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Editor in Chief

Message from the Editor-in-Chief

As we close the year 2025, I am pleased to share the final issue of GMJ. This year, as planned, we published four issues containing high-quality scientific work from various fields.

In this December issue, we present eight original articles, one review article, and two case reports. Our editorial team continues to prioritize publishing studies from a wide range of scientific disciplines to support knowledge sharing and academic progress.

As the year comes to an end, I would also like to acknowledge the season. December is a time for reflection, appreciation, and renewed energy. We hope that the articles in this issue will inspire you and add value to your work in the year ahead.

I sincerely thank all authors, reviewers, and editors for their contributions throughout 2025.

Wishing our community health, happiness, and success in the new year.

M. Ali Gülçelik, M.D., Prof.
Editor-in-Chief

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The role of family in mobilization exercises for post-stroke patients in Southeast Asia: a scoping review

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ABSTRACT

Despite facing barriers such as a lack of information, healthcare support, and physical and emotional burdens, families have an important role in supporting stroke patients' mobilization through assistance in physical exercise, changes in body position, and activities of daily living. Mobilization exercises in stroke patients have been reviewed, but the role of the family in the exercise process has not been evaluated. Families are the primary caregivers supporting post-stroke patients over time. We aimed to identify literature related to mobilization exercises for post-stroke patients, including types, family roles, and barriers faced by families. We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Review framework to search PubMed, ScienceDirect, Clinical Key, Global Index Medicus, EBSCO, Scopus, ProQuest, Cochrane Library, Google Scholar, and Garuda from inception to May 1, 2023. Fourteen relevant primary studies were evaluated using inductive thematic analysis. The findings indicate that mobilization exercises include range of motion, ambulation, and daily activities. Families play a crucial role through active participation, motivation, and support. The main barriers are a limited understanding and a lack of information. These findings highlight the crucial role of families in post-stroke mobilization despite challenges. Enhancing family education and support may improve patient outcomes. However, further review is required to assess the effectiveness of family intervention to improve mobilization exercises. Therefore, a systematic review on this topic is recommended.

Introduction

Stroke is a non-communicable disease that is the second leading cause of death worldwide (1). More than 62% of strokes occur between the ages of 49 and 70, and 34% of these individuals experience death (2). The most significant increase in the incidence, morbidity, and mortality of ischemic stroke is highest at the regional level in areas such as North Africa, the Middle East, and Southeast Asia (SEA) (3), highlighting the importance of stroke prevention.

As many as 80% of post-stroke patients will experience hemiplegia or hemiparesis, resulting in impaired mobilization (4). In addition, limb weakness due to stroke can limit daily activities, making eating, dressing, and moving difficult (5).

Stroke sufferers may feel useless due to the lack of physical activity and inability to perform self-care, defined as a series of actions performed to maintain or promote health (6). As a consequence, post-stroke paralysis can burden families due to the required care (7,8). Thus, rehabilitation programs have an important role in improving activities of daily living in stroke patients. Appropriate rehabilitation programs can prevent neurological, structural, and functional disabilities after stroke, is mobilization, which aims to gradually increase the physical activity, strength, balance, coordination, and motor function of patients with a multidisciplinary medical team, including neurologists, rehabilitation physicians, nurses, physiotherapists, occupational therapists, social work assistants, psychologists, and patient families (9). Families assist with daily living activities and provide psychosocial support, which not only enhances patients' cognitive function but also contributes to improved outcomes and greater independence (10). Therefore, the family must play a role in the mobility exercise of stroke patients. Mobilization exercises prevent complications due to immobility, such as decubitus ulcers, joint stiffness, and respiratory problems. Stroke rehabilitation is crucial for patient recovery, with family support ensuring regular mobilization exercises (11). Their role in mobilization exercises is vital and cannot be ignored.

Few review articles explore the family's role in supporting mobilization exercises for post-stroke patients. One review discussed the contribution of nurses in stroke rehabilitation and showed that they maximize patient independence in performing daily activities (12). However, these two reviews do not discuss the role of the family in mobilization exercises in post-stroke patients. One study describes the diversity of support systems among family caregivers of stroke sufferers in Asia (13). However, it did not explain the role of families in mobilization exercises. A review study conducted in China suggests that family caregiving is not always perceived positively, has various needs, and can be a burden for caregivers who provide care due to extrinsic motivation (14). However, this review does not explain the role of family in mobilization exercises in post-stroke patients.

Therefore, we aim to explain the role of family for mobilization exercises with post-stroke patients, especially in SEA countries that include Brunei, Malaysia, Indonesia, Thailand, Singapore, the Philippines, Vietnam, Laos, Cambodia, Myanmar, and East Timor. By identifying the types of mobilization, barriers, and the role of family in the rehabilitation and mobilization process, we can better understand the challenges and support systems involved. These findings will provide valuable insights for designing future research and developing effective interventions to improve family participation in post-stroke rehabilitation.

Methods

This study protocol is registered in the Open Science Framework (osf.io/8e5hk). The Optional Preferred Reporting Items for Systematic Reviews and Meta-Analyses Extension for Scoping Reviews were used to optimize reporting. We used the five stages to perform this review based on guidance for conducting scoping reviews (15).

Stage 1: Research questions

What role do families play in mobilization exercises for post-stroke patients in SEA?

SEA countries include Brunei, Malaysia, Indonesia, Thailand, Singapore, the Philippines, Vietnam, Laos, Cambodia, Myanmar, and East Timor.

Stage 2: Relevant studies and search terms

This review explores family participation in mobilization exercises performed by post-stroke patients, based on evidence from the scientific literature on SEA. Terms searched were: post-stroke or stroke or cerebrovascular accident and family role or family participation or family and mobility exercises or movement routines or activity drills.

An initial search retrieved titles, abstracts, and content to identify terms and keywords, including alternative words or synonyms, across languages and cultures.

The inclusion and exclusion criteria for the review were based on the context, concept, and population PCC model (Table 1). Studies were included if they focused on stroke patients, utilized qualitative or quantitative primary data, and were published in English or Bahasa Indonesia between 2014 and 2023. Articles that did not align with these criteria, such as those focusing on non-stroke patients or published in other languages, were excluded. This approach ensures a focused analysis relevant to the SEA population while acknowledging the limitation that studies from different linguistic contexts may not be fully represented.

Table 1. Article eligibility criteria

Criterion	Element
Population	Post-stroke
Concept	The role of family in mobility exercises
Context	Research conducted in SEA, a sub-region of Asia consisting of eleven countries: Brunei, Malaysia, Indonesia, Thailand, Singapore, Philippines, Vietnam, Laos, Cambodia, Myanmar, and East Timor

SEA: Southeast Asia

Stage 3: Study selection

Study extraction from the databases

Figure 1 illustrates the process, screening results, and manuscript extraction criteria after the initial search based on the study inclusion and exclusion criteria. In summary, 751 relevant abstracts were collected from 10 databases, and 252 additional manuscripts were identified through Google Scholar. After duplicate articles were removed, 958 articles remained. Titles were then screened for relevance, narrowing the selection to 61 for further screening. Subsequently, full articles were read, and abstracts were reviewed.

A third search stage involved screening the reference lists of the selected articles by reading their full text. This process led to the exclusion of 47 articles because of irrelevance to stroke, not focusing on mobilization exercises, lacking a discussion of family roles, being unrelated to SEA countries, or for being categorized as literature reviews. Ultimately, 14 primary research studies met the inclusion criteria and were included in the analysis.

Database search

Using 10 databases is considered adequate to capture a wide range of relevant studies in Indonesian and English (PubMed, ScienceDirect, Clinical Key, Global Index Medicus,

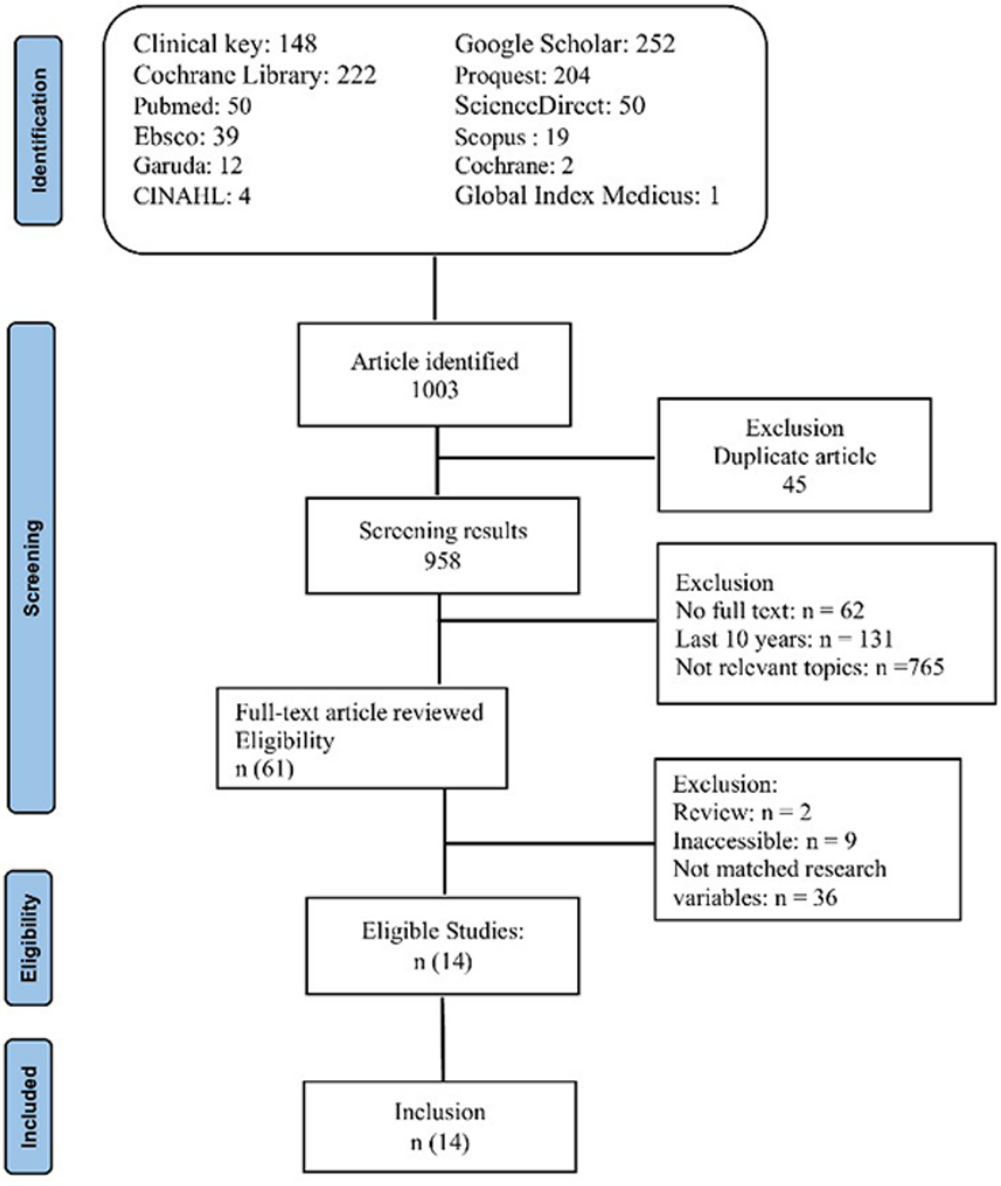

Figure 1. PRISMA-ScR flowchart of the study

PRISMA-ScR: Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews

EBSCO, Scopus, ProQuest, Cochrane Library, Google Scholar, and Garuda). Please refer to the supplementary file for details.

Study extraction constraints

All abstracts from the article search were downloaded into the Mendeley software reference manager, duplicates were removed, and then they were exported into the Rayyan software program (16). Rayyan is a web-based software designed for screening and analyzing articles in systematic reviews, featuring import, grouping, evaluation, and team collaboration tools (16). This application establishes clear boundaries between reviewers and the articles they screen-based on inclusion and exclusion criteria. Two reviewers sampled titles, abstracts, and full text, using the manual Joanna Briggs Institute method (17). There was a disagreement between the two reviewers on a small number of studies during the screening process. Specifically, out of the total number of screened articles, disagreements occurred in 34 articles. These differences were resolved through review discussions until a consensus was reached, ensuring full agreement at each sampling stage.

Stage 4: Data

The data were extracted to obtain important information, such as the study location, research methods, objectives, and the role of the family in mobilization exercises (Table 2).

Stage 5: Thematic summary and key findings

Inductive thematic analysis identified key emerging themes based on Braun and Clarke's (18) work across multiple studies. Their method includes six phases: familiarization with the data, generating initial codes, searching for themes, reviewing themes, defining and naming themes, and producing the report. This analysis required familiarization with each research finding and generated initial codes that were refined to arrive at the final themes reported in this article.

Results

Study characteristics

Of the 14 studies reviewed, 80% were conducted in Indonesia (19-30), one in Thailand (31), and one in Singapore (32). There were three qualitative (19,27,29,30) and eleven quantitative (19-27,29,30) research findings.

Types of mobilization exercises

Only two articles mentioned the type of mobilization exercises provided (24,29). These exercises were range of motion (ROM) exercises, which are carried out by the family of the post-stroke patients at home with guidance from healthcare workers, including filling out questionnaires, practicing active and passive movements, and evaluation with checklists to improve motor function and prevent complications (33) and exercises, such as ambulation, walking, and supporting the patient's daily activities occur for six months at home through a three-stage program: pre-education to provide knowledge about stroke; intervention with mobilization exercises assisted by family caregivers; and periodic monitoring and evaluation using the Barthel Index to increase the patient's functional capacity and reduce the family's care burden (29).

Family role

To identify the family's role in the mobilization exercise, different measurement tools were used. The most frequent questionnaire used is the Family Support Questionnaire (20,21,25-27), whereas some studies utilized interview guides to explore the family's role in mobilization exercise (19,31,32). Ten articles mentioned that the family actively participated in mobilization exercises (19,21-24,26,29-32), six articles mentioned that families provided motivation (20,22,23,25-27) to perform mobilization exercises that support the patient's recovery and independence, and two articles described coordination between families and healthcare workers (23,32). Three articles stated that families played a role in supervising, providing spiritual and psychological support, and assisting with physical activity while caring for stroke patients (20,23,28).

Barriers

This review article showed that the obstacles experienced by families include a lack of understanding about ROM exercises (24), mobilization (21,26,30,31), and ambulation and walking exercises (29). Family support in accompanying the patient's daily activities was limited (20,27) due to the family's lack of information (19).

Discussion

This review highlights that families play a key role in supporting post-stroke patients through mobilization exercises, motivation, and coordination with healthcare providers. However, the findings also reveal significant barriers, such as limited knowledge about exercises and reduced family engagement due to information gaps.

Types of mobilization exercises

The type of mobilization exercises carried out by the family for post-stroke patients includes ROM exercises, early mobilization, ambulation exercises, balance and coordination exercises, muscle strength exercises, and exercises that imitate daily activities (34). During the acute phase of stroke rehabilitation, early mobilization, positioning, functional mobility exercises, Activities of Daily Living (ADL) exercises, ROM, splinting, and bed mobility are important interventions (31).

