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From the Editor

Dear Esteemed Readers,

As we approach the conclusion of 2023, we take great pleasure in presenting the final issue of the year. This compilation comprises a selection of articles meticulously chosen to engage and captivate healthcare professionals, with a special emphasis on primary care physicians. Our unwavering commitment is to provide an invaluable compass for those navigating the ever-evolving landscape of healthcare.

In this issue, we are proud to showcase six research articles and two reviews that shed light on groundbreaking advancements across critical healthcare domains. From exploring geographical trends in breast cancer mortality and the correlation between caregiver anxiety and malnutrition risk to delving into the perspectives of patients and caregivers receiving home health care, the articles featured cover a diverse array of topics. Notably, our exploration extends to the relationship between smartphone addiction levels, psychological symptoms, and sleep quality among medical students, as well as the potential impact of improving female students' physical fitness index on reducing cardiovascular risk.

As the foremost primary care journal in Turkey, we consider it a profound honor to serve as an indispensable resource for healthcare professionals in the region. We express our sincere gratitude for your continued interest in our journal, and we remain committed to delivering the latest research findings and evidence relevant to primary care.

We invite you to delve into the thought-provoking articles within these pages, trusting that they will both intrigue and inspire you. Your engagement and support drive our mission to foster knowledge and innovation in the field of primary care.

Stay tuned for our upcoming edition, which promises to be equally enlightening and thought-provoking.

Prof. Dr. Ahmet Keskin

ANKARA MEDICAL JOURNAL

Contents

ANKARA MEDICAL JOURNAL

Research Article

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GEOGRAPHICAL DISTRIBUTION AND TRENDS OF WOMEN BREAST CANCER MORTALITY IN TURKEY BETWEEN 2009-2019

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Abstract

Objectives: Breast cancer is the most common malignancy in women all over the World. It is in the first line, causing deaths because of cancer in women worldwide. However, its progress differs regarding the counties' socioeconomic and cultural features. The aim of this study is to estimate breast cancer mortality rates in Turkish women by geographic region and to evaluate 11-year mortality trends.

Materials and Methods: Joinpoint Regression Analysis was used to estimate the trends of mortality from breast cancer by gender and age groups for every geographic region. Also, we used the world standard population (100,000 women) was used to estimate the age-standardized mortality rates as a reference to calculate age-standardized mortality rates.

Results: We found that nearly 39,000 women died from breast cancer between the years 2009-2019. During this 11-year period, the age-standardized mortality rate in Turkey was 6.84 per 100,000 women in 2009, while it rose up to 8.16 in 2019 with a significant increase of 1.78 per year (Confidence Interval: 0.57:3.00) p=0.009). This change was observed especially in TR2, TR7, TR9, TRA, TRB and TRC regions. According to the age groups examined, significant increases were observed in all age groups in Turkey.

Conclusion: Breast cancer is still a very important health problem in Turkish women of all ages. It is essential to take measures to reduce the breast cancer mortality rate and increase early diagnosis opportunities in our country.

Keywords: Breast cancer, mortality rate, joinpoint regression analysis.

Introduction

In the World, cancer is the most common cause of death worldwide. It caused approximately 10 million deaths in 2020. Cancer was found to be the most common cause of mortality in 57 of 127 nations analyzed, including Turkey. According to the same research, by the turn of the century, cancer-related deaths will rise and overtake all other causes of early death in the majority of countries.[3]

Breast cancer is the most commonly diagnosed cancer in terms of new cancer cases in 2020. It is the most important public health problem, leading to the most frequent cancer-related deaths among women worldwide. In 2020, the World Health Organization reported that there were 2.2 million (25.4%) cases of breast cancer in women, and in the same year, globally, breast cancer-related deaths accounted for 15.5% (684 996) of total deaths.[1] The World Health Organization predicts that the incidence and deaths of breast cancer in women will double by 2040.[2]

Due to delayed diagnosis and limited access to cancer care, breast cancer survival rates in low- and middle-income countries are lower than those in high-income nations. Because of improvements in prevention, screening, and treatment, there have been fewer fatalities from cancer in several parts of the world, particularly in high-income nations. In 12 different parts of the world, breast cancer also ranks first in terms of cancer deaths.[1]

Breast cancer was identified as the leading cause of death for women in a 2020 study carried out in Turkey. The study indicates that the incidence of breast cancer has increased over time.[4] When only taking into account deaths in city and district centers between 1987 and 2008, the average annual standardized death rate was reported by Doğan et al. in 2014 to be 11.9 (per 100,000 women).[5] According to Teker et al.'s study, there has been an increase in cancer-related fatalities in recent years.[5,6] According to Li, one of the most significant indicators for tracking the health of breast cancer patients is mortality.[7] Trend analysis is a method for determining patterns of change or trends in a variety of observations, both globally and locally, in order to guide local control methods.

This study aimed to evaluate trends in breast cancer death rates among women in Turkey over time by years, age groups, and geographic regions.

Materials and Methods

An ecological study was carried out, taking into account all women breast cancer fatalities that occurred in Turkey from 2009 to 2019. The Turkish Statistical Institute has been compiling and publishing annual death

records at the national level in Turkey since 1931. Prior to 2009, only the province and district centers were included in the death records; however, in the years that followed, the death lists from the villages were added, and the entire country of Turkey was covered. The International Classification of Diseases, Tenth Revision (ICD-10) has also been utilized since 2009 in the classification system for causes of death.[8] The C50 code from the ICD-10 revision was used to assess the cause of death from breast cancer in women. Statistical information on breast cancer deaths is available from 2009 to 2019 and is segmented by year and age in 12 areas for each year in 5 age groups up to 85+ years.

Data from TurkStat is based on the death notification system and previous data generated by the Ministry of Health, General Directorate of Public Health. The breast cancer mortality data was obtained through an official request to the relevant institution, which did not impose any restrictions on information sharing and analysis. For this reason, ethics committee approval was not received.

The General Directorate of Public Health of the Ministry of Health and prior data are the foundations for TurkStat's statistics. Data on breast cancer deaths were obtained by asking for an official petition from the relevant institution; no restrictions were placed on the sharing and analysis of information.[9] Specific rates were calculated for different age groups (<45, 45-54, 55-64, 65-74, and 75+) based on data on deaths considering year and region.

Age-standardized mortality rates (ASMR) were calculated using the direct standardization approach and the world standard population as a reference. Rates are given in terms of fatalities per 100,000 people. For the age range of 0 to 85, age-specific mortality rates were computed across 5-year intervals. By accounting for population age structure variations, this method eliminates the impact of historical events on the age structure and is used to compare different cities or nations.[10] For each region, the same strategy was employed.

Statistical analysis

A statistical modeling method called Joinpoint Regression Analysis (JRA) uses piecewise linear regression to describe the relationship between two variables. In epidemiological studies, this method is frequently used to model time trends in mortality or incidence series. In the JRA, the change point is defined as a "joinpoint," and in 2000, the Grid Serch method proposed by Lerman was used to find these change points by Kim et al.[11] The analysis starts with the minimum point of change and tests each time whether the change point is significant and should be added to the model. The number of change points is determined by the Monte Carlo Permutation test.[11] The final model obtained shows optimal changeover points where the ratio does/is not significantly changed. For each statistically significant change point, annual percentage change (APC), average annual percentage change (AAPC), and their 95% confidence intervals (CI) are calculated. AAPC is the average of the APC values at all breakpoints. Analyzes were performed using the Joinpoint Regression Program (version

4.9.1.0–2021) prepared by the US National Cancer Institute (National Cancer Institute, 2021). A value of P<0.05 was considered statistically significant.

Nomenclature of Territorial Units for Statistics (NUTS): In order to gather and develop regional data, analyze the socioeconomic makeup of the regions, set regional policies, and create a database that can be compared to the European Union Regional Statistical System, NUTS definitions are created (Figure 1).

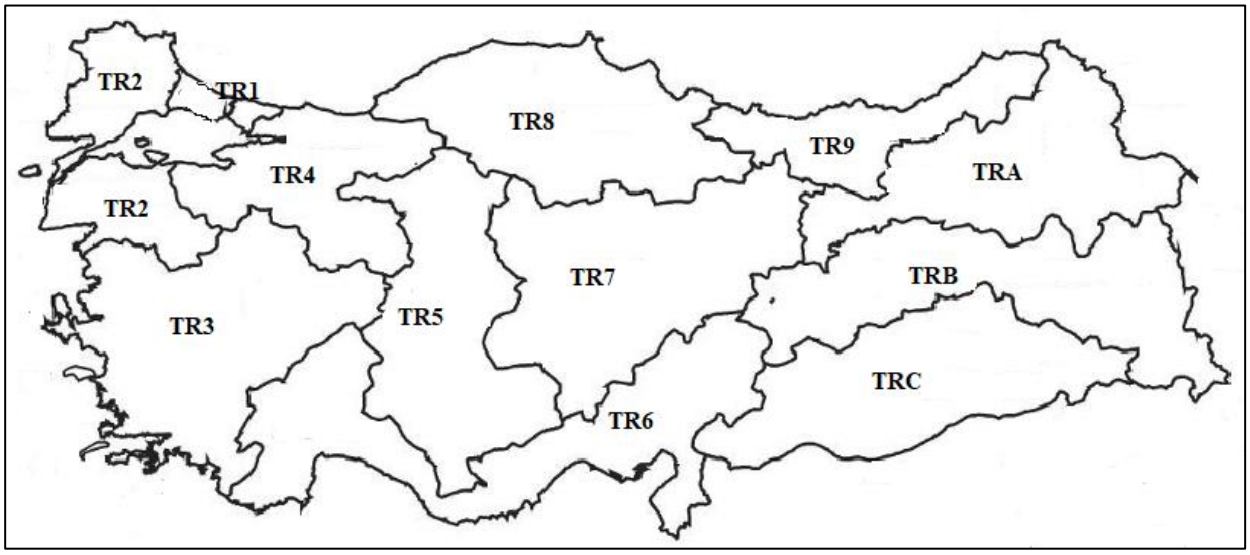


Figure 1. 12 regions in NUTS1 in Turkey

Region Classification of Nomenclature of Territorial Units for Statistics definitions is created in order to gather and develop regional data, analyze the socioeconomic make of the regions, create regional policies, and create a database that can be compared to the Regional Statistical System of the European Union. Figure 1 depicts of Turkey's 12 regions (TR1-Istanbul; TR2- Western Marmara; TR3- Aegean; TR4- Eastern Marmara; TR5- Western Anatolia; TR6- Mediterrenian; TR7- Central Anatolia; TR8- Western Black Sea; TR9- Eastern Black Sea; TRA- Northeastern Anatolia; TRB- Central Eastern Anatolia; TRC- Southeastern Anatolia.

Results

In Turkey, approximately 39000 women died from breast cancer in the period of 2009-2019. The ASMR rose from 6.84/100,000 in 2009 to 8.16/100,000 in 2019. When evaluated according to regions, annual ASMR increases were 2.28 in the TR1 region, 4.03 in the TR7 region, 2.94 in the TR9 region, 4.71 in the TRA region, 5.63 in the TRB region and 4.26 in the TRC region (Table 1).

Table 1. Age-standardized mortality rate and average annual percentage change (AAPC) of women breast cancer mortality according to region and year, 2009:2019.

Region	ASMR			
	2009	2019	AAPC	95%CI
TR1	10.60	10.14	-0.44	-1.65;0.80
TR2	6.63	8.75	2.81*	0.48;5.20
TR3	6.65	7.76	1.56	-0.55;3.70
TR4	8.08	9.19	1.30	-0.84;3.50
TR5	7.79	8.24	0.56	-0.44;1.58
TR6	6.52	7.87	1.89	-0.25;4.08
TR7	5.04	7.47	4.03*	0.62;7.55
TR8	5.66	6.23	0.96	-1.05;3.10
TR9	4.92	6.59	2.94*	0.23;5.73
TRA	4.51	7.22	4.71*	0.98;8.57
TRB	4.19	7.42	5.63*	2.48;8.88
TRC	3.77	5.71	4.26*	0.02;8.67
Turkey	6.84	8.16	1.78*	0.57;3.00

ASMR: Age-Standardized Mortality Rates; CI: Confidence Interval *Significant change

According to the Joinpoint Regression Analysis, a statistically significant increase in deaths from breast cancer was observed during this period (AAPC:1.78 (CI: 0.57:3.00) p=0.009). When evaluated by regions, significant increases were observed in the TR2 region until 2013, in the TR5 region until 2012, and in the TRC region until 2017. Non-significant decreases were observed for all three regions from these years until the end of the period (Table 2, Figure 2).

According to the age groups examined, significant increases were observed in all age groups in Turkey. When the determined age groups were examined according to the regions, it was seen that there were significant increases, especially in the 65 and over age groups, according to the results obtained. Breast cancer death rate in women is strongly associated with age, which is the highest in the elderly population (Table 3, Figure 3). There were decreases only in the 55 and over age group in the TR1 region, in the 45-54 age group in the TR8

region, in the 45-54 age group in the TR9 region, and in the 65-74 age group in the TR5 region, although they were not statistically significant.

Table 2. Annual rate of women breast cancer mortality between 2009-20019.

	AAPC(95% CI) (2009-2019)	Period I		Period II	
		Years	APC (95% CI)	Years	APC (95% CI)
Overall	1.78 (0.57;3.00) (p=0.009)				
TR1	-0.47 (-1.59;0.67) (p=0.372)				
TR2	3.61 (0.48;6.84) (p=0.023)	2009-2013	9.22 (0.5;18.65) (p=0.040)	2013-2019	0.03 (-3.12;3.28) (p=0.981)
TR3	1.65 (0.15;3.17) (p=0.034)				
TR4	1.37 (-0.36;3.14) (p=0.107)				
TR5	1.03 (-0.77;2.86) (p=0.263)	2009-2012	4.58 (-2.32;11.98) (p=0.016)	2012-2019	-0.45 (-1.75;0.86) (p=0.428)
TR6	1.95 (0.15;3.77) (p=0.037)				
TR7	4.14 (1.83;6.51) (p=0.003)				
TR8	1.13 (-0.39;2.68) (p=0.127)				
TR9	3.51 (2.56;4.47) (p<0.001)				
TRA	4.68 (0.86;8.63) (p=0.021)				
TRB	5.63 (2.43;8.93) (p=0.003)				
TRC	3.72 (-0.52;8.15) (p=0.086)	2009-2017	7.19 (4.94;9.49) (p<0.001)	2017-2019	-9.06 (-28.92;16.35) (p=0.382)

CI: Confidence Interval; AAPC: Average Annual Percent Change; APC: Annual Percent Change.

Table 3. Women breast cancer mortality rates (100,000) and average annual percentage change (AAPC), by age groups, in Turkey and region, 2009-2019.

Region	<45 years of age			45-54 years of age			55-64 years of age			65-74 years of age			>74 years of age		
	2009	2019	AAPC	2009	2019	AAPC	2009	2019	AAPC	2009	2019	AAPC	2009	2019	AAPC
TR1	4.70	5.05	0.73	19.53	23.98	2.07	32.64	31.94	-0.22	52.00	45.08	-1.42	95.88	88.11	-0.84
TR2	3.66	5.93	4.94	16.53	21.53	2.68	23.41	28.29	1.91	28.49	36.76	2.58	33.93	57.41	5.40*
TR3	4.16	4.51	0.82	15.18	18.26	1.87	20.84	24.33	1.56	17.04	21.33	2.27*	43.09	61.35	3.60*
TR4	4.99	5.41	0.81	18.06	20.50	1.27	26.15	31.52	1.89	35.29	40.41	1.36	45.57	63.51	3.38
TR5	3.97	4.84	2.01	16.00	18.87	1.66	24.49	26.60	0.83	34.98	34.92	-0.02	63.00	63.51	0.08
TR6	3.53	5.42	4.37*	16.53	17.83	0.76	22.18	25.19	1.28	25.84	33.67	2.68*	33.76	53.62	4.74*
TR7	3.43	5.13	4.09	13.03	18.42	3.52	15.64	24.71	4.68	18.58	30.25	5.00*	26.70	50.16	6.51*
TR8	3.76	4.57	1.97	16.82	13.56	-2.13	16.33	20.82	2.46	20.15	24.14	1.82	32.34	45.26	3.42
TR9	4.13	3.99	-0.34	14.55	18.23	2.28	14.30	19.11	2.94	15.86	27.28	5.57*	23.55	46.54	7.14*
TRA	2.85	4.28	4.14	8.72	21.63	9.51*	14.00	22.75	4.97	29.66	42.94	3.77	36.89	38.78	0.50
TRB	3.59	4.46	2.20	9.17	22.04	9.16*	13.37	23.40	5.76	14.07	26.12	6.38*	17.93	45.82	9.84*
TRC	3.40	4.81	3.55	10.19	16.91	5.19*	12.36	21.46	5.67	15.65	24.53	4.59*	19.31	36.85	6.67*
Turkey	4.00	4.90	2.05*	15.72	19.40	2.13*	21.84	26.06	1.78*	28.84	33.84	1.61*	44.49	58.48	2.77*

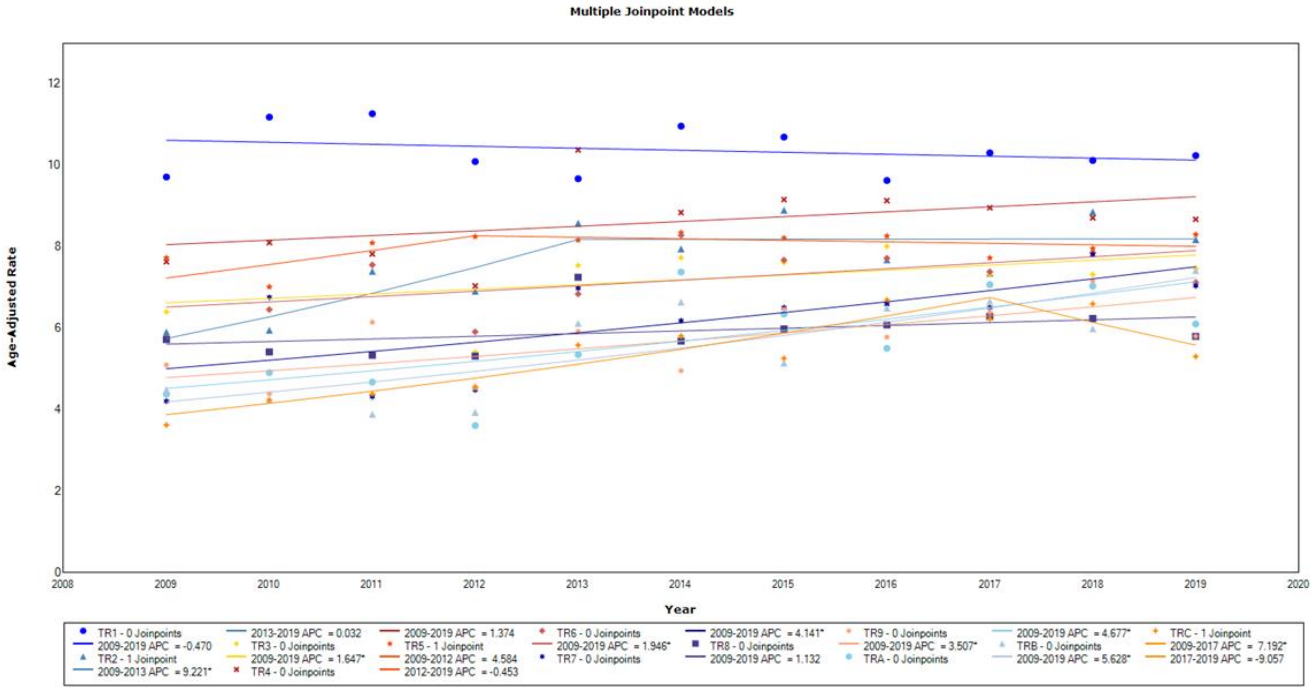
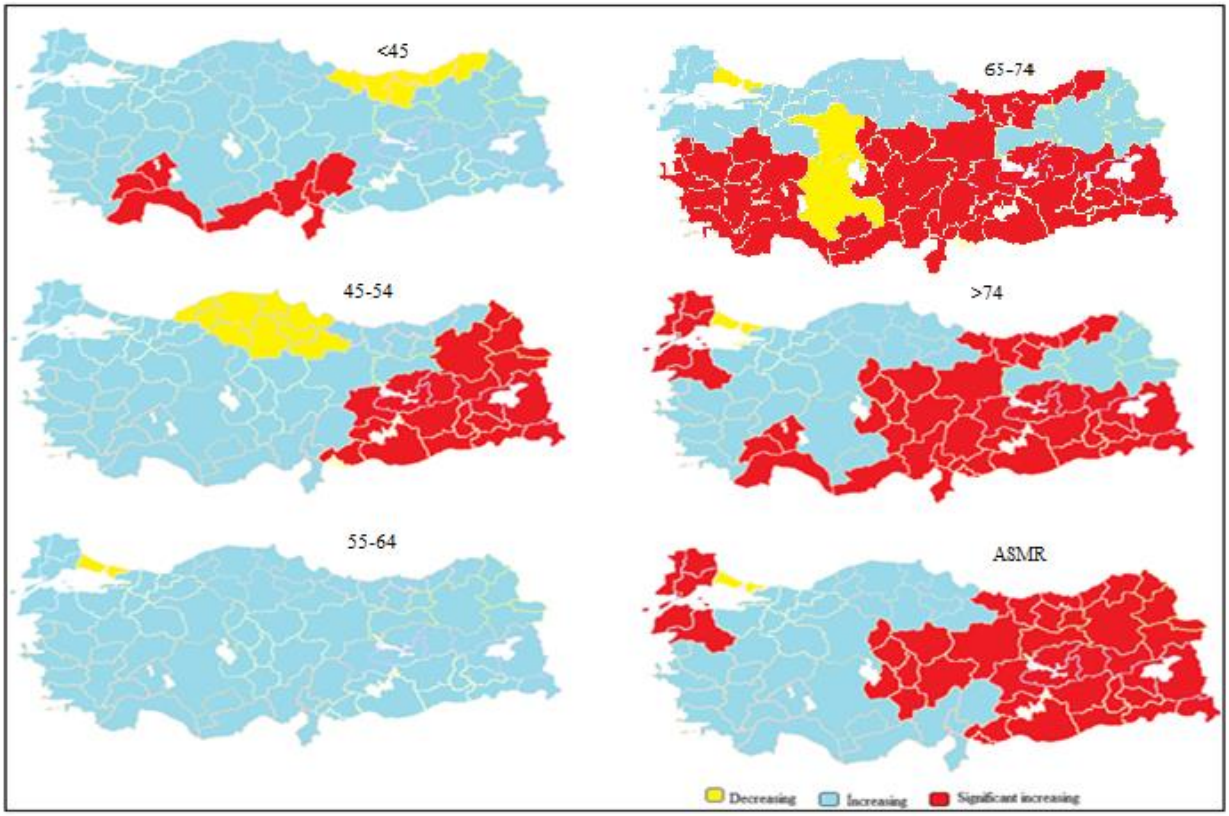


Figure 2. Trends in mortality from women breast cancer mortality in Turkey, results of JRA, 2009–2019



(ASMR: Age-standardized mortality rate.)

Figure 3. Trend of women breast cancer mortality, according to age group, for Turkey and its region, 2009-2019

Discussion

In this study, breast cancer mortality trends in women in Turkey and geographical regions from 2009 to 2019 were evaluated. The results show a significant annual increase of 1.78% in breast cancer-related deaths between 2009 and 2019. It has been observed that there are inequalities in breast cancer deaths by geographical regions. It was determined that the highest significant annual increase was in the Central Eastern Anatolia region, with 9.84%.

