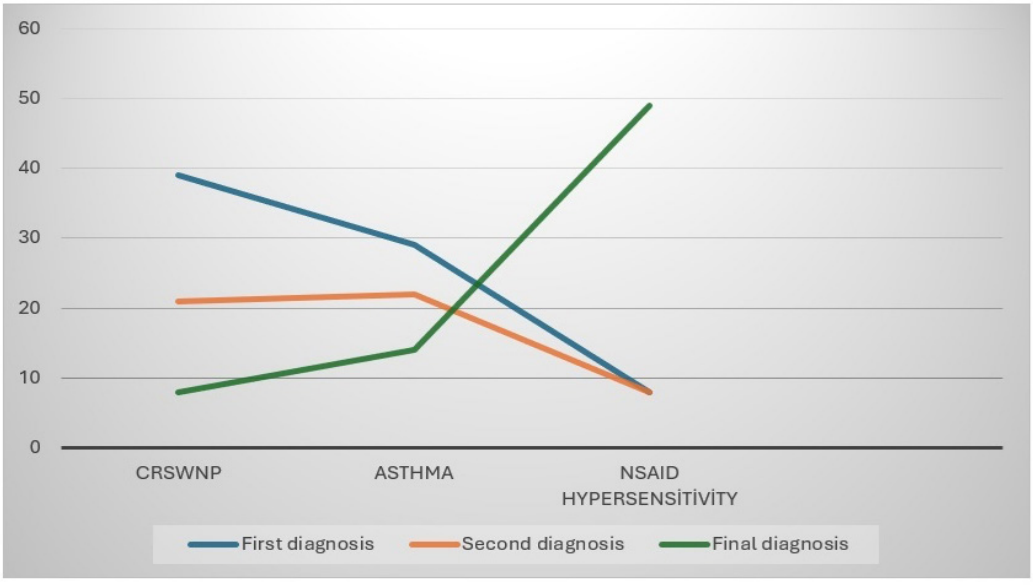

Figure 2. Chronological order of the N-ERD triad

NSAID: non-steroidal anti-inflammatory drug, CRSwNP: chronic rhinosinusitis with nasal polyps, N-ERD: non-steroidal anti-inflammatory drug-exacerbated respiratory disease

Of the patients in the group with diagnostic delay, 25 (64.1%) were female, and 14 (35.9%) were male. The mean age at which women received their first N-ERD diagnosis was 39.3±12.2 (IQR: 11.0-65.0) years, whereas this value was 38.2±10.4 (IQR: 19.0-65.0) years for men, with no significant difference found between the two (P = 0.774). The mean age at which the first symptoms began was 28.6±10.5 (IQR: 4.0-58.0) years, and there was no significant difference according to sex (P = 0.332).

Chronologically, the first diagnosis was CRSwNP in 39 (36.4%) patients, asthma in 29 (27.1%), asthma + CRSwNP in 19 (17.7%), and NSAID hypersensitivity in eight (7.4%). The second diagnosis was asthma in 22 (20.5%) patients, CRSwNP in 21 (19.6%), and NSAID hypersensitivity in eight (7.4%). The final diagnosis was NSAID hypersensitivity in 49 (45.7%) patients, asthma in 14 (13.0%), CRSwNP in eight (7.4%), simultaneous asthma + NSAID hypersensitivity following the CRSwNP diagnosis in 12 (11.7%), simultaneous CRSwNP + NSAID hypersensitivity following the asthma diagnosis in 11 (10.2%), and simultaneous asthma + CRSwNP following the NSAID hypersensitivity diagnosis in two (1.8%) (Figure 2). The remaining 10 (10.2%) patients were diagnosed with CRSwNP, asthma, and NSAID hypersensitivity simultaneously.

DISCUSSION

In our study, we found that 36.4% of patients diagnosed with N-ERD experienced an average diagnosis delay of seven years, and this was observed more frequently in women (64.1%). Consistent with previous reports, we determined that N-ERD usually started in the third or fourth decade of life and had a higher prevalence among women. The mean age at the diagnosis of N-ERD was previously reported to be 46 years by Roland et al.[14] and 30 years by Szczeklik et al.[9]