Table 2. **Articles that explore the role of family in mobilization exercises.**

Author, year, Country	Objective	Research method	Sample	Measurement tool	Results	Recommendations	Family role in mobilization exercises	Barriers
Audia et al. (19), (2017), Indonesia	To explore the experience of caring for stroke patients among Banjar families, understanding the changes experienced by caregivers, and investigating the impact of caregiving activities on daily life and the need for support.	Quantitative with descriptive research.	6 family members	Interview guide exploring family experiences in caring for stroke patients	Home care for post-stroke patients was primarily provided by spouses, children, or siblings, involving daily assistance, exercise support, spiritual needs, treatment management, and socialization. Challenges included patient non-compliance, emotional changes, and the need for immediate response to patient demands.	Providing information, education and structured homeward planning, family caregivers can face the challenges that exist while caring for stroke patients.	Providing passive movement assistance and provide spiritual support after a stroke at home.	The challenges faced by families in caring for stroke patients include physical, emotional, social, and spiritual changes, as well as a lack of information and support from health services.
Tyagi et al. (32), (2021), Singapore	To describe caregiver support systems for stroke survivors in Singapore, highlighting different caregiver identities.	Qualitative with semi-structured interviews	61 respondents : 35 family members 26 stroke survivors	Interview guide	This study identified four key themes in stroke survivors' caregiving support: cultural influences, caregiver support systems, caregiving disruptions, and relationship dynamics. Spousal caregivers preferred direct support from family, while adult child caregivers tended to rely on distributed support with paid care workers.	Future research should explore caregiver identity in support systems and develop strategies for enhancing family-centered care in stroke rehabilitation.	Providing physical assistance and coordinate with health workers.	-
Karunia (20), (2016), Indonesia	To analyze the relationship between family support and independence in performing ADL after stroke.	Quantitative with cross-sectional design	47 stroke patients and family members	Barthel Index Questionnaire and Family Support Questionnaire	Most post-stroke respondents (aged 43-61, male, unemployed) received strong family support, enhancing their independence. Chi-square analysis showed a significant relationship between family support and ADL independence ($p = 0.018$, $\alpha = 0.05$), but no association with age, sex, or occupation. Families should foster a supportive environment and encourage activities that promote independence.	Future research should explore specific family interventions that can further optimize patient recovery and independence, considering different socio-de	Creating a supportive environment, motivate patients, help with basic needs, and provide positive reinforcement.	Lack of family support prevents post-stroke patients from achieving independence in daily activities.

Table 2. Continued

Author, year, Country	Objective	Research method	Sample	Measurement tool	Results	Recommendations	Family role in mobilization exercises	Barriers
Putri Utami et al. (23), (2023), Indonesia	To know the relationship between family involvement in home physiotherapy programs and daily activities (ADL) in post-stroke patients at home.	Quantitative with cross-sectional design	15 family members	Family involvement questionnaire	There was a relationship between family involvement in the Physiotherapy home program and ADL in post-stroke patients.	To enhance family member involvement in physiotherapy home programs to improve the independence of post-stroke patients in performing activities of daily living (ADL).	Assisting patients in improving physical abilities, managing mental health, providing instrumental assistance, motivating them, ensuring adherence to rehabilitation programs, acting as an intermediary between patients and medical services, and assisting with home exercises without physiotherapy.	-
Sari et al. (24), (2023), Indonesia	To know the relationship between knowledge, self-efficacy, and family skills in performing a healthy range of motion in post-stroke patients.	Qualitative with a cross-sectional study approach.	55 family members	Range of Motion (ROM) Exercise Knowledge Questionnaire Self-efficacy questionnaire in performing ROM exercises ROM skill observation checklist	There was a significant relationship between family knowledge ($r = 0.613$, $p = 0.00$) and self-efficacy ($r = 0.497$, $p = 0.00$) with family skills in performing range of motion exercises. Community nurses should enhance interventions and home visits for post-stroke families.	Community nurses should provide health education and range of motion training to empower families in post-stroke care, supporting long-term rehabilitation and improving patient outcomes.	Actively participating in ROM exercises to aid recovery and optimize the patient's health skills.	Family lacks knowledge
Setyoadi et al. (25), (2018), Indonesia	To know the relationship between family support and the independence of stroke patients at the rehabilitation center	Qualitative with a cross-sectional study approach.	57 family members	Family support questionnaire and barthel index	Statistical analysis showed significant value = 0.00 whereas its sig value $<\alpha = 0.05$ These numbers show a strong connection between family support with independence, which means that there is a correlation between family support and stroke patients independence.	Increasing its role in providing education about the importance of family support for family members of stroke patients because the family plays an important role in the recovery process.	Supporting and motivating patients to perform mobilization exercises for recovery and independence.	

Table 2. Continued

Author, year, Country	Objective	Research method	Sample	Measurement tool	Results	Recommendations	Family role in mobilization exercises	Barriers
Utaisang et al. (31), (2021), Thailand	To seek understanding of stroke family caregivers in relation to care experiences	Qualitative with phenomenological study	16 family members	Interview guide	The experiences of family caregivers of stroke patients included lack of knowledge, challenges of distance, limited family support, and minimal access to health services.	A specific program should be developed to prepare caregivers for stroke patient care, incorporating social support, stress relief, and relationship-building activities.	Providing care to stroke patients and conducting mobilization exercise guidance	Families lack specialized knowledge, skills, patience, and understanding, leading to stress, anxiety, fatigue, and other health problems.
Nugraha (26), (2018), Indonesia	To know family support in motivating patients to mobilize	Quantitative with descriptive research.	54 family members	Family Support Questionnaire	There was a significant relationship between family support and the ability of post-stroke patients to perform ADL at Persahabatan Hospital, Jakarta with a p value=0.001.	Nurses play a crucial role in educating families on providing informational, emotional, and instrumental support to enhance post-stroke patient independence in ADL.	Motivating post-stroke patients to perform mobilization exercises by providing support, helping patient independence, and increasing patient motivation to exercise.	Some families also lack an understanding of post-stroke recovery procedures.
Wardhani and Martini (27), (2015), Indonesia	To know the relationship between stroke patient characteristics and family support with rehabilitation compliance.	Qualitative with a cross-sectional study approach.	22 family members	Family support questionnaire and rehabilitation compliance questionnaire	Family support can affect the compliance of stroke patients in undergoing rehabilitation.	To enhance rehabilitation compliance through family support, healthcare provider involvement, and socioeconomic considerations.	Supporting families in improving patient compliance and motivation during the rehabilitation process.	Lack of family support for stroke patients.
Agustiani et al. (28), (2023), Indonesia	To explore the family's experience in caring for non-hemorrhagic stroke patients in depth.	Qualitative research with a descriptive phenomenological approach	5 family members	Interview guide	Experience in treating patients was to be more patient and sincere, but also feel sad, sad and surprised by the illness suffered by patients. Family support was also provided to their family members including spiritual, psychological and social support. Families also experienced obstacles or obstacles in caring for stroke patients including time or busyness and daily activities. Families have knowledge of what the patient needs as well as the concept of strokes.	Family knowledge during caring for non-hemorrhagic stroke patients, namely increasing knowledge of what patients need, management or care that can be given to patients, and the concept of stroke.	Supervising, providing spiritual and psychological support, and assisting with physical activities while caring for stroke patients.	-

Table 2. Continued

Author, year, Country	Objective	Research method	Sample	Measurement tool	Results	Recommendations	Family role in mobilization exercises	Barriers
Dharma et al. (29), (2018), Indonesia	To know the effect of a caregiver empowerment program based on an adaptation model (CEP-BAM) on functional capacity and quality of life of post-stroke patients.	Quantitative with a quasi-experimental design.	80 family members	Questionnaire Barthel Index and Stroke-Specific Quality of Life Scale (SSQoL)	There was a significant improvement in functional capacity and quality of life in the intervention group compared to the control group six months post-intervention.	To develop an assessment tool to measure family support in adaptive training and to evaluate its effectiveness in caring for stroke patients with complex conditions.	Training with exercises such as ambulation, walking, joint exercises, and basic daily activities such as bathing, toileting, dressing, and eating to help patients with mild to moderate disabilities after stroke.	Lack of knowledge and awareness of families regarding ambulation training and walking in stroke patients
Atmojo, (30), (2020), Indonesia	To determine the family knowledge level regarding the prevention of post-stroke pressure sores.	Quantitative with descriptive method.	15 family members	Questionnaire	Majority of the respondent were male and majority age were 60. The level of family knowledge about the prevention of post-stroke pressure sores is very low, this will increase the risk of pressure sore while the patient is treated at home.	-	Performing consistent mobilization every 2-3 hours.	Lack of family knowledge and awareness to mobilize
Vellyana D and Rahmawati A. (21), (2021), Indonesia	To determine the relationship between family support and early mobilization in post-stroke patients to support increasing the degree of health and reducing morbidity in post-stroke patients.	Quantitative with cross-sectional design	24 family members	Family support questionnaire and mobilization implementation questionnaire	There was a relationship between family support and the implementation of early mobilization in post-stroke patients at Pringsewu Hospital.	-	Educating and supporting post-stroke patients in early mobilization, thus contributing to the patient's overall health and well-being.	Families lack knowledge about post-stroke mobilization.
Sihombing (22), (2023), Indonesia	To know the relationship between the effectiveness of therapeutic communication by nurses and a decrease in family behavior in mobilizing stroke patients.	Quantitative with cross-sectional design	30 family members	Family mobilization action questionnaire, nurse role questionnaire, family behavior questionnaire	The therapeutic communication of nurses carried out as a nursing intervention in the mobilization of stroke patients provided a significant relationship to the decrease in the level of family members attitudes towards mobilizing stroke.	To prepare a Standard Operating Procedure (SOP) for mobilizing stroke patients as a guide for family members in helping to mobilize patients.	Assisting with movement during the acute and rehabilitation phases, maintaining a positive attitude, and providing the necessary for motivation.	-

Recommendations for mobilization programs for post-stroke patients include various exercises adjusted to the rehabilitation phase and patient condition, such as active and passive ROM exercises performed 2-3 times a day for 15-20 minutes, aimed at increasing joint flexibility and preventing contractures (35). Ambulation and walking exercises performed 3-5 times a week help restore walking and balance abilities through assistive devices such as walkers (36). Patients also need to be trained in ADL, such as eating, dressing, and using the toilet. These activities are carried out every day to encourage independence (37). In addition, aerobic and water-based exercises, such as brisk walking or shallow pool exercises performed three to four times a week, can improve motor function and cardiovascular health (38). Thus, involving the family in rehabilitation through regular assistance and exercise can accelerate patient recovery and improve the functional capacity, quality of life, and independence of post-stroke patients. Therefore, the implementation of a multifaceted rehabilitation program that integrates ROM exercises, ambulation, joint exercises, and daily functional activities has the potential to optimize neuromuscular recovery, improve functional capacity, and facilitate the reintegration of post-stroke patients into daily life more effectively than rehabilitation approaches that focus on one aspect alone. Implementing a comprehensive rehabilitation program that includes these interventions improves post-stroke patient management. It can potentially increase long-term disability prevention, optimize neuromuscular function recovery and functional capacity, and accelerate the reintegration of patients into daily routines. This multifaceted approach may improve patients' quality of life by facilitating independence, lowering the risk of complications secondary to prolonged immobilization, and maximizing the potential of brain neuroplasticity to support optimal recovery of function. Additionally, this strategy is intended to improve the efficiency of rehabilitation programs by integrating various aspects of care in one holistic approach, promoting the development of structured and comprehensive rehabilitation protocols, and emphasizing the importance of rehabilitation interventions from the acute phase to optimize long-term recovery in stroke patients.

Family role

Findings from the review indicate that the family's role is crucial in rehabilitating post-stroke patients. They provide physical and spiritual support, as well as coordination with healthcare providers, which helps patients improve their physical abilities and ensure compliance with rehabilitation, especially in carrying out mobilization exercises.

Family support plays a crucial role in the rehabilitation and quality of life of stroke patients. Family support, encompassing emotional, appreciative, instrumental, and informational aspects, creates a sense of security for patients, while providing essential physical and psychological comfort to help them cope with illness and treatment processes (39). The family support system, as the most important resource for stroke patients, directly impacts their quality of life. Given the high incidence of stroke in Indonesia and its associated disabilities, it plays a crucial role in rehabilitation by improving patients' overall well-being and functional abilities (40).

Family members play an essential role in assisting with self-care activities, providing motivation, and facilitating daily exercises that contribute to the patient's recovery. Stroke patients often face significant physical and emotional challenges, requiring continuous encouragement and a supportive environment to participate actively in rehabilitation. By ensuring that basic needs such as security, emotional support, and self-confidence are met, families help create a positive atmosphere that enhances the patient's willingness to engage in recovery efforts. Additionally, the involvement of healthcare professionals in guiding families on effective caregiving strategies further strengthens the rehabilitation process, improving the overall well-being and functional abilities of stroke patients.

Family can provide emotional support, motivation, and practical assistance in daily activities and mobilization exercises. Motivation and a supportive environment can increase the patient's enthusiasm and compliance with the rehabilitation program. Regular mobilization exercises and physical activity also help maintain and improve the functional abilities of post-stroke patients. Coordination and cooperation between family, healthcare providers, and patients are important to achieve optimal results in the rehabilitation process. Healthcare providers can offer education and exercise about proper care for chronic diseases (41,42), including exercise for stroke patients to families. The family can partner in the rehabilitation process, providing important information about the patient's condition and helping implement rehabilitation programs at home.

Meanwhile, patients need to be actively involved in the rehabilitation process and comply with recommendations from healthcare workers, and receive support from their families. Therefore, there is a need to improve education and training for family members about the care and rehabilitation of stroke patients at home. Families must gain adequate knowledge and skills to provide appropriate support and assistance. Exercise can include mobilization exercise techniques, stress management, effective communication, and motivational strategies. Strengthening community health support and services is also necessary to assist families in caring for stroke patients. These services can include home visits by healthcare workers, online consultations, or resource centers that provide families with the information and tools they need to care for stroke patients. Raising public awareness of the need for rehabilitation and social support for stroke patients is important. Educational and advocacy campaigns can be conducted to destigmatize and increase public understanding of the conditions faced by stroke patients and the importance of family support and involvement in the rehabilitation process. The development of affordable and accessible rehabilitation programs and facilities is also needed within health facilities and the community. This change will

make it easier for patients and families to access the needed rehabilitation services and encourage active participation in rehabilitation programs. Close collaboration between health workers, patients, and families in designing rehabilitation programs is essential.

Barriers

In this review, a lack of family knowledge about the rehabilitation process for post-stroke patients was noted, especially regarding mobilization and recovery procedures, and support for mobilization exercises to foster independence in daily activities.

Lack of family knowledge can hinder the patient's adaptation to their new stroke rehabilitation process (43). Increased family knowledge can facilitate effective adaptation for patients and families. Implementing health education programs can improve family readiness to care for stroke patients (44). Physiological adaptation interventions and ROM exercises effectively enhance patient independence, but family knowledge about these techniques is lacking (45). Strategic steps are needed to overcome the obstacles in post-stroke patient rehabilitation by developing a structured education program for families consisting of identifying needs, compiling material on mobilization, providing ongoing support, and conducting regular evaluations (46).

In contrast, to overcome obstacles from a lack of family knowledge in post-stroke patient rehabilitation, strategic steps are needed, such as structured education to increase family understanding of mobilization techniques, recovery procedures, and the importance of their support, along with practical exercises by physiotherapists to provide direct skills. Providing guides, instructional videos, or mobile applications can make it easier for families to assist patients (47). In addition, regular consultations with medical personnel and community-based programs, such as support groups, can strengthen the family's role. This approach aims to increase the effectiveness of family support, speed recovery, and encourage patient independence (48). Telerehabilitation-based stroke education programs, such as the Stroke Education Program, have increased knowledge, independence, and mobilization among post-stroke patients and their families by integrating technology-based distance exercise into the rehabilitation process (49). Comprehensive interventions aimed at families of stroke patients are a crucial component of a holistic rehabilitation strategy. Improved family health literacy, particularly in aspects of post-stroke management, has the potential to be a catalyst in optimizing rehabilitation outcomes.