In contrast, Istanbul, one of 12 geographical regions with a decreasing trend in mortality rates, is located in the Western part of the country. This region has the lowest poverty rates and the highest oncological workforce compared to the eastern region. Therefore, easier and quicker access to health services and more opportunities to diagnose cancer in the population living in Istanbul may have a positive effect on early diagnosis of cancer.

Socioeconomic determinants that influence disparity in breast cancer mortality include poverty, culture, and social injustice. Poverty is a critical social factor driving health inequality.[12] Low-income women have significantly lower breast cancer screening rates, a higher probability of late diagnosis, and often receive inadequate and different treatment, resulting in higher death rates from breast cancer.[13]

It can be thought that the high mortality rates among people living in underdeveloped regions are associated with limited access to diagnosis and treatment opportunities and also the lower quality of health services and information about cancer. According to studies, breast cancer survival rates are lower in low- and middle-income countries due to such disparities, late diagnosis and poor access to cancer care compared to high-income countries. In high-income countries, successful screening programs and effective treatment and care have led to reductions in breast cancer-related deaths. Conversely, breast cancer-related deaths have increased in low- and middle-income countries.[14]

According to the results of a study covering European Union countries, the death rate due to breast cancer, which was 17.9 per hundred thousand in 2002, decreased to 15.2 per hundred thousand in 2012. The greatest regression was observed in the age group 49 years and younger. It was stated that early diagnosis, effective treatment methods and regular screenings reduce the deaths from breast cancer in Europe.[15]

In another study conducted in 24 EU countries, including the United Kingdom, it was stated that breast cancer deaths tend to decrease in all countries except Croatia, France and Poland.[16]

It is conceivable that the improvement in life expectancy in Istanbul may not be accompanied by healthier habits, access to health services and preventive medicine. Because the opportunities to access health services and information sources about health and economic standards are higher than in the eastern parts of the country, mortality rates tend to decrease in Istanbul.

The aim of cancer screening in our country is to reduce cancer-related deaths in the target population. Screenings are carried out free of charge in primary healthcare institutions, including Cancer Early Diagnosis, Screening and Training Centers (KETEM), Community Health Centers, Healthy Life Centers, Family Health Centers, and Mobile Cancer Screening Vehicles. KETEM enables the diagnosis and treatment of cancer in active stages by providing the importance of early diagnosis and public awareness. The breast cancer screening program for early detection of breast cancer in Turkey was started in 2012. The program includes the evaluation of women aged 40-69 with mammography every two years.[17. Early] diagnosis and screening both prevent deaths and improve the disease with simpler and cheaper treatments.

This screening practice tends to increase correct and early cancer diagnosis and consequently decreases death rates. Therefore, the higher mortality rate in the eastern regions and the higher mortality rate in older ages

may reflect the impact of the cancer screening program. However, it may be considered too early to see the benefits of this nationwide program to reduce mortality rates.

For community outreach, work has begun in areas such as educating Health supporters and ensuring patients adhere to their treatment regimens.

Family history is one of the most widely acknowledged risk factors for breast cancer. Breast cancer risk factors in families vary depending on the affected family members, their ages at diagnosis, and the number of unaffected women in the lineage. A woman is more likely to develop breast cancer if a first-degree relative has the disease when they are young or if they have multiple relatives who have the disease.[18] It can be thought that the high mortality rate in the eastern region of Turkey is due to genetic predisposition due to the high rate of consanguineous marriage, which is 4% in 2021, and most of them are in the East and Southeast parts of Turkey.[9]

In the breast cancer mortality rates in women in Turkey, a statistically significant increase was observed in seven regions (TR2, TR3, TR6, TR7, TR9, TRA, TRB) except TR1 in the 2009-2019 period, and non-significant increases were observed in other regions. The heterogeneity found in this study may be a reflection of economic factors, information sources about cancer, and changing situations to access health care for both early detection and adequate treatment.

Conclusion

In this study, regional differences in the breast cancer mortality trends over 11 years were found. Significant increases were observed during this period, especially in the eastern regions. When evaluated by age groups without regard to the geographical region, there are statistically significant increases in all age groups.

To our knowledge, this is the first study in Turkey to analyze breast cancer mortality trends by geographic region at the national level using JRA. Breast cancer is still a very important health problem in Turkish women of all ages. It is essential to take measures to reduce the breast cancer mortality rate and increase early diagnosis opportunities in our country.

Ethical Considerations: Ethics committee approval is not required for the study due to publicly available data has been used.

Conflict of Interest: The authors declare that they have no conflict of interest.

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ANKARA MEDICAL JOURNAL

Research Article

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IS THE RISK OF MALNUTRITION AMONG CARETAKERS RELATED TO CAREGIVER ANXIETY?

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Abstract

Objectives: This study aims to investigate the association between caregiver anxiety and the risk of malnutrition among caretakers.

Materials and Methods: A total of 200 caregivers whose patients were hospitalized in internal medicine clinics were included in a cross-sectional study. Patients were screened with the Nutritional Risk Screening (NRS) 2002 and divided into two groups: Patients with scores <3 (patients without nutritional support) and with scores ≥3 (patients with nutritional support). Caregiver distress was assessed using the State-Trait Anxiety Inventory (STAI).

Results: Anxiety scores were high for all caregivers (mean state anxiety score 42.4 (min=20, max=70, median=42) and median trait anxiety score 41 (min=25, max=64, mean=41.4). However, the anxiety scores of caregivers of patients with malnutrition did not differ from those of caregivers of patients without malnutrition(for NRS score < 3 versus ≥3, state anxiety score 41.4±10.1 versus 42.7±10.1, p=0.428, and trait anxiety score 40±12 versus 41±13, p=0.494, respectively). Caring for patients for more than one year without support or with minimal support was significantly associated with higher anxiety scores compared to caring for more than one year with support or caring for less than six months without support (for state and trait anxiety, 50.4±9.1 vs 41.0± 9.7, p < 0.001 and 49±10 vs 40±12, p < 0.001, respectively).

Conclusion: The absence of a support system and the duration of caregiving were found to be associated with an increased risk of caregiver anxiety, especially when both factors were present. However, no effect was observed on malnutrition status based on levels of anxiety among caregivers.

Keywords: Caregivers, malnutrition, anxiety, caregiver burden.

Introduction

Caregivers are essential in providing the emotional and physical needs of people who require additional care and support, and they are also referred to as caretakers. Caregivers may be involved in decision-making about the patient's progress in addition to their general responsibilities. These tasks may be of short duration or lifelong and have psychological implications. Torres et al. reported depression in 32% of elderly caregivers.[1] Hahn et al. also reported increased depressive signs in caregivers providing care for longer than two years. [2] In their study, Lai et al. found a significant prevalence of depression and anxiety in individuals affected by rare bone disease and their caregivers. The research revealed that up to 50% of caregivers suffered from anxiety symptoms.[3] Previous studies have shown that female gender, advanced age, and partner dissatisfaction are factors associated with increased risk for psychological distress among caregivers.[4-6] This underscores the importance of recognizing and addressing caregivers' psychological distress to promote their well-being.

Several scales exist to assess mood disorders in caregivers. The Hospital Anxiety and Depression Scale, the Center for Epidemiologic Studies Depression Scale, and the Beck Depression Inventory are among these instruments for measuring depression in caregivers.[7,8] The State-Trait Anxiety Inventory (STAI) consists of two questionnaires and can be used to assess caregiver distress.[9] Malnutrition encompasses the inadequate or excessive intake of nutrients, as well as imbalances in essential nutrient distribution and impaired utilization. The dual challenge of malnutrition comprises both undernourishment and overweight/obesity, along with noncommunicable diseases linked to diet.[10] The impact of malnutrition on both the quality of life and morbidity rates is significant, with potentially fatal consequences. The prevalence of this issue differs depending on the specific context or setting. The literature reports 14.5% malnutrition in elderly patients living at home and 20-50% in hospitalized patients.[11,12] Assessment of factors contributing to malnutrition is crucial, as it is an important predictor of mortality.[13]

Because caretaker well-being often depends on the caregiver, we hypothesized that the malnutrition status of the caretaker may be affected by caregiver anxiety. The purpose of this study is to investigate an association between caregiver anxiety and the risk of malnutrition among caretakers. Furthermore, we aimed to assess the factors contributing to caregiver anxiety.

Materials and Methods

This prospective cross-sectional study was conducted with patients hospitalized in internal medicine clinics between January 1, 2018, and June 31, 2018. The study protocol was approved by the hospital ethics committee and conducted in accordance with the Declaration of Helsinki. All participants gave their informed consent.

Subjects

The nutritional status of patients admitted to the internal medicine clinics was assessed using the Nutritional Risk Screening (NRS) 2002 by the same nutrition nurse, and two groups were formed: Patients with a score <3 (patients not requiring nutritional support) and with a score ≥3 (patients requiring nutritional support).

Caregivers were eligible to participate in the study if they were at least 18 years old, lived with patients in the same home, and had supervised or directly cared for them for at least 4 hours per day in the three months before participating in the study. Caregivers were excluded if they had cognitive impairment or an active psychiatric illness.

The State-Trait Anxiety Inventory (STAI), a widely used psychological inventory, was designed to assess and measure the level of anxiety in individuals. It consists of 20 items assessing state anxiety (STAI 1), which measures the current feelings of anxiety that an individual is experiencing, and 20 items measuring trait anxiety (STAI 2), which assesses the enduring trait of anxiety that individuals experience over the course of their lives. The State-Trait Anxiety Inventory, developed by Spielberger et al., is a reliable and valid instrument for assessing anxiety in both clinical and research settings.[9] The Turkish version is also available and was used in our study.[14] STAI scores are often categorized as indicating "absence or minimal anxiety" (20-37 points), "moderate levels of anxiety" (38-44 points), and "high levels of anxiety" (more than 44 points).[15] Caregivers of both groups were assessed using STAI 1 and STAI 2. STAI 1 was presented on the first day of hospitalization, and STAI 2 was presented on the second day. They also completed a questionnaire to obtain background information.

Caregiver anxiety scores were compared using two categories: Scores below three and scores equal to or above 3. Furthermore, caregiver characteristics were examined to identify groups at high and low risk for anxiety based on their relation with anxiety scores.

Statistical Analysis

Statistical analysis was performed using SPSS version 16 software. The normality of variables was tested using visual (histogram) and analytical methods (Kolmogorov-Smirnov/Shapiro-Wilk's test) to determine whether they were normally distributed. Data was analyzed by calculating the mean and standard deviation (SD) for normally distributed variables and the median and interquartile range (IQR) for non-normally distributed variables. Comparisons between normal distributions were made using the Student's t-test, while the Mann-Whitney U-test was used to compare non-normal continuous variables. Pearson and Spearman were used to test correlations between variables.

The correlation between the NRS score and the situational anxiety and trait anxiety scores was analyzed using Spearman correlation analysis, and the correlation coefficient (rho) was calculated. If the value of Rho is less than 0.2, it is considered to have a very weak correlation; between 0.2-0.4 indicates a weak correlation, between 0.4-0.6 suggests a moderate correlation, and above 0.6 represents a high correlation in academic studies. If the correlation coefficient was negative, it indicated that there was an inverse relationship between the variables - if one increased, the other decreased (or vice versa). On the other hand, if the coefficient was positive, it indicated a direct relationship - if one variable increased, so did the other (or if one variable decreased, the other also decreased). An overall 5% type-I error level was used to infer statistical significance.

Results

A total of 200 caregivers were included. The mean age of the participants was 53.40±12.60 years. There were 181 female caregivers (90.50%), and 48 of them were housewives (n=96).

A significant proportion (n=73) had completed middle school education as their highest level attained, accounting for approximately 36.50 % of the group. Out of the participants, 73% (n=146) were unemployed. Chronic illness was reported by 40% (n=80) of participants, while 11.50 % (n=23) had a history of psychiatric illness. The majority of caregivers had no prior training in caregiving, accounting for 90% (n=180). First-degree relatives made up most of the caregivers at 63% (n=126). A significant percentage, 72%, had been caring for patients for more than one year. Caregivers included non-native speakers, some of whom had language communication problems (approximately 5.55 %). Of the total patient population, a significant proportion (73.50%, n=147) required nutritional support. Of those who received this support, 57.1% relied on oral feeding, while the remaining 42.9% used tube feeding (Table 1).

STAI scores

The mean state anxiety level of participants was 42.40 (min=20, max=70, median=42), with 72 participants (36%) reporting little or no anxiety, 41 participants (20.50%) displaying moderate levels of anxiety, and 87 participants (43.50%) showing a high level of anxiety. The trait anxiety score was 41 (min=25, max=64, mean=41.40).

No significant difference was found between the anxiety levels among caregivers whose patients had NRS scores of 3 or higher and those whose NRS scores were below 3. Additionally, there was no correlation between NRS scores and the state and trait anxiety scores (p=0.986 and p=0.346, respectively) (Table 2).

ANKARA MEDICAL JOURNAL

Table 1. The baseline characteristics of caregivers and their anxiety scores

Variables	Data (n=200)
Age, median (IQR)	54 (17)
Gender, (n/%)	
Female	181 / 90.50
Male	19 / 9.50
Nationality, (n/%)	
Native	164 / 82.00
Nonnative	36 / 18.00
Marital status, (n/%)	
Single	56 / 28.00
Couple	144 / 72.00
Occupation, (n/%)	
Housewife	97 / 48.50
Retired	19 / 9.50
Caregiver/nurse	23 / 11.50
Others	61 / 30.50
Education status, (n/%)	
Illiterate	16 / 8.00
Elementary school	52 / 26.00
High school	73 / 36.50
University	59 / 29.50
Working, (n/%)	
Yes	54 / 27.00
No	146 / 73.00
Chronic illness, (n/%)	80 / 40.00
Active psychiatric illness, (n/%)	23 / 11.50
Alcohol and/or cigarette use (n/%)	45 / 22.50
Received training for care?, (n/%)	
Yes	20 / 10.00
No	180 / 90.00
Degree of kinship with the patient, (n/%)	
1. degree	126 / 63.00
Relative	23 / 11.50
Other	51 / 25.50
Duration of caring? , (n/%)	
Three months	31 / 15.50
4-6 months	25 / 12.50
Longer than a year	144 / 72.00
Time for caring?, (n/%)	
All day	119 / 59.50
Not all-day	81 / 40.50
Support status, (n/%)	
Little or no	45 / 22.50
Yes	155 / 77.50
Is there another person responsible for care?	
Yes	50 / 25.00
No	150 / 75.00
Duration of sleep near the patient, (n/%)	
2-3 hours	73 / 36.50
4-5 hours	74 / 37.00
6-8 hours	16 / 8.00
Not staying at night	37 / 18.50
Nutritional support?	
Yes	147 / 73.50
No	53 / 26.50
Nutrional route*, (n/%)	
Oral	84 / 57.14
With tube	63 / 42.86
NRS score, median (IQR)	4 (3)
NRS score groups, (n/%)	
<3	54 / 27.00
≥3	146 / 73.00
State anxiety score, mean (SD)	42.40 (10.10)
State anxiety status, (n/%)	
Little or no	72 / 36.00
Moderate	41 / 20.50
High	87 / 43.50
Trait anxiety score, median (IQR)	41 (12)
Trait anxiety status, (n/%)	
Little or no	74 / 37.00
Moderate	56 / 28.00
High	70 / 35.00

*Calculations were made on 147 patients receiving nutritional support.
n; number, IQR; interquartile range, SD; standard deviation, NRS;

Table 2. The correlation between NRS and anxiety scores

Correlation	Correlation coefficient	p-value
NRS and state anxiety	0.001	0.986
NRS and trait anxiety	-0.067	0.346

NRS; Nutritional Risk Screening

Caregiver anxiety scores were assessed according to patients' nutritional and caregivers' social characteristics (Table 3). Although the differences were not statistically significant, the lack of adequate training for providing care led to an increase in both state and trait anxiety (p=0.379 and p=0.553, respectively). When the patients' care was provided by a first-degree family member rather than others, trait anxiety scores were similar (p=0.957). However, being a first-degree relative of the patient caused higher levels of anxiety than being a non-first-degree relative, and this difference was almost statistically significant (p=0.090). There was no difference in anxiety scores according to total time spent with the patient (all day vs. night or daytime, p=0.500). Caregivers of patients with nutritional support did not have higher anxiety scores than caregivers without nutritional support (p=0.500), and the route of nutritional support did not affect caregivers' anxiety scores (oral vs. tube, p=0.080).

There was a statistically significant difference between the trait anxiety score of caregivers who had been working for more than one year and caregivers who had been working for only 4-6 months (p=0.196), whereas no significant difference was observed for state anxiety (p=0.196). Participants who had been caring for their patients for less than six months had lower scores on both state anxiety and trait anxiety than participants who had been caring for their patients for over a year.

Results showed that the presence of support statistically significantly affected both state anxiety (p=0.002) and trait anxiety (p=0.003). Individuals who had little to no support had higher scores for both state anxiety and trait anxiety than those who had support in their lives. Based on the results of the comparisons, which can be seen in Table 3, participants were divided into a high-risk group and a low-risk group for anxiety. The high-risk group included individuals caring for patients for more than one year without support (n=29). In contrast, the low-risk group consisted of individuals who either received assistance or had been providing care for less than six months without any assistance (n=171). When comparing these two groups, participants in the high-risk group had significantly higher levels of both state anxiety and trait anxiety compared to those in the low-risk group ($p < 0.001$ for both).

Table 3. Comparison of anxiety scores among some demographic variables

Variable	n / %	State anxiety score (Mean / SD)	p-value	Trait anxiety score (Median / IQR)	p-value
Training received for care?					
Yes	20 / 10.00	40.50 / 10.89	0.379	40 /12	0.553
No	180 / 90.00	42.62 / 10.11		41 / 13	
Degree of kinship with the patient, (n/%)					
1. degree	126 / 63.00	43.33 / 10.74	*0.090*	41 / 14	0.957
Other	74 / 37.00	40.82 / 8.99		40 / 11	
Duration of care? , (n/%)					
Less than six months	56 / 38.00	40.91 / 9.850	0.196	38 / 8	**0.01**
More than one year	144 / 72.00	42.92 / 10.20		42 / 14	
Support status, (n/%)					
None or minimal	45 / 22.50	46.60 / 10.15	**0.002**	45 / 16	**0.003**
Yes	155 / 77.50	41.19 / 9.82		40 / 11	
Nutrition route*, (n/%)					
Oral	84 / 57.14	42.82 / 11.08	0.879	42 / 13	0.138
With tube	63 / 42.86	42.55 / 8.96		40 / 12	
Alcohol and/or cigarette use (n/%)					
Yes	45 / 22.50	43.27 / 10.64	0.542	41 / 10	0.337
No	155 / 77.50	42.17 / 10.06		41 / 13	
NRS score groups, (n/%)					
<3	54 / 27.00	41.46 / 10.16	0.428	40 / 12	0.494
≥3	146 / 73.00	42.75 / 10.19		41 / 13	
In terms of patient care and support, (n/%)α					
Caring for more than one year and having no or little support	29 / 14.50	50.41 / 9.17	**<0.001**	49 / 10	**<0.001**
"Caring for more than one year but have support" or "caring less than six months and have no support."	171 / 85.50	41.05 / 9.73		40 / 12	

* Calculations were made on 147 patients receiving nutritional support.
α Individuals participating in the study were divided into two distinct groups based on their susceptibility to anxiety. The high-risk group consisted of caregivers who had cared for their patients for more than one year without significant support. The low-risk group included participants who had cared for their patients with assistance for more than one year or those who had provided care without assistance for less than six months.
(P values in bold indicate statistical significance. The p-value in italics indicates a trend towards statistical significance.)
(n; number, IQR; interquartile range, SD; standard deviation, NRS; nutritional risk score)

Discussion

In this study, although there was no association between patients' malnutrition status and STAI scores, caregivers had high levels of anxiety. The risk of patient malnutrition did not affect caregiver anxiety scores, but duration of care, especially when there was no or minimal support, was associated with higher anxiety scores.

The relationship between caregiver stress and malnutrition is possibly bidirectional. Tana et al. have shown that poor patient nutritional status negatively affects caregiver stress.[16] Rullier et al. have shown that

malnutrition occurs in both caregivers and dementia patients.[17] These findings suggest that caregivers' distress includes somatic manifestations beyond psychological defects. Anxiety is a highly distressing condition that caregivers should take seriously in the context of caregiving.[18] Furthermore, it is important to recognize that anxiety can have a significant impact on both the well-being of caregivers and the quality of care they provide to their care recipients.

As life expectancy and the number of people needing care increases, family caregivers continue to be the primary providers of people in both developed and developing countries.[19] Often, family caregivers are family members, spouses, or children, also referred to as informal caregivers. Unlike professional caregivers, these informal caregivers often provide unpaid, continuous assistance with daily activities or tasks for people with chronic illnesses or disabilities.[20] A majority of caregivers assume responsibilities associated with medical tasks that are usually carried out by medical professionals such as nurses and therapists.[21] The results of our study suggest that the lack of proper training in caregiving contributes to an increase in both state and trait anxiety, although these differences were not statistically significant. In the study conducted by Pars et al., caregivers who were trained in the use of gastrostomy tubes were more proficient in providing home care. This resulted in a reduction in stress, anxiety, and challenges associated with home care.[22] Both of these results suggest that adequate education and training of caregivers may enhance their ability and confidence in caring for patients effectively.

Hahn et al. also reported an increase in depressive signs in caregivers over a 2-year period.[2] This finding underscores the fact that continuous assessment of caregiver distress is needed. Geriatric facilities often assess patients in less than three months. Caregiver distress screening can be integrated into these assessments to prevent or detect the problem earlier.

Identifying the factors that contribute to increased levels of anxiety in informal caregivers is critical for early detection and prevention of these symptoms, as they can significantly impact the daily lives of caregivers and ultimately affect the well-being of both the caregiver and the care recipient.[23] Understanding the factors that contribute to increased levels of anxiety in informal carers in order to early identification and prevention of these symptoms.

Research suggests that caregiver burden is associated with a range of adverse reactions while performing the primary caregiving task. In the study by Liu et al., they found that caregiver burden can stem from inadequate financial resources, competing responsibilities, and a lack of social activities.[24] In our study, the trait anxiety scores of caregivers working for a longer period of time were higher than those of caregivers with shorter care durations. In addition, individuals who did not have sufficient support exhibited higher scores on both state anxiety and trait anxiety compared with individuals who had a support system. Furthermore, caring for

patients for an extended period of time combined with inadequate or no support emerged as the highest risk factor for anxiety. These results likely indicate the cumulative effect of various risk factors while also pointing to two important factors that may be modifiable. These findings suggest that social and familial support plays a critical role in the management of anxiety and depression in people caring for the chronically ill.

The study has several limitations, starting with its cross-sectional design, which prevents the establishment of a definitive causal relationship between the parameters. Secondly, it was conducted in a hospital where medical assistance can be provided at any time. This may have lowered the state anxiety scores of the caregivers.

In conclusion, in our study, caregiving elicited anxiety regardless of the patient's nutritional status. The factors associated with increased caregiver anxiety were the duration of care and the presence of a support system.