In a study undertaken by Kshirsagar et al.,[15] 24.4% of patients diagnosed with N-ERD had a diagnosis delay of one year or more from the onset of symptoms, and patients with allergies were found to be diagnosed earlier. The authors explained this finding by suggesting that patients with allergies possibly consult specialists more frequently. However, no relationship was detected between diagnostic delay and various factors, including age, sex, race, obesity, alcohol consumption, tobacco use, diabetes mellitus, and sleep apnea. In contrast, we did not find any relationship between allergy status and diagnostic delay. This may be because they evaluated the allergy status of their patients based on the International Classification of Diseases codes in their files, while we record allergies based on the findings from the anamnesis, skin prick tests, and specific IgE blood test results. Similar to the study by Kshirsagar et al.,[15] we determined that age, sex, smoking, comorbidities, number of nasal polypectomies, and treatment methods used were not risk factors for delayed diagnosis of N-ERD. Furthermore, we observed that the total IgE and eosinophil levels of the patients in the group without diagnostic delay were slightly higher, although the difference did not reach statistical significance. This may also be the reason why patients are referred to allergists in a timely manner. Our study additionally revealed that individuals with a diagnostic delay had a higher prevalence of thyroid dysfunction among comorbidities. Among the comorbidities observed in our study, thyroid dysfunction, particularly hypothyroidism and Hashimoto's thyroiditis, was found to be more common in patients with delayed N-ERD diagnoses. This observation aligns with previous studies reporting a higher prevalence of Hashimoto's thyroiditis in women, especially those with non-allergic asthma.[16] Thyroid dysfunction, including hypothyroidism and hyperthyroidism, can present with respiratory manifestations such as respiratory muscle weakness, upper airway obstruction, and dyspnea. These symptoms may obscure or mimic the clinical presentation of N-ERD, complicating the diagnostic process.[17-19]

The majority of patients with N-ERD first develop chronic rhinosinusitis, followed by asthma, and then aspirin or NSAID sensitivity, conditions that gradually progress over years.[10] In a previous study, Szczeklik et al.[9] first detected rhinitis, then followed by asthma, aspirin intolerance, and nasal polyposis in their patients. In the current study, we found that upper respiratory tract symptoms appeared first, followed by asthma, and finally NSAID hypersensitivity. While some patients were diagnosed with NSAID hypersensitivity first (7.4%), others (11.2%) received all three diagnoses simultaneously. The literature contains research in which N-ERD phenotyping was performed on patients according to their clinician diagnoses,[20] but there is still a clear need for further studies to investigate the effect of the initial condition of patients on disease severity and progression to offer a better understanding of the heterogeneous structure of N-ERD.

A recent study found that the mean delay in diagnosis three years for patients who were unaware of NSAID hypersensitivity.[20] NSAID hypersensitivity may be underdiagnosed due to the lack of routine aspirin challenge testing in asthmatic patients who do not report a history of drug allergies. However, the delayed identification of NSAID hypersensitivity can have direct consequences for patients. Marquette et al.[2] reported that 25% of asthmatic patients diagnosed with N-ERD required urgent mechanical ventilation. In a recent study, patients with a delayed diagnosis of N-ERD were found to be more likely to receive two or more courses of systemic steroids.[20]

Berges-Gimeno et al.[10] determined that N-ERD developed in patients within an average of 13 years from the onset of the first symptom. In our study, N-ERD developed within an average of seven years from the onset of the first symptom. At the time of the emergence of the first symptom, it may be difficult for clinicians to anticipate that a patient will develop N-ERD. In our study, patients with asthma and CRSwNP, having completed the N-ERD triad, were diagnosed with NSAID hypersensitivity after an average of three years. The diagnosis of N-ERD should be excluded by performing the aspirin challenge test in appropriate patients presenting with asthma and CRSwNP. Although clinicians may be hesitant due to potential reactions with the aspirin challenge test, studies have shown that it is a reliable method if performed under the supervision of qualified professionals according to defined protocols.[1] The emergence of a classification system encompassing all phenotypes, including incomplete and pseudoforms of N-ERD, is deemed crucial.[21,22] Moreover, early diagnosis can facilitate the consideration of treatment interventions such as ATAD and biological therapies, known for their effectiveness.

While raising awareness may reduce diagnostic delays, the retrospective nature of this study limits its scope, highlighting the need for future research.

CONCLUSION

While raising awareness may reduce diagnostic delays, the retrospective nature of this study limits its scope, highlighting the need for future research. Despite recent significant advances in understanding the pathomechanism of N-ERD, this study revealed that the diagnosis of patients was delayed in clinical practice. The observed delay in diagnosis may be attributed to the low awareness of N-ERD among non-allergist physicians, such as pulmonologists and otolaryngologists the physicians' reluctance to perform aspirin provocation tests, as well as the limited availability of these tests in all centers. The other reasons for delayed diagnosis could be patients' non-compliance and sociocultural or socioeconomic issues. Failure to initiate proper treatment in patients with N-ERD may lead to an increased frequency of asthma exacerbations, nasal polyp recurrence, additional surgery requirements, and severe NSAID hypersensitivity reactions.

Ethics

Ethics Committee Approval: The study protocol was approved by the Hacettepe University Hospital (approval number: 24/239, date: 02.04.2024).

Informed Consent: Retrospective study.

Presented in: This manuscript was previously presented as an oral presentation at the European Academy of Allergy and Clinical Immunology (EAACI) Congress 2024 and the Turkish Thoracic Society Congress.

Footnotes

Authorship Contributions

Surgical and Medical Practices: M.C., H.K., Ç.T., Concept: M.C., E.D., G.K., A.F.K., Design: M.C., A.F.K., G.K., E.D., Data Collection or Processing: M.C., H.K., Ç.T., Analysis or Interpretation: M.C., H.K., Ç.T., Literature Search: M.C., H.K., Ç.T., Writing: M.C., E.D., G.K., A.F.K.