Furthermore, integrating the family as an active partner in the multidisciplinary rehabilitation team can improve the continuity of care and accelerate the patient's recovery. Thus, developing a comprehensive educational program targeted at the patient's family is a priority, focusing on improving understanding of mobilization techniques, ROM exercises, and post-stroke recovery procedures. Implementing interventions that involve the whole family can improve the effectiveness of care and support the family's adaptation to their new role as caregivers. Integrating cultural approaches in educational programs to ensure relevance and acceptance in the patient's socio-cultural context is also important. Establishing community-based support groups for families of stroke patients can facilitate the exchange of knowledge and experience. From a policy perspective, developing national guidelines that emphasize the importance of family involvement in the stroke rehabilitation process is crucial. Overall, it emphasizes the importance of a holistic and family-focused approach in optimizing recovery and improving the quality of life of post-stroke patients.

This review provides a focused analysis of family involvement in mobilization exercises for post-stroke patients in SEA, an area with limited existing research. The use of both qualitative and quantitative studies enhances the comprehensiveness of the findings. Furthermore, the systematic approach to study selection and thematic analysis strengthens the validity and reliability of the review. However, we acknowledge that using only two languages (English and Indonesian) is a limitation of this review. As a result, relevant articles in other languages that may have met the inclusion and exclusion criteria were not analyzed. In addition, the review is limited to studies published between 2014 and 2023, which may exclude relevant older research.

Conclusion

Although few studies detail the type and role of family in exercise for post-stroke patients, most emphasize active participation and family support as key factors for successful rehabilitation. Family involvement in providing motivation, spiritual and psychological support, and physical activity assistance is significant for consistent mobilization exercises that improve patients' independence and quality of life. However, a lack of family knowledge and awareness was a major barrier. Therefore, the development of comprehensive, family-focused educational programs and national guidelines that emphasize family involvement, integrate cultural approaches into interventions, and establish community-based support groups are important. Thus, effective coordination of the family with healthcare professionals is important in developing mobilization exercise programs that suit the individual patient's condition.

Thus, a holistic approach involving active family participation, ongoing motivational-psychological support, and coordination with healthcare professionals is key to successful mobilization exercises and post-stroke recovery.

Footnotes

Authorship Contributions

Concept: N.N., A.M.I, A.S., Design: N.N., A.M.I, A.S., Data Collection or Processing: N.N., Analysis or Interpretation: N.N., A.M.I., A.S., N.A.A., Literature Search: N.N., Writing: N.N., A.M.I., N.A.A.

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Supplementary File: Keywords for databases

No.	Database	Keywords	Article	Access Date
1	PubMed	((((Post-stroke) OR (stroke)) OR (cerebrovascular accident (CVA))) AND ((((Family role) OR (family participation)))) OR (family))) AND (((mobility exercises) OR (movement routines)) OR (activity drills))	50 Articles	May 1, 2024
2	Garuda	Mobilization of stroke patients	12 Articles	May 1, 2024
3	ScienceDirect	Post-stroke OR stroke OR cerebrovascular accident (CVA) AND family role OR family participation OR family AND mobility exercises OR movement routines OR activity drills	50 Articles	May 1, 2024
4	Clinical Key	Post-stroke OR stroke OR cerebrovascular accident (CVA) AND family role OR family participation OR family AND mobility exercises OR movement routines OR activity drills	391 Articles	May 1, 2024
5	Global Index Medicus	Post-stroke OR stroke OR cerebrovascular accident (CVA) AND family role OR family participation OR family AND mobility exercises OR movement routines OR activity drills	1 Article	May 1, 2024
6	EBSCO	Post-stroke OR stroke OR cerebrovascular accident (CVA) AND family role OR family participation OR family AND mobility exercises OR movement routines OR activity drills	39 Articles	May 1, 2024
7	Scopus	Post-stroke OR stroke AND family AND mobility AND exercises	19 Articles	May 1, 2024
8	Proquest	Post-stroke OR stroke OR cerebrovascular accident (CVA) AND family role OR family participation OR family AND mobility exercises OR movement routines OR activity drills	204 Articles	May 1, 2024
9	Cochrane Library	Post-stroke OR stroke OR cerebrovascular accident (CVA) AND family role OR family participation OR family AND mobility exercises OR movement routines OR activity drills	222 Articles	May 1, 2024
10	Google Scholar	Post-stroke OR stroke OR cerebrovascular accident (CVA) AND family role OR family participation OR family AND mobility exercises OR movement routines OR activity drills and Indonesia	252 Articles	May 1, 2024

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Investigation of suicide deaths in Artvin: a retrospective analysis of autopsy findings

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ABSTRACT

Aims: Suicide is defined as an act committed by an individual deciding to end their own life. It is one of the leading causes of death. The aim of this study is to reveal the multidimensional structure of suicide deaths and to contribute to the development of policies for the prevention of suicide through analyzing the data on suicide deaths in Artvin.

Methods: In this retrospective descriptive study, data from suicide cases autopsied by the Artvin Forensic Medicine Branch Directorate between 2016 and 2024 were analyzed. Only cases confirmed as suicides, as determined by a non-prosecution decision from the prosecutor's office or court, were included in the analysis. Cases currently under investigation for suspected suicides were excluded. The evaluation included age, gender, marital status, body mass index (BMI), time interval, season, location of the incident, suicide method, and medical history documented in electronic health records.

Results: A total of 50 suicide cases were analyzed. The mean age was 52.9±19.6 years, and most of the participants were male (76%). The majority were married (68% of them) and in the 50-64 age group (34% of them). Based on BMI, 42% were overweight, 26% obese, and 6% morbidly obese. Firearms were the most common method (42%), followed by hanging (38%). Most suicides occurred at home or in annexes (62%), and during spring (32%) or summer (30%). Systemic disease was present in 73.5%, psychiatric disorders or medication use in 46.9%, and both in 34.7%. Significant differences were found for age, gender, marital status, oncological disease, and suicide method ($p<0.05$), while no associations were noted with BMI, location, season, time, or health history ($p>0.05$).

Conclusions: This study examined suicide autopsies and showed that most cases involved middle-aged, married men. Suicides generally occurred at home during spring and summer, with firearms being the most commonly used method. Many cases had systemic or psychiatric illnesses and were overweight.

Introduction

Suicide is defined as an act committed by an individual to end their own life (1). The World Health Organization reports that suicides have increased globally in recent years, that one person attempts suicide every 40 seconds, and that this act ranks among the top ten causes of death. It is known that the number of deaths due to suicide worldwide is higher than the number of deaths due to causes such as human immunodeficiency virus/acquired immunodeficiency syndrome, breast cancer, malaria, war, and homicide (2). Parallel to global trends, the number of suicide deaths in Türkiye has also increased in recent years, with official data indicating that 4,061 individuals lost their lives due to suicide in 2023 (3). Suicides not only end the life of the individual but also leave long-term psychological effects on family members, the close environment, society; strain the health system; and cause economic losses. Therefore, suicide has become an increasingly important public health problem in Türkiye in recent years (4). Despite research and preventive efforts to address this major issue, suicide rates have not decreased to the desired levels (5).

Suicide cases are complex phenomena influenced by a combination of biological, psychological, socio-economic, and cultural factors (6). These factors include a variety of risk and causal elements that may provide early warning signs. Reported risk factors for suicide include socio-cultural variables such as age, gender, marital status, employment status, economic condition, family structure and relationships, and place of residence (6), in addition to obesity, chronic systemic diseases (7), psychiatric disorders (8), and the impact of the natural environment (9).

In developing strategies for suicide prevention, it is crucial to accurately analyze the various risk factors and their effects. A thorough examination of individuals' demographic characteristics and mental states enhances our understanding of these factors and aids in implementing effective preventive measures (10). Consequently, understanding the causes, trends, and demographic characteristics associated with suicide cases is critically important from both scientific and social perspectives.

Although there are studies addressing suicide cases across Türkiye (11,12), autopsy-based retrospective research conducted in small and geographically isolated provinces is quite limited. The literature emphasizes that socio-cultural factors, regional differences, and access to methods of suicide play a decisive role in suicidal behavior (3,13). In particular, the province of Artvin- located in the mountainous and forested northeastern region of Türkiye has been reported to display distinct seasonal and demographic patterns of suicide compared to other regions (3).

In our study, we aim to uncover the multidimensional structure of suicide deaths and contribute to the development of preventive policies by analyzing data on suicide deaths in Artvin.

Methods

Study design and participants

In this retrospective descriptive study, we examined 261 cases autopsied by the Artvin Forensic Medicine Branch Directorate between 2016 and 2024.

Only cases confirmed as suicides, as determined by a non-prosecution decision from the prosecutor's office or court, were included in the analysis.

Cases that were still under investigation for suspected suicide (n=5), as well as those determined to have died from non-suicidal causes such as natural death, accident, or homicide (n=206), were excluded. A total of 50 cases that met the inclusion criteria were analyzed.

We conducted a retrospective analysis of crime scene investigation reports, death examination reports, autopsy reports, and electronic health records (E-Pulse) for these cases. We evaluated various factors, including age, gender, marital status, body mass index (BMI), suicide time, season, location of the incident, method of suicide, and relevant medical conditions documented in the E-Pulse records. The E-Pulse system contains individuals' health records provided by the relevant doctor. Additionally, medical histories were verified through clinical records. This study was approved by the Ministry of Justice's Forensic Medicine Institute Education and Scientific Research Commission (decision no.: 21589509/2024/1104, date: 03.09.2024). The research was conducted in accordance with the principles of the Declaration of Helsinki.

The decision of the Artvin Çoruh University Scientific Research and Publication Ethics Committee (decision no.: E-18457941-050.99-152405, date: 09.10.2024), determined that "approval of compliance with scientific research and publication ethics is not required" for our study.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). The normality of data distribution was evaluated using the Shapiro-Wilk test. Descriptive statistics were presented as percentages, means, and standard deviations. Differences between categorical variables were analyzed using Fisher's exact test, as the expected frequency in some cells was less than 5. A p-value of <0.05 was considered statistically significant.

Results

Demographic characteristics

A total of 50 suicide cases were analyzed. The mean age was 52.94±19.61 years, and the majority were male (76%, n=38). Suicides were most frequently observed in the 50-64 age group (34%, n=17), followed by individuals aged 65 and older (26%, n=13).

Regarding marital status, 68% (n=34) were married, 22% (n=11) were single, and 10% (n=5) were widowed. Based on BMI classifications, 42% (n=21) were overweight (BMI: 25-29.9 kg/m²), 26% (n=13) were obese (BMI: 30-39.9 kg/m²), and 6% (n=3) were morbidly obese (BMI ≥40 kg/m²).

Suicide characteristics (methods, location, and time)

Firearms were the most commonly used method of suicide (42%, n=21), followed by hanging (38%, n=19) and jumping from a height (14%, n=7). Two individuals committed suicide by drowning, and one by using a sharp instrument. Among the firearm suicides, 66.7% (n=14) involved pistols and 33.3% (n=7) involved shotguns. The head was the most frequently targeted region (66.7%, n=14), followed by the chest (28.6%, n=6) and the neck (4.7%, n=1).

Most suicides occurred at home or its annexes (62%, n=31), followed by open areas (34%, n=17). In 80% (n=40) of the cases, death occurred at the scene, whereas 20% (n=10) occurred in the hospital.

Seasonal distribution showed that suicides were most frequently reported during the spring (32%) and summer (30%). The most common time interval for suicide was between 06:00 and 12:00 (42%).

Medical and psychiatric history

Health records of all 50 cases were reviewed using the E-Pulse system integrated with the National Judiciary Informatics System. Health information for 49 cases was accessed; however, data for 1 case could not be obtained due to the individual's foreign nationality. Among the analyzed cases, 73.5% (n=36) had at least one systemic disease, 4.1% had at least one oncological disease, and 46.9% (n=23) had at least one psychiatric disorder or a history of psychiatric medication use. Additionally, 34.7% (n=17) of the cases had both systemic diseases and psychiatric disorders (Table 1).

Statistically significant differences were found regarding age (p=0.033), gender (p=0.012), marital status (p=0.005), the presence of oncological disease (p=0.017), and preferred method of suicide (Table 2). However, no statistically significant associations were found between the method of suicide and factors such as BMI, location of suicide, season, and time of suicide, or records of systemic diseases and psychiatric disorders (p>0.05) (Table 2).

Table 1. Demographic, clinical, and forensic characteristics of suicide cases in Artvin province (n=50)

		n	%
Gender	Male	38	76
	Female	12	24
Age (years)	≤18	1	2
	19-29	7	14
	30-39	6	12
	40-49	6	12
	50-64	17	34
	≥65	13	26
Marital status	Married	34	68
	Single	11	22
	Widow	5	10
Body mass index (kg/m²)	Underweight (<18.5)	1	2
	Normal weight (18.5-24.9)	12	24
	Overweight (25-29.9)	21	42
	Obese (30-39.9)	13	26
	Morbidly obese (>40)	3	6
Suicide method	Firearm	21	42
	Hanging	19	38
	Throwing from a height	7	14
	Sharp instrument	1	2
	Drowning	2	4
Injury site in firearm suicides (n=21)	Head	14	66.7
	Neck	1	4.7
	Chest	6	28.6
Suicide season	Spring	16	32
	Summer	15	30
	Autumn	14	28
	Winter	5	10
Suicide time	24.00-6.00	5	10
	06.00-12.00	21	42
	12.00-18.00	13	26
	18.00-24.00	11	22
Scene	Home and its annexes*	31	62
	Open spaces	17	34
	Others	2	4
Place of death	Scene	40	80
	Hospital	10	20
Systemic diseases (n=49)**	Yes	36	73.5
	No	13	26.5
Oncological diseases (n=49)**	Yes	2	4.1
	No	47	95.9
Psychiatric disorder (n=49)**	Yes	23	46.9
	No	26	53.1
Systemic diseases and psychiatric disorder (n=49)**	Yes	17	34.7
	No	32	64.3

*Residence and annexes include places such as houses, barns, serenders, coal storage areas, balconies, and apartment stairwells as reported in forensic investigation files and crime scene reports, **E-Pulse data could not be accessed for one case involving a foreign national, while data for 49 other cases was successfully evaluated.

Table 2. Comparison of suicide methods by demographic, temporal, and clinical variables

		Suicide Method					x^2	p
		Firearm	Hanging	Throwing from a height	Sharp instrument	Drowning		
		n (%)	n (%)	n (%)	n (%)	n (%)		
Age (years)	≤64	16 (43.3)	14 (37.8)	7 (18.9)	0	0	11,051	0.026
	≥65	5 (38.5)	5 (38.5)	0	1 (7.6)	2 (15.4)		
Gender	Male	20 (52.6)	13 (34.2)	3 (7.9)	0	2 (5.3)	12,873	0.012
	Female	1 (8.3)	6 (50)	4 (33.4)	1 (8.3)	0		
Marital status	Married	14 (41.2)	16 (47.1)	3 (8.8)	0	1 (2.9)	22,168	0.005
	Single	6 (54.5)	1 (9.1)	4 (36.4)	0	0		
	Widow	1 (20)	2 (40)	0	1 (20)	1 (20)		
Body mass index (kg/m^2)	Underweight	0	1 (100)	0	0	0	11,839	0.755
	Normal weight	6 (50)	4 (33.4)	1 (8.3)	0	1 (8.3)		
	Overweight	10 (47.6)	9 (42.8)	1(4.8)	0	1 (4.8)		
	Obese	4 (30.7)	4 (30.7)	4 (30.7)	1 (7.9)	0		
	Morbidly obese	1 (33.3)	1 (33.3)	1 (33.3)	0	0		
Suicide season	Spring	7 (43.8)	5 (31.2)	3 (18.8)	0	1 (6.2)	7,276	0.839
	Summer	6 (40)	4 (26.6)	3 (20)	1 (6.7)	1 (6.7)		
	Autumn	6 (42.9)	7 (50)	1 (7.1)	0	0		
	Winter	2 (40)	3 (60)	0	0	0		
Suicide time	24.00-6.00	4 (80)	0	1 (20)	0	0	9,216	0.684
	06.00-12.00	8 (38.1)	9 (42.9)	3 (14.3)	0	1 (4.7)		
	12.00-18.00	5 (38.4)	4 (30.8)	2 (15.4)	1 (7.7)	1 (7.7)		
	18.00-24.00	4 (36.4)	6 (54.5)	1 (9.1)	0	0		
Systemic diseases (n=49)	Yes	15 (41.7)	14 (38.9)	4 (11.1)	1 (2.8)	2 (5.5)	2,065	0.724
	No	5 (38.5)	5 (38.5)	3 (23)	0	0		
Oncological diseases (n=49)	Yes	0	1 (50)	0	0	1 (50)	12,031	**0.017**
	No	20 (42.6)	18 (38.3)	7 (14.9)	1 (2.1)	1 (2.1)		
Psychiatric disorder (n=49)	Yes	6 (26.2)	11 (47.9)	4 (17.4)	1 (4.3)	1 (4.3)	4,650	0.325
	No	14 (53.9)	8 (30.8)	3 (11.5)	0	1 (3.8)		

x^2: Fisher's exact test

Discussion

This retrospective autopsy-based study analyzed 50 confirmed suicide cases in Artvin, a province in northeastern Türkiye. Most cases involved middle-aged, married individuals, with the most frequently used methods being firearms and hanging. Suicides predominantly occurred at home or in their annexes, particularly during the spring months and morning hours. A considerable proportion of the decedents had a history of systemic disease, psychiatric disorder, or both.