Ethical Considerations: The study protocol was approved by the Istanbul Medeniyet University, Istanbul Goztepe Training and Research Hospital Ethics Committee (2018/0413-09/01/2028)

Conflict of Interest: The authors declare no conflict of interest.

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Research Article

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CARE BURDEN AND INFLUENCING FACTORS OF ELDERLY PATIENTS RECEIVING HOME HEALTH CARE: PERSPECTIVES OF PATIENTS AND CAREGIVERS

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Abstract

Objectives: The aim of the study was to determine the care burden and influencing factors of patients receiving home health care.

Materials and Methods: The study was cross-sectional descriptive and was conducted with patients who benefited from a tertiary hospital's home health care unit. A 25-question demographic data questionnaire was prepared by the researchers by scanning the literature, and the BARTHEL daily living activities index was applied to the patients.

Results: A total of 416 people participated in the study, 34.86% (n=145) of whom were male, and 65.14% (n=271) were female. According to the Barthel daily living activities index, 43.75% (n=182) of the patients were entirely dependent, 38.46% (n=160) were severely dependent, and their average score was 34.14±29.27. No significant relationship was found between the gender of the caregiver, closeness with the patient, education level of the patient and the perceived burden of care. On the other hand, a significant relationship was found between the education level of the caregiver, the profession, the dependency degree of the patient, and the perceived burden of care ($p=0.001$, $p=0.031$, and $p<0.001$, respectively).

Conclusion: To reduce the care burden of caregivers, it is necessary to increase the quality and accessibility of home healthcare services, provide education and support for patients and caregivers, and take measures to maintain and improve patients' independence.

Keywords: Home care services, caregiver burden, burden of illness, physical functional performance.

Introduction

Many individuals who need care for reasons such as old age, chronic illness, and injury prefer to stay in their homes and receive home health care.[1,2] Home health care services are a service model that provides medical or supportive care to these individuals in their homes. Home healthcare services can help improve individuals' quality of life, independence, and health. In addition, home healthcare services can be more economical, more comfortable, and equally effective compared to places such as hospitals or nursing homes.[3]

The level of dependency on daily living activities of individuals receiving home health care services is an essential indicator for both themselves and the people who provide care for them.[4] Daily living activities are the skills required to meet basic physical needs such as nutrition, personal care, dressing-undressing, toileting, bladder and bowel control, transfer (bed-chair), mobility on level ground, and stair climbing.[5] A frequently used tool to measure these skills is the Barthel Index. The Barthel Index is an ordinal scale that scores each activity according to the individual's ability to perform the task independently.[6]

The level of dependency on daily living activities of individuals receiving home health care services is not only related to the physical conditions of the individuals but also to the characteristics of the people who provide care for them.[7] Caregivers are usually relatives, friends, or acquaintances of the patients. The occupations, education levels, and closeness to the patients of the caregivers can affect the quality and quantity of the care process[7]. In addition, how the caregivers perceive their patients' care burden is also essential. Care burden can be defined as the caregiver's physical, psychological, social, and economic difficulties. As the care burden increases, the caregiver's quality of life and health can be negatively affected.[8]

This study aims to measure the level of dependency on daily living activities of patients who benefit from home health care services and to examine the factors that affect the care burden of caregivers.

Materials and Methods

Population

The study was cross-sectional and descriptive. The research was conducted with patients over 65 who received service from the Erzincan Binali Yıldırım University Hospital home health unit between 01.02.2023 and 01.04.2023.

The sample size was calculated using the G Power program. The confidence interval of the research was determined as 99%, the margin of error as 5%, and the variance as 50%. According to these values, it was found

that the sample size should be 385. Approximately 5% margin of error was also added, and the sample size was calculated as 404. In this context, interviews were conducted with 416 people.

Data collection tools

A 25-question questionnaire prepared by the researchers by scanning the literature and questioning the demographic data of the patients and caregivers, the time spent by the caregivers on care, and the chronic diseases of the patient were applied to the patients who reside in Erzincan city center and agree to participate in the study. Moreover, the 11-item BARTHEL daily living activities index, developed by Mahoney and Barthel in 1965 and modified by Shah et al. in 2000, was used to measure the level of dependency on patients' daily living activities. Küçükdeveci et al. validated the Turkish version in 2000 and applied it to the patients.[6] The total score on the scale ranges from 0 to 100. A higher score means higher independence.

Ethics committee approval

Written and oral informed consent forms were obtained from all participants who agreed to participate in the study and from the legal guardians of the patients who could not consent. The principles of the modified version of the Helsinki Declaration were followed in every stage of the study. Approval was obtained from the Erzincan Binali Yıldırım University Clinical Research Ethics Committee with decision no 2023-02/1 for the study.

Statistical methods

The researchers entered the study data into the IBM SPSS Statistics 23 (SPSS, Chicago, IL) package program. Descriptive analyses were presented using mean ± standard deviation (SD) for normally distributed variables, median and range (min-max) for non-normally distributed variables and the number of cases (n) and (%) for nominal variables. The normality assumption was checked using the Kolmogorov-Smirnov test. Students' t-tests and the Mann-Whitney U test were used to compare means and medians between the two groups, respectively. One-way ANOVA was employed for comparing means across more than two groups. The chi-square test was used to examine the association between categorical variables.

The level of statistical significance was taken as $p<0.05$.

Results

A total of 416 people participated in the study. 34.86% (n=145) of the participants were male, and 65.14% (n=271) were female. The mean age was 74.75 (min=65, max=111). The other demographic data of the participants are given in Table 1.

Table 1. Demographic data of the participants

		n	%
Marital status	Married	156	37.51
	Single	47	11.29
	Widow	213	51.20
Occupation	Housewife	141	33.89
	Worker	20	4.80
	Officer	8	1.92
	Retired	131	31.5
	Not working	116	27.88
Education	illiterate	168	40.38
	Primary school	191	45.91
	Middle school	27	6.49
	High school	22	5.28
	University	8	1.92
Social security	Public insurance	272	65.38
	Special insurance	78	18.75
	None	66	15.86

The most common pathologies in the participants were the circulatory system, with 54.80% (n=228), and the nervous system, with 48.31% (n=201). The last seen pathology was visual pathology, with 1.92% (n=8).

The most frequently used services by the patients within the scope of home health care services were examination with 39.42% (n=164) and hospital transfer services with 22.83% (n=95).

The degree of kinship, marital status, and occupation of the person primarily responsible for the patient's care is given in Table 2.

The mean time spent on the patient's daily care was 11.86 ± 8.84 hours. The mean score of the patients from the Barthel daily living activities index was 34.14±29.27. According to this, 43.8% (n=182) of the patients were entirely dependent, 38.46% (n=160) were severely dependent, and 17.78% (n=74) were moderately mildly dependent or completely independent.

The caregivers' mean perceived care burden score, which was asked as 1= lowest, 10= highest, was 7.27±2.3. The relationship between perceived care burdens and various parameters is given in Table 3.

Table 2. The degree of closeness, marital status and occupation of the person primarily responsible for the care of the patient

		n	%
The primary person responsible for the care	Their children	206	49.51
	Partner	55	13.22
	Bride-groom	51	12.25
	Mom dad	25	6.00
	Caregiver	25	6.00
	Brother	13	3.12
	Other	41	9.85
Occupation of the person primarily responsible for the care	Housewife	176	42.30
	Worker	99	23.79
	Retired	58	13.94
	Officer	32	7.69
	Not working	51	12.25
The education level of the person primarily responsible for the care	Illiterate	32	7.69
	Primary school	167	40.14
	Middle school	59	14.18
	High school	95	22.83
	University	63	15.14

Table 3. Relationship between perceived care burdens and demographic data and dependency levels

		n	Perceived Care Burden (Mean±SD)	p
Gender	Male	145	7.32±2.36	0.728
	Female	271	7.24±2.34	
Education	İlliterate	168	7.43±2.35	0.403
	Primary School	191	7.09±2.42	
	Middle School	27	7.48±1.88	
	High School	22	6.91±2.22	
	University	8	8.25±1.90	
Education Level of The Caregiver	İlliterate	32	7.03±2.63	**0.001**
	Primary School	167	7.76±2.10	
	Middle School	59	7.56±2.23	
	High School	95	6.79±2.50	
	University	63	6.54±2.38	
Degree of Disability	Fully Dependent	182	8.07±1.94	**<0.001**
	Highly Dependent	160	7.22±2.11	
	Moderately Dependent	53	5.79±2.56	
	Mildly Dependent	13	4.31±2.49	
	Fully İndependent	8	4.75±3.15	
Occupation of The Caregiver	Housewife	176	7.51±2.18	**0.031**
	Employee	99	7.39±1.91	
	Officer	32	6.25±2.39	
	Retired	58	7.33±2.57	
	Not Working	51	6.76±3.08	
The Degree of Closeness of The Caregiver	Child	206	7.17±2.33	0.111
	Partner	55	7.58±2.25	
	Bride-Groom	51	7.82±2.08	
	Mom Dad	25	7.32±2.68	
	Caregiver	25	7.76±1.87	
	Brother	13	6.62±2.66	
	Other	41	6.54±2.62	

Discussion

Home healthcare services are an increasingly demanded service area with the increase in the elderly population.[9] Home health care services reduce hospitalizations, lower infection risk, and improve quality of life by enabling patients to receive care in home environments.[9] However, the care burden perceived by the caregivers of these patients and the factors affecting this burden have yet to be well known. In our study, a significant relationship was found between the perceived care burden of the caregivers and the education level, occupation, and dependency level of the person responsible for care.

The mean age of the patients participating in the study was 74.75, and 65.14% of them were female. In a study conducted by Acar Tek et al. with patients receiving home care services in Ankara/Turkey, 65.1% of 407 patients were also female. The patients' mean age was 72.8±6.67.[10] Although only patients over 65 were included in our study, the average age in the studies was very close to each other. Because most of the patient population is elderly, excluding patients who receive home health care because of acute problems such as bone fractures, these results also show that home health care services are preferred more by elderly and female individuals in Turkey. Among the reasons for the preference for home health care services by elderly and female individuals in Turkey, sociocultural factors, gender roles, and differences in access to health services can be mentioned[11]. While often taking on the role of caregiver within the family, older women may have difficulty finding someone to care for themselves. In addition, older women may have lower income and education levels, limiting their access to health services.[11] Home health care services may be a suitable option for older women.

In our study, 54.80% of the patients had a circulatory system, and 48.31% had nervous system diseases. Similarly, in another study by Selçuk et al. in Turkey, it was observed that patients receiving home health care had the most cardiac disorders with 42.7%.[12] Among the reasons why most of the patients who benefit from home health care services have circulatory system and nervous system diseases are old age, genetic factors, lifestyle, and environmental factors. Similarly, a study conducted by Nair et al. in India found that 70% of the elderly patients receiving home health care had chronic diseases such as hypertension, 50% had diabetes, and 40% had dementia.[13] These diseases can increase the level of dependency on the patient's daily living activities and raise the perceived care burden of the caregivers. Therefore, home healthcare services must provide medical and psychosocial support to prevent or treat these diseases. On the other hand, these findings highlight the importance of integrating chronic disease management into home health care. This may include providing caregivers with special training in managing these conditions.

The most frequently used services by patients within the scope of home health care services are examination and hospital transfer services. This finding has been similarly reported in studies conducted in other

countries.[3,14] These services are essential for monitoring the health status of the patients, updating their treatment plans, and referring them to the hospital when necessary. Patients who cannot receive adequate examination and hospital transfer services within the scope of home health care services may experience deterioration in their health status, recurrent hospitalizations, and decreased quality of life. This highlights a critical aspect of home healthcare - the need for continuous medical monitoring and the ability to respond quickly to changes in the patient's condition.

According to the degree of closeness of the person primarily responsible for the patient's care, it was seen that the most common ones were their children, spouse, and daughter-in-law/son-in-law, respectively. On the other hand, the most common occupations of the caregivers were housewife (42.30%), worker (23.79%), and retired (13.94%). These results show, in line with similar studies conducted in Turkey, that home healthcare services are carried out within the family and that family members play an essential role.[10] As expected, most caregivers are away from or have low income from working life, and most are primary school graduates. This reflects traditional family structures and caregiving norms but also raises questions about the support available to these family caregivers, who may be balancing caregiving with other personal and professional responsibilities.

The level of dependency on the patient's daily living activities was measured by the Barthel Index. The mean Barthel score of the patients was 34.14±29.27, and 43.75% were classified as entirely dependent and 38.46% as severely dependent. In a study conducted by Güdük et al. with 525 home health patients in Istanbul/Turkey, these rates were found to be 37% and 20%, respectively.[15] These results show that most patients who benefit from home healthcare services are severely dependent on daily living activities. The high dependency levels observed suggest that home healthcare services are catering to a significantly impaired population, which underscores the need for comprehensive care plans that address both medical and functional needs.

Care burden can be defined as a subjective experience perceived by the caregiver as a result of providing care.[16] The caregivers were asked to score between 1 and 10 to evaluate their perceived care burden. The caregivers' mean perceived care burden score was 7.27±2.3, which indicates that the caregivers feel a moderate-high level of care burden. A significant relationship was found between the perceived care burden of the caregivers and the education level, dependency level, and occupation of the person responsible for care. These results show that the caregivers feel more of a care burden as the caregiver's education level decreases, the patient's dependency level increases, and the occupation of the caregiver is housewife or worker. This finding is crucial for healthcare policymakers and practitioners, highlighting the need for interventions to reduce caregiver burden, such as respite care, caregiver training, and psychological support.

Increasing the education level of caregivers can improve both the health status and quality of life of the patient and the caregiver.[17] Education programs should provide information about the nature, course, treatment, and

complications of the disease and include caregiving skills, problem-solving strategies, stress management, and coping methods. Moreover, education programs must be culturally appropriate and respectful of the beliefs and values of the caregivers.[17]

As the patient's dependency level increases, the caregiver has to spend more time, energy and resources. In a study conducted in Turkey that included 177 patients and caregivers, it was found that caregivers felt the burden of care the most in terms of time.[18] This can lead to physical, psychological and social exhaustion. Therefore, appropriate home health services should be provided according to the patient's dependency level, and caregivers should be given respite opportunities.

The caregiver's occupation can also affect the care burden.[19] Caregivers who are housewives or workers may feel more of a care burden.[19] Because these occupational groups may be disadvantaged both economically and socially. Therefore, particular policies and programs should be developed for these occupational groups. For example, workers who are caregivers can be provided with opportunities such as flexible working hours, paid leave or financial support. Housewives who are caregivers can be offered services such as social security, psychosocial support or help with household chores.

Although the perceived care burden was higher in daughters-in-law and sons-in-law and lower in children, this difference was not statistically significant. Similarly, the gender of the person responsible for the care and the patient's education level did not significantly affect the care burden. These results are consistent with some studies in the literature, as well as some studies that have findings that female caregivers feel more of a care burden than male caregivers and close relatives feel more of a care burden than other relatives and non-blood relatives.[20] Among the reasons for these differences, it can be mentioned that the studies were conducted in different countries and cultures, different scales were used, different sample groups were selected, and different statistical analysis methods were applied. Moreover, these factors may affect the care burden not alone but in interaction with other factors. Therefore, there is a need for more comprehensive and comparative studies to understand the factors determining the care burden.

Among the limitations of this study is that it was single-centered, data based on self-reports of the patients and caregivers participating in the study were used, and the study had a cross-sectional design. Therefore, the generalizability of the results of this study is limited. On the other hand, the burden of care could not be measured with a standard scale to avoid asking too many questions and affecting the participation of patients and their relatives in the study. In future studies, it is recommended to use larger and multicenter sample groups using completely standardized scales.

In conclusion, this study showed that the dependency levels of the patients who benefit from home health services in daily living activities were high, creating a severe burden on the caregivers. Therefore, it is necessary

to increase the quality and accessibility of home health services, provide education and support for the patients and caregivers, and protect and improve the patient's independence.

Ethical Considerations: Ethical approval was acquired from the local Ethics Committee (Date: 19.01.2023, App. No: 2023-02/1).

Conflict of Interest: The authors declare no conflict of interest.

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THE RELATIONSHIP BETWEEN SMARTPHONE ADDICTION LEVELS AND PSYCHOLOGICAL SYMPTOMS AND SLEEP QUALITY AMONG MEDICAL STUDENTS

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Abstract

Objectives: In this study, it was aimed to determine the level of smartphone addiction in medical students and its relation to some psychological symptoms and sleep quality.

Materials and Methods: The research data were composed of four parts. A sociodemographic data form consisting of 30 questions was prepared by the researcher, including the Smartphone Addiction Scale-Short Version (SAS-SV), the Brief Symptom Inventory (BSI), and the Pittsburgh Sleep Quality Index (PSQI).

Results: According to the evaluation made by considering the cut-off points of the SAS-SV, 34.41% of the students were found to be at risk of smartphone addiction. SAS-SV scores were highest in those who used their smartphones for eight hours or more daily and those who checked their smartphones 51 times or more in a day. The highest risk of smartphone addiction was found among those who left their phones in bed or under the pillow at night, those who checked their phones within one minute after waking up in the morning, and those who charged their smartphones more than once daily. Students' BSI three global indices and median scores of all sub-dimensions were higher in those at risk of smartphone addiction. In addition, significant positive correlations were found between the SAS-SV scores and the PSQI total scores.

Conclusion: The results indicate that psychological symptoms and sleep quality are associated with smartphone addiction. This may lead to depression and/or anxiety, which can consecutively result in sleep problems. Responsible use of smartphones may have a positive effect on students' mental health and sleep.

Keywords: Smartphone, addiction, psychological symptoms, sleep quality.

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Introduction

Today, the smartphone has become a ubiquitous device for everyone because it serves much more than just as a communication tool. Although a smartphone is very small in size, it is designed on a mobile computing platform with more advanced computing capability and connectivity. It serves as a media player, digital camera, GPS navigator, games, and much more. Since smartphones are extremely portable, they provide very convenient and instant access to the internet. They offer multitasking functions like computers, which could promote dependence to a greater degree.[1] The above-mentioned features of smartphones make them a center of attraction for every individual around us.

Over the past few years, there has been a noticeable increase in the proportion of people owning and using smartphones in developed and developing countries. As in almost every country in the world, an uninterrupted and rapid increase in smartphone ownership is observed in our country. As of 2020, the number of smartphone users worldwide is approximately six billion. The number of mobile cellular subscriptions is expected to exceed seven billion worldwide by the end of 2024.[2]

Smartphone addiction is defined as the lack of control over using the smartphone despite all the negative effects on its users, including financial, psychological, physical, and socially harmful consequences.[3] In the literature, researchers have variously named these behaviors as “smartphone addiction”, “problematic smartphone use,” and “excessive smartphone use,” and referred to the use of mobile phones other than smartphones.

Although smartphone addiction is not currently recognized as an official clinical disorder in the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) or the International Classification of Diseases (ICD-10), many aspects of this behavior seem to share similarities with other behavioral addictions.[4] Smartphone addiction consists of four main components: obsessive use, tolerance, feelings of withdrawal or agitation when there is no phone, and functional impairment that interferes with other life activities and harms social relationships.[5]

There are numerous adverse effects associated with excessive smartphone use. It can lead to an attention deficit as well as other mental disorders such as social anxiety, depression, impulsivity, and loneliness. It has been found that anxiety is more common in adolescents who use their smartphones in a problematic way due to device interaction or distraction.[6]

Depression is a common mental disorder worldwide. It is characterized by persistent sadness and a lack of interest or pleasure in previously rewarding or enjoyable activities. Fatigue and poor concentration are common, and they can also disturb sleep and appetite. Depression is a leading cause of disability around the world and contributes greatly to the global burden of disease.[7]

The main feature of anxiety disorder is excessive worry about a series of events or activities. The intensity, duration, or frequency of anxiety is not proportional to the actual probability or impact of the anticipated event. The individual finds it difficult to control his anxiety and prevent the worrying thoughts from paying attention to the tasks at hand. Adults with generalized anxiety disorder often worry about everyday, routine life situations, such as job responsibilities, health, finances, the health of family members, or other minor issues. Anxiety is accompanied by at least three of the following additional symptoms: restlessness or nervousness, easy fatiguability, difficulty concentrating, irritability, muscle tension, and insomnia.[7]

Sleep is one of the basic requirements to lead a quality and healthy life. Therefore, quality sleep is very important. It has positive effects on physical and mental health. Poor sleep quality is believed to be widespread in modern society, and about one-third of adults complain of poor sleep quality, though in most studies, prevalence estimates are based upon insomnia-related symptoms.[8] Sleep deprivation has both short- and long-term effects on individuals. In the short term, it causes a decrease in concentration, a deterioration in the quality of life, a decrease in productivity, and an increase in domestic accidents; in the long term, it can lead to increased morbidity and mortality, traffic accidents, problems with memory, and depression.[9]

Materials and Methods

Participants

This study was planned as a cross-sectional descriptive study. The population of the research consisted of students studying at Selcuk University Faculty of Medicine during the 2020-2021 academic year. It was aimed to include all (1423) students from the 1st to the 6th grades. However, after taking into consideration the statistical analyses, it was planned to reach 80 percent of the targeted audience since students could not come to university due to the COVID-19 pandemic lockdowns. As a result, the study sample consisted of 1,177 participants, including 667 female and 510 male medical students.

Measures

The data in the study was collected using a sociodemographic data form, the Smartphone Addiction Scale-Short Version (SAS-SV), the Brief Symptom Inventory (BSI) and the Pittsburgh Sleep Quality Index (PSQI). A sociodemographic data form consisting of 30 questions was developed by the researcher to collect information from the participants regarding their age, gender, class year, and other sociodemographic characteristics of the students, the frequency of smartphone use, sleep habits, and the conditions which are thought to affect the purpose of the research.

Smartphone Addiction Scale-Short Version (SAS-SV)

The Smartphone Addiction Scale-Short Version (SAS-SV) is a self-report scale that measures smartphone addiction level consisting of 10 six-point Likert-type items that were developed by Kwon et al.[10] The test is valid and reliable in Turkish.[11] The total score obtained from the scale varies between 10 and 60. It is considered that the higher the score obtained from the scale, the higher the risk of addiction. In the Korean sample, the cut-off points were 31 for men and 33 for women.

Brief Symptom Inventory (BSI)

The Brief Symptom Inventory (BSI) is a scale composed of 53 items developed by Derogatis to catch psychiatric problems in various medical cases.[12] The inventory is valid and reliable for Turkish youth.[13] The scale has a nine-factor structure and three global indices of distress: the Global Severity Index, the Positive Symptom Distress Index, and the Positive Symptom Total. The factors are somatization, obsession-compulsion, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism.

Pittsburgh Sleep Quality Index (PSQI)

The Pittsburgh Sleep Quality Index (PSQI) is a self-report scale developed by Buysse et al.[14,] which measures the quality of sleep and provides information on the type and severity of sleep disorders for the previous month. The test is valid and reliable in Turkish.[15] The total index score above five indicates poor sleep quality.

Procedure

Due to the pandemic, the study was conducted online as an e-survey. Whatsapp groups were reached via the student representative of each class. The participants were asked to fill in the survey questions and scales by sending reminder messages from time to time. After reaching all the students, the data were evaluated.

While e-survey applications offer several advantages, they also have negative aspects that could impact the study's results. Some of the problems that might be encountered when working with e-surveys are the inability to connect with people from remote areas, sampling issues, response bias and delay, survey fatigue and dropout, increase in errors, and high chances of survey fraud.