Conflict of Interest: Gül Karakaya has performed lectures or acted as an advisor for Novartis, GSK, AstraZeneca, Takeda, and Acino. Other authors declare no conflict of interest.

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Letter to the Editor

Evaluation of Cases of Long-Coronavirus Disease-2019 Reported as being Readmitted to Intensive Care Units Due to Acute Respiratory Failure: Correspondence

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DEAR EDITOR,

We would like to comment on the publication "Evaluation of Long-Coronavirus Disease 2019 Cases Readmitted to Intensive Care Units Due to Acute Respiratory Failure: Point Prevalence Study."[1] The evaluation of long-term Coronavirus disease-2019 (COVID-19) patients was the goal of a study conducted by the Turkish Thoracic Society's Intensive Care and Respiratory Care Unit. The sample consisted of 41 individuals with an average age of 66 years who were recruited from 11 different centers. The study found that heart failure (27%) was the most common comorbidity, followed by high blood pressure (27%), diabetes (51%), lung and other malignancies (34%), and diabetes (51%). Eighty percent of the patients had received COVID-19 vaccination. Participants experienced mild respiratory failure due to hypoxia despite vaccination, and tests like the Acute Physiology and Chronic Health Evaluation II and Sequential Organ Failure Assessment scores showed a markedly severe illness in this group.

Although this study provides valuable insights into the characteristics and treatment response of patients with long-term COVID-19, it also has several obvious shortcomings and weaknesses. The relatively small sample size (41 patients) prevented generalizability of the results. Furthermore, the lack of a control or comparison group made it difficult to draw clear conclusions about the effectiveness of the treatment or the long-term outcomes of the patients. The study relied primarily on observational data. This may introduce bias due to differences in treatment protocols among participating centers. In addition, the cross-sectional study design may limit our understanding of the long-term progression of COVID-19 symptoms and associated complications over time.

Increasing the sample size and adding a control group can improve the robustness of the results in subsequent research. Long-term cohort studies could offer more thorough insights into COVID-19's long-term tendencies of COVID-19, which could enhance our comprehension of the acute and chronic stages of the illness. Involving various geographic and demographic groups may aid in identifying variations in disease presentation and consequences, resulting in the development of suitable therapies. Standardizing treatment plans and diagnostic standards throughout facilities may also make it possible to compare and assess data collected more accurately.

There is great potential for novel approaches to long-term COVID-19 management that use interdisciplinary methods. Using modern imaging techniques and biomarkers, researchers can investigate the underlying pathophysiology of long-

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term COVID-19 symptoms, potentially revealing particular targets for therapeutic intervention. Furthermore, research into rehabilitation programs, mental health assistance, and interdisciplinary care strategies could help inform long-term COVID-19 management procedures. Given the ongoing pandemic and the possibility of new mutations, more research into the long-term effects of COVID-19 will be critical in shaping healthcare policies and treatment frameworks in the post-pandemic period.

Footnotes

Authorship Contributions

Surgical and Medical Practices - Concept - Design - Data Collection or Processing - Analysis or Interpretation - Literature Search - Writing: All authors contributed equally to all contribution sections.

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Letter to the Editor

In Response to: Evaluation of Long-Coronavirus Disease-2019 Cases Readmitted to Intensive Care Units due to Acute Respiratory Failure: Point Prevalence Study

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TO THE EDITOR,

I greatly appreciate the Thoracic Research and Practice policy of having an open forum where scientific disagreements can be discussed. We would like to thank the reviewer for their insightful comments on our study evaluating patients with Long-Coronavirus disease re-admitting intensive care unit (ICU) due to acute respiratory failure (ARF).[1]

The letter raised interesting points concerning the generalizability of the results due to the small sample size and study design. Since we aimed to evaluate the ICU re-admission of long-Coronovirus disease (the symptoms lasting for 4-12 weeks); Coronavirus disease-2019 (COVID-19) patients who were discharged and re-admitted to the ICU due to ARF were included in the study.[2] Therefore, the inclusion criteria inevitably limited the study population. In addition, even if the study was multicenter, larger sample sizes were difficult to achieve in a cross-sectional, 1-day point prevenance study. However, despite the small sample size, this study revealed observational data (demographic and radiologic features, ICU data) of this specific group of patients in various regions and approaches such as treatment.

As the letter mentioned, there was a lack of comparison groups and observational data in the current study. We agree and also mentioned in the conclusion section that it is not possible to evaluate and define the risk factors for the long-term effects of COVID-19 in a cross-sectional study. However, this study serves as a preliminary investigation that could lead to more detailed prospective cohort and case-control studies.

In summary, the current preliminary study provides snapshot features of on-going symptomatic COVID-19 cases. In order to reveal the association between ICU re-admission and the presence of comorbidity, malignancy risk analysis should be performed through the control group.

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