The majority of suicide cases (76%) involved males, consistent with a national study in Türkiye, reporting 79.1% male involvement in suicide deaths (13). Similar male predominance is observed in the United States of America and European countries (14). Other research consistently shows that males significantly outnumber females in suicide cases (12,13,15). These findings align with existing literature. Men tend to choose more lethal methods such as firearms, hanging, or jumping from heights. In contrast, women often prefer less fatal means, like poisoning or overdose with psychiatric medication (16). This difference may partly explain the higher suicide mortality among males. One study found that suicide attempts were 3.4 times more likely to be fatal in men, largely due to the lethality of the methods chosen (16).

Suicides were most commonly observed among individuals aged 50 to 64, with a mean age of 52.94±19.61 years. While suicides occur across all age groups, certain age ranges exhibit higher rates. Previous research indicates that suicides typically occur in the age range of 24.2 to 41.6 years (12,13,15,17). According to data from the Turkish Statistical Institute, suicide

deaths in our country over the past decade have been most frequently reported in individuals over 60, and those aged 40 to 59 (3). This finding supports the trend that suicide risk is higher in middle-aged and elderly individuals. Factors such as increasing loneliness, chronic diseases, physical losses, and psychosocial issues may contribute to the elevated risk among the elderly population.

A considerable proportion (68%) of suicide cases involved married individuals. However, research on marital status and suicide presents varied findings. Some studies (11,15) report higher rates among married individuals, while others (7) suggest single or widowed individuals are at greater risk. Although marriage is often viewed as protective, it may also pose a risk when stress, conflict, or increased responsibilities are present.

When cases were classified by BMI, approximately three-fourths had a BMI of 25 kg/m² or above. Obesity has both physical and psychosocial consequences (18), and is considered a potential factor influencing suicides (7). A high BMI not only impacts physical health but also significantly affects mental well-being. Recent studies indicate a complex relationship between obesity, high BMI, and suicide risk (18,19). Literature reports increased suicidal ideation and suicide attempts among overweight (BMI: 25-29.9) and obese (BMI: 30 and above) individuals (19). One study found that obesity was associated with higher rates of suicidal thoughts and attempts (18). It has been suggested that obesity leads to chronic systemic inflammation (20), and suicide risk is elevated in people with such inflammation (21,22). However, despite the increased prevalence of suicidal ideation and attempts in individuals with high BMI (18,19), the same pattern is not consistently seen in suicide deaths. Literature presents conflicting findings regarding the relationship between elevated BMI and suicide mortality. While some studies (7,23) report a positive association, others find no significant link or even suggest an inverse relationship (7,24). In our study, elevated BMI and obesity among suicide cases may have interacted with other contributing factors. This aligns with findings that high BMI and obesity often coexist with chronic diseases and psychiatric disorders (23). Obese individuals often face low self-esteem and depression due to social stigmatization and marginalization. Moreover, a decline in quality of life due to chronic diseases and eating disorders is an important factor that can increase suicidal tendencies (18).

Firearms were the most common suicide method (42%), followed by hanging (38%). There are regional variations in preferred suicide methods worldwide. While firearms are commonly used in South America and Africa, hanging remains the most prevalent method globally (25). In Türkiye, hanging is recognized as the leading method, followed by firearms (3). The choice of method may be influenced by customs, accessibility of means, and socio-cultural norms. The widespread use of firearms in some regions may stem not only from cultural familiarity with hunting or self-sufficiency but also from evolving perceptions of safety and personal protection (26). Historically used for hunting and food provision, firearms have increasingly become tools for household defense. Factors such as gender, age, income level, urban versus rural residence, and perceived safety influence firearm ownership (27). The higher prevalence of firearm use in our study, compared to national trends, may reflect unique regional characteristics. In the Eastern Black Sea region, for example, challenging terrain and scattered rural settlements may contribute to a greater reliance on firearms for both utility and protection (28). In some areas, residents also use firearms to guard against wildlife, a factor shaping local attitudes toward weapon ownership. These dynamics are reflected in national reports. According to a civil organization monitoring gun violence, the northern region of Türkiye, including the Black Sea area, ranked second in firearm-related incidents in 2023 (29). As firearm ownership rises, so does the risk of firearm-related deaths (26). There also appears to be a gender-related pattern in suicide methods. Our findings indicate a higher rate of firearm use among males, consistent with evidence that men tend to choose more lethal, accessible, and often irreversible methods; suggesting male suicides may be more premeditated and intentional.

The head was identified as the most frequently targeted region in firearm suicides, accounting for 66.7% of cases. This aligns with existing literature indicating that head injuries are most common, followed by those to the chest and abdomen (30). The preference for the head may reflect a desire for a rapid and irreversible outcome in suicide attempts.

Suicides occurred most frequently during the spring (32%) and summer (30%) months. However, the timing of suicides varies across the literature. Some studies (31,32) report that suicides peak in winter and spring, while others (3,33) indicate that suicides peak in spring and summer. Data from the Turkish Statistical Institute also show that suicide deaths in Türkiye are most frequent in the spring and summer (3). The seasonal prevalence in our study may reflect how seasonal changes influence suicide risk. One study found that each 1°C increase in temperature corresponded to a 2.18% rise in suicides (33). Similarly, research conducted in East Asia revealed comparable findings, indicating that the relationship between rising temperatures and suicide rates did not vary by age or gender (34).

Most suicides were committed at home or in annexes, with 80% of deaths taking place at the scene. This aligns with previous studies showing that both suicide attempts and deaths predominantly occur at home (11,13). The home may be preferred due to its privacy and low likelihood of intervention. Additionally, an individual's psychological state may be affected by household social dynamics, with stressors in this setting potentially increasing suicide risk. People may prefer the

home for its privacy and reduced chance of being interrupted. Furthermore, household stress and interpersonal dynamics may worsen mental health and elevate suicide risk. That most deaths occurred at the scene suggests the methods used tend to be highly lethal, limiting chances for intervention.

Approximately three-fourths of individuals had at least one chronic systemic disease. Chronic diseases significantly diminish quality of life, often causing social isolation, occupational limitations, and emotional issues. Their ongoing nature and the treatment process create substantial stress that deeply affects patients' lives. This negatively impacts mental health and further reduces quality of life. Additionally, the financial burdens associated with treatment exacerbate their mental health challenges. Chronic diseases often bring social, occupational, and emotional challenges. These combined difficulties place additional strain on mental health. Research indicates suicidal ideation risk is higher among patients with chronic diseases (35,36).

A study examining suicide attempts among adults over 50 from various countries found that suicidal ideation was especially common among patients with chronic systemic diseases, with the risk increasing for those with multiple chronic conditions. Furthermore, chronic diseases may contribute to suicidal thoughts by creating psychological effects that lead individuals to despair and perceive life as intolerable (37). Suicides may be linked not only to the presence of chronic diseases but also to the treatments administered for these conditions. One study reported that certain medications increased the risk of suicide by heightening suicidal thoughts (38).

Approximately half of the cases examined were found to have at least one psychiatric disorder and a history of medication use. The presence of these disorders is a significant factor in both suicide attempts and suicide deaths. Research indicates that a vast majority of suicide deaths are linked to an underlying psychiatric disorder (39). While psychiatric disorders alone do not fully account for suicidal behavior, they are among the most critical risk factors influencing the suicide process. One study highlighted that the impact of psychiatric disorders on suicides arises from a combination of factors, including the occurrence of psychiatric episodes, access to methods of suicide, lack of help or social support, and inadequate coping skills (40). Our findings are consistent with existing literature, suggesting that psychiatric disorders adversely affect individuals' cognitive, emotional, and behavioral functioning, thereby increasing the likelihood of suicidal thoughts and behaviors.

This study has several limitations due to its retrospective design and single-center nature. The small sample size restricts the generalizability of the findings. Moreover, the lack of data on the socio-economic status, and the recent life events of the victims before suicide are among the limitations of the study.

Conclusion

This study, which examined suicide autopsies in Artvin, found that most of those who committed suicide were middle-aged, married men. Suicides predominantly occurred at home during spring and summer, with firearms being the most common method. Many victims had systemic or psychiatric illnesses and were overweight. These findings suggest that suicide prevention efforts should focus on stricter firearm regulations, improved mental health screenings, and community-based psychosocial support-especially for the elderly and the chronically ill.

Ethics

Ethics Committee Approval: This study was approved by the Artvin Çoruh University Scientific Research and Publication Ethics Committee (decision no.: E-18457941-050.99-152405, date: 09.10.2024)

Informed Consent: Retrospective study.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: B.K., Concept: B.K., Design: B.K., Data Collection or Processing: B.K., A.S., Analysis or Interpretation: B.K., Literature Search: B.K., A.S., Writing: B.K., A.S.

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Microbiological evaluation of air quality and surface contamination in the surgical room at West Kalimantan Regional General Hospital

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ABSTRACT

Aims: This study aimed to evaluate the microbiological quality of airborne and surface bacterial contamination in surgical rooms.

Methods: This descriptive study was conducted at West Kalimantan Regional General Hospital (WKRGH) from October to December 2023 to evaluate microbiological contamination of air and floor surfaces. Air samples were collected using the settling plate method, while floor surface samples were obtained using the swab method. Surgical rooms with the highest frequency of procedures were selected through purposive sampling.

Results: The airborne bacterial counts ranged from 52.37 colony forming unit (CFU)/m^3 to 995.13 CFU/m^3, while surface bacterial counts ranged from 2.66 CFU/m^2 to 48 CFU/m^2. Post-disinfection, the airborne bacterial counts were, i.e., median 0 CFU/m^3 and surface bacterial counts ranged from median 0 CFU/m^2 to 1.33 CFU/m^2. According to the Italian National Institute for Occupational Safety and Prevention, surgical rooms 1 (median: 209.5) and 2 (median: 995.13) did not meet the criteria for airborne microbial contamination during surgery, as the levels exceeded 180 CFU/m^3. Post-surgical evaluations of both air and floor surface samples showed complete compliance with the established criteria.

Conclusions: Overall, the quality of airborne and surface bacteria in the surgical rooms at WKRGH meets the acceptable standards. However, certain rooms still exceed this limit and require improvement to comply with the recommended standards.

Introduction

The cleanliness standards of hospital environments must be carefully addressed due to the potential transmission of infection-causing bacteria through droplets, airborne particles, and direct contact. The presence of bacteria in hospital air can contribute to diseases, including nosocomial infections, which are infections acquired within healthcare facilities and can impact patients undergoing treatment (1). Nosocomial infections can result from the transmission of pathogenic bacteria originating within the hospital environment, facilitated by air contamination, surfaces such as floors and walls, and medical equipment (2).

Patients face a heightened risk of acquiring nosocomial infections, particularly when surgical room conditions do not meet established standards. Surgical site infections (SSIs) contribute 14-17% of hospital-acquired infections and 38% in surgical patients (3). According to the World Health Organization, up to 77% of deaths among surgical patients are associated with SSIs (4).

The urgency of evaluating microbiological contamination is underlined by a significant increase in surgical procedures in the Central Surgery Unit of West Kalimantan Regional General Hospital (WKRGH) which rose from 1,690 in 2021 to 3,501 in 2022 (5). The increase by more than 50% may indirectly elevate the risk of nosocomial infections. If not adequately monitored, surgical rooms can harbor airborne and surface pathogens that compromise surgical outcomes and patient safety.

Microbiological monitoring is essential to identify pathogens such as *Escherichia coli* and *Pseudomonas aeruginosa*, both of which are common causes of postoperative infections (6,7). Furthermore, consistent evaluation of microbial contamination supports infection control protocols by determining the source of contamination, allowing for targeted interventions (8,9).

Despite the well-established importance of environmental monitoring, no previous study has evaluated the microbiological quality of air and floor surfaces in the surgical rooms of WKRGH. This represents a critical knowledge gap, as hospital infection prevention strategies often rely on general guidelines without supporting regional and local microbiological data.

This study aims to address that gap by evaluating the microbiological contamination of air and floor surfaces in the surgical rooms of WKRGH. This study will provide baseline data for hospital infection prevention policies and inform future improvements in surgical room hygiene practices, in line with national and international health standards.

Methods

Study design, setting and sampling

This study was conducted at WKRGH from October to December 2023 using a descriptive observational research design. The population under investigation comprises the central surgical installation at WKRGH, and the sample selection uses purposive sampling. The selection criteria were determined based on the most frequently performed surgical procedures, specifically ophthalmic and orthopedic surgeries, as documented in the 2022 surgical activity report of WKRGH. These surgeries are conducted in operation room No. 1, No. 2, No. 3 of the hospital. The sample collection area in each room was determined based on the surgical room's area. In this study, seven areas were identified for each room, using the formula number of areas (NL)=√A, where NL denotes the number of areas, and "A" represents the area of the room in square meters (m^2) (10). As a result, seven sampling areas were identified per room, leading to 14 samples per room (7 during surgery and 7 after disinfection); and 84 samples in total from all rooms.

Disinfection and post-disinfection sampling

Airborne bacteria sampling in the surgical room was conducted both during surgery and after disinfection using the settling plate method on blood agar. The sampling areas in a room should encompass areas with minimal air movement, zones of airflow convergence, or turbulence. These locations typically include spots near the entrance, air grilles, high-efficiency particulate arrestance filters, and the corners of the room (Figure 1) (10). Petri dishes were strategically positioned at predefined locations with lids placed adjacent to the dishes to ensure full exposure of the agar surface to the room air. Care was taken to avoid any contact with the agar surface and to prevent any object from passing over the open dish. The petri dishes were left open for 15 minutes and then closed. Following exposure, the area surrounding the dish was cleansed by spraying alcohol, to eliminate any residual media or condensation from the lid that might compromise the room's cleanliness (11).