Statistical Analysis

All statistical analyses were performed using IBM SPSS 22 package software. Descriptive statistics for the data were presented as mean±standard deviation, median (minimum – maximum) or median (distance between

quartiles) for numerical variables, and numbers (n) and percent (%) for categorical variables. The reliability of the obtained sample was checked with the Cronbach Alpha coefficient. While evaluating the scales, total scores were taken as a basis. The normality of data was checked with Q-Q plots and the Anderson-Darling normality test. Comparisons between groups of variables showing a normal distribution were performed using Student-t, and comparisons of variables not showing a normal distribution were performed using Mann-Whitney U and Kruskal Wallis tests. Multiple comparisons of the groups found to be significant with the Kruskal-Wallis test were made with the Dunn test and Bonferroni correction. Spearman's rho correlation analyses were performed to determine the relationship between numerical variables. Relationships between categorical variables were examined using Chi-square analysis and Yates continuity correction or Fisher's exact test, according to appropriate situations. Logistic regression models were used to determine the factors affecting smartphone addiction. Statistical tests were performed at the 5% significance level.

Results

The study included 1177 students, 56.67% of whom were female (n=667) and 43.33% of whom were male (n=510). Whereas 464 participants (39.42%) were between the ages of 18 and 20, 533 (45.28%) were between the ages of 21 and 23, and 180 (15.29%) were 24 years of age or older. The median age was 21 years old.

The mean score of the students from the SAS-SV was 28.42±10.37. According to gender, the mean SAS-SV score for females was 29.70±10.36 and for males was 26.80±10.16. Females had a higher mean score than males, and a statistical difference was found between them ($p<0.001$). According to our evaluation based on the cut-off values of the scale (33 points for females and 31 points and above for males), 34.41% of the students included in the study were at risk of smartphone addiction.

The SAS-SV mean score was statistically significantly higher in the group in which students used their smartphones for eight hours or more daily than those who used them less. Additionally, the SAS-SV mean score was statistically significantly lower in the group in which students checked their smartphones 20 times or less than in groups that checked their phones 21 times or more ($p<0.001$) (Table 1). There was a statistically significant higher smartphone addiction risk in students who left their phones in the bed or under the pillow, those who checked their phones within one minute after waking up in the morning, those who charged their phones more than once daily, those who carried portable chargers (power banks) continuously, those who changed their phones every two years or less, and those who evaluated themselves as smartphone-addicted individuals compared to students in other groups of each category (Table 2).

Table 1. Smartphone Addiction Risk According to Students' Smartphone and Internet Usage Characteristics and Multiple Comparison Analyses Between Groups

Characteristic	SAS-SV M ± SD	Mdn (Min-Max)	Z/X^2	p	Multiple Comparison
Age of First Use of Smartphone			-0.692*	0.489	
Under the age of 15	28.6 ± 10.4	28.0 (10-60)			
15 years and older	28.2 ± 10.3	27.0 (10-60)			
Smartphone Usage Time Per Day (hours)			89.682**	**<0.001**	
0-4 hours (a)	25.9 ± 9.4	25.0 (10-56)			**p_1 <0.001**
5-7 hours (b)	30.7 ± 10.3	30.0 (10-60)			**p_2 <0.001**
8 hours and above (c)	34.4 ± 11.6	36.0 (10-60)			**p_3= 0.008**
Internet Usage Time Per Day (hours)			51.551**	**<0.001**	
0-4 hours (a)	25.7 ± 9.4	25.0 (10-56)			**p_1 <0.001**
5-7 hours (b)	30.0 ± 10.4	29.0 (10-60)			**p_2 <0.001**
8 hours and above (c)	30.7 ± 10.9	30.0 (10-60)			p_3= 0.781
Frequency of Checking Smartphone Per Day			60.310**	**<0.001**	
20 times and below (a)	26.5 ± 9.4	25.0 (10-60)			**p_1 <0.001**
21-50 times (b)	31.6 ± 10.9	31.0 (10-58)			**p_2 <0.001**
51 times and above (c)	31.8 ± 11.4	29.0 (10-60)			p_3= 0.992

* The Mann-Whitney U test was used
** The Kruskal-Wallis test was used
SAS-SV: Smartphone Addiction Scale-Short Version; M: mean; SD: standart deviation; Mdn: median
(p_1: a vs b; p_2: a vs c; p_3: b vs c)

Scores obtained from all "somatization, interpersonal sensitivity, depression, anxiety, etc." sub-dimensions of the BSI and the three global indices were statistically significantly higher in the group at risk of smartphone addiction than in the group with no risk (Table 3). There was a positive and statistically significant correlation between participants' SAS-SV scores with all three global indices scores of the BSI and the PSQI total score (p<0.001) (Table 4).

55.82% of the students had poor sleep quality. The sleep quality and PSQI scores of the students who participated in the study based on their risk of smartphone addiction revealed that 66.91% of the students at risk of smartphone addiction had poor sleep quality, whereas 50% of the students who had no risk of addiction had poor sleep quality. The difference between the two groups was statistically significant (p<0.001). Whereas the average PSQI score of students at risk of smartphone addiction was 7.41±3.67, the average PSQI score of students not at risk of smartphone addiction was 6.42±4.00, and the difference between these groups was determined to be statistically significant. (p<0.001) (Table 5).

Table 2. Smartphone Addiction Risk Status According to Students' Smartphone Usage Characteristics

Characteristic	Smartphone Addiction Risk				Total		X^2	*p*
	Yes		No					
	n	%	n	%	n	%		
Place of Leaving Smartphone While Going to Sleep at Night							25.324*	**<0.001**
Outside the bedroom or away from the bed	89	25.87	255	74.13	344	100.00		
Somewhere near the bed	259	35.92	462	64.08	721	100.00		
In the bed or under the pillow	57	50.89	55	49.11	112	100.00		
Time to Check the Phone After Waking Up in the Morning							56.792*	**<0.001**
As soon as waking up within 1 minute	197	46.79	224	53.21	421	100.00		
Within 1-5 minutes	148	32.39	309	67.61	457	100.00		
Within 6-15 minutes	29	21.01	109	78.99	138	100.00		
After 15 minutes	31	19.25	130	80.75	161	100.00		
Frequency of Charging the Phone							44.727*	**<0.001**
More than once per day	137	48.41	146	51.59	283	100.00		
Once daily	232	32.86	474	67.14	706	100.00		
Once every two or more days	36	19.15	152	80.85	188	100.00		
Status of Carrying a Portable Charger							16.403*	**<0.001**
Yes	63	47.73	69	52.27	132	100.00		
Sometimes	87	38.84	137	61.16	224	100.00		
No	255	31.06	566	68.94	821	100.00		
Frequency of Changing the Smartphone							9.252*	**0.010**
Every two years or less	40	48.19	43	51.81	83	100.00		
Every 3-4 years	252	34.71	474	65.29	726	100.00		
Every five years or more	113	30.71	255	69.29	368	100.00		
Self-Evaluation of Smartphone Addiction							258.173*	**<0.001**
Addicted	180	70.04	77	29.96	257	100.00		
Maybe addicted	185	36.42	323	63.58	508	100.00		
Not addicted	31	8.66	327	91.34	358	100.00		
No idea	9	16.37	45	83.33	54	100.00		
Total	405	34.41	772	65.59	1177	100.00		

*Chi-square test was used

Table 3. Distribution of Students According to Their Smartphone Addiction Status by Scores Obtained From the BSI and its Sub-Dimensions

BSI Sub-Dimension	Smartphone Addiction Risk	n	M ± SD	Mdn (Min-Max)	*Z**	*p*
Somatization	Yes	405	5.39 ± 5.02	4.00 (0-28)	10.450	**<0.001**
	No	772	2.77 ± 3.76	1.00 (0-25)		
OCD	Yes	405	9.96 ± 5.77	9.00 (0-24)	12.783	**<0.001**
	No	772	5.59 ± 4.56	5.00 (0-21)		
Interpersonal sensitivity	Yes	405	5.48 ± 4.32	4.00 (0-16)	9.661	**<0.001**
	No	772	3.11 ± 3.33	2.00 (0-16)		
Depression	Yes	405	8.31 ± 6.07	7.00 (0-24)	9.987	**<0.001**
	No	772	4.93 ± 5.08	3.00 (0-23)		
Anxiety	Yes	405	6.02 ± 5.20	5.00 (0-23)	10.976	**<0.001**
	No	772	3.06 ± 3.90	2.00 (0-23)		
Hostility	Yes	405	5.73 ± 4.68	5.00 (0-20)	10.934	**<0.001**
	No	772	3.00 ± 3.35	2.00 (0-20)		
Phobic anxiety	Yes	405	4.04 ± 3.85	3.00 (0-18)	8.659	**<0.001**
	No	772	2.23 ± 2.88	1.00 (0-19)		
Paranoid ideation	Yes	405	6.12 ± 4.43	5.00 (0-20)	9.662	**<0.001**
	No	772	3.67 ± 3.66	3.00 (0-19)		
Psychoticism	Yes	405	4.92 ± 4.48	4.00 (0-20)	8.880	**<0.001**
	No	772	2.76 ± 3.34	2.00 (0-18)		
Global Severity Index	Yes	405	1.14 ± 0.77	0.98 (0.02-3.74)	11.866	**<0.001**
	No	772	0.64 ± 0.59	0.49 (0.02-3.58)		
Positive Symptom Total	Yes	405	30.17 ± 13.80	31.00 (1-53)	11.205	**<0.001**
	No	772	20.03 ± 14.01	19.00 (1-53)		
Positive Symptom Distress Index	Yes	405	1.82 ± 0.67	1.72 (0-3.98)	8.469	**<0.001**
	No	772	1.50 ± 0.57	1.33 (0-4)		

*Mann-Whitney U test was used; BSI: Brief Symptom Inventory; SAS-SV: Smartphone Addiction Scale-Short Version; M: mean; SD: standart deviation; Mdn: median

Table 4. The Relationship Between the SAS-SV Scores and Global Indices Scores of the BSI and the PSQI Total Score

	SAS-SV Score	
	r_s*	*p*
Global Severity Index	0.432	**<0.001**
Positive Symptom Total	0.410	**<0.001**
Positive Symptom Distress Index	0.317	**<0.001**
PSQI Total Score	0.197	**<0.001**

*Spearman correlation test was used.
SAS-SV: Smartphone Addiction Scale-Short Version; PSQI: Pittsburgh Sleep Quality Index

Table 5. Sleep Quality of the Students According to Their Smartphone Addiction Risk Status

	Sleep Quality						PSQI Score	
	Good		Bad		Total			
Smartphone Addiction Risk	**n**	**%**	**n**	**%**	**n**	**%**	**M ± SD**	**Mdn (Min-Max)**
Yes	134	33.09	271	66.91	405	100.00	7.41 ± 3.67	7.00 (0-20)
No	386	50.00	386	50.00	772	100.00	6.42 ± 4.00	5.50 (0-21)
Total	520	44.18	657	55.82	1177	100.00	6.76 ± 3.92	6.00 (0-21)
Test statistic	X^2= 30.814* ***p* <0.001**						Z= 5.089** ***p* <0.001**	

*Chi-square test was used;
**Mann-Whitney U test was used;
PSQI: Pittsburgh Sleep Quality Index; SAS-SV: Smartphone Addiction Scale-Short Version; M: mean; SD: standard deviation; Mdn: median

Discussion

Smartphones, which we never separate from ourselves, have many functions and applications that facilitate internet access, an easy approach to information, and high functionality that makes everyday life easier. Apart from compulsory usage fields such as instant communication, accessing information, and so on, individuals can spend most of the day on the phone checking notifications from social media applications. In this context, the time spent with the smartphone increases, and smartphone addiction arises as a result of this situation.

In the study conducted by Noyan et al., those who controlled their smartphones more than 40 times a day on average had a statistically significantly higher mean SAS-SV score than those who controlled them less. Likewise, those who spent five hours or more per day on their phones had a higher mean SAS-SV score, creating statistical significance compared to the groups that used their phones for a lesser amount of time.[11] In another study conducted in Switzerland, it was found that those who spent more than six hours a day with their smartphones had an 11-fold risk of addiction compared to those who spent less than 60 minutes.[16] A study done earlier found the ratio of those who checked their smartphones 40 or more times a day was significantly higher in the high-level smartphone use group than in the low-level use group.[17] These data support our study findings in terms of the association of smartphone addiction risk with high rates of daily checking and time spent on smartphones.

It can be said that keeping the phone device near all the time or even leaving it under the pillow until late at night in order to check it frequently can increase the risk of addiction, and as a result, it can negatively affect the quality of sleep and life. In this study, it was determined that the risk of smartphone addiction was found

in half of those who left their phones in bed or under the pillow before going to bed at night, and a statistically significant difference was found in this relationship in comparison to other groups. In a study conducted in Turkey, it was found that those who left their phones at an accessible distance while going to bed got significantly higher scores on the Smartphone Addiction Scale (SAS) than those who left their phones in an inaccessible place.[18] Those who leave their phones in bed or under the pillow in order not to miss important calls or messages, even if they do this with good intentions, are actually putting their own health at risk. This can seriously impair their sleep quality. Smartphones emit high levels of radiation that can cause dysfunction or imbalance in humans' biological clocks. That way, sleeping next to the phone can actually cause more nightmares and can lead to restlessness and frequent wakings during the night.

In this study, the risk of smartphone addiction was found in nearly half of those who checked their phones as soon as they woke up, and this group was found to be at a higher addiction risk than those who checked after 15 minutes of waking up. Haug et al. found that approximately two-thirds of those at risk of smartphone addiction checked their phones in the first five minutes after waking up in the morning and had the highest rate compared to those who checked them in other periods.[16] In an earlier study done with medical students in Egypt, it was found that 80% of those who checked their phones within the first five minutes after waking up had a risk of smartphone addiction. This rate was found to be statistically significantly higher than the other groups.[19] In light of this information, we can say that adolescents who use social media intensively, whose first thing to do is to look at the smartphone before going to the toilet after waking up in the morning or to check their messages and notifications before sleeping at night, increase their predisposition to smartphone addiction.

Considering the relationship between the frequency of smartphone charging and the risk of smartphone addiction in this study, the risk of smartphone addiction was found in almost half of those who charged their phones more than once a day. This addiction rate decreased significantly as the charging frequency decreased. In a qualitative study conducted with young employees in China, it was found that participants felt withdrawn when their smartphones ran out of charge, and a few young employees stated that they were very impatient in such situations. According to the participant interviews in the study, an employee stated that he charges his phone every night and never lets the battery level fall below 20%. Another employee, who seems to be a heavy smartphone addict, stated that phone battery levels below 40% were unacceptable for him.[20] In a previously conducted study, the average SAS score of students who used their phones while charging was found to be significantly higher than that of those who used them after charging a little bit and those who never used them while charging.[18] Based upon these facts, it can be said that the increase in the frequency of phone charging in adolescents, using the phones even while charging, being impatient, and exhibiting nervous behaviors when the battery is close to draining are closely related to smartphone addiction.

The presence of psychiatric symptoms may lead to problematic smartphone use or the continuation of the problematic use. Likewise, in some other cases, problematic smartphone use can lead to the development of psychiatric symptoms. Additionally, an underlying genetic risk or environmental factors may lead to both the development of psychiatric symptoms and problematic smartphone use.[17] Depressed individuals use mobile phones as a coping method to cope with their depressive and negative emotions.[21] Thus, smartphone use can function as an experiential avoidance strategy to deflect disturbing emotional content; however, experiential avoidance is ineffective for this purpose and may lead to negative emotional consequences.[22]

On the other hand, there is evidence in the literature suggesting that increased levels of technology use may cause psychopathology types. For example, in a study of university students, it was found that those classified as heavy computer, social media, and cell phone users reported higher levels of long-term stress, depression, and sleep disturbance.[23] In the study conducted by Demirci et al., depression, anxiety, and PSQI daytime dysfunction scores were found to be higher in the high-risk smartphone addiction group than in the low-risk addiction group. A positive correlation was found between the SAS scores and depression, anxiety levels, and some sleep quality scale scores. The findings of the study showed that depression and/or anxiety play a mediatory role in smartphone overuse and sleep quality. It has been thought that excessive use of smartphones may cause depression and/or anxiety, which may lead to sleep problems.[24]

Similar to this study, Firat et al. evaluated the relationship between problematic smartphone use and psychiatric symptoms in adolescents who were referred to a psychiatry outpatient clinic in Turkey. The results of the study showed significant differences in somatization, interpersonal sensitivity, depression, anxiety, obsessive-compulsive, phobic anxiety, hostility, and other sub-dimensions scores of the BSI between problematic smartphone use and non-problematic smartphone use groups.[25] The results of another study conducted with undergraduate university students revealed a significant positive relationship between smartphone addiction and both anxiety and depression. It has been found that smartphone addiction has a significant effect on anxiety and is a predictor of depression.[26] This information explains the correlation between smartphone addiction and bad mental health.

Sleep disturbance is an important risk factor for adolescent mental health and affects the relationship between addictive behaviors and psychological symptoms. The results of this study indicate that higher smartphone addiction risk leads to poorer sleep quality. Several studies reported similar findings. In a study conducted among Chinese university students, significant positive correlations were found between sleep latency, short sleep duration, and poor sleep quality variables in relation to smartphone addiction. It has been found that procrastination is significantly and positively associated with smartphone addiction.[27] In another large cross-sectional study done in the United Kingdom, a statistically significant relationship was found between poor sleep quality and smartphone addiction; while 68.7% of those at risk of smartphone addiction had poor sleep

quality, 57.1% of those who were not at risk had poor sleep quality.[28] In a study conducted with medical students, there were significant correlations between mobile phone dependency with each subjective sleep quality and sleep latency domains of the PSQI, and nearly two-thirds of the participants had poor sleep quality.[29]

Based on the results of this study and the information found in the literature, it can be said that there is a relationship between smartphone addiction, poor sleep quality, and psychological symptoms. Dealing with smartphones for a long time in the evenings and not being aware of the time spent due to social media and internet use causes the eyes to be tired by the bright light. This may lead to disruption of the circadian rhythm, difficulty falling asleep, as well as delayed sleep. As a result, conditions such as decreased sleep efficiency and duration, daytime dysfunction, and negative effects on mental and physical health may occur. Therefore, this situation can lead to a decrease in academic performance and disruptions in social life.

In conclusion, psychological symptoms and sleep quality are associated with smartphone addiction. Such addiction may lead to depression, anxiety, and/or other mental issues, which can consecutively result in sleep problems. This indicates the importance of intervention to reduce smartphone addiction among medical students to improve overall sleep quality and avoid negative psychological impacts that can arise.

Ethical Considerations: The local clinical research ethics committee approved the study (Approval No. 2020/454, dated 14/10/2020).

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IMPROVING FEMALE STUDENTS' PHYSICAL FITNESS INDEX MAY REDUCE CARDIOVASCULAR RISK

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Abstract

Objectives: Evidence suggests that lower cardiovascular disease risk is among the most important factors for decreasing premature mortality rates in non-communicable diseases. Physical fitness is a potentially important factor for cardiovascular disease prognostication. We aim to analyze the correlation between physical fitness and the risk of cardiovascular disease in female students.

Materials and Methods: 76 participants completed all examinations. Cardiovascular disease risk factors were assessed by measuring body fat percentage, blood pressure, and lipid profiles. Physical fitness was measured using the modified Harvard step test to compute the physical fitness index., Spearman correlation was used to determine the correlation between variables in this study.

Results: A negative correlation between physical fitness index with body mass index, fat percentage, systolic blood pressure, and diastolic blood pressure (r = -0.443; r = -0.409; r = -0.370; r=-0.280). We also found that the physical fitness index did not significantly correlate with the lipid profile.

Conclusion: The physical fitness index might predict individual cardiovascular disease risk. Physicians should encourage patients to exercise regularly to maintain or improve their fitness levels to prevent cardiovascular disease.

Keywords: Cardiorespiratory fitness, dyslipidemia, fatness, screening, sustainable development goals.

Introduction

Cardiovascular disease (CVD) is the major contributor to premature mortality in non-communicable diseases, as stated in Sustainable Development Goals (SDGs) indicator 3.4.[1] According to data from Global Burden Diseases (GBD) 2019, there are nearly two-fold prevalent cases, from 271 million total CVD in 1990 to 523 million in 2019.[2] Cardiovascular disease deaths grew steadily from 12.1 million in 1990 to 18.6 million in 2019; 58% of CVD death in 2019 occurred in Asia.[2,3] In high-income Asian nations, the percentage of premature CVD fatalities to total CVD deaths was notably lower but considerably higher in several low- and middle-income Asian nations, including Indonesia.[3] Roughly one-third of deaths in Indonesia are caused by cardiovascular disease.[4]

In descending order, several modifiable risk factors for CVD include hypertension, dietary risk, dyslipidemia, smoking behavior, diabetes, obesity, and a lack of physical activity.[5] Low cardiorespiratory fitness (CRF) levels have been strongly linked to an increased risk of cardiovascular disease and a more accurate predictor of mortality than other CVD risk factors. Integrating CRF into risk classification offers opportunities to improve patient management and encourage lifestyle-based strategies for reducing cardiovascular risk.[6] A 17% reduction in risk for every 1-MET increase in CRF supports the idea that it effectively predicts mortality risk in women.[7] CRF-improving initiatives must be regularly integrated into the physical examination .[6]

Limited studies assessed cardiovascular risk and physical fitness in female students; therefore, this study focused on female university students for several reasons. Globally, the prevalence of less physical activity is higher in women than men.[8] Research in Qatar shows that female students tend to be less active than male students and do not enjoy doing exercise regularly.[9] Awareness of the risks and dangers of CVD is also required to prevent it in the future, but awareness among women in this age group remains low. According to an American Heart Association (AHA) survey, approximately 41% of women aged 25-34 did not know that CVD was the leading cause of death in women.[10] In the following AHA survey of women between the ages of 15 and 24, only 10% of participants knew that CVD is the top cause of death in women.[11]

The American Heart Association (AHA) recommends that young adults over 20 assess their CVD risk factors every 4-6 years.[12] However, Indonesia has not yet adopted this recommendation in primary health centers. Measuring the physical fitness index is one tool for assessing cardiorespiratory fitness as screening CVD risk. This study aims to assess the correlation between physical fitness and the risk of cardiovascular disease in female students. This study's findings will contribute to implementing physical fitness as one of the inexpensive tools for screening individual cardiovascular risk.

Materials and Methods

Participants

The research participants were students at the Faculty of Medicine Universitas Andalas who voluntarily participated by filling out a Google form. We distributed the Google form via WhatsApp to the students' chairman in every grade. The recruitment is open to participants with the following criteria: female students at the Faculty of Medicine Universitas Andalas who are not pregnant and are not currently taking anti-hypertension and cholesterol-lowering drugs. Eighty-one female students enrolled in this study, but only 76 students completed all examinations.

Physical Fitness Index

Physical activity and fitness are inextricably linked. A person's ability to perform physical activities is called physical fitness. Physical activity assessments using a simple, self-reported questionnaire are prone to measurement errors or misclassification.[13,14] Physical fitness provides more objective data about one's health and is more reproducible than physical activity.[14,15] Physical fitness is a stronger predictor of adverse health outcomes and mortality than smoking, hypertension, high cholesterol, and diabetes.[6]

Physical fitness consists of several components: flexibility, muscle strength, cardiorespiratory fitness (CRF), and body composition. We measured the physical fitness index using a modified Harvard step test to assess cardiorespiratory fitness. The test requires minimal tools and can be done in limited indoor space, so it can be applied to screening cardiovascular risk in a primary health care setting.[16] We asked participants to step on 30 cm high stairs with each click sound from the step test timer, and the stepping rate is 96 beats per minute (4 clicks = one cycle, step up and down) for 5 minutes. The participant counted their pulse rate at minutes 1, 3, and 5 after the step test for one minute full. The physical fitness index formula is 100 x step test duration (300 seconds) / the sum of pulse rate at minutes 1, 3, and 5. We divided PFI into tertile based on the PFI range of the participants: lowest (71.43–89.63), middle (89.64–107.84), and highest (107.85–126.05)

Cardiovascular Risk Factors

Cardiovascular risk factors assessed in this study are family history of cardiovascular diseases, body mass index, body fat percentage, blood pressure, and lipid profile. Family history of cardiovascular was assessed by an online questionnaire consisting of six questions: are there any in your family history of heart disease, obesity, diabetes Mellitus, dyslipidemia, hypertension, and stroke? Enumerators using standard procedures examined body mass index, body fat percentage, and blood pressure. Height was measured using a stadiometer,

and the data was input to BIA TANITA BC-418 to get body mass index and body fat percentage. Blood pressure using Omron automatic blood pressure monitor.

Blood samples were taken from each participant to examine lipid profiles in the morning with subjects fasting 8-10 h since evening. An accredited laboratory examines lipid profiles. The traditional approach for CVD risk assessment is LDL-C and triglycerides, but a recent study found that the concentration of non-high-density lipoprotein cholesterol (non-HDL-C) is superior to LDL-C in predicting CVD.[17] Therefore, we measured non-HDL-C (total cholesterol minus HDL-C) and non-HDL-C to HDL-C ratio (atherogenic coefficient).

Statistical analysis

We performed data analysis using the IBM SPSS 29.0.1.0 trial version (until 25 June 2023). We run a normality test on all numerical data. Normal distribution data are presented in mean ± standard deviation, and non-normal distribution data are presented in median (minimum-maximum). Spearman rank correlation was used to measure the correlation between variables in this study.

Results

Subject Characteristic

We analyzed data from 76 female students who participated in this study. Table 1 provides descriptive data for subject characteristics and family history of cardiovascular diseases. We found that the average age was 19.9 years old, with a range of 18–23 years old. The mean body weight was 61.73 kg with a range of 39.50–97.60 kg, and the mean height was 1.56 m with a range of 1.46–1.69 m. A family history of diabetes and hypertension were higher than others, 42.11% and 38.16%, respectively.

Table 1. Subject Characteristic

Characteristic*	Total (n=76)
Age	19.91 ± 1.04 years old
Body Weight	61.73 ± 13.96 kg
Body Height	1.56 ± 0.05 m
Family History*	
1. Heart Disease	
Absent	63 (82.89%)
Present	13 (17.11%)
2. Obesity	
Absent	57 (75.00%)
Present	19 (25.00%)
3. Diabetes Mellitus	
Absent	44 (57.89%)
Present	32 (42.11%)
4. Dyslipidemia	
Absent	66 (86.84%)
Present	10 (13.16%)
5. Hypertension	
Absent	47 (61.84%)
Present	29 (38.16%)
6. Stroke	
Absent	70 (92.11%)
Present	6 (7.89%)

*Values are presented as mean ± standard deviation or number (%)

Anthropometric and Blood Pressure

Table 2 shows that the mean body mass index was 25.59 kg/m2, with nearly half of the subjects being obese. In fat percentage, more than half of the total subjects were overfat (fat percentage > 45%). The most surprising aspect of the data is that 25% of these young female participants were suspected hypertension-based JNC VIII category.

Lipid Profile

The lipid profile characteristics of participants are summarized in **Table 3**. Based on the NCEP-ATP III classification, we found that almost all participants have normal triglyceride, and more than one-third have normal HDL. For non-HDL, we found that more than half of the participants have less than 130 mg/dL (at risk).

Table 2. Anthropometric and Blood Pressure of Participant

Characteristic*	Total (n=76)
BMI	24.55 (17.87–35.80) kg/m^2
Underweight	5 (6.58%)
Normal	30 (39.47%)
Overweight	4 (5.26%)
Obese	37 (48.68%)
Body Fat Percentage	36.50 (23.00–49.00) %
Underfat	1 (1.3%)
Ideal	34 (44.7%)
Overfat	41 (53.9%)
Blood Pressure	
Systolic Blood Pressure	112.01 ± 13.39 mmHg
Diastolic Blood Pressure	70 (53–101) mmHg
Blood Pressure Profile	
Hypertension	19 (25.00%)
Prehypertension	5 (6.58%)
Normal	52 (68.42%)

*Values are presented as mean ± standard deviation or number (%)

Table 3. Lipid Profile of Participant

Characteristic*	Total (n=76)
Triglycerides	73.5 (35–174) mg/dL
Risk (<150 mg/dL)	2 (2.63%)
Normal (≥150 mg/dL)	74 (97.37%)
HDL-C	55.18 (10.25) mg/dL
Low (<50 mg/dL)	23 (30.26%)
Normal (≥50 mg/dL)	53 (69.74%)
Non-HDL-C	133.08 ± 33.63 mg/dL
Risk (<130 mg/dL)	39 (51.32%)
Normal (≥130 mg/dL)	37 (48.68%)
Atherogenic Coefficient	2.50 ± 0.80

*Values are presented as mean ± standard deviation or number (%)

Correlation of Cardiovascular Risk and PFI

We categorized all the variables based on the PFI tertile (**Figure 1**). We can see that most obese students are in the lowest tertile, as do the overfat students. Two-thirds of prehypertension and hypertension students were also in the lowest tertile. For the lipid profile, there was no difference in PFI in triglyceride, HDL, and non-HDL.

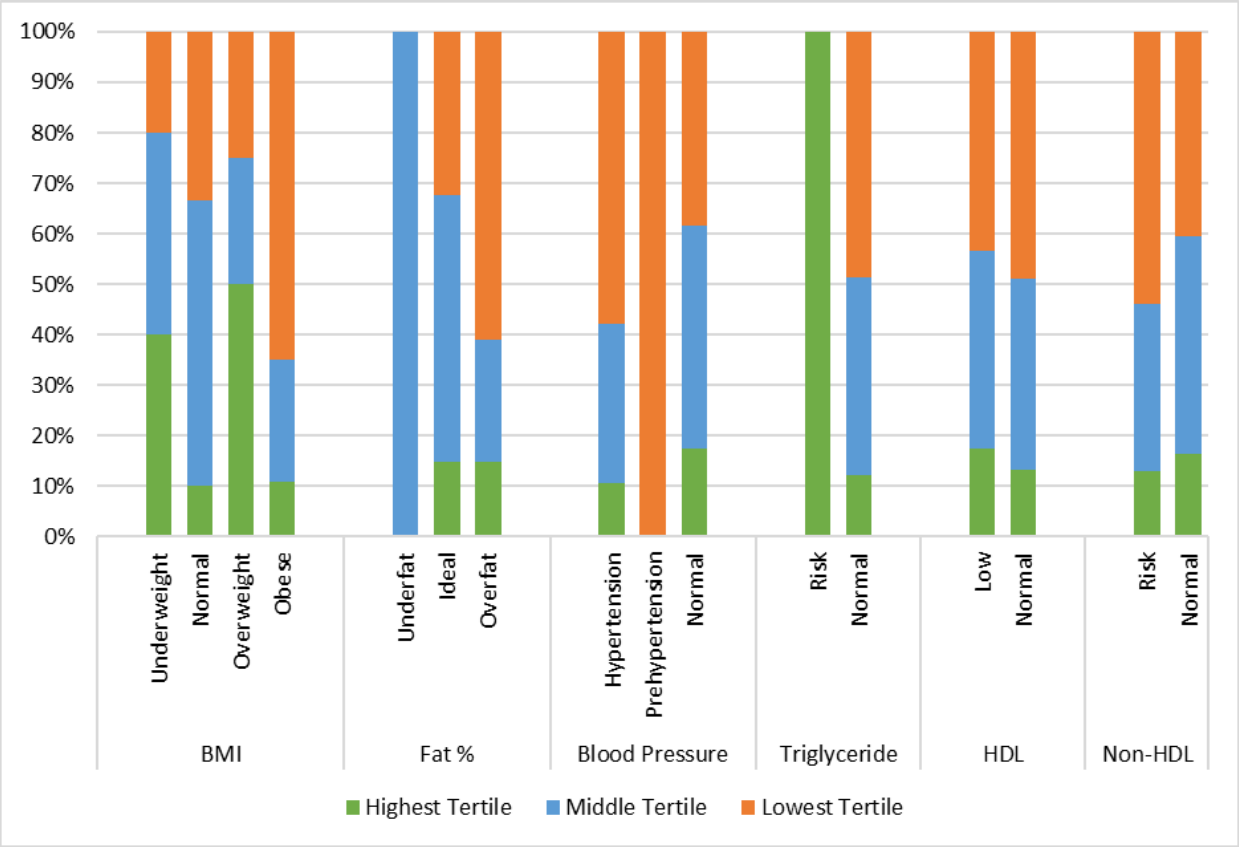


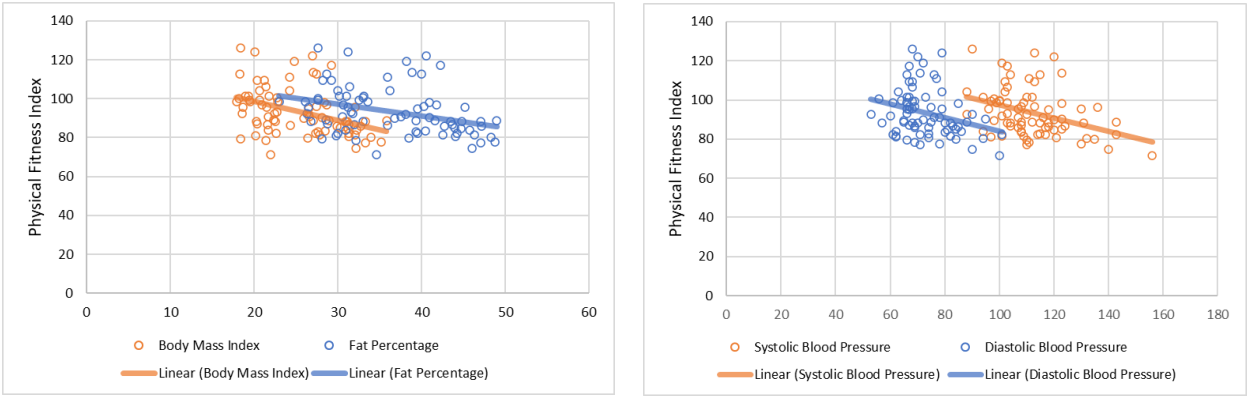
Figure 1. Cardiovascular risk based on PFI tertile

Further analysis determined the correlation between variables (**Table 4**). We found that PFI negatively correlates with BMI, body fat percentage, systolic blood pressure, and diastolic blood pressure (r = -0.443; r = -0.409; r = -0.370; r = -0.280), as shown in **Figure 2**. Increasing the physical fitness index led to a reduction in BMI, fat percentage, and blood pressure. The Spearman rank correlation did not show any correlation between PFI and all lipid profiles.

Table 4. Correlation between physical fitness index, fat percentage, blood pressure, and lipid profile

	PFI	BMI	Fat %	SBP	DBP	TG	Non-HDL-C	HDL-C	AC
PFI	1.000								
BMI	-0.443†	1.000							
Fat %	-0.409†	0.971†	1.000						
SBP	-0.370†	0.526†	0.549†	1.000					
DBP	-0.280†	0.475†	0.515†	0.708†	1.000				
TG	0.146	0.137	0.086	0.055	0.109	1.000			
Non-HDL-C	-0.04	0.163	0.182	0.169	0.166	-0.363†	1.000		
HDL-C	0.085	-0.250*	-0.213	-0.110	-0.012	0.487†	-0.099	1.000	
AC	-0.074	0.278*	0.267*	0.176	0.137	0.611†	0.804†	-0.613†	1.000

P-values were calculated by Spearman rank correlation.
PFI, Physical Fitness Index; SPB, Systolic Blood Pressure; DPB, Diastolic Blood Pressure; TG, HDL-C; High-Density Lipoprotein Cholesterol; AC, Atherogenic Coefficient.
* P<0.05; † P<0.01



A B

Figure 2. A. Correlation of physical fitness index with body mass index and fat percentage; B. Correlation between physical fitness index and blood pressure

Discussion

Our study found that more than one-third of our participants have a family history of cardiovascular disease, mainly obesity and diabetes mellitus. These results are consistent with those of Purohit et al.[18], who found that 77% of overweight medical students in Gujarat have a family history of CVD, and Costa et al.[19] found that 71.1% of female students at the University in Sao Paolo have a family history of diabetes melitus. This family history increases the participants' susceptibility to CVD in their later life.

One interesting finding is that hypertension was found in 25% of these young participants. In accordance with the present results, previous studies have demonstrated that the prevalence of hypertension in Damietta University students was 26.5% and 18.1% of students in Port-Said University.[20] This might be an alarm situation because these young populations were less aware of their blood pressure status.[21] The elevated oxidative stress from hypertension causes an inflammation response, which leads to a buildup of atherosclerotic plaque.[22] Coronary artery disease has this plaque formation within the endothelium as its primary cause. Atherosclerotic plaque may erode or rupture, causing thrombosis at first and, subsequently, a vascular closure that causes cardiovascular disease such as myocardial infarction, stroke, and limb ischemia.[23] There is, therefore, a definite need for screening blood pressure and educating students about healthy lifestyles to prevent hypertension.

The way the heart, lungs, and blood vessels effectively transport oxygen to the muscle used during continuous physical work is represented by cardiovascular fitness, which is measured by the physical fitness index in this study. Further analysis showed that the physical fitness index inversely correlates with blood pressure. This finding is consistent with the results of a previous study in men by Chase et al.[24] that found an inverse relationship between higher CRF levels and a lower risk of hypertension. Barlow et al.[25] suggested that if all unfit women in their population sample became fit, it might reduce hypertension by 22 percent. A study by Díez-Fernández et al.[26] found that adiposity mediates the association between cardiorespiratory fitness and blood pressure. A high level of cardiorespiratory fitness may attenuate the rate of progression from prehypertension to hypertension but might not neutralize the adverse effects of adiposity on blood pressure. Increasing individual fitness levels and maintaining a healthy body composition through enhanced physical activity should be a keystone of primary hypertension prevention.

Another finding from this study was that most obese students were in the lowest tertile and had a negative correlation between physical fitness index, body mass index, and fat percentage. This finding is similar to that of Chung et al.[27], who studied 124 Taiwanese youth. They found that CRF negatively correlates with body fat percentage ($r = -0.662$, $p<0.001$). Anwar et al.[28] also found a significant correlation between body fat percentage and aerobic and anaerobic performances. Apart from the percentage of fat, physical fitness also has an inverse correlation with other body composition indices like body mass index (BMI), waist circumference (WC), and waist-height ratio (WHtR).[29]

This study did not find a significant correlation between the physical fitness index with the HDL-C, non-HDL-C, and atherogenic coefficient. In contrast to earlier findings, Watanabe et al.[30] evaluated CRF and non-HDL-C in 4067 Japanese men and found an inverse relationship between CRF level and non-HDL-C. Physical activity can decrease the non-HDL-C, the numerator of the atherogenic coefficient, with several possible mechanisms: it activates the AMP-activated protein kinase in skeletal muscle, increases LPL, and improves insulin sensitivity.

These results must be interpreted cautiously due to a small sample size from a single population. These findings might not be generalized to other populations. Another limitation of this present study was using only one fitness parameter, and the cross-sectional design cannot assess the effect of physical fitness on the event of cardiovascular disease. Further research is needed to evaluate the correlation between various physical fitness parameters and the novel atherogenic coefficient with a bigger sample size in other populations.

The results of this investigation show that physical fitness is inversely correlated with body mass index, fat percentage, and blood pressure. These results suggest that the physical fitness measurement should be used as screening for cardiovascular risk factors since it is a simple and inexpensive test. Physicians should counsel their patients to engage in routine exercise to achieve higher fitness levels, maintain fitness over time, and decrease the fat percentage to prevent cardiovascular disease.

Ethical Considerations: The Research Ethics Committee of the Faculty of Medicine Universitas Andalas has approved this research.

Conflict of Interest: The authors declare no conflict of interest.

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Research Article

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COMPARISON OF HEALTH-RELATED QUALITY OF LIFE BETWEEN DIALYSIS PATIENTS AND KIDNEY RECIPIENTS

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Abstract

Objectives: Health-related quality of life (HRQOL) assessment is important for patients with end-stage kidney disease. This study aimed to determine the contribution of demographic factors to HRQOL in affected kidney recipients and dialysis patients on the waiting list for kidney transplantation in Iran.

Materials and Methods: This was a comparative survey. We required 196 patients in the Sina Organ Procurement Unit. HRQOL of 100 kidney recipients was measured using Study Short-Form 36 and compared with 96 dialysis patients. The factors investigated were age, gender, and cause of kidney failure; data were evaluated using SPSS 16.0 software.

Results: The scores of both groups were ordered from high to low in the following three dimensions: physical functioning, emotional well-being, and vitality. The mean physical component scores in kidney recipients and dialysis patients were 14.44±4.32 and 5.91±4.60, respectively. The mean mental component summary scores in kidney recipients and dialysis patients were 5.91 ± 4.60 and 5.12 ± 2.11, respectively. There were significant differences in all domains of HRQOL except role limitations due to emotional problems and emotional well-being in both groups (t = 0.963, P = 0.420). Age made the largest unique contribution (β = 0.211) to the physical component, while marital status was the greatest contributing factor to the mental component.

Conclusion: HRQOL improved after successful kidney transplantation compared to dialysis patients, despite kidney transplant patients suffering the effect of using immunosuppressive medicine and being subject to infectious complications and tumors. This study shows that we have reached the primary goal of transplantation, which is to improve the HRQOL of kidney recipients.

Keywords: Health-related quality of life, SF36 questionnaire, dialysis patients, kidney recipient, transplantation.

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Introduction

Available kidney replacement therapies include peritoneal dialysis, hemodialysis, and kidney transplantation. Dialysis and transplantation are two available treatments for end-stage renal disease (ESRD).[1] Kidney disease patients who need renal replacement therapy have impaired health-related quality of life.[2]

Between 2001 and the end of 2021, 54162 kidney transplantations (from living: 38899, from deceased: 15263) have been performed in Iran. In 2021, 1777 patients with ESRD underwent kidney transplantation from deceased and living donors in Iran.[3]

Kidney transplantation is the most reliable treatment for patients with end-stage kidney disease and offers improved survival compared with dialysis.[4] According to the World Health Organization (WHO), kidney transplantation is accepted as one of the best treatments for chronic kidney disease.[5] Kidney transplantation reduces mortality and improves the health-related quality of life for most patients when compared with dialysis.[6]

Both end-stage renal disease (ESRD) and kidney transplants have a large impact on several aspects of everyday life and thus affect their health-related quality of life (HRQOL),[7] which was defined by the WHO as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their aims, expectations, standards, and concerns". [8]

HRQOL, an individual's quality of physical, emotional, and social function in the face of a medical or health problem, is a multidimensional concept.[9] It goes beyond direct measures of general health, such as life expectancy and causes of death, and focuses on the impact that health status has on a patient's daily life.[10]

Reducing the effect of ESRD could potentially improve HRQOL. Several studies have reported an overall improvement in HRQOL after transplantation[11,12]. The SF-36 tool (SF-36) has become the standard measure used worldwide. It is considered a valid and reliable tool useful for assessing the HQOL of kidney patients.[13] Patient self-reported HRQOL scores provide outcome measures for assessing the efficacy of treatment and disease severity.[14]

The level of health-related quality of life of patients undergoing dialysis decreases in the various stages of kidney disease; this may be attributed to many factors.[15] The transplantation goal is not only to ensure their survival but also to offer patients a higher quality of life compared with the condition before transplantation, achieving a good balance between the functional efficacy of the organ and the patient's psychological and physical components.[16] Therefore, we submitted the SF-36 questionnaire to both patients who underwent

kidney transplantation from deceased donors and dialysis patients on a waiting list. We then compared the HRQOL of the life of kidney transplant patients with that of dialysis patients on the waiting list.

The purpose of this study was to examine differences between aspects of life quality among patients receiving renal transplants compared with dialysis patients.

Materials and Methods

The present descriptive correlational study was conducted on the Sina Organ Procurement Unit (OPU).

Using the Cochran Sample Size Formula, 189 individuals were enrolled in the study.

Convenience sampling was chosen to be the sampling method as the patients who visited the Sina organ procurement unit for periodical visits after transplantation, as well as dialysis patients who had registered on the kidney waiting list, were selected as the sample size. All patients agreed to answer the questionnaire. All patients knew that the topic of the study was their health-related quality of life. Eventually, with a probability of 10% of sample dropout, the sample size was 207 people (103 kidney recipient patients and 104 dialysis patients on the waiting list between 2020-2022).

Inclusion criteria for kidney recipients were three months or more post-renal transplantation and a functional renal graft (the patient does not need dialysis). Inclusion criteria for dialysis patients in the waiting list were three months or more in the waiting list. Additional inclusion criteria were being at least 18 years old, the ability to speak and read in Farsi, and availability and willingness to participate in this study.

Patients with multiple organ transplants or those who had more than one renal transplant, patients with transplantation from a living donor, and patients on a living donor waiting list were excluded from this study.

The HRQOL standardized questionnaire (SF-36) was completed for all participants. Demographic information was collected at the same time, including current age, gender, employment status, level of education, marital status, family financial income, cause of kidney failure, and the duration of dialysis before transplantation (in months).

Health-related quality of life / SF-36

The SF-36 tool assessment is used to evaluate the physical, psychological, and social domains of health, seen as distinct areas that are influenced by a person's experiences, beliefs, expectations, and attitudes.[16] The SF-36 has eight scaled scores; the scores are weighted sums of the questions in each section. Scores for each of the

eight health concepts range from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state). Higher scores declare better self-perceived health. Questions including Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), and Mental Health (MH). There are 2 component summary scores: the physical component summary (PCS) and the mental component summary (MCS).[17,18] The Cronbach's α = 0. 0.888 of SF-36 tool were calculated [19]. The survey began in March 2022, and the last response was collected in July 2022. Clinical and demographic data were collected from patient records in the Sina OPU. Each interview was conducted by the transplant coordinator, suitably trained and qualified to work with questionnaires, following instructions given by the study designers.

The present descriptive correlational study was conducted after obtaining approval from the ethics committee of the Tehran University of Medical Sciences. The aim, risks, and benefits of this study were explained to both groups before their participation. The participation was voluntary, and refusal to participate would not influence their clinical care.[20]

Statistical analysis

The Kolmogorov–Smirnov test was used to test the data distribution. Results showed a normal distribution of all dependent variables. Both the Chi-square and an independent sample t-test were used to compare the demographic variables in both groups. Moreover, the Chi-square test was conducted to compare the SF-36 health domain scores between kidney transplant recipients and dialysis patients on the waiting list. The students' t-test was also used to assess differences in SF-36 scores between the two populations. ANOVA was used if there were more than two groups. A multiple linear regression model also was used for data analysis. Statistical analyses were performed using SPSS16. The significance level was set at $P<0.05$.

Results

Demographic and Clinical Characteristics

During the two years under review, 207 patients were eligible for this study; of these, 196 completed the questionnaires (Dialysis patients on the waiting list [n=96], Kidney recipients [n=100]).