Bacterial sampling of the surgical room floor surface was conducted using the swab method on blood agar, both during surgery and after disinfection. The positioning of the sample collection area is determined by potential sources and pathways of bacterial exposure, as well as the activities occurring around the area to be swabbed (Figure 1). Care was taken to confirm that the surface at each sampling area was dry. A sterile cotton

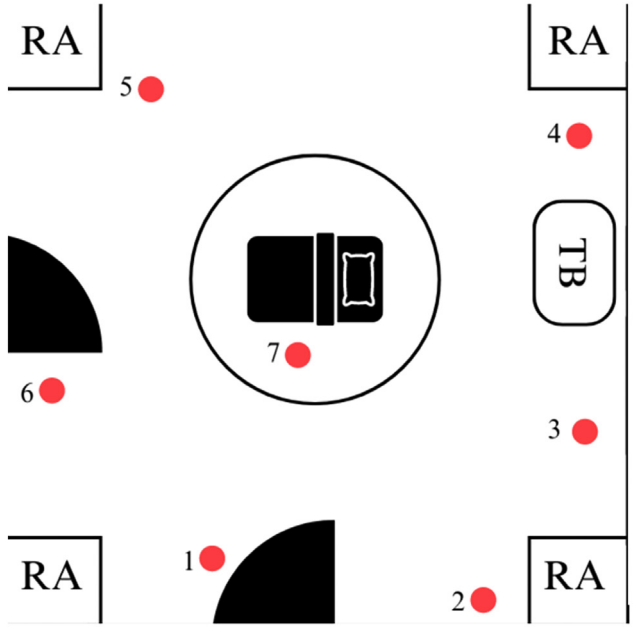

Figure 1. Sampling area RA, TB (●)
RA: Return air, TB: Trash bin

swab was immersed in a 0.9% Natrium Chloride (NaCl) solution and then gently pressed against the side of the tube to remove excess liquid. The sterile cotton swab was then used to swab the sampling area, covering a wide area of 5x5 cm, in horizontal, vertical, and diagonal directions for 30 seconds at a 30° angle (10). Bacterial cultivation at each sampling area is performed in three replications. Incubation is carried out at 37ºC for 24 hours (12). The number of bacterial colonies that grew was subsequently counted.

The disinfection process at WKRGH involved the use of ultraviolet (UV) light, and the floor surfaces were cleaned with 0.5% chlorine solution. Post-disinfection sampling was conducted 30 minutes after the completion of the disinfection procedure.

Microbiological analysis and identification

All collected samples were incubated at 37°C for 24 hours. Following the colony count, additional macroscopic observations were carried out, including examining the shape, size, margin, color, and elevation of the bacterial colonies on the blood agar plate. Subsequently, Gram staining was conducted to examine the cell morphology. Blood agar plates were prepared using Nutrient Agar (Merck, Germany) supplemented with fresh sheep blood. The cultivation of microorganisms from surface samples was conducted using the spread plate method. Swab samples suspended in a tube containing 0.9% NaCl solution were collected and 0.1 mL of the suspension was dispensed onto the agar surface, evenly spread and subsequently incubated.

The maximum concentration of airborne microorganisms in a surgical room during activity is 180 colony forming unit (CFU)/m^3, while after the disinfection process, it is reduced to 10 CFU/m^3 (13). In contrast, the permissible concentration for floor surfaces is only specified for post-disinfection conditions, with a maximum of 5 CFU/m^2 (14).

Ethics considerations

This research has been reviewed and approved by the Health Research Ethics Committee of Dr. Soedarso Regional General Hospital (approval no.: 89/RSUD/KEPK/X/2023, date: October, 2023). As it did not involve human subjects, the research focused on the microbiological evaluation of air quality and surface contamination in the surgical room, with additional institutional authorization provided through Research Permit No. 000.9/20308/RSUD.

Statistical Analysis

IBM SPSS Statistics for Windows, version 30.0 (IBM Corp., Armonk, NY, USA, 2023) was used for statistical analysis. The normality of the data was assessed using the Shapiro-Wilk test. According to the normality test results, normally distributed data are reported as the mean with standard deviation, while non-normally distributed data are reported as the median along with the minimum and maximum values (15).

Results

The results of airborne bacterial count observation

At each designated air sampling area, the findings exclusively indicated the presence of bacterial colonies. The air bacterial counts recorded during surgical procedures are detailed in Table 1. This investigation demonstrated that observable bacterial colonies vary across different sampling areas. For instance, in surgical room No. 1 during the second scheduled operation,

Table 1. Airborne bacterial levels in the surgical room by sampling time and number of personnel

Sample area	CFU/m^3					
	During operation			After disinfection		
	R1	R2	R3	R1	R2	R3
1	471.38	628.5	261.87	0	52.37	157.12
2	209.50	2.514,02	0	0	0	0
3	52.37	419	52.37	0	0	0
4	157.12	523.75	209.5	52.37	0	0
5	733.25	1.099,88	52.37	0	0	0
6	314.25	995.13	52.37	0	0	0
7	0	2.566,40	0	0	0	0
CFU/m^3 [Median (Range)]	209.50 (0-733.25)	995.13 (419-2.566,40)	52.37 (0-209.5)	0 (0-52.37)	0 (0-52.37)	0 (0-157.12)
Room	**Samples were taken during the operation**			**Number of personnel in the room**		
1	2			4		
2	4			6		
3	1			5		

CFU: Colony forming unit

sampling was conducted at a temperature of 17.60°C with four personnel present during ophthalmic surgery. The highest bacterial count of 733.25 CFU/m^3 was observed at area 5, whereas area 7 showed the lowest bacterial count at 0 CFU/m^3.

In surgical room 2, sampling was conducted during the fourth scheduled operation at a temperature of 17.70°C. Six personnel were present during the orthopedic surgery, with individuals entering and exiting the room during the sampling process. The highest bacterial count, 2,566.40 (CFU/m^3), was recorded at area 7, while the lowest bacterial count, 419 (CFU/m^3), was observed at area 3.

In surgical room 3, sampling was performed during the first scheduled operation at a temperature of 17.70°C. Five personnel were present during the orthopedic procedure. The highest bacterial count, 209.50 CFU/m^3, was detected at area 4, while the lowest bacterial count, 0 CFU/m^3, was found in areas 2 and 7.

The Table 1 presents the bacterial counts in surgical rooms 1, 2, and 3 during surgical procedures. The highest bacterial count, 2,556 CFU/m^3, was recorded in area 7 in room 2. Conversely, the lowest bacterial count, 0 CFU/m^3, was observed in several areas. According to the Italian National Institute for Occupational Safety and Prevention (ISPESL), the acceptable air quality threshold during surgery is 180 CFU/m^3. Surgical rooms 1 and 2 did not meet this hygiene criterion, whereas surgical room 3 complied with the standard (13).

The growth of airborne bacterial colonies in surgical rooms 1, 2, and 3 was significantly reduced after disinfection compared to during surgery. In surgical room 1, the number of bacterial colonies at each air sampling area decreased following the disinfection process. Area 4 exhibited the highest bacterial count at 52.37 CFU/m^3, whereas no bacterial colonies were detected in the other sampling areas.

In surgical room 2, area 1 recorded the highest bacterial count at 52.37 CFU/m^3, with no bacterial colonies detected in the other sampling areas. In surgical room 3, area 1 had the highest bacterial count, measuring 157.12 CFU/m^3.

The highest bacterial count, 157.12 CFU/m^3, was observed in area 1 in room 3. According to ISPESL, the acceptable air quality threshold during surgery, which is 10 CFU/m^3; surgical rooms 1, 2, and 3 met the air hygiene standard.

Observation results of floor surface bacterial counts

The timing and type of operation for floor surface sampling in each room followed the same protocol as air sampling. Table 2 shows the bacterial counts on the floor surfaces of surgical rooms 1, 2, and 3 during surgery. The highest bacterial count, 170.66 CFU/m^2, was recorded at area 2 in room 2. Additionally, several areas showed no bacterial colonies. It is important to note that there are neither local regulatory standards nor international guidelines governing floor surface contamination during surgical procedures.

Following the disinfection process, sampling was conducted sequentially in surgical rooms 1, 2, and 3. The results from these rooms demonstrated a decrease in bacterial counts compared to those collected during surgery. Table 2 displays the bacterial counts in surgical rooms 1, 2, and 3 during surgery. The highest bacterial count, 6.66 CFU/m^2, was observed at area 6 in room 2, with several areas showing no bacterial colonies. Notably, the limits set by Dancer (14) for floor surface contamination following disinfection are set at 5 CFU/m^2, a threshold that was met by all three rooms in the study.

Table 3 presents the cell morphology findings, which included the most frequently identified bacteria: gram-positive cocci, comprising 49.4% of the total, followed by gram-negative cocci

Table 2. Floor bacterial levels in the surgical room

Sample area	CFU/m^3					
	During operation			After disinfection		
	R1	R2	R3	R1	R2	R3
1	6.66	208	4	0	0	1.33
2	2.66	170.66	2.66	1.33	1.33	1.33
3	2.66	4	0	1.33	0	0
4	8	49.33	0	1.33	0	0
5	22.66	46.66	4	0	2.66	1.33
6	25.33	48	6.66	0	66.6	0
7	38.66	24	2.66	0	66.6	0
CFU/m^3 [Median (Range)]	8 (2.66-38.66)	48 (4-170.66)	2.66 (0-6.66)	0 (0-1.33)	0 (0-66.6)	1.33 (0-1.33)
Room	**Samples were taken during the operation**			**Number of personnel in the room**		
1	2			4		
2	4			6		
3	1			5		

CFU: Colony forming unit

Table 3. Morphological characteristics of bacterial cell according to gram staining

Gram type	Cell shape		Total n (%)
	Coccus	*Basil*	
Positive	78 (49,4%)	23 (14,5%)	101 (63,9%)
Negative	36 (22,8%)	21 (13,3%)	57 (36,1%)

at 22.8%. Based on gram staining, gram-positive bacteria constituted the predominant type (64%) of the bacteria found in the surgical rooms of WKRGH.

Discussion

Airborne and surface bacterial contamination

The median concentrations of airborne bacteria in surgical rooms 1, 2, and 3 during surgery were 209.50 CFU/m^3, 995.13 CFU/m^3, and 52.37 CFU/m^3, respectively. According to the ISPESL guidelines, which set a maximum acceptable limit of 180 CFU/m^3 for airborne microorganisms during surgical procedures, rooms 1 and 2 exceeded the permissible threshold, while room 3 remained within acceptable limits. Most countries have established a bacterial threshold limit of 50-150 CFU/m^3 for surgical procedures conducted in conventionally ventilated surgical rooms, with some regulations allowing a maximum of 180 CFU/m^3 (16). According to ISPESL recommendations, the acceptable concentration of airborne microorganisms in surgical environments during general surgery is 180 CFU/m^3 (16). The findings indicate that while room 3 adhered to these microbiological safety standards, rooms 1 and 2 exhibited microbial contamination levels surpassing the acceptable threshold, potentially posing a risk to surgical sterility and patient safety. According to the acceptable limits set by Dancer (14), the contamination level should not exceed 5 CFU/m^2.

These findings align with previous research conducted at the Central Surgical Installation of Dr. Moewardi Hospital, where airborne bacterial levels similarly did not meet the established quality standards for air bacterial concentration (17).

The median airborne bacterial counts in surgical rooms 1, 2, and 3 at WKRGH after disinfection are 0 CFU/m^3, 0 CFU/m^3, and 0 CFU/m^3, respectively. The results for rooms 1, 2, and 3 decreased to within the normal range for bacterial counts of 10 CFU/m^3. The findings from this study in the surgical room were believed to be influenced by the duration of disinfection, which raised concerns about suboptimal disinfection procedures that may not have aligned with recommended practices.

The median floor surface bacterial counts in surgical rooms 1, 2, and 3 during surgery were 8 CFU/m^2, 48 CFU/m^2, and 2.66 CFU/m^2, respectively. These results indicate that bacterial counts vary across different area during surgery, The results of this study suggest that bacterial counts fluctuate across different areas during surgical procedures.

The median floor surface bacterial counts in surgical rooms 1, 2, and 3 after disinfection, were 0 CFU/m^2, 0 CFU/m^2, and 1.33 CFU/m^2, respectively, all of which fall within the acceptable limits for bacterial density.

The findings of this study revealed a noticeable reduction in airborne bacterial counts both during surgical procedures and following the disinfection process. All recorded measurements met the acceptable bacterial limits outlined by the ISPESL, which provides guidelines specifically for infection prevention and control in healthcare facilities. This regulation sets specific thresholds for microbial contamination in medical environments to ensure patient safety and minimize the risk of healthcare-associated infections. The results indicate that, despite the presence of some microbial activity, the surgical rooms met the prescribed standards for bacterial levels, suggesting that both the surgical practices and disinfection protocols employed were effective in maintaining a controlled and sterile environment (14).

Factors affecting microbial load and disinfection efficacy

The findings of this study are likely influenced by multiple factors. First, the level of activity in the surgical area during procedures may contribute to microbial contamination, as bacteria tend to accumulate in high-traffic areas. Second, the duration of the surgical procedure at the time of sampling could also play a significant role, as prolonged operations may increase exposure to airborne and surface contaminants. Third, the effectiveness of the disinfection process during surgical breaks is a crucial factor, as inadequate or incomplete disinfection may leave certain areas untreated, thereby compromising sterility (18).

Research conducted at RGH Brigjend H. Hasan Basry Kandangan suggested that the most effective UV sterilization duration for reducing airborne bacteria was 2 hours, whereas the UV sterilization duration in this study was 1 hour (19).

The study results showed a reduction in airborne bacteria during surgery and after disinfection. This suggests that room disinfection can influence airborne bacterial levels and is anticipated to decrease the risk of surgical wound infections in patients. Several factors can impact the effectiveness of disinfection, including the concentration and potency of the disinfectant. Higher concentrations of disinfectant can enhance effectiveness and shorten the time required to kill microbes. Additionally, physical and chemical factors such as temperature, pH, and humidity also play a role in disinfection efficacy (20). Higher temperatures generally enhanced the effectiveness of most disinfection processes in the past, although excessively high temperatures could lead to degradation of the disinfectant and reduce its activity. Increased pH is known to enhance the antimicrobial activity of certain disinfectants like quaternary ammonium compounds, but it could decrease the activity of others, such as phenol,

hypochlorite, and iodine. Additionally, humidity played a crucial role in influencing the activity of disinfectant gases like chlorine dioxide and formaldehyde (21).

According to standard disinfection protocols, specific cleaning procedures must be performed during each surgical break. These include floor cleaning, disinfecting the operating table surface, and properly disposing of medical waste. However, observations in the surgical room revealed that by the end of the procedure, the floor had not been adequately cleaned, and medical waste remained uncollected. Furthermore, subsequent surgeries were scheduled immediately after the previous ones, without sufficient time allocated for thorough sterilization. This lack of proper disinfection and waste management compromises the sterility of the surgical room, increasing the risk of post-surgical infections in subsequent patients.

Several factors may influence the bacterial load on floor surfaces, including the number of surgeries performed, the timing of sample collection, and the number of individuals present in the surgical room prior to sampling. These variables can significantly impact microbial contamination levels. For instance, in room 3, samples were collected during the first surgical procedure of the day, whereas in room 2, sampling occurred during the fourth operation. This difference in sampling time may have contributed to variations in bacterial counts, as surgical rooms subjected to multiple consecutive procedures are more likely to accumulate microbial contamination due to increased exposure to personnel movement, surgical activity, and airborne particulates. Additionally, the number of samples collected at each time point differed, further influencing the observed bacterial distribution. These findings highlight the importance of considering procedural timing and room utilization when assessing microbial contamination in surgical environments (22).

Additionally, the number of bacterial colonies is affected by the activities of surgical room personnel, such as walking, which can deposit microorganisms on the floor. The presence of microorganisms on the floor is also influenced by the cleanliness of the surgical room.

Bacterial identification and clinical relevance

The observation of bacterial colonies in the surgery rooms, based on cell morphology, revealed that gram-positive cocci were the most commonly found at 49.4%, followed by gram-negative cocci at 22.8%, gram-positive bacilli at 14.6%, and gram-negative bacilli at 13.2%. According to gram staining, gram-positive bacteria (63.9%) were predominantly present in the surgical rooms of the hospital, compared to gram-negative bacteria (36.1%). These findings are consistent with the study conducted by Abdilah et al. (23), which also found a higher prevalence of gram-positive bacteria in surgical rooms.