The sample covered a wide range of ages from 18 years to 79 years. Overall, the patients were predominantly male (135/68.87%) with a mean age of 47.28 ± 13.30 years with a median age of 47 years.

Altogether, there were 64 causes of ESRD, with hypertension the most common, followed by diabetes mellitus, Polycystic kidney disease (PKD), proteinuria, kidney stones, infection, and 56 other causes. The demographic and clinical characteristics data of the participants are summarized in Table 1.

Table 1. Sociodemographic and clinical characteristics of the participants (n = 196)

	Total (n = 196)	**Dialysis patients on waiting list (n = 96)**	**Kidney recipients (n = 100)**
Age, years (mean)	47.28± 13.30 (Median=47)	46.42± 13.51 (Median=45)	48.07± 13.23 (Median=48)
Marital Status			
Single	29 (14.79)	15 (15.63%)	14 (14%)
Married	159 (81.13)	77 (80.20%)	82 (82%)
Other	8 (4.08)	4 (4.17%)	4 (4%)
Number of children (among married and others)			
0	24 (14.20 %)	26 (27.08%)	9(10.98)
1-2	84(49.70%)	38 (39.59%)	45 (54.88%)
3-4	47 (27.82%)	23 (23.95%)	23 (28.05%)
More than 5	14 (8.28%)	9 (9.38%)	5 (6.09)
Sex			
Female	62 (31.63%)	33 (34.37%)	29 (29%)
Male	134 (68.37%)	63 (65.63%)	71 (71%)
Job			
Freelancer	65 (33.16%)	32 (33.33%)	33(33%)
Housewife	46 (23.46%)	22 (22.90%)	24 (24%)
Retirement	32 (16.33%)	14 (14.59%)	18 (18%)
Employee	22 (11.23%)	8 (8.33%)	14 (14%)
Worker	7 (3.57%)	5 (5.22%)	2 (2%)
Student	6 (3.07%)	3 (3.13%)	3 (3%)
Unemployment	18 (9.18%)	12 (12.50%)	6 (6%)
Level of Education			
Under diploma	87 (44.39%)	52 (54.17%)	35 (35%)
Diploma	77 (39.29%)	30 (31.26%)	47 (47%)
BSc/ Master	27 (13.77%)	11 (11.45%)	16 (16%)
Doctorate	5(2.55%)	3 (3.12%)	2 (2%)
Cause of ESRD			
Hypertension	63 (32.14%)	27 (28.13%)	36 (36%)
Diabetes Mellitus	35 (17.86%)	28 (29.17%)	7 (7%)
Infection	5 (2.55%)	1 (1.04%)	4 (4%)
PKD	20 (10.21%)	12 (12.50%)	8 (8%)
Kidney stone	7 (3.57%)	4 (4.16%)	3 (3%)
Proteinuria	10 (5.10%)	4 (4.16%)	6(6%)
Other	56 (28.57%)	20 (20.84%)	36 (36%)

Health-Related Quality of Life

According to Student's t-test, comparing the SF-36 scores of dialysis patients with the scores of kidney recipients, there were significant differences in all SF-36 dimensions except role limitations due to emotional problems (t = 0.963, P = 0.420) and emotional wellbeing (t = 4.711, P = 0.070).

In addition, there is a significant difference in the overall physical dimension (t = 6.652, P = 0.001) and emotional dimension (t = 2.763, P =0.001) between the two groups. Comparisons of the mean scores of SF-36 scores between kidney transplant recipients and dialysis patients are shown in Table 2.

According to the ANOVA test, there were statistically significant differences between the physical function (F = 2.7, P = 0.017), energy (F = 3.2, P = 0.006), general health (F = 3.7, P = 0.002), physical component summary (F = 3.05, P = 0.009), and job in kidney recipients.

Based on this test, there were not any significant differences between the genders based on HRQOL dimensions in dialysis patients.

This test didn't show any significant differences between each dimension of HRQOL and the cause of ESRD in recipient patients. This test showed that there are no significant differences between each dimension of HRQOL and the number of children in recipient patients.

Table 2. Comparisons of the mean scores of SF-36 between kidney transplant recipients and dialysis patients on the waiting list

Dimension	Kidney recipients	Dialysis patients	t	P
	M ± SD	M ± SD		
Physical functioning	71.82 ± 32.00	45.11 ± 34.89	5.551	0.001
Role limitations due to emotional problems	13.05 ± 13.21	11.59 ± 14.90	0.963	0.420
Role limitations due to physical health	10.80 ± 12.51	6.66 ± 11.50	2.392	0.009
vitality	26.59 ± 9.91	20.62 ± 11.12	3.980	0.001
Emotional well being	33.33 ± 10.92	30.35 ± 11.81	4.711	0.070
Social functioning	12.80 ± 4.81	9.82 ± 3.72	4.373	0.001
Bodily pain	17.34 ± 4.85	13.23 ± 6.11	5.281	0.001
General Health	17.33 ± 8.22	13.92 ± 7.89	3.760	0.001
Physical component summary	14.44 ± 4.32	9.83 ± 4.00	6.652	0.001
Mental component summary	5.91 ± 4.60	5.12 ± 2.11	2.763	0.001

According to Spearman analysis, there were statistically significant differences between the physical function (r = -3.62, P = 0.001), physical dimension (F = -2.65, P = 0.008), overall health-related quality of life (F = -2.65, P = 0.008) and age in kidney recipients. This test showed significant differences between general health (F = -1.81, P = 0.008) and the age of dialysis patients.

This test didn't show any significant differences between each dimension of HRQOL and the level of education and marital status in both groups.

According to the ANOVA test, there were significant differences between the genders with respect to physical function, energy, pain, and physical component summary. However, there were not any significant differences between the genders based on HRQOL dimensions in dialysis patients.

This test didn't show any significant differences between each dimension of HRQOL and the cause of ESRD in recipient patients. However, there were statistically significant differences between the physical function, energy, general health, physical component summary, and job in kidney recipients.

This test showed that there are no significant differences between each dimension of HRQOL and the number of children in recipient patients. This test also showed that there were no statistically significant differences between emotional well-being and the number of children in dialysis patients (Table 3).

According to Spearman analysis, there were statistically significant differences between the physical function (r = -3.620, P = 0.001), physical dimension (F = -2.652, P = 0.008), overall health-related quality of life (F = -2.650, P = 0.008), and age in kidney recipients. This test showed significant differences between general health (F = -1.813, P = 0.008) and the age of dialysis patients. This test didn't show any significant differences between each dimension of HRQOL and the level of education and marital status in both groups.

Multiple Linear Regression of Associations with HRQOL in Participation

The PCS score was associated with age (P = 0.022), gender (P = 0.021), level of education (p = 0.005), cause of ESRD (P = 0.020), and the number of children (P = 0.013). The model explains 4.50% of the variance in PCS. Marital status (P = 0.032) was associated with MCS. The model explains 37% of the variance in MCS. Age made the largest unique contribution (β = 0.211) to the PCS, while marital status (β = 0.213) was the greatest contributing factor to MCS (Table 4).

Table 3. Differences between gender, Number of children, and cause of brain death with SF_{36} dimensions in dialysis patients

	Component	**F**	**P**
Gender	Physical function	8.811	0.004
	Energy	3.724	0.040
	Pain	6.682	0.010
	Physical component summary	9.570	0.003
Cause of ESRD	Physical function	2.304	0.041
	Pain	3.331	0.005
	General Health	2	0.040
	Physical component summary	2.691	0.019
Number of children	Social function	2.645	0.008
	General Health	2.231	0.021

Table 4. Multiple linear regression between predictors variables and physical and mental component summary in all participants

Variable	**β**	**t**	**p**	**R^2**
Physical component summary				
Age	0.211	2.302	0.022	0.045
Gender	0.162	2.333	0.021	
Type of Job	0.001	0.040	0.960	
Level of education	0.201	2.811	0.005	
Cause of ESRD	0.152	2.201	0.020	
Lance of dialysis	0.073	0.952	0.344	
Marital status	0.102	1.112	0.265	
Number of children	0.170	2.500	0.013	
Mental component summary				
Age	0.050	0.573	0.561	0.370
Gender	0.083	1.131	0.253	
Type of Job	0.042	0.535	0.592	
Level of education	0.081	1.111	0.264	
Cause of ESRD	0.002	0.110	0.915	
Date of transplant	0.000	0.083	0.933	
Marital status	0.213	2.184	0.032	
Number of children	0.097	1.291	0.192	

Discussion

Nowadays, HRQOL is an issue of interest about outcomes after kidney transplantation, as well as a cause of concern for those under dialysis in that varying degree of disease-specific physical and psychological impairments are attributed to drug adverse effects.[21]

The results of this study show a worse HRQOL in dialysis patients compared to kidney recipients, typically in the areas of role limitation due to physical health problems, social functioning, and role limitations due to emotional problems.

We observed that patients after kidney transplantation have a higher HRQOL compared to dialysis patients. Similar to our study, Dew et al. demonstrated statistically significant pre- to post-transplant improvements in physical function, mental health, cognitive status, and overall HRQOL situation, [22] whereas others find no difference between the recipients and dialysis patients.[23]

Regarding our results, there were significant differences between the genders related to physical function, energy, pain, and physical component summary. However, in dialysis patients, a significant difference was not shown between the female/male and HRQOL dimensions. Mittal et al. declared that men have higher physical function scores than women in chronic kidney disease at the dialysis stage; however, mental function scores were similar.[24] In contrast, according to Esen et al., male patients with chronic kidney disease have better general health, vitality, and mental health scores.[25]

In spite of the improvement of physical function, pain, general health, and overall physical dimension, the cause of ESRD did not significantly influence HRQOL in recipient patients. Compatible with our research, Essue et al.[26] showed that kidney disease is associated with dietary and social restrictions, which make treatment acceptance difficult and may decrease HRQOL.

Physical function, physical dimension, overall HRQOL, and age exhibited statistically significant differences among kidney recipients. Dialysis patients also displayed a significant difference between general health and age.

Similar to our results, several studies showed that the HRQOL score is higher in younger patients than in older patients in both groups.[27,28] In contrast, another research[29] has shown that there was no significant association between age and HRQOL.

The result showed that there is a significant difference between each dimension of HRQOL and the level of education and marital status in both groups. In addition, there were statistically significant differences between emotional well-being, social function, general health, and the number of children in dialysis patients.

These results were the same as Ong et al.,[30] which showed that married patients in dialysis reported better health-related quality of life scores than those patients who were single, separated, and widowed, in favor of family support in coping and managing the illness, as well as in times of stressful situations.

Several important limitations of our study should also be noted. Kidney recipients and dialysis patients from only a single center were enrolled. In addition, the cross-sectional nature of our research does not allow us to draw conclusions about the relationship between treatment modality and HRQOL. Our sample size had similar social and demographic characteristics. Consequently, this is unlikely to have caused a systematic bias in our results.

It is advisable to design and implement an intervention program of support and follow-up of HRQOL for dialysis patients.

In conclusion, HRQOL improved after kidney transplantation compared to dialysis patients. Based on the results, SF36 was a useful tool as it allowed the transplant team to focus on different aspects of the HRQOL of kidney patients.

According to our knowledge, this study compares, for the first time in Iran, the quality of life of dialysis patients and kidney recipients, and also examines the demographic indicators and the quality of life in both groups in detail.

Regular evaluation of HRQOL may help to identify high-risk patients who may benefit from increased attention and risk modification interventions. Therefore, considering emotional problems is necessary in the recipient group by continuous access to mental and physical health support services. They also reinforce the need for longitudinal and intervention studies for dialysis patients. It is advisable to design and implement an intervention program of support and follow-up of HRQOL for dialysis patients.

Ethical Considerations: The present descriptive correlational study was conducted after obtaining approval from the ethics committee of the Tehran University of Medical Sciences, with approval ID: IR.TUMS.SINAHOSPITAL.REC.1401.080, on 17.11.2022.

Conflict of Interest: The authors declare that they have no conflict of interest.

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ASSESSMENT OF PHYSIOLOGICAL AND PSYCHOLOGICAL DEPENDENCE ON TOBACCO

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Abstract

Objectives: Smoking is recognized as the most important preventable public health problem in the world with known carcinogenic, mutagenic and addictive effects on many organs and systems.

Materials and Methods: Our study was conducted with 380 first-year students of Trakya University who were tobacco users in the 2020-2021 academic year. The 62-question questionnaire included questions about socio-demographic characteristics and smoking, as well as the 6-question Fagerstrom Nicotine Dependence Test (FTND) and the 25-question Test to Assess the Psychological Dependence on Smoking (TAPDS).

Results: Our study consisted of 185 male (48.69%) and 195 female (51.31%) students. Of the participants, 94 (24.73%) were from health-related faculties and 286 (75.27%) were from non-health-related faculties. It was observed that 364 (95.78%) of the participants smoked cigarettes and 16 (4.22%) used non-cigarette tobacco products. When the participants were classified according to their FTND scores, the most crowded category was very "slightly addicted" with 210 participants (55.27%), while the most crowded category was "moderately addicted" with 190 participants (50%) according to their TAPDS scores. It was also observed that using cigarettes as a tobacco product, having a smoker in the family and living alone at home made a statistically significant difference for both physical and psychological addiction. In our study, it was determined that there was a statistically significant, linear, same-directional and moderate relationship between physical dependence and psychological dependence.

Conclusion: In order to better understand the factors affecting smoking addiction and to make individualized treatment selection, it is important to differentiate between physical and psychological addiction.

Keywords: Cigarette, tobacco, physiological, psychological, dependence, family medicine.

Introduction

Tobacco use is recognized as the most important preventable public health problem in the world. It is known to cause more than 8 million deaths each year, 7 million of which are directly caused by tobacco use and 1.2 million of which are non-smokers exposed to second-hand smoke, and it is estimated that if this continues, smoking-related deaths will reach 10 million by 2030.[1] It is known that approximately 4000 chemicals such as carbon monoxide, cyanide, tar, nicotine, ammonia, carcinogenic and mutagenic substances in cigarettes are harmful to various organs and systems of the human body with synergistic effect and they cause serious diseases.[2] Nicotine, which enters the body when smoking, acts on the central nervous system and affects the release levels of neurotransmitters such as dopamine, acetylcholine, serotonin and noradrenaline. By affecting nicotinic acetylcholine receptors, dopamine increases, and the "nucleus accumbens", the pleasure and reward center in the brain, is affected. At the same time, the release of noradrenaline from the locus coeruleus causes seeking behavior and restlessness. This neurotransmitter system interacts with each other and with many complex systems, such as glutamatergic systems, and plays a role in the development of addiction.[3,4] As the act of smoking continues, the number of nicotinic receptors in the body increases, resulting in the fact that the same amount of cigarettes consumed becomes not enough to saturate the receptors (tolerance). The compulsive use of cigarettes and the emergence of conditions such as irritability, craving and seeking behavior (withdrawal) when cigarettes cannot be accessed are defined as "Physical Dependence".[5,6]

"Psychological addiction" has been recognized as important as physical addiction in recent years and has become an important issue in preventing smoking addiction and determining treatment preferences. Apart from the active and addictive psychostimulant substances in cigarettes, smoking behavior can cause people to keep smoking by citing such factors as a pretext as social acceptance, accompaniment of activity, relaxation, stress control, self-reward, self-expression and image. These factors provide psychological support for smoking addiction or help to develop psychological addiction.[7-10] This shows that smoking addiction is an addiction that needs to be examined multidimensionally. Many scales have been developed and used to help diagnose and treat the types and parameters of smoking/tobacco addiction.[9, 11, 12] In our study, we aimed to examine the physical and psychological dependence of smokers on cigarettes, the factors affecting them and the relationships between them in order to better understand their reasons why they smoke, and to eventually guide them in determining the appropriate steps to quit smoking.

Materials and Methods

Our study is a cross-sectional and descriptive study conducted among Trakya University first-year students in the 2020-2021 academic year. The study, which was conducted during the COVID-19 pandemic period, reached all first-year students studying at Trakya University (a total of 11,005 people), and all of them were invited to

the study. The data forms of 380 first-year students who volunteered to participate in the study and who were smoking/tobacco users were included in the sample.

The data were collected with a questionnaire consisting of 62 questions. The questionnaire included 31 questions about sociodemographic characteristics, smoking, smoking cessation status and factors that may affect smoking, as well as the Fagerstrom Test for Nicotine Dependence (FTND) consisting of 6 questions and the Test to Assess the Psychological Dependence on Smoking (TAPDS) consisting of 25 questions. The FTND is a scale that measures the severity of physical dependence on nicotine, which was created by revising the "Fagerstrom Tolerance Test" created by Karl-Olov Fagerström in 1978, and the reliability study of the Turkish version was conducted by Uysal et al.[3, 13] The results are analyzed in five groups as very low dependence, low dependence, moderate dependence, high dependence and very high dependence. The TAPDS was developed by Ponciano-Rodriguez et al. in 2015 to assess the psychological dependence on smoking, and the Turkish validity and reliability study was conducted by Bardakcı et al. in 2021.[8, 9]

Statistical Analysis

Median, minimum, and maximum values were given for descriptive statistics, and categorical variables were calculated as numbers and percentages. Mann Whitney U test was used for two independent group comparisons, and Pearson Chi-Square, Fisher's Exact and Fisher Freeman Halton tests were used for comparisons of differences between categorical variables according to groups. Kruskall Wallis H test was used for comparisons of more than two independent groups. Spearman rho correlation coefficient (r-value) was used to analyze the relationship between variables. Statistical analyses were performed with the Jamovi project (2021), Jamovi (Version 2.0.0.0), and JASP (Version 0.14.1.0) programs. A p-value lower than 0.05 was considered statistically significant.

Results

Of the 380 participants, 185 (48.68%) were male, and 195 (51.32%) were female, with a median age of 20 years (18-52). 361 (95%) of the participants had not repeated a grade, and 286 (75.27%) were studying in faculties not related to health. The socio-demographic characteristics of the participants are summarized in Table 1.

305 (80.26%) of the participants had a family member who smoked, and the median number of tobacco users in their family was 2 (0-10). Most of the 268 (70.52%) participants' close circle of friends were regular smokers, and 245 (64.47%) of the participants stated that they were sometimes asked whether they smoked when they applied to a health institution for any reason. 349 (91.85%) thought that smoking/tobacco use was harmful to

health. 248 (65.34%) of the participants reported that they currently smoked cigarettes/tobacco every day, and 364 (95.78%) of the participants used cigarettes as a tobacco product. The median age at initiation of smoking was 16 years, and 232 (61.05%) of the participants reported smoking for less than five years. Participants had smoked for a median of 4 years.

Table 1. Socio-demographic characteristics of the participants

Category		n (%)
Age	≥ 20 years	147 (38.68)
	< 20 years	233 (61.32)
Gender	Male	185 (48.68)
	Female	195 (51.32)
Faculty/department	Faculties related to health	94 (24.73)
	Faculties not related to health	286 (75.27)
Siblings	No siblings	57 (15)
	Have siblings	323 (85)
Person living with	At home, alone	14 (3.68)
	With my family	343 (90.32)
	Other	23 (6)
Where respondents spend most of their lives	Village	43 (11.31)
	District center	146 (38.43)
	Provincial center	191 (50.26)

Among the students, 172 (45.26%) stated that they did not plan to quit smoking, 243 (63.94%) participants had tried to quit smoking before, and 105 (43.2%) stated that they were able to quit smoking for 1-14 days in their most recent quitting attempt. 227 (59.73%) of the participants stated that they had not consulted any health institution in their last attempt to quit smoking.

The most frequently cited reason (65.84%) for participants to try to quit smoking was knowing that it could cause serious health problems in the future. The most important reason given by participants who did not consult a healthcare provider to quit smoking was that they thought they could quit of their own will (47.1%) without using any method. 215 (56.6%) of the participants stated that they tried to quit smoking voluntarily without using any method. The most common method (23.04%) used by the participants to quit smoking was to try to quit all at once without gradually cutting down (Table 2).

Participants scored a median of 2 (min 0, max 10) on the FTND and a median of 47 (min 25, max 75) on the TAPDS. According to the FTND, the most common group was the very slightly dependent group, with 210 (55.27%) participants, whereas the most common group was the moderately dependent group, with 190 (50%) participants, according to TAPDS. (Table 3).

Table 2. Participants' smoking/tobacco use characteristics

Description		n (%)
Smoking use in the family	No	75 (19.74)
	Yes	305 (80.26)
The density of regular tobacco users in participants' close circle of friends	Nobody uses it	5 (1.31)
	The majority do not use it	29 (7.64)
	Majority use it	268 (70.52)
	They all use it	78 (20.53)
The frequency with which participants were questioned about their smoking/tobacco use in health institutions	Never	92 (24.22)
	Sometimes	245 (64.47)
	Always	43 (11.31)
Participants' opinions on the harm of smoking to health	Not harmful	31 (8.15)
	Harmful	349 (91.85)
Smoking status of the participants	I smoke occasionally now; I never used to smoke at all.	38 (10)
	I smoke occasionally now; I used to smoke occasionally	74 (19.5)
	I smoke occasionally now; I used to smoke every day	20 (5.26)
	I smoke every day now	248 (65.34)
Which tobacco product did the participants use	Cigarette	364 (95.78)
	Non-cigarette tobacco products	16 (4.22)
How many years the participants have been smoking	< 5 years	232 (61.05)
	5-10 years	137 (36,05)
	> 10 years	11 (2.9)
Whether participants have ever attempted to quit smoking/tobacco	No	137 (36.06)
	Yes	243 (63.94)
How long the participants did not smoke/tobacco in their last attempt to quit smoking/tobacco	1-14 days	105 (43.20)
	15-30 days	38 (15.63)
	1 month – 3 months	46 (18.93)
	3 months - 6 months	30 (12.34)
	6 months - 1 year	20 (8.24)
	More than 1 year	4 (1.66)
Whether the participants who have attempted to quit smoking/tobacco have applied to any health institution	Those who do not apply to a health institution	230 (94.65)
	Applicants to a health institution	13 (5.35)
How participants realized their attempts to quit smoking/tobacco use	Quitting suddenly	124 (51.03)
	Those who have tried and failed to quit smoking	63 (25.93)
	By reducing the number of cigarettes per day	56 (23.04)
Participants' reasons for attempting to quit smoking use	Knowing that smoking can cause serious health problems in the future	160 (65.84)
	Monetary burden/loss	135 (55.55)
	My close circle of relatives asking me to quit for my own sake	55 (22.63)
	Smoking takes up/wastes my time	50 (20.57)
	My close environment is uncomfortable with my smoking	30 (12.34)
	I have existing health problems	21 (8.64)

Table 3. Grouping of Participants According to Scale Scores

Scale Scores		n (%)
Fagerstrom Test for Nicotine Dependence (FTND)	Very low dependency	210 (55.27)
	Low dependency	76 (20)
	Moderate dependency	41 (10.78)
	High dependency	38 (10)
	Very high dependency	15 (3.95)
Test to Assess the Psychological Dependence on Smoking (TAPDS)	Mild dependence	118 (31.05)
	Moderate dependence	190 (50)
	Severe dependence	72 (18.95)

Gender and being enrolled in a health-related/non-health-related faculty did not create a significant difference according to the TAPDS, whereas males and being enrolled in a non-health-related faculty were found to be associated with significantly higher dependency scores according to the FTND.

Living alone at home, having a smoker/tobacco user in the family, having more smokers in the close circle of friends, not thinking that smoking is harmful to health, smoking more frequently, preferring cigarettes as the tobacco product used, not thinking about quitting smoking and not having tried to quit smoking were found to be associated with higher addiction scores according to both FTND and TAPDS (Table 4).

A statistically significant, linear, same-directional and moderate relationship was found between FTND scores and TAPDS categories (Figures 1 and 2).

Table 4. Evaluation of sociodemographic and smoking characteristics according to TAPDS and FTND scores

Socio-demographic and smoking characteristics	**TAPDS** [min-max]	**p**	**FTND** [min-max]	**p**
Age				
Under 20	49 [25 – 73]	0.083	1 [0 – 9]	0.153
20 and over	46 [25 – 75]		2 [0 – 10]	
Gender				
Male	47 [25 – 75]	0.931	3 [0 – 10]	**0.025**
Female	47 [26 – 75]		1 [0 – 10]	
Faculty / Department				
Related to health	48 [26 – 75]	0.724	1 [0 – 10]	**0.047**
Not related to health	47 [25 – 75]		2 [0 – 10]	
The current environment				
Home, alone	57 [32 – 68]	**0.044**	5 [0 – 8]	**0.008**
With my family	47 [25 – 75]		2 [0 – 10]	
Other	41 [26 – 75]		2 [0 – 7]	
Whether there is a smoker in their family				
No	45 [26 – 64]	**0.033**	1 [0 – 9]	**<0.001**
Yes	48 [25 – 75]		2 [0 – 10]	
Regular smokers in the close circle of friends				
Nobody uses it	36 [34 – 67]	**0.002**	1 [0 – 10]	**<0.001**
The majority don't use it	43 [29 – 60]		0 [0 – 10]	
Majority use it	47 [25 – 75]		2 [0 – 9]	
They all use it	52 [31 – 73]		4 [0 – 9]	
Thinking that smoking is harmful to health				
I don't think it's harmful	56 [33 – 75]	**<0.001**	4 [0 – 9]	**0.003**
I think it is harmful	47 [25 – 75]		2 [0 – 10]	
How they describe their smoking/tobacco use				
I smoke occasionally now; I never used to smoke at all	38 [26 – 64]	**<0.001**	0 [0 – 7]	**<0.001**
I smoke occasionally now; I used to smoke occasionally	41 [25 – 75]		0 [0 – 7]	
I smoke occasionally now; I used to smoke every day	41 [29 – 65]		0 [0 – 6]	
I smoke every day now	51 [26 – 75]		4 [0 – 10]	
Type of tobacco product used				
Cigarette	48 [26 – 75]	**0.004**	2 [0 – 10]	**0.001**
Non-cigarette tobacco products	40.5[25 – 58]		0 [0 – 7]	
Smoking cessation attempt				
Not attempting to quit	50 [28 – 75]	**0.003**	3 [0 – 9]	**0.011**
Attempting to quit	46 [25 – 73]		2 [0 – 10]	
The status of applying to any health institution in a smoking cessation attempt				
Non-applicants	46 [25 – 73]	**0.008**	1 [0 – 10]	**<0.001**
Applicants	51 [34 – 66]		5.5 [0 – 9]	
How did they realize their smoking cessation attempts				
I tried to quit smoking/tobacco but failed	53[29 – 73]	**<0.001**	3 [0 – 10]	**<0.001**
By reducing the number of cigarettes per day	43.5 [26 – 67]		1 [0 – 7]	
Quitting suddenly	45 [25 – 69]		1 [0 – 10]	

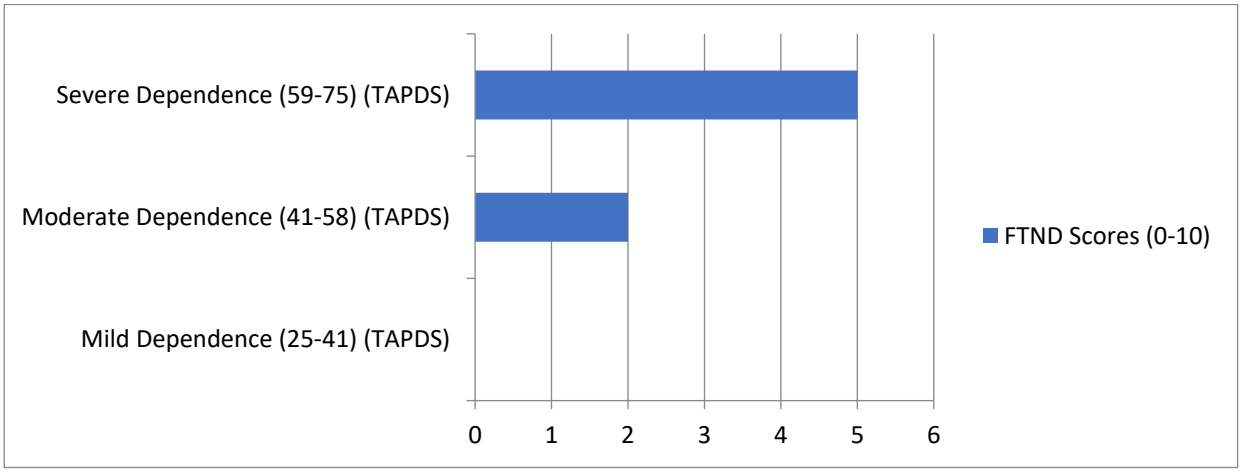

Figure 1. The relationship between participants' TAPDS and FTND scores

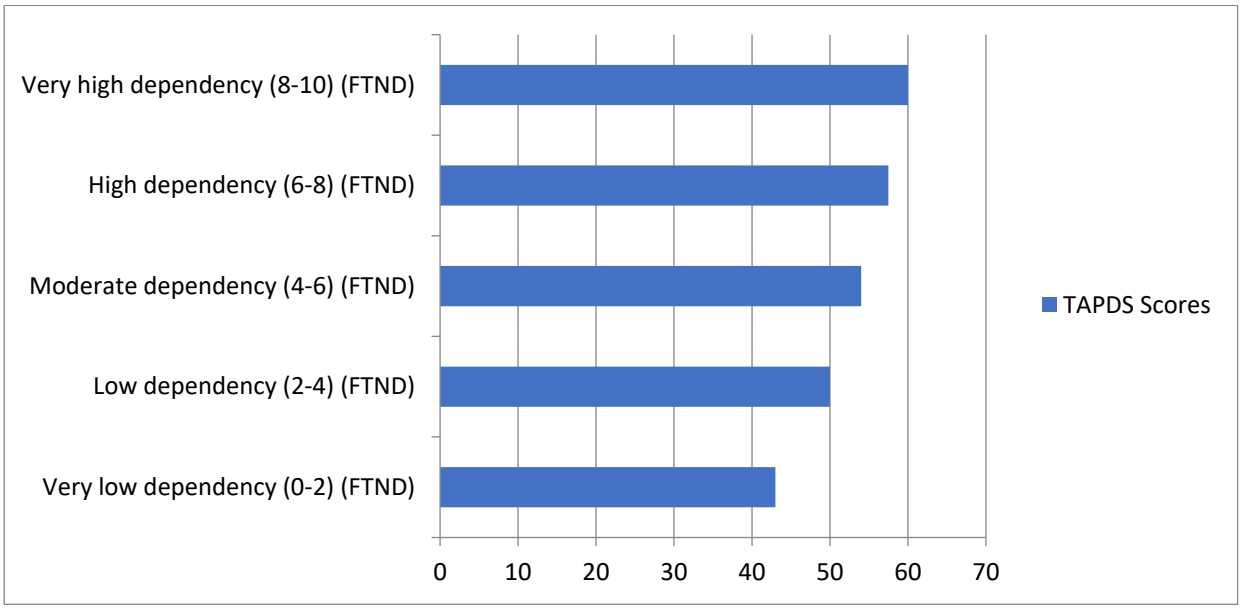

Figure 2. The relationship between participants' FTND and TAPDS scores

Discussion

Smoking/tobacco use is one of the leading preventable public health problems in our country and in the world. The struggle to protect society from smoking and its effects includes both the cessation of smoking by smokers and the protection of non-smokers from the harmful effects of smoking. Therefore, it is necessary to examine all factors that are thought to have an effect on smoking and to investigate the characteristics of psychological addiction as well as physical addiction.

In our study, significantly higher dependence was found in males compared to females according to FTND, whereas no significant difference was found according to TAPDS. In 2012, in the comprehensive Global Adult Tobacco Survey (GATS) conducted in Turkey, smoking rates were found to be 47.9% in men and 15.2% in women in the whole population.[1] Similarly, many researchers have reported that the smoking prevalence of men is significantly higher than that of women, while a study conducted on university students reported that gender did not make a significant difference in the examination of smoking addiction.[14-17] In a study conducted in a smoking cessation center in Mexico, in line with our study, significantly higher dependence was found in men compared to women, according to FTND, while no significant difference was found according to TAPDS.[9] In a study conducted in a smoking cessation center in Turkey, no significant difference was found between genders according to both FTND and TAPDS.[10] The high prevalence of smoking and nicotine addiction in men, which is generally accepted in the literature, has been interpreted as the gender roles attributed to men in a patriarchal society and the fact that smoking is seen as a sign of power, self-confidence and independence. However, the fact that there was no significant difference, especially in terms of psychological dependence, suggests that psychological factors are less affected by gender.

In our study, both physical and psychological dependence levels were found to be significantly higher in those who had smokers in their families. In the literature, many studies conducted in medical faculties concluded that the effect of having parents and siblings who smoke significantly increased the likelihood of smoke addiction, which is consistent with our study.[18-20] People are influenced throughout their lives by the environments in which they are born and raised. Many behaviors of the people in the family who care, protect and serve as role models are taken as examples by the child. It is expected that the likelihood of this behavior will increase in members of families with smoking/tobacco use. In addition, while the prohibition and intimidation of authority figures at home can play a preventive role against harmful habits, an authority figure who is a bad example of smoking/tobacco use will have difficulty in prohibiting this behavior for other members.

It was found that as the regular smoking/tobacco use status of the friends of those students who participated in our study increased, smoking addiction increased according to both FTND and TAPDS. Friends are together in one or more activities during the day; they help each other, they talk to each other, and they can share many things. Therefore, it is inevitable that they are influenced by each other. For this reason, smoking is also an activity that is suitable for doing together and for friends to encourage each other. Many studies in the literature have emphasized that having friends who smoke is an important risk factor for smoking addiction.[21,22]

In our study, health-related faculties had significantly lower FTND scores than non-health-related faculties. Many studies have been conducted to investigate the relationship between the smoking addiction levels of university students who smoke and the faculties in which they study. In studies conducted in Egypt, England and Turkey, students studying in medical faculties were found to have lower smoking rates than students studying in non-health-related departments.[18,23,24] In another study conducted in Turkey, it was reported that FTND scores of medical faculty students were also lower than those of other students.[25] Unlike the general literature, there are also studies that conclude that smoking addiction scores do not differ significantly according to the faculties of study.[26] In light of these data, it can be said that the FTND results of our study are compatible with the literature. In our study, no significant difference was found in TAPDS scores in terms of psychological dependence, which has not been sufficiently examined in the literature. It should be considered that these differences may vary according to which faculties were examined and how they were grouped. In general, although it is observed that both smoking rates and nicotine addiction rates of students in departments with more knowledge about the harms of smoking are lower, it will be important to evaluate the types of smoking addiction separately in future studies.

In our sample, 95.8% were cigarette smokers, and 4.2% were users of non-cigarette tobacco products such as pipes, cigars, hookahs, and electronic cigarettes. Similarly, in many studies, it is noteworthy that cigarettes are used at the highest rate among tobacco products.[1,27] In addition, in our study, it was observed that cigarette smokers had significantly higher dependence on FTND and TAPDS than non-cigarette smokers. The fact that cigarettes have a more standardized form and are more easily accessible than other tobacco products may have caused them to be used more than other tobacco products. The fact that cigars, pipes, electronic cigarettes and hookahs are relatively more difficult to access may leave addicted individuals in a difficult situation when they experience withdrawal; therefore, it can be expected that people who use non-cigarette tobacco products are mostly composed of people with lower addiction levels.

In our study, when the participants who wanted to quit smoking were asked why they wanted to quit smoking, health-related concerns ranked first in line with the literature.[3,28] Moreover, in our study, it was found that people who thought of quitting smoking due to health concerns were less dependent, according to both the FTND and the TAPDS.

The FTND is the scale that is considered to best assess the building blocks of physical dependence, such as withdrawal and tolerance.[8] In our study, FTND was used to measure physical dependence, and the most populous group was the very slightly dependent group, with 55.3%, which is consistent with the literature. In studies conducted in universities, the group with the lowest level of dependence score according to FTND constituted the largest percentage; Yengil et al. found 51.6%, Okutan et al. 40.9%, Selçuk et al. 54.4%. [18, 29, 30]

As the pathophysiology of smoking addiction is examined, it is understood that it is a multidimensional process that is formed by the combination of many complex and mutually reinforcing factors. It is thought that it would be incomplete to consider smoking only as a physical addiction, and similarly, the psychosocial aspect should also be examined separately.[8, 9] Karlıkaya et al. emphasized the importance of genetic factors and nicotine addiction as well as psychosocial factors in smoking behavior and its continuation.[4] Examples include people with psychiatric illnesses starting to smoke earlier and more intensely than the general population, the tendency of individuals to see smoking as a solution when they are under distress and stress, and individuals with neglectful parents seeking to compensate for emotional deprivation in addictive substances such as cigarettes show the importance of examining the psychological dimension of smoking.[10] In our study, we tried to measure the psychological dependency levels of the students with TAPDS. While those with moderate psychological dependence constituted the largest group with 50%, those with severe psychological dependence constituted the smallest group with 18.9%. When it is remembered that the most crowded group in the same sample with the FTND was the group with very low dependency at 55.3%, it can be seen that the two scales asked different questions according to different parameters as intended and as a result, they could evaluate different dependencies.

In our study, in which we compared both scales, it was found that there was a statistically significant, linear, same-directional, and moderate correlation between FTND scores and TAPDS scores. Ponciano-Rodríguez et al. found a same-directional and weak correlation, while Hezer and Karalezli found a moderate, same-directional, linear relationship.[9,10] These scales, which reveal two dimensions of smoking addiction, emphasize the need for a multidimensional approach to smoking addiction. Using both scales together in smoking addiction studies will provide more complementary and more accurate results.

In conclusion, since smoking addiction is a multidimensional process formed by the combination of many complex and mutually reinforcing factors, it would be insufficient to treat it only as a physical addiction. For this purpose, FTND and TAPDS are considered to be meaningful, correlated and preferable scales for the examination of physical and psychological addiction to cigarettes separately and can be easily applied in primary care.

Limitations

The fact that the study was conducted during the COVID-19 Pandemic should be taken into consideration that the study data may reveal different results compared to routine life.

Ethical Considerations: Approval was obtained from the Trakya University Faculty of Medicine Scientific Research Ethics Committee (Trakya -BAEK 2021/106).

Conflict of Interest: The authors declare no conflict of interest.

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HISTORICAL ASPECTS OF NON-ALCOHOLIC FATTY LIVER DISEASE: STUDIES AND CLASSIFICATIONS

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Abstract

Non-alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases worldwide and is currently the second leading indication for liver transplantation. The global obesity pandemic is linked to metabolic syndrome, so the prevalence of NAFLD will increase progressively and become a real burden on the economy and public health worldwide. Assuming that assessment of the history of a disease can improve clinical practice and provide efficient clues for research, the aim of this article is to review the background of nonalcoholic fatty liver disease (NAFLD) in adults and children. We have reviewed the evolution of the definition and classification of NAFLD as a distinct nosological form and started our consideration with the year 1836. The review performed covers the first guidelines issued by the scientific community throughout current clinical guidelines. We have also considered diseases associated with this pathology, from early steps to more recent studies confirming that NAFLD is a risk factor for cardiovascular disease, hepatocellular carcinoma, and other malignancies. This article discloses current differences in the International Classification of Diseases (ICD) 10 and ICD 11. In the updated ICD 11th revision, NAFLD is presented as a separate heading (DB92 - nonalcoholic fatty liver disease), which is closer to modern nomenclature. This classification allows a better understanding of research and clinical approaches to the diagnosis, treatment, and prevention of the disease.

Keywords: Non-alcoholic fatty liver disease, liver steatosis, obesity, metabolic syndrome.

Introduction

Nonalcoholic fatty liver disease (NAFLD) is a chronic liver disease of metabolic genesis in individuals without exogenous factors of toxic liver damage (e.g., exogenous ethanol), caused by lipid accumulation in liver lobe composing cellular elements, morphologically confirmed by steatosis, steatohepatitis, fibrosis, cirrhosis or adenocarcinoma. NAFLD is diagnosed when lipid accumulation in the form of triglycerides (TG) is more than 5-10% of hepatocyte mass or when more than 5% of hepatic cells contain lipid deposits.[1]

NAFLD includes a wide range of diseases of varying severity with different prognoses: steatosis, nonalcoholic steatohepatitis, fibrosis, cirrhosis, and hepatocellular carcinoma.[2]

NAFLD is the most common liver disease worldwide and is currently the second leading indication for liver transplantation in the United States, second only to alcohol-related liver disease.[2,3] The highest NAFLD prevalence is in Latin America at 44.37%, then Middle East and North Africa at 36.53%, South Asia at 33.83%, Southeast Asia at 33.07%, North America at 31.20%, East Asia at 29.71%, Asia Pacific at 28.02%, Western Europe 25.10%.[4] In Russia, according to the DIREG2 multicenter study, the prevalence of NAFLD in outpatients was as high as 37.3%.[5]

The rates of decompensated cirrhosis with nonalcoholic steatohepatitis (NASH) are predicted to increase up to 168%, as NASH complicated by hepatocellular carcinoma up to 137% in the period 2015- 2030.[6] As the global obesity pandemic fuels metabolic conditions, the prevalence of NAFLD will increase progressively and become a real burden on the economy and public health worldwide.[4]

Non-alcoholic fatty liver diseases as a separate nosological form: history of definition

T. Addison coined the term "fatty liver" in 1836 when describing the liver in patients suffering from alcohol abuse.[7] In 1838, an Austrian physician and pathologist, Carl von Rokitansky, documented the accumulation of liver fat in hepatic cells in autopsy specimens, suggesting that it might be the cause of cirrhosis of this organ.[8]

Subsequently, for decades, pathologists determined the similarity of changes in the histological structure of the liver observed in patients with diabetes mellitus and obesity.[9, 10]

In 1938, Ch. Connor described fatty liver infiltration, which could lead to cirrhosis in diabetic patients. He reported two cases of bleeding from esophageal varices (one case was fatal because of severe hemorrhage) in patients with diabetes mellitus and fatty liver dystrophy.[11]

In 1958, J. Westwater and D. Feiner reported on histological findings of fatty liver infiltration in obese patients. They confirmed that hepatic test abnormalities and morphological changes improved after weight reduction. In 1962, H. Thaler added certain clinical and pathological descriptions of the disease by investigating liver pathology in diabetes mellitus, which he described as steatosis with an inflammatory response.[12]

In 1960-1970. S.D. Podimova described several cases of liver changes corresponding to steatosis with signs of inflammation in patients who did not abuse alcohol.[13]

In 1980, the term non-alcoholic steatohepatitis was coined by J. Ludwig et al. (Mayo Clinic, USA) to describe a progressive form of fatty liver disease that histologically resembled alcoholic steatohepatitis. Most of the patients were obese women, and many of them had diabetes mellitus.[14]

In 1983, J. Moran et al. extended these findings to obese children. In the children, abnormal liver enzymes and nonspecific abdominal pain accompanied by steatohepatitis.[15]

In 1986, F. Schaffner and H. Thaler were the first to use the term "nonalcoholic fatty liver disease".[16]

Diseases associated with non-alcoholic fatty liver disease

By the early 2000s, it had already become clear that NAFLD was associated with certain somatic pathologies, with hepatocellular carcinoma, as well as with extrahepatic cancer diseases.[17-26]

Non-alcoholic fatty liver disease and the risk of cardiovascular diseases

In 2004 and 2005, G. Targher and co-authors were the first to report that NAFLD was more closely associated with an increased risk of cardiovascular diseases in patients with type 2 diabetes mellitus.[17,18]

In 2016, G. Targher and co-authors found that patients with NAFLD had a higher risk of cardiovascular diseases, arterial hypertension, atherosclerotic disease, etc., compared with the control group without NAFLD.[19]

In 2021, M. Yoneda and co-authors evaluated the relationship of NAFLD with cardiovascular diseases using a Japanese nationwide database from April 2013 to March 2019. The results of this meta-analysis showed that the identification rate of patients with cardiovascular diseases is higher in NAFLD compared to the control group. Among patients with NAFLD, the frequency of complications with diabetes mellitus and hypertriglyceridemia is high, which in turn can contribute to the development of cardiovascular diseases.[20]

According to a systematic review and meta-analysis of prospective studies published from 1966 to 2021, NAFLD was associated with an increased risk of stroke, myocardial infarction and atrial fibrillation. The

analysis also confirms that mortality from cardiovascular diseases was the same in the groups with and without NAFLD.[21]

Risk of cancer in nonalcoholic fatty liver disease

In 2002, two major studies reported on the risk of hepatocellular carcinoma (HCC) in NAFLD. E. Bugianesi et al. studied patients with hepatocellular carcinoma because of cirrhosis and noted that hypertriglyceridemia, diabetes mellitus, and increased aminotransferases were risk factors for hepatocellular cancer, suggesting that it may represent a late complication of cirrhosis resulting from NASH.[22]

Currently, according to the data provided by the European, American and Italian Liver Foundations, HCC in patients is a definite finality of the natural course of liver diseases, including NAFLD.[2,23,24]

In 2003, H. Sørensen et al. compared data from the Danish general population (7326 people) with alcoholic liver disease or nonalcoholic fatty liver dystrophy. The results showed that the patients with nonalcoholic fatty liver dystrophy had an increased risk of pancreatic cancer and renal cancer.[25]

Various types of extrahepatic cancer, including colorectal adenoma and carcinoma, are currently commonly identified as NAFLD-associated diseases.[26]

According to 2019 data, NAFLD is more associated with an increased risk of gastrointestinal and uterine cancers than with obesity.[27]

National guidelines and clinical recommendations for diagnostics and treatment of non-alcoholic fatty liver

Subsequently, scientific associations around the world began their work on clinical guidelines focused on diagnostic criteria and management of NAFLD. Interestingly, a decade-long gap separates the first clinical and pathological signs of NAFLD from the first recommendations issued by scientific associations. This probably reflects an initial lack of evidence-based data in favor of strong recommendations. Continued growth in incidence, advances in diagnostic techniques, and the results of research and clinical trials of new drug regimens have played a critical role in making the publication and updating of clinical guidelines for NAFLD an ongoing challenge for scientific liver associations.

The Asian Pacific Association issued the first guidelines on NAFLD for the study of the liver (APASL) in 2007. They involved information for clinicians regarding a new common disease.[28,29] Despite the lack of evidence-

based data, the authors were able to formulate general principles in the management of NAFLD. This document, proposed by the Asian Scientific Association, paved the way for the guidelines on NAFLD in Europe.

In 2010, the European Association for the Study of the Liver (EASL) summarized the results of the 2009 NAFLD/NASH Special Conference.[30] This article outlined expert opinions regarding the diagnosis and treatment of patients with NAFLD. The main ones are:

1) In patients with elevated alanine aminotransferase (ALT) on the biochemical blood count or with hepatic steatosis on ultrasound, noninvasive methods to assess fibrosis should be the first-line procedure.