Gram-positive bacteria found in surgical rooms are part of the normal skin flora, which can be released into the air from the skin of patients, doctors, and medical staff during surgery. These bacteria have the potential to cause wound infections, particularly post-surgery infections. These bacteria commonly form spores to protect themselves from adverse environmental conditions. Bacterial spores are highly resistant to disinfectants and high temperatures (24). Because these bacteria are normal flora, almost everyone has them on the skin, nose, or throat.

Based on the Gram staining results, the majority of the gram-positive cocci bacteria are presumed to be *Staphylococcus* species. *Staphylococcus* colonies typically appear round, smooth, raised, and shiny on culture media. Specifically, colonies of *Staphylococcus aureus* usually exhibit a gray-to-yellow coloration, whereas colonies of *Staphylococcus epidermidis* typically appear gray to white (25). In this study, gram-positive *cocci* exhibited colony morphology characterized by round, convex shapes and a white to yellow coloration. Therefore, it can be suspected that the gram-positive cocci bacteria found in this surgical room are *Staphylococcus* aureus and *Staphylococcus* epidermidis.

The findings of Spagnolo et al. (3) indicated that *Staphylococcus* was the most frequently detected bacterium in surgical room examinations. This high prevalence was attributed to *Staphylococcus* being a normal flora on human skin. This finding aligned with research conducted at Jimma University Specialized Hospital, which identified bacteria contaminating the walls and floors, revealing that 33.3% of the bacteria were *Staphylococcus aureus*. Additionally, gram-negative bacteria, specifically *Escherichia coli* and *Klebsiella* spp. each with 11.1% (26).

Microorganism identification was conducted solely based on macroscopic colony morphology and microscopic Gram staining, to provide a general characterization of the bacteria, as this study focused on evaluating the bacterial load in surgical rooms before and after surgery. This study was conducted in the operating rooms of a single hospital; therefore, the results cannot be generalized to all healthcare facilities with different operational characteristics or infection control systems.

Conclusion

The microbiological quality of airborne and surface bacteria in the surgical rooms at WKRGH generally falls within acceptable standards. However, some rooms, specifically rooms 1 and 2, exceeded the recommended threshold of 180 CFU/m^3 during surgical procedures. Inadequate conditions within the surgical room can lead to infections in patients' surgical wounds and facilitate the transmission of diseases to healthcare workers. Consequently, it is essential to enforce standardized procedures within the surgical unit, alongside effective sanitation practices, to ensure a hygienic environment. This is a critical component of infection prevention and control strategies. Infection prevention

and control programs play a vital role in minimizing the occurrence of healthcare-associated infections and ensuring patient and healthcare worker safety.

Ethics

Ethics Committee Approval: This research has been reviewed and approved by the Health Research Ethics Committee of Dr. Soedarso Regional General Hospital (approval no.: 89/RSUD/KEPK/X/2023, date: October, 2023).

Informed Consent: As it did not involve human subjects, the research focused on the microbiological evaluation of air quality and surface contamination in the surgical room, with additional institutional authorization provided through Research Permit No. 000.9/20308/RSUD.

Footnotes

Authorship Contributions

Concept: A.R., M.M., M.M., Design: A.R., M.M., M.M., D.F.L., R.A.M., Data Collection or Processing: A.R., M.M., M.M., D.F.L., R.A.M., Analysis or Interpretation: A.R., M.M., M.M., D.F.L., R.A.M., Literature Search: A.R., M.M., M.M., D.F.L., R.A.M., Writing: A.R., M.M., M.M., D.F.L., R.A.M.

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Incidence and predictors of postoperative pneumonia after cardiothoracic surgery

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ABSTRACT

Aims: The objective of this study was to examine risk factors and predictors that contribute to the development of postoperative pneumonia (POP) following cardiothoracic surgery.

Methods: This was a prospective, observational study including patients who underwent major cardiothoracic surgery and survived the initial 48 postoperative hours. POP was diagnosed based on the Centers for Disease Control and Prevention criteria. Preoperative, intraoperative, and postoperative variables were analyzed to determine their association with the occurrence of POP.

Results: A total of 278 consecutive patients (mean age: 51±22.91 years, male sex 68%) were included in the study. POP incidence was 6.87 per 1000 days of hospitalization. Significant risk factors for POP were identified as history of renal disease [odds ratio (OR) 3.9, 95% confidence interval (CI) 1.1-13.5, p=0.040)], central nervous system disorder (OR 12.8, 95% CI 4-40.5, p<0.001), postoperative aspiration (p=0.008), absence of respiratory exercise after surgery (OR 2.5, 95% CI 1-6.3, p=0.041), and presence of postoperative complications other than pneumonia (e.g. acute renal failure) (OR 7.2, 95% CI 2.3-22, p=0.002). Patients with POP had significantly longer mechanical ventilation (p<0.001), hospitalization (p<0.001), and mobilization durations (p=0.006) than those without pneumonia. Multivariate analysis revealed that prolonged postoperative mobilization duration (OR 1.8, 95% CI 1.08-2.84, p=0.022), presence of postoperative complications other than pneumonia (OR 12.7, 95% CI 1.73-92.31, p=0.012), and longer postoperative hospitalization duration (OR 1.1, 95% CI 1.02-1.19, p=0.011) were independent predictors of POP.

Conclusions: This study demonstrates that POP remains a considerable complication after cardiothoracic surgery. Pre-existing renal and neurologic disorders, postoperative aspiration, and inadequate respiratory exercises were identified as major risk factors. Prolonged postoperative mobilization duration, and longer postoperative hospitalization duration along with the presence of other postoperative complications, were identified as independent predictors of POP, highlighting the need for early risk stratification and targeted preventive strategies.

Introduction

Postoperative pneumonia (POP) is a nosocomial pneumonia or ventilator-associated pneumonia (VAP) in patients who are in the postoperative period (1). POP is one of the most frequent nosocomial infections after major surgery, which is associated with increased mortality, morbidity, and prolonged hospitalization (2). The incidence of POP differs among patients, hospitals, and types of surgery, and varies from 5% to 80% (3,4). To the best of our knowledge, there is no study regarding surveillance and risk factors of POP in our country. This study sought to identify potential risk factors for POP following cardiothoracic surgery, with the aim of reducing its incidence by targeting modifiable risks.

Methods

Patient population

This study had a prospective and observational design and was performed at the Cardiovascular Surgery and Thoracic Surgery units of Gazi University Hospital between June 2010 and May 2011. Patients who had major cardiothoracic surgery and survived the first 48 postoperative hours were consecutively included in the study. Patients who underwent minor surgical procedures and who were hospitalized for less than 48 hours were excluded from the study. The epidemiological and clinical data of the patients were recorded. Approval for the study was obtained from the Ethics Committee at the Gazi University Medical Faculty Institutional Review Board (decision number: 018, date: 02.06.2010), which stated that informed consent from participants was unnecessary due to the absence of any intervention.

Surveillance

Active prospective surveillance was performed by visiting patients every day. Patient characteristics were recorded on the POP surveillance form. The following data were included on the POP surveillance form: demographic characteristics, underlying diseases, previous surgery, survival status, risk factors for infections, invasive materials (e.g., chest tube, urinary catheter), type of surgery, surgery date, mean duration of surgery, surgical wound classification (clean, clean-contaminated, contaminated, dirty-infected), American Society of Anesthesiologists (ASA) score, the other characteristics of surgery (open or laparoscopic, emergent or elective, general or local anesthesia), prophylactic or therapeutic antibiotics, postoperative complications, infections (surgical site infections, urinary tract infections, intraabdominal infections), cultures, and antimicrobial susceptibility results. Risk factors for POP were categorized and analyzed based on the timing: preoperative, operative, and postoperative.

Prophylactic antibiotics were administered 60 minutes before the surgical incision to ensure optimal tissue concentration during surgery according to current clinical guidelines. The duration of prophylaxis did not exceed 24 hours postoperatively (1). Respiratory exercise was administered to all patients with thoracic intervention. However, patients who underwent surgery with local anesthesia or those who had peripheral vascular surgery did not receive respiratory exercise unless they had significant respiratory disease.

Nosocomial pneumonia and VAP were diagnosed according to the Center for Diseases Control (CDC) and Prevention criteria (4). According to the CDC criteria used to define nosocomial infections for the diagnosis of nosocomial pneumonia in adults, one of the following criteria must be present:

1. Rales or dullness to percussion on physical examination of chest and any of the following:
   a. New onset of purulent sputum or change in character of sputum
   b. Organism isolated from blood culture
   c. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy.
2. Chest radiographic examination shows new or progressive infiltrate, consolidation, cavitation, or pleural effusion and any of the following:
   a. New onset of purulent sputum or change in character of sputum
   b. Organism isolated from blood culture
   c. Isolation of pathogen from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy
   d. Isolation of virus or detection of viral antigen in respiratory secretions
   e. Diagnostic single antibody titer (immunoglobulin M) or fourfold increase in paired serum samples (immunoglobulin G) for pathogen
   f. Histopathologic evidence of pneumonia.

Isolation site of microorganisms were from specimen obtained by transtracheal aspirate, bronchial brushing, or biopsy and blood culture. According to our study design cultures were obteined beyond the 48 hour following surgery.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 20.0 (IBM Corp., Armonk, NY, USA). Continuous variables were presented as means with standard deviations, and 95% confidence intervals (CIs) if normally distributed, or as medians with interquartile ranges when the distribution was skewed. Discrete variables were reported as percentages. Comparisons of variables were made using the chi-square test, Fisher's exact test, Mann-Whitney U test, and logistic regression (LR) analysis. LR analysis was used to identify the prognostic factors for the occurrence of POP. The Backward LR method was applied in the LR analysis. Univariate

analyses were performed before the regression model was created. Statistically significant variables in univariate analyses and significant ones in literature were added to the model. p<0.05 was considered statistically significant. The final model in the LR analysis was presented.

Results

Patient characteristics

A total of 278 patients (68% male) were included in the study. The mean age was 51±22.91 years. Of these, 200 (71.9%) were hospitalized in the cardiovascular surgery department and 78 (28.1%) in the thoracic surgery department. Demographic characteristics, underlying diseases, risk factors, and type of surgery are presented in Table 1. Perioperative antimicrobial prophylaxis was given to all patients. A single dose of intravenous prophylactic antibiotics was given within 60 minutes before the incision. Cefazolin 2 g (82.7%), ampicillin-sulbactam 3 g (10.8%), and other drugs (6.5%) were used for the antimicrobial prophylaxis. Dose adjustment was made according to creatinine clearance as recommended (1). The mean duration of the surgery was 264.75±112.75 minutes, and the mean duration of hospitalization was 13.6±12.32 days.

Nosocomial infection rate and the incidence of pneumonia

Fifty-six of 278 patients (20.1%) had a nosocomial infection after surgery. The most frequent nosocomial infection was pneumonia (26, 9.4%), followed by surgical site infection (22, 7.9%), bloodstream infection (3, 1.1%), intra-abdominal infection (2, 0.7%), and urinary tract infection (1, 0.4%). POP incidence was found to be 6.87 per 1000 hospitalization days. Eleven of the POP cases (42.3%) were diagnosed with VAP. The incidence of VAP in the mechanically ventilated population was 26 per 1000 ventilation days.

The microorganisms

The microorganisms responsible for POP in this study were *Acinetobacter baumannii* (15.4%), *Klebsiella species* (11.5%), *Escherichia coli* (11.5%), and *Pseudomonas aeruginosa* (7.7%). Gram-positive pathogens were not isolated. Culture results were negative in 53.8% of the cases.

Risk factors for postoperative pneumonia

History of renal disease [odds ratio (OR) 3.9, 95% CI 1.1-13.5, p=0.040] and central nervous system disorder (OR 12.8, 95% CI 4-40.5, p<0.001), aspiration after surgery (p=0.008), absence of respiratory exercise after surgery (OR 2.5, 95% CI 1-6.3, p=0.041), presence of postoperative complications other than pneumonia (e.g. acute renal failure) (OR 7.2, 95% CI 2.3-22, p=0.002) were significant preoperative risk factors for POP (Table 2). As shown in Table 3, patients with POP had markedly longer durations of mechanical ventilation [median 1.5 (0-30)

Table 1. Demographic characteristics (n=278)

Characteristic	n (%)
Sex, male	189 (68)
Department, cardiovascular surgery/thoracic surgery	200/78 (71.9/28.1)
Underlying diseases	
Atherosclerotic heart disease	123 (44.2)
Hypertension	101 (36.3)
Diabetes mellitus	71 (25.5)
Malignant neoplasm	68 (24.5)
Peripheral vascular disease	35 (12.6)
Hyperlipidemia	20 (7.2)
Previous myocardial infarction	18 (6.5)
Renal disease	15 (5.4)
Congestive heart failure	15 (5.4)
Central nervous system disorder	14 (5)
Respiratory failure/chronic obstructive pulmonary disease	11 (4)
Obesity	11 (4)
Pulmonary hypertension	6 (2.2)
Severe ventricular dysfunction (EF <30%)	4 (1.4)
Immunosuppression	3 (1.1)
The use of H_2 receptor blockers	186 (66.9)
The use of steroid	2 (0.7)
Smoking	85 (30.6)
Alcohol use	7 (2.5)
Hospitalization in the last 6 months	58 (20.9)
Use of antibiotics in the last 6 months	58 (20.9)
Previous surgery other than cardiac surgery	94 (33.8)
Previous cardiac surgery	19 (6.8)
Previous cardiac surgery (in the last 1 year)	2 (0.7)
Indication (surgery)	
Elective	258 (92.8)
Emergent	20 (7.2)
American Society of Anesthesiologists score	
1	2 (0.7)
2	152 (54.7)
3	120 (43.2)
4	4 (1.4)
5	-
Type of surgery	
Coronary artery surgery	104 (37.4)
Pulmonary resection	67 (24.1)
Congenital disease surgery	32 (11.5)
Valvular replacement	25 (9)
Coronary artery bypass grafting surgery	17 (6.1)
Arterial embolectomy	13 (4.7)

Table 1. Demographic characteristics (n=278)	
Characteristic	**n (%)**
Thoracic wall surgery	12 (4.3)
Aortic surgery	8 (2.9)
Surgical wound classification	
Clean	275 (98.9)
Clean-contaminated	2 (0.7)
Contaminated	1 (0.4)
Dirty-infected	-
Type of surgery	
Open	275 (98.9)
Thoracoscopic	3 (1.1)
Type of anesthesia	
General	270 (97.1)
Local	6 (2.2)
Spinal/epidural	2 (0.7)
Mortality	31 (11.2)
EF: Ejection fraction	

Table 2. Significant risk factors for postoperative pneumonia			
Variables	**OR**	**95% confidence interval**	**p-value**
History of renal failure	3.9	1.1-13.5	**0.040**
Central nervous system disorder	12.8	4-40.5	**<0.001**
Aspiration after surgery	-	-	**0.008**
Absence of respiratory exercise after surgery	2.5	1-6.3	**0.041**
Presence of postoperative complications	7.2	2.3-22	**0.002**

vs. 0 (0-38) days, p<0.001], postoperative hospitalization [15 (6-44) vs. 6 (0-52) days, p<0.001], and postoperative mobilization [4.5 (1-41) vs. 1 (0-147) days, p<0.001] than those without pneumonia. Among survivors, postoperative mobilization time also remained significantly prolonged [2 (1-10) vs. 1 (0-10) days, p=0.006].

Multivariate analysis revealed that prolonged postoperative mobilization duration (OR 1.8, 95% CI 1.08-2.84, p=0.022), presence of postoperative complications other than pneumonia (OR 12.7, 95% CI 1.73-92.31, p=0.012), and longer postoperative hospitalization duration (OR 1.1, 95% CI 1.02-1.19, p=0.011) were independent predictors of POP (Table 4).