2) In patients with other chronic liver diseases, an ultrasound examination should be performed to identify metabolic risk factors and steatosis.

3) During elective surgical procedures, such as bariatric surgery for obesity (high risk of NASH) and cholecystectomy (common risk factors between NAFLD and cholelithiasis), liver biopsy should be performed.

4) Treatment of patients with NAFLD should primarily include weight loss (5-10% weight loss may be sufficient to normalize aminotransferase and improve liver architectonics with steatosis), lifestyle changes, and physical exercises.

In 2012, a collaborative effort of the three major American Hepatology Associations, the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association, and the American College of Gastroenterology, published a regulatory document on NAFLD. They proposed:

1) Screening family members for NAFLD is not recommended;

2) Assessment of fibrosis by noninvasive diagnostic methods in patients with NAFLD is a useful tool for identification of fibrosis and/or cirrhosis;

3) Liver biopsy for suspected NAFLD should be considered in patients with other comorbid chronic liver disease;

4) Metformin has no significant effect on liver morphology and is not recommended as a specific treatment for NASH;

5) Vitamin E (α-tocopherol) administered at a daily dose of 800 IU/day can improve liver histology in adult patients with NASH without diabetes and, therefore, can be considered as first-line pharmacotherapy for the patients;

6) Ursodeoxycholic acid (UDCA) is not recommended for the treatment of NAFLD;

7) Omega-3 fatty acids can be considered for the treatment of hypertriglyceridemia in NAFLD patients;

8) Statins should not be used for specific treatment of NASH; they can only be used to treat dyslipidemia in patients with NAFLD.[31]

In 2014, the World Gastroenterology Organization published its regulatory document on basic principles of diagnosis and treatment of NAFLD.

Here are some of them:

1) NAFLD and NASH are a serious global pandemic public health problem and affect both rich and poor countries;

2) Diet and exercise should be recommended for all patients;

3) Not everyone with fatty liver dystrophy needs aggressive therapy;

4) Liver puncture biopsy should be performed in patients who have risk factors for NASH and/or other liver diseases; 5) NAFLD and NASH are also an increasing problem in pediatric patients, including those under ten years of age.[32]

Consensus and practice guidelines based on recommendations from national associations were also published between 2007 and 2014. These include the Italian Association for the Study of the Liver (AISF), 2010 Chinese Association for the Study of Liver Diseases, 2011, Korean Association for the Study of the Liver, 2013, Japanese Society of Gastroenterology and Japanese Society of Hepatology, 2015.[33-36]

Classification of nonalcoholic fatty liver disease

Since the 1920s, Austrian, Swedish, and Spanish authors have reported on the association of arterial hypertension, diabetes mellitus, obesity, hyperuricemia, and cardiovascular disease. Over the past years, several international organizations have tried to form a reference of what is included in the terms "metabolic syndrome" and "insulin resistance," proposing different definitions for them.[37]

A considerable amount of information has recently been published supporting the change in the nomenclature of nonalcoholic fatty liver disease to metabolic fatty liver disease (MFLD). "Consensus" statements have been made, as well as a number of articles that have attempted to emphasize the need for this change.[38]

In 2020, an international expert consensus statement was issued. The statement proposed a new concept - metabolically associated fatty liver disease (MAFLD). According to the authors of this consensus, this interpretation of the disease allows both focusing on the systemic and multifactorial pathogenesis of liver parenchyma damage and making medical care more personalized for various clinical options of comorbidity associated with MAFLD.[39,40]

Nevertheless, is this really the case? In 2021, Sh. Singh et al., in their study on the pathogenesis of NAFLD, deeply disagreed with a possible change in the nomenclature of this disease. In their opinion, NAFLD is a heterogeneous disease with different pathogenetic mechanisms, one of which is liver steatosis caused by metabolic dysfunction. The authors believe that instead of changing nomenclature without strong scientific support, efforts should be directed toward understanding the pathogenesis of NAFLD in different populations, which can potentially help develop new therapeutic options.[38]

Russian experts who compile clinical guidelines agree with the authors of the NAFLD Consensus but nevertheless recommend clinicians use the WHO-approved codes in their daily practice, as specified both in the current ICD-10 and in the soon-to-be-released ICD-11.[1]

The International Classification of Diseases is a regulatory document with generally accepted statistical classification of diagnoses. It is used in public health to standardize methodological approaches and international comparability of materials.[41] The current ICD 10th revision was adopted by the World Health Assembly in 1990 in Geneva and has been translated into 43 languages, being used in 117 countries.

According to the ICD-10 codes, the diagnosis of NAFLD is made by the leading clinical disease, syndrome and/or symptom:

K76.0 - fatty liver degeneration not classified under other headings;

K73.0 - chronic persistent hepatitis, not classified under other headings;

K73.9 - chronic hepatitis unspecified;

K74.6 - other and unspecified cirrhosis of the liver.[41]

For NAFLD diagnosis, ICD-10 recommends code K76.0 (fatty degeneration of the liver not classified under other headings). For clinically confirmed NAFLD or cirrhosis, code K 74.6 (other and unspecified cirrhosis of the liver) is recommended. Given the long history of the classification of NAFLD as a distinct nosological form,

the first papers which were issued long before the release of ICD-10 revision, one can inadvertently conclude that ICD-10 coding for NAFLD is imperfect.

Undoubtedly, since the entry into force of ICD-10 (in Russia, it was approved as an official document in 1997 by order of the Ministry of Health), a real breakthrough in gastroenterology occurred: new diagnostic tools and techniques appeared, new mechanisms of etiology and pathogenesis were identified, as well as new potential therapeutic goals. Thus, the classification in the field of gastroenterology is actively evolving, due to which there is a need to edit it. Nowadays, we are still encouraged to use the ICD-10 classification for coding diagnoses, which is already far from the current classification of gastroenterological diseases, especially in terms of hepatology.

Such inconsistencies exist both in hepatology and in other areas of medicine. Therefore, a revision of the ICD has long been necessary. To date, ICD-11, which was adopted by the WHO in 2019, has been developed; the official beta version, available on the Internet, has been developed in the Russian Federation.

In ICD-11, which is still planned to be approved in the Russian Federation, NAFLD will have the codes corresponding to its international name:

DB92 - nonalcoholic fatty liver disease

DB92.0 - nonalcoholic fatty liver disease without nonalcoholic steatohepatitis

DB92.1 - non-alcoholic steatohepatitis

DB92.Y - other clarified non-alcoholic fatty liver disease

DB92.Z - nonalcoholic fatty liver disease, not specified

DB93 - hepatic fibrosis or cirrhosis

DB93.0 - hepatic fibrosis

DB93.1 - peripheral cirrhosis

DB93.2 - definite liver fibrosis or cirrhosis.[42]

ICD-11 is clear to be more closely aligned with modern nomenclature. Finally, the special codes "nonalcoholic fatty liver disease" and "nonalcoholic steatohepatitis" have been introduced. They eliminate the existing contradictions in ICD-10.

Thus, with the introduction of ICD-11, the scientific and statistical approaches to the classification of diagnoses will coincide. In the future, science will continue to move forward, and the understanding of liver diseases will deepen. Perhaps we will see how the nomenclature will differ from the fixed structure of the classification.

Conclusion

We can conclude that a thorough understanding of the history of NAFLD as a distinct nosology allows us to better understand the disease itself as well as anticipate directions for future research. From early assumptions to current research, NAFLD has been shown to be an independent risk factor for cardiovascular disease, hepatocellular carcinoma, and other malignancies. However, as in practical medicine, we cannot move forward without proper and clearly defined statistics.

The updated International Classification of Diseases 11 revision (ICD-11) eliminates the current contradictions of ICD 10 about NAFLD. In ICD-11, it is allocated in a separate heading (DB92 - nonalcoholic fatty liver disease), which is closer to up-to-date nomenclature. This classification contributes to a better understanding of research and clinical approaches to the diagnosis and treatment of the disease.

Ethical Considerations: Since public data and related literature were analyzed in our study, there was no ethical violation.

Conflict of Interest: The authors declare no conflict of interest.

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Review

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VIRAL HEPATITIS B AND C AND NEUROLOGICAL IMPAIRMENT

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Abstract

Viral Hepatitis B and C are characterized as systemic diseases with a wide range of extrahepatic manifestations caused by various immunological disorders. Neurological disorders are among the most important extrahepatic manifestations, which can serve as indicators of the presence of viruses and play a major role in the clinical picture of the disease. This review article describes the most frequently manifested neurological disorders detected in patients with chronic viral hepatitis, particularly Hepatitis B and C.

Keywords: Viral hepatitis, Guillain-Barré syndrome, Parkinson's Disease, peripheral neuropathy, cognitive impairment, stroke.

Introduction

Parenteral forms of hepatitis are systemic diseases in which there is a wide range of neurological disorders of manifestations caused by various immunological disorders. Pathological processes in them are caused by the replication of viral agents both in the liver tissue and outside its borders.[1]

Neurological disorders in viral hepatitis, both in acute and chronic form, can manifest not only from the side of the brain but also from the side of the spinal cord and peripheral nervous system, according to the severity from subclinical changes to neurocritical states.[2,3] These disorders are caused by both the direct neurotoxic effect of viral particles on brain cells and the indirect effect caused by the influence of viruses on the immune system or as a result of using antiviral therapy.[4] Neurological disorders and deterioration of the quality of life associated with health in patients with viral hepatitis may occur even at the non-cirrhotic stage of infection, regardless of the stage of fibrogenesis and the genotype of the virus. [5]

Neurologists often participate in the consultation of patients with viral hepatitis, and it is important for them to detect the main neurological symptoms in patients with viral hepatitis in time, which will further facilitate the adoption of timely tactics of diagnostic and therapeutic measures. [2,3]

The present review aims to investigate the neurological impairment of patients with viral Hepatitis B and C. A systematic literature search of English-language studies was performed in Medline, Embase, Web of Science, Scopus and The Cochrane Library from January 2013 to August 2023. The systematic literature search resulted in 589 hits. The screening of titles and abstracts identified 122 potentially eligible articles. Finally, 51 studies were included in this review. The selection algorithm is shown in Figure 1.

Guillain-Barré syndrome

Guillain-Barre syndrome is one of the most frequent and severe acute peripheral neuropathies and is characterized by protein-cytological dissociation, which is detected in the analysis of cerebrospinal fluid.[5-7] The mechanism of formation of Guillain-Barre syndrome is a demyelinating lesion of peripheral nerves, which occurs due to a previous infection, which is the trigger of a further cross-autoimmune reaction.[7] Currently, there are many cases of Guillain-Barre Syndrome associated with many infectious agents, such as Haemophilus influenzae, Campylobacter jejuni, Zika virus, SARS-CoV-2 and universal interest among both scientists and healthcare professionals.[5,7-9] It is noteworthy that most patients report respiratory or gastrointestinal symptoms a few weeks before the development of Guillain-Barre Syndrome.[5]

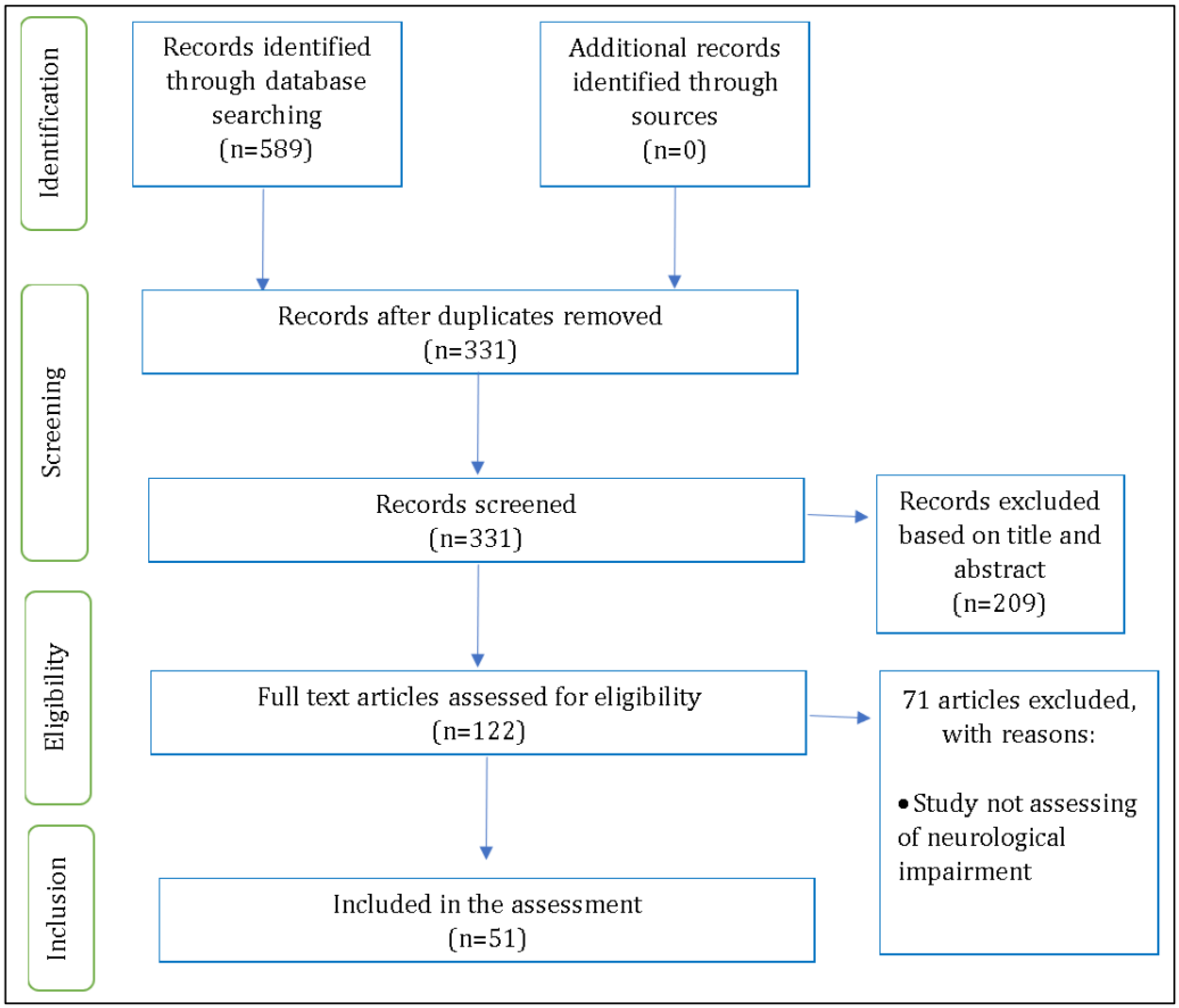

Figure 1. Flow diagram of the of the literature search

Hepatitis viruses can also form postinfectious autoimmune peripheral neuropathy and manifest acute limb paralysis.[6] However, in the modern literature, there are a small number of cases of Guillain-Barre syndrome in viral hepatitis, while most of the research is devoted to the study of the disease after viral hepatitis A and E.[7] However, the rare triggers for the development of Guillain-Barre Syndrome are viral Hepatitis B and C.[5-7,10,11] At the same time, the pathogenesis of the syndrome formation remains completely unexplored. One of the links in the pathogenesis of Guillain-Barre syndrome in viral Hepatitis B is the positive immunofluorescence labeling of HBsAg around endoneural small blood vessels and in the endoneurium of affected individuals, as well as significantly higher levels of HBsAg immune complexes in both serum and cerebrospinal fluid.[7] Besides, immune complexes can be deposited in the endoneurium through the hemato-nervous barrier and damage

nerve fibers, serving as important pathogenic agents. In addition, the Hepatitis B virus has some components similar to peripheral nerves and circulating immune complexes that can cause an imbalance of T-cell subpopulations and reduce the suppressive activity of T-cells in the peripheral blood of patients.[7] The Hepatitis B virus can cause the production of autoantibodies and activation of monocytes through molecular mimicry, leading to immune damage to myelin and axons.[7] It is known that with viral Hepatitis B, Guillain-Barre syndrome manifests itself with a severe course, which responds well to therapy with intravenous immunoglobulin, plasmapheresis, a long course of corticosteroids, immunosuppressants, appropriate antiviral therapy, the use of hepatoprotection, acupuncture, and timely rehabilitation.[5,10-12] According to some authors, there is a link between Guillain-Barre syndrome, viral Hepatitis C and mixed cryoglobulinemia.[7] A case related to acute reactivation of chronic viral Hepatitis C, which led to the formation of Guillain-Barre syndrome, is also described.[5] In addition, according to some authors, the course of Guillain-Barre syndrome can take on a severe character with a coinfection of viral Hepatitis C and HIV infection.[13]

Peripheral neuropathy

According to the latest data, there is no replication of hepatitis viruses in peripheral nerves, unlike brain cells, where this pathological process occurs.[14] Of the total number of peripheral neuropathies, 86% of cases occur in patients with existing mixed cryoglobulinemia associated with HCV infection.[14] However, a recent study found that peripheral neuropathy had a close relationship with age and Hepatitis C virus and not with cryoglobulinemia, while neuropathic pain had a correlation with damage to nociceptive pathways, which was assessed using laser-induced potentials.[15] Many studies also confirm the widespread prevalence of peripheral sensory-motor neuropathy in patients with viral Hepatitis C.[16,17] There are reports that the Hepatitis C virus can lead to peripheral neuropathy associated with eosinophilic infiltration and granuloma formation, which have been confirmed by biopsy.[18] Other studies have evaluated the role of vitamin B12 in the development of peripheral neuropathies in patients infected with viral Hepatitis C. However, as a result, no significant association was found.[19] There is evidence of the role of HCV-E2 glycoprotein in the formation of peripheral neuropathy in patients infected with the Hepatitis C virus, regardless of the presence of cryoglobulin. According to the authors, damage to peripheral nerves occurred due to immune-mediated mechanisms triggered by the Hepatitis C virus.[20] Currently, antiviral therapy used in the treatment of viral hepatitis can have a negative effect on the peripheral nervous system, causing neurological complications, which in some cases limit their use in the future.[21] However, according to other authors, the use of antiviral therapy and the eradication of the virus contributes to the regression of neurological symptoms in patients with viral hepatitis.[16,18,22,23]

Stroke

Cerebrovascular diseases are one of the main causes of mortality among the world's population.[24] Bacteria and viruses can lead to the risk of stroke, in particular, hemorrhagic stroke.[25] However, there are currently few studies on the development of ischemic stroke due to viral hepatitis.[26] The analysis showed that hepatitis viruses are one of the factors in the development of atherosclerosis of the carotid arteries.[26] The pathogenesis of ischemic stroke in patients infected with viral hepatitis includes a complex mechanism, one of the links of which are replication of the hepatitis virus in the walls of arteries, pathological secretion of inflammatory cytokines, oxidative stress, mixed cryoglobulinemia, violations of cellular and humoral immunity.[27,28] Thus, it was found that patients with chronic viral Hepatitis C have a higher level of inflammation in the endothelial cells of the brain, and it was assumed that this category of patients is more at risk of stroke.[24] In a recent study involving 2,444 patients with cirrhosis of the liver, it was found that 160 participants had a history of ischemic stroke, and 32 patients first developed ischemic stroke during hospitalization, which increased the risk of mortality.[29] According to some authors, there is a hypothesis that the elimination of the Hepatitis C virus with interferon therapy helps to reduce the risk of ischemic stroke and, consequently, mortality.[27] Patients with chronic viral hepatitis also have an increased risk of intracerebral hemorrhages, especially in patients with relatively young age.[30] Thus, it was found that patients with a history of chronic viral hepatitis have a 2.33% higher chance of recurrent intracerebral hemorrhage than patients without viral hepatitis.[30] According to the assumption of other authors, patients with decompensated cirrhosis of the liver associated with the Hepatitis B virus have a higher risk of developing countless cerebral microbleeds.[31] There are also reports that patients infected with the Hepatitis B virus have an increased risk of cerebral aneurysm rupture.[32]

Alzheimer's Disease

Alzheimer's disease is a neurodegenerative disease with a complex and multifactorial etiology that leads to irreversible loss of neurons, intellectual abilities, memory and reasoning.[33,34] Many authors confirm the undoubted role of neurotropic viruses in the development of Alzheimer's disease, but in recent years, more and more research has focused on studying the relationship between the Hepatitis C virus and dementia.[35] However, at present, the mechanism of dementia development in viral Hepatitis C remains poorly understood. This is due to the fact that viral agents can both directly and indirectly neurotoxically affect brain cells, causing systemic and/or local inflammation through the action of inflammatory markers.[35] Hepatitis viruses may have the ability to directly infect endothelial cells and penetrate the blood-brain barrier into the central nervous system. During the replication of pathogens, their constituent molecules, called pathogen-associated molecular structures, are released. When the central nervous system is damaged during infection, inflammatory mediators such as TNF-α, IFN-γ, IL-1β, IL-6, IL-18, and chemokines are released.[35] A recent multi-year large-scale study has shown that patients with a history of viral Hepatitis C significantly increase the risk of developing Alzheimer's disease.[36]

Parkinson's Disease

Parkinson's disease is a disease belonging to the group of neurodegenerative diseases and is caused by the progressive death of neurons of the substantia nigra and the formation of Levi's bodies.[37-40] Clinically, the disease includes motor symptoms such as bradykinesia, rigidity, rest tremors, and postural instability.[37] According to modern literature, the development of Parkinson's disease is due to a combination of various factors, such as genetic and environmental.[41] According to various authors, bacteria and viruses can serve as potential triggers for the development of Parkinson's disease, although at the moment, there is a small amount of work devoted to the study of the formation of the disease.[38-41] According to another author, the pathogenesis of Parkinson's disease in viral hepatitis is associated with the potential for penetration through the blood-brain barrier and the ability of hepatitis viruses to multiply in macrophages and microglial cells of the brain, resulting in increased release of pro-inflammatory cytokines and chemokines that have a neurotoxic effect on neurons and cause their death.[37,41] In addition, recent studies conducted on rats have shown that the hepatitis virus leads to the loss of dopaminergic neurons in the brain of rodents.[37,41,42] There are several proven studies in which patients with chronic viral hepatitis had a higher risk of developing Parkinson's disease.[37,43,44] Thus, a large nationwide population-based study conducted in Taiwan with the participation of 49,967 patients infected with viral Hepatitis C, it was found that this category of patients is more vulnerable to Parkinson's disease than patients without a history of viral hepatitis.[45] There are similar data from other researchers who report significant evidence of a more significant vulnerability of patients with viral hepatitis to Parkinson's disease, but the authors recommend conducting further large-scale studies to obtain more reliable data.[37,46] However, according to the results of a study by other authors, no significant link was found between Parkinson's disease and hepatitis viruses. The authors explain this fact by the fact that liver disease, in particular, in its terminal stage, leads to the formation of Parkinsonism, which in turn is mistakenly regarded as Parkinson's disease.[47-49] Despite this, many authors believe that the use of antiviral therapy in patients infected with viral hepatitis leads to a significant reduction in the risk of Parkinson's disease.[50,51]

Conclusion

Most patients with chronic viral Hepatitis B and C may have various neurological manifestations of the existing viral infection. These neurological disorders can be observed in both acute and chronic course of the disease. We recommend that patients with suspected various neurological diseases and without obvious previous acute respiratory or gastrointestinal diseases be screened for viral hepatitis.

Conflict of Interest: The authors declare no conflict of interest.

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