Mortality

Overall mortality was 11.2% (31 patients). Mortality was significantly higher in patients with POP (OR 11.38, 95% CI 4.43-29.48, p<0.001) and nosocomial infections other than pneumonia (OR 3.56, 95% CI 1.29-9.64, p=0.010), and in patients who needed inotropic support (OR 2.54, 95% CI 1.02-6.22, p=0.044). A high ASA score was a significant risk factor for mortality as well (Table 5). No statistically significant relationship was identified between the type of surgery and mortality outcomes.

Discussion

According to our results, POP incidence was 6.87 per 1000 admission days and significant risk factors for POP were as follows: history of renal disease, central nervous system disorder, high ASA score, aspiration after surgery, absence of respiratory exercise after surgery, presence of postoperative complications other than pneumonia (e.g., acute renal failure), duration of mechanical ventilation, duration of postoperative hospitalization days, and duration of postoperative mobilization days. The significant risk factors for mortality were pneumonia and other nosocomial infections, the necessity of inotropic support, and a high ASA score.

POP, a type of nosocomial pneumonia, is one of the important postoperative complications after abdominal and cardiothoracic surgeries. Possible causes of POP are colonization of microorganisms at the secretion retention area, unresolved atelectasis area, or unnoticed aspiration of pathogenic microorganisms. Therefore, patients who require prolonged respiratory support and are unable to expel tracheobronchial secretions are at higher risk for the development of POP (5,6).

Pneumonia was the most frequent nosocomial infection after surgery in our study population, with 26 cases (9.4%), and 11 patients (42.3%) were diagnosed with VAP. POP incidence was 6.87 per 1,000 hospitalization days. There are few studies in the literature on the prevalence of POP, which show that the prevalence of POP after cardiac surgery varies between 1.02% and 15.3% (7-9). Some studies have reported a higher prevalence of POP compared to previous findings. Since most previous studies included patients undergoing major cardiac surgery, the prevalence may be expected to be higher. The number of POP/the patient days x1000 formula was used to calculate the incidence of POP in our study. However, “POP rate=number of POP/number of surgery x100” formula was commonly used for the incidence of POP in most of the previous studies. Therefore, as far as we know, our study is the first in which POP incidence was calculated using hospitalization days. The length of hospital stay is an important factor in the context of nosocomial infections for several reasons. The longer a patient stays in the hospital, the greater their exposure to the hospital environment, including surfaces, equipment, and healthcare workers, all of which can harbor infectious agents. This increased exposure heightens the risk of acquiring an infection. Extended hospital stays often involve prolonged use of medical devices such as catheters, ventilators, or intravenous lines, which are common sources of

Table 3. Significant postoperative time-related risk factors for the development of postoperative pneumonia

Postoperative risk factors	Pneumonia	No pneumonia	p-value
	Median (min-max)	Median (min-max)	Median (min-max)
Duration of mechanical ventilation days	1.5 (0-30)	0 (0-38)	**<0.001***
Duration of postoperative hospitalization days	15 (6-44)	6 (0-52)	**<0.001***
Duration of postoperative mobilization days	4.5 (1-41)	1 (0-147)	**<0.001***
Duration of postoperative mobilization days (survivors)	2 (1-10)	1 (0-10)	**0.006***

*Mann-Whitney U Test, min-max: Minimum-maximum

Table 4. Predictors of postoperative pneumonia

*Variables	OR	95 % confidence interval	p-value
Mobilization days	1.8	1.08-2.84	**0.022**
Presence of postoperative complications	12.7	1.73-92.31	**0.012**
Postoperative hospilization days	1.1	1.02-1.19	**0.011**

Backward logistic regression method was applied
*The model contains renal failure, central nervous system disorder, presence of aspiration after surgery, presence of respiratory exercise after surgery, presence of postoperative complications, ASA score, need for transfusion, duration of postoperative hospitalization days, duration of postoperative mobilization days
ASA: American Society of Anesthesiologists, OR: Odds ratio

nosocomial infections. The risk of infection generally increases with the duration of device use. Furthermore, longer stays involve more interactions with healthcare workers, which can increase the risk of cross-contamination, especially if infection control protocols are not strictly followed.

The incidence of POP was reported to range from 2% to 25% in previous studies (10,11). This may be justified by the presence of mixed populations with variable age groups, underlying conditions, and differences in pneumonia definitions. Clinical and radiological symptoms and signs were considered sufficient for the diagnosis of pneumonia in some studies, which reported higher rates. Considering microbiologically documented infection as a requirement for the diagnosis of pneumonia may lead to a lower incidence. When microbiologically documented infection is considered to be a necessity for the diagnosis of pneumonia, it can lead to a low incidence. Another problem in POP incidence studies is the evaluation of pneumonia and related complications (atelectasis and secretion retention) together. For these reasons, the true incidence of POP is unknown, although it is estimated to be approximately 10% (10,12).

The incidence of VAP in the mechanically ventilated patient population was 26 per 1000 ventilation days in our study population. In the study by Hortal et al. (12), the incidence of VAP was 45.9% in the patients who remained ventilated for more than 48 hours. The incidence of VAP was 7.87% in the patients undergoing cardiac surgery in the study by Bouza et al. (13). The variation in results may be attributed to the presence of patient populations with diverse underlying diseases.

Microbiological documentation of POP was made in only 46.2% of our patients. The difficulty of obtaining a culture specimen in non-VAP nosocomial pneumonias and the early empirical administration of antibiotics may reduce the percentage of microbiological documentation in these cases. The most frequently isolated microorganisms from POP were *Acinetobacter baumannii* (15.4%), *Klebsiella species* (11.5%), *Escherichia coli* (11.5%), and *Pseudomonas aeruginosa* (7.7%). Although the majority of our patients (61.5%) developed early-onset pneumonia, isolated microorganisms were mostly late-onset pneumonia pathogens in our study. Similarly, Giantsou et al. (14) showed that both early-onset and late-onset VAP were mainly caused by potentially multiresistant gram-negative bacteria and *methicillin-resistant Staphylococcus aureus*. Therefore, distinguishing between early-onset and late-onset VAP according to the isolated microorganisms is considered no longer clinically valuable (13).

Duration of mechanical ventilation and the need for blood component transfusions were found to be significant postoperative risk factors for POP in a study conducted in our country. Consistent with our findings, the use of postoperative mechanical ventilation and the duration of mechanical ventilation have been reported as the most significant risk factors for the development of POP (15). Many reported studies have commented that shortening the duration of mechanical ventilation or encouraging non-invasive mechanical ventilation would reduce the development of postoperative VAP (16,17).

There is an increased risk of aspiration in patients who have neurological dysfunction due to the affected swallowing reflex. This situation leads to the aspiration of microorganisms that colonize the oropharynx and to the development of hospital-acquired pneumonia. The presence of neurological dysfunction before the surgery was a significant risk factor for POP in Bouza et al. (13) and Leal-Noval et al. (18) studies, consistent with our study.

The incidence of postoperative complications after lung resection was 24-48% (19,20). The following postoperative complications can develop in patients undergoing cardiothoracic surgery: acute renal failure, low cardiac output syndrome, bleeding, and others. The risk of developing POP also increases

in patients who experience postoperative complications. The presence of at least one of the postoperative complications was found to be a significant risk factor for POP in our study. In the study of Lee et al. (20), the presence of postoperative complications was a significant risk factor for the development of POP, similar to our results.

A high ASA score was also significantly associated with the development of POP in our study, which is consistent with previous reports (13,21). There was a linear relationship between a high ASA score and the development of POP.

Cardiopulmonary physical therapy is frequently used to prevent and treat sputum retention, atelectasis, pneumonia, and bronchopulmonary infections. Prolonged immobilization increases the risk of atelectasis, while cardiopulmonary physical therapy helps reduce pulmonary complications and shortens the postoperative recovery period (22). The absence of respiratory exercise after surgery was a significant risk factor for the development of POP in our study (p=0.041). The presence of aspiration after surgery, prolonged postoperative hospitalization, and mobilization days were also found to be significant risk factors for POP.

The overall mortality rate in our study population was 11.2%, and this rate was significantly higher in patients with POP, nosocomial infections other than pneumonia, inotropic support requirements, and those with high ASA scores. Consistent with our results, Garibaldi et al. (23) reported that a high ASA score was an independent risk factor for the development of POP. However, it wasn't a significant risk factor for mortality. Hypotension was also reported to be associated with higher mortality in the study by Dupont et al. (24) and in our results.

Our study has several key limitations. Firstly, it is a single-center study with a relatively small patient sample. Given the limited sample size and the insufficient number of cases for each surgical category, the incidence of POP was not stratified

Table 5. The risk factors for mortality

	Non-survivors		Survivors		OR	%95 confidence interval	p-value
	n	%	n	%			
Sex							
Male	23	12.2	166	87.8	-	-	0.561*
Female	8	9.0	81	91.0			
Pneumonia	14	53.8	12	46.2	11.38	4.43-29.48	**<0.001***
Nosocomial infection	8	26.7	22	73.3	3.56	1.29-9.64	**0.010***
Atherosclerotic heart disease	11	8.9	112	91.1	-	-	0.395*
Hypertension	13	12.9	88	87.1	-	-	0.624*
Diabetes mellitus	6	8.5	65	91.5		-	0.536*
Malign neoplasm	5	7.4	63	92.6	-	-	0.356*
Need for inotropic support	10	20.4	39	79.6	2.54	1.02-6.22	**0.044***
ASA score							
1	-	-	2	100	-	-	**<0.001***
2	8	5.3	144	94.7			
3	21	17.5	99	82.5			
4	2	50.0	2	50.0			
Type of surgery							
Valvular replacement	4	16.0	21	84.0	-	-	0.081*
Coronary artery surgery	9	8.7	95	91.3			
Congenital disease surgery	8	25.0	24	75.0			
Aortic surgery	1	12.5	7	87.5			
Arterial embolectomy	3	23.1	10	76.9			
Coronary artery bypass grafting surgery	2	11.8	15	88.2			
Pulmonary resection	4	6.0	23	94.6			
Thoracic wall surgery	-	-	12	100.0			
Age, mean ± SD	51±31		51±22		-	-	0.359**

*Chi-square test, **Mann-Whitney U Test
OR: Odds ratio, ASA: American Society of Anesthesiologists, SD: Standard deviation

by surgical type. The influence of institutional experience on outcomes is undeniable, meaning these findings may not be generalizable to other centers. Several risk factors that were not evaluated in our study may contribute to the development of POP. Additional clinical studies with a prospective and randomized design are necessary to validate our findings. Despite these limitations, we believe our results highlight the need for further research.

Conclusion

In conclusion, this study demonstrates that POP remains a considerable complication after cardiothoracic surgery. Pre-existing renal and neurologic disorders, postoperative aspiration, and inadequate respiratory exercises were identified as major risk factors. Prolonged postoperative mobilization duration, and longer postoperative hospitalization duration, along with the presence of other postoperative complications, were identified as independent predictors of POP. Early identification of high-risk patients and implementation of targeted preventive strategies may reduce the incidence of POP and improve postoperative survival.

Ethics

Ethics Committee Approval: The study was approved for the study was obtained from the Ethics Committee at the Gazi University Medical Faculty Institutional Review Board (decision number: 018, date: 02.06.2010).

Informed Consent: Informed consent from participants was unnecessary due to the absence of any intervention.

Footnotes

Authorship Contributions

Surgical and Medical Practices: S.S.Y., G.T.D., M.D., Concept: S.S.Y., G.T.D., M.D., Design: S.S.Y., G.T.D., M.D., Data Collection or Processing: S.S.Y., G.T.D., E.A., M.D., Analysis or Interpretation: S.S.Y., Z.K., E.A., M.D., Literature Search: S.S.Y., Z.K., G.T.D., E.A., M.D., Writing: S.S.Y., Z.K., G.T.D., E.A., M.D.

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Associations between intuitive eating, body self-compassion, and orthorexia nervosa in young adults: a cross-sectional analysis

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ABSTRACT

Aims: Orthorexic tendencies are increasingly recognized as an emerging problem in eating behavior, while intuitive eating and body self-compassion (i.e., treating one's body with kindness and acceptance) are adaptive factors supporting healthier eating and body image. Recognizing the protective role of these constructs is crucial. This study aimed to examine the relationship between intuitive eating, body self-compassion, and orthorexia nervosa (ON) in university students.

Methods: This descriptive cross-sectional study was conducted with university students aged 18-25 years. A convenience sampling method was used to recruit participants. Socio-demographic characteristics and anthropometric measurements were assessed using a structured questionnaire. The risk of ON was evaluated with the Orthorexia Nervosa Risk Assessment Scale, intuitive eating with the Intuitive Eating Scale-2, and body self-compassion with the Body Self-Compassion Scale. Data were collected through face-to-face interviews and analyzed using descriptive, correlational, and linear regression analyses.

Results: The study included 500 students (mean age: 19.67±1.65 years; 51.4% female). The mean body mass index (BMI) was 22.55±3.02 kg/m²; 74.4% of participants were classified as normal weight, while 15.4% were overweight. ON scores were negatively correlated with intuitive eating ($r=-0.404$, $p<0.001$) and body self-compassion ($r=-0.372$, $p<0.001$). Regression analysis showed that intuitive eating ($\beta=-0.391$, $p<0.001$) and body self-compassion ($\beta=-0.258$, $p<0.001$) were significantly associated with ON. Emotional eating was positively associated with BMI ($r=0.315$, $p<0.001$) and identified as the strongest factor ($\beta=0.308$, $p<0.001$).

Conclusions: This study found that higher intuitive eating and body self-compassion scores were linked to lower orthorexic tendencies and healthier weight-related behaviors, while higher BMI was related to maladaptive patterns. Promoting intuitive eating and body self-compassion may help protect against disordered eating. From a public health perspective, integrating these constructs into interventions could support healthier eating behaviors among young adults.

Introduction

Eating disorders have become increasingly common and pose a serious threat to health. Eating disorders, defined as negative eating behavior by the World Health Organization (WHO), are characterized by body weight control, body image anxiety, and low self-esteem (1). The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), categorizes eating disorders into five main types: anorexia nervosa (AN), bulimia nervosa, binge eating disorder, and two additional categories for specified and unspecified feeding and eating disorders (2). Although orthorexia nervosa (ON) is not officially recognized as a distinct eating disorder in the DSM-5, it shares certain characteristics with clinically diagnosed eating pathologies and is increasingly examined in the context of disordered eating (1). ON is a newly emerging concept related to eating disorders, derived from the Latin word “orthos”, meaning correct. Although researchers define it as an obsession with healthy and proper nutrition, it shares similarities with other eating disorders. Unlike AN and bulimia nervosa, ON focuses on the health, purity, and quality of food rather than quantity. Individuals may prefer to remain hungry instead of consuming foods considered impure or harmful to health which can lead to malnutrition and weight loss, similar to what is seen in AN. In ON, individuals spend much of their time contemplating the foods they will consume and adhering to strict rules, which resembles obsessive-compulsive disorder (3). While ON has gained increasing attention in recent years, it is important to distinguish between a healthy interest in nutrition and ON, as these terms are often used interchangeably in public discourse. Healthy orthorexia reflects a flexible, health-conscious approach to eating without obsessive behaviors or emotional distress. In contrast, ON is characterized by rigid dietary rules, preoccupation with food purity, and compulsive behaviors that interfere with social and psychological functioning. Individuals with ON may exhibit anxiety, guilt, or avoidance when confronted with foods perceived as unhealthy. This pathological fixation is thought to contribute to disruptions in self-regulation and is associated with disordered eating patterns and psychological distress (4).

Recently, it has been suggested that individuals may adopt eating patterns aimed at weight loss under the guise of healthy eating. In this regard, it is noteworthy that ON may be related to body weight and body image (5).

Body image encompasses an individual’s perceptions, attitudes, and behaviors related to their physical appearance (6). Prior studies have suggested that negative body image may play a key role in the development of orthorexic tendencies, as individuals with high appearance-related anxiety may adopt rigid dietary rules to attain perceived ideals of health and purity (7,8). In eating behavior disorders, there is excessive preoccupation with food, body, weight, and body dissatisfaction, and this preoccupation may impair body image. There are data suggesting a relationship between negative body image and symptoms of ON (9,10). Given this connection, understanding how individuals relate to their bodies—particularly through constructs like self-compassion—may offer insight into mitigating the psychological burden of ON.

Self-compassion, which has a reducing effect on eating behavior disorders and negative body image, draws attention (11). Self-compassion refers to treating oneself with kindness and understanding, especially during difficult moments. There are studies showing that self-compassion is associated with positive eating behaviors, less body image anxiety, and also prevents risk factors for eating behavior disorders and body image anxiety (12-14). In light of this restrictive pattern, intuitive eating emerges as a promising counter-approach, emphasizing flexibility, internal cues, and a non-judgmental stance toward eating (15,16). Both intuitive eating and body self-compassion promote self-acceptance and internal awareness, encouraging individuals to respond to their physical and emotional needs without guilt or rigid control (13,17,18). Individuals with higher body self-compassion are more likely to respect their body’s signals and detach from societal body ideals, which in turn facilitates intuitive eating behaviors (12,14). Therefore, these two constructs may not only buffer the psychological impact of disordered eating but also support each other in fostering a healthier relationship with food and body image (13,18).

In this context, it becomes increasingly important to understand the potential role of intuitive eating in transforming these rigid and rule-driven eating behaviors commonly observed in individuals with ON. Changing restrictive eating behaviors in individuals with ON is a long and challenging process. In this context, intuitive eating has been proposed as a potential approach to alleviate symptoms (19). Intuitive eating is defined as having a strong connection with hunger and satiety signals and consuming nutrients in response to these signals (15). Intuitive eating behavior does not categorize foods as “healthy” or “unhealthy”, but instead focuses on individuals’ hunger signals. This perspective sets intuitive eating apart from restrictive patterns (20). Intuitive eating behavior has been linked to positive eating patterns and lower body image anxiety (18). However, some evidence suggests that ON may not show a consistent association with intuitive eating (4,21).

Upon reviewing the studies, it is observed that the relationship between intuitive eating behavior, body image, and eating behavior disorders is generally evaluated (4,18,21). However, studies on the mediating role of intuitive eating behavior in this context are needed. Therefore, this study aims to clarify the mediating role of intuitive eating behavior on ON and body self-compassion, contributing new insights to the literature.

Methods

Study desing and participants

This cross-sectional study was conducted between January and March 2024 among university students aged 18-25 at Health Sciences University. The cross-sectional design was selected for its practicality in assessing multiple variables simultaneously within a limited timeframe and resource availability. A convenience sampling method was used to recruit participants. Eligible university students were contacted and invited to participate in the study through scheduled face-to-face appointments. This method was preferred over online data collection to ensure controlled conditions, minimize distraction, and reduce data loss or misunderstanding during the survey. University students were chosen as the target population due to their heightened vulnerability to disordered eating behaviors, given the transitional nature of this life stage and the increasing societal pressures surrounding body image and healthy eating. After individuals read and signed the voluntary consent form, they were evaluated by researchers based on inclusion and exclusion criteria. The inclusion criterion for the study was being aged between 18 and 25, while the exclusion criteria included being pregnant or breastfeeding, having any chronic illness, syndrome or systemic disease, using medications that could affect appetite (such as corticosteroids, antidepressants, metformin, etc.), receiving hormone supplementation, and following an energy-restricted diet.

To determine an adequate sample size for the study, an a priori power analysis was performed using G*Power software (version 3.1), which indicated that a minimum of approximately 320 participants would be sufficient to detect a medium effect size (f^2=0.15) with 95% power at α=0.05. To increase the reliability and generalizability of the results, a larger sample was targeted. Accordingly, 500 students who met the inclusion criteria were included in the study. Since all participants fulfilled the eligibility requirements, no data loss occurred.

The study protocol approved by the Gülhane Scientific Research Ethics Committee of University of Health Sciences Türkiye (decision no.: 2024-22, date: 03.01.2024). All procedures were conducted in accordance with the Helsinki Declaration. Before data collection, participants were provided with detailed study information and asked to sign a written informed consent form.

Data collection

Individuals eligible for the study were invited by appointment for face-to-face questionnaire administration, during which their socio-demographic characteristics were recorded and anthropometric measurements, including body weight and height, were taken by the researcher using a standardized method. The risk of ON in individuals was assessed using the Orthorexia Nervosa Risk Assessment Scale (ORTO-11), intuitive eating behavior levels were assessed with the Intuitive Eating Scale-2 (IES-2), and their body-related self-compassion was assessed through the Body Self-Compassion Scale (BSCS).

ORTO-11 Scale

To assess the risk of ON, this study utilized the ORTO-11 Scale which is a modified version of the original ORTO-15 developed by Donini et al. in 2005 (3). The Turkish validity and reliability of the scale were established in 2008 by Arusoğlu et al. (22), who refined the tool by eliminating specific items. The final version includes eleven items rated on a four-point Likert scale ranging from “always” to “never”. Higher total scores indicate a lower risk of ON as the scale is reverse-coded; lower scores reflect more rigid and obsessive eating-related attitudes (22).

Intuitive Eating Scale (IES)

To assess intuitive eating behaviors, the IES-2 was used. The IES-2 consists of 23 items rated on a five-point Likert scale (1=strongly disagree to 5=strongly agree) and covers four subscales: unconditional permission to eat, eating for physical rather than emotional reasons, reliance on hunger and satiety cues, and body–food choice congruence. Items 1, 2, 3, 6, 7, 8, and 9 are reverse-coded, consistent with the original version developed by Tylka and Kroon Van Diest (15). Higher scores indicate a stronger tendency toward intuitive eating. The Turkish adaptation was conducted using standard back-translation procedures and validated by Bas et al. (23), ensuring conceptual and linguistic equivalence with the original scale.

Body Self-Compassion Scale (BSCS)

The original form of the BSCS developed by Altman et al. (24) is a 23-item, five-point Likert-type measurement tool consisting of three sub-dimensions (dissociation, common human values, and bodily acceptance).

The scale items are rated on a five-point Likert scale ranging from 1 (never) to 5 (always), with intermediate options including rarely, sometimes, and most of the time. The Cronbach alpha internal consistency coefficient of the scale was found to be 0.92, 0.92, 0.91, and 0.87 for the total score, dissociation, common human values, and bodily acceptance sub-dimensions of the BSCS, respectively. It was determined that the sub-dimensions showed a positive and significant relationship with each other (0.25, 0.43, 0.61). The items in the dissociation dimension of the measurement tool (1, 2, 3, 4, 5, 11, 12, 14, 15) are reverse scored. The scores that can be obtained from the scale range from 23 to 115. High scores obtained from the scale indicate a high level of body self-compassion (24-26).

Anthropometric measurements

Participants' body weight and height were measured directly by the researcher. During the assessments, individuals wore lightweight clothing, and metal accessories or objects were removed to avoid measurement bias. Body weight was recorded using a TANITA BC 418 ST body composition analyzer, and height was measured with a fixed wall stadiometer and a flexible, non-elastic measuring tape. Body mass index (BMI) was calculated as weight in kilograms divided by height in meters squared. BMI classifications followed WHO standards, with underweight defined as <18.50 kg/m², normal weight as 18.50-24.99 kg/m², overweight as 25.00-29.99 kg/m², and obesity as ≥30.00 kg/m² (27).

Statistical Analysis

All statistical analysis were performed using IBM SPSS Statistics version 26.0 (IBM Corp., Armonk, NY, USA). The normality of the data was evaluated through distribution tests and skewness values, with results expressed as mean ± standard deviation or median (minimum-maximum). Group comparisons were carried out using either independent samples t-tests or Mann-Whitney U tests, depending on the data distribution. For categorical data, chi-square tests (Pearson or Fisher's exact) were used where appropriate. Associations between variables were explored through correlation coefficients, including Pearson, Spearman, and eta. To identify predictors of intuitive eating scores, linear regression analysis was conducted. In cases of non-normally distributed data, logarithmic transformation was applied. Statistical significance was defined as $p<0.05$.

Results

A total of 500 university students participated in the study (female: 257, male: 243) with an average age of 19.67±1.65 years. Of the university students who participated in the study, 91.6% did not have any health problems, 30.2% exercised regularly, and 32.4% had a smoking habit. The mean ORTO-11 total score was 27.90±4.33, the mean intuitive eating score was 2.79±0.44, and the mean body self-compassion total score was 69.49±13.20. 74.4% of the students had normal body weight according to the BMI classification. The socio-demographic, anthropometric, and psychometric characteristics of the students who participated in the study are shown in Table 1.

The relationship between the ORTO-11 scores of university students participating in the study, intuitive eating, body self-compassion, and BMI levels was evaluated (Table 2). Accordingly, a positive, weak, and significant correlation was observed between the total ORTO-11 score and intuitive eating, as well as its sub-dimensions: unconditional eating permission, physical eating, and trust in hunger signals. Additionally, a positive, weak, and significant relationship was found between the total score of the BSCS and its sub-dimensions, namely dissociation and body acceptance. As the level of intuitive eating increased, the level of body self-compassion also increased. Furthermore, the sub-dimensions of body self-compassion—dissociation and body acceptance—showed a positive, weak, and significant relationship with the total intuitive eating score. In addition, the study examined the correlation between BMI and the scale assessments, revealing that as BMI increased, intuitive eating scores decreased, demonstrating a significant, negative, and weak relationship with the sub-dimensions of intuitive eating: unconditional eating, physical eating, and trust in hunger signals. Moreover, it was found that as BMI increased, both the total body self-compassion score and its sub-dimensions (dissociation and physical acceptance) exhibited a decrease.

Table 3 and Figure 1 present the results of the linear regression analysis conducted to predict intuitive eating scores. The overall model was statistically significant ($R^2=0.129$; $p<0.001$), indicating a meaningful relationship between the predictor variables and intuitive eating levels. Among the predictors, ORTO-11 total score [$\beta=0.157$, 95% confidence interval (CI): 0.008 to 0.025, $p<0.001$] and body self-compassion score ($\beta=0.262$, 95% CI: 0.006 to 0.012, $p<0.001$) showed significant positive associations with intuitive eating. This suggests that individuals with fewer orthorexic tendencies and higher body self-compassion are more likely to eat intuitively. Conversely, BMI was negatively associated with intuitive eating ($\beta=-0.106$, 95% CI:-0.028 to -0.003, $p=0.014$), indicating that higher BMI predicted lower intuitive eating levels. Gender also emerged as a significant predictor ($\beta=0.114$, 95% CI: 0.026 to 0.176, $p=0.008$), with female participants reporting higher intuitive eating scores.

Figure 1 provides a visual summary of the standardized beta coefficients. The strongest contributor to intuitive eating was body self-compassion, followed by ORTO-11 total score and gender, while BMI showed a negative relationship. This figure highlights the direction and relative strength of each predictor's association with intuitive eating.

Discussion

This study demonstrated that orthorexic tendencies were negatively associated with both intuitive eating and body self-compassion among young adults. Individuals with higher intuitive eating scores also reported greater body self-compassion, while both constructs showed significant negative correlations with BMI. Additionally, intuitive eating was found to be higher among male participants than females. Regression analyses further indicated that ORTO scores, body self-compassion, BMI, and gender were significant predictors of intuitive eating. These findings highlight the protective role of intuitive eating and body self-compassion in relation to orthorexic tendencies and weight-related outcomes.

Growing awareness of rigid dietary patterns and their psychological consequences has led to increased interest in ON in recent literature (25,28). Findings supported the hypothesis that higher levels of intuitive eating and self-compassion are related to lower ON risk and healthier BMI outcomes. The obsessive focus on consuming pure and natural foods observed in ON is known to be associated with physical and mental health issues (25). There is a strong relationship between negative body image perception, a factor affecting an individual's physical and mental health, and eating behavior. This relationship has led to an increase in interest in ON. However, due to the insufficient number of studies on the subject in the literature, the results appear to be conflicting (4). One study found that individuals with ON did not exhibit negative body image (29). In another study, it was observed that ON, was positively associated with negative body image attitudes (4). In addition, it is suggested that self-compassion and intuitive eating will be effective as a protective measure against negative eating behavior and negative body image perception (30).

Table 1. Socio-demographic, anthropometric, and psychometric characteristics of participants by gender

Variables	Female		Male		Total		p-value
	n	%	n	%	n	%	
Gender	257	51.4	243	48.6	500	100.0	-
Regular exercise status							
Yes	55	21.4	96	39.5	151	30.2	**p<0.001***
No	202	78.6	147	60.5	349	69.8	
Food preferences							
Fatty foods	30	11.7	27	11.1	57	11.4	
Carbohydrate foods	122	47.5	48	19.8	170	34.0	**p<0.001***
Protein foods	80	31.1	157	64.6	237	47.4	
Vegetable-based foods	25	9.7	11	4.5	36	7.2	
Body weight perception							
Very weak	3	1.2	3	1.2	6	1.2	
Weak	36	14.0	29	11.9	65	13.0	0.018
Normal	140	54.5	168	69.1	308	61.6	
Light overweight	67	26.1	38	15.6	105	21.0	
Obese	11	4.3	5	2.1	16	3.2	
Presence of health problems							
Yes	20	7.8	22	9.1	42	8.4	0.62
No	237	92.2	221	90.9	458	91.6	
Smoking habit							
Yes	60	23.4	102	42.8	162	32.4	**p<0.001***
No	197	76.7	141	58.0	338	67.6	
BMI classification (kg/m²)							
Underweight (<18.5)	32	12.5	6	2.5	38	7.6	
Normal (18.5-24.99)	189	73.5	183	75.3	372	74.4	**p<0.001***
Overweight (25-29.99)	28	10.9	49	20.2	77	15.4	
Obese (≥30)	8	3.1	5	2.1	13	2.6	
	Mean ± SD		**Mean ± SD**		**Mean ± SD**		
Age (years)	19.67±1.50		19.67±1.79		19.67±1.65		0.232
BMI (kg/m²)	21.94±3.22		23.19±2.65		22.55±3.02		**p<0.001***
ORTO-11 total score	27.73±3.99		28.08±4.66		27.90±4.33		0.254
Intuitive eating score	2.75±0.41		2.84±0.46		2.79 ±0.44		0.073
Unconditional permission to eat	3.50±0.64		3.21±0.68		3.36±0.67		**p<0.001***
Physical eating	2.84±0.87		3.29±0.80		3.06±0.86		**p<0.001***
Relying on hunger satiety signals	3.35±0.79		3.26±0.96		3.31±0.87		0.236
Harmony of body-nutrient selection	3.24±0.83		3.34±0.93		3.29±0.88		0.210
Body self-compassion total score	69.33±15.26		69.67±10.63		69.49±13.20		0.994
Dissociation	31.63±8.77		33.62±7.40		32.60±8.19		**0.041***
Bodily acceptance	16.10±4.51		16.07±4.43		16.09±4.46		0.928
Common human values	21.58±6.59		19.97±6.00		20.80±6.36		**0.006***

Mann-Whitney U test, chi-square test *p<0.05, **p<0.001.
BMI: Body mass index, ORTO-11: Orthorexia Nervosa Risk Assessment Scale, SD: Standard deviation

Table 2. Evaluation of the relationship between ORTO-11, intuitive eating, body self-compassion and BMI levels of individuals

	ORTO-11 total score	Intuitive eating score	Unconditional permission to eat	Physical eating	Relying on hunger satiety signals	Harmony of body-nutrient selection	Body self-compassion total score	Dissociation	Bodily acceptance	Common human values
ORTO-11 total score	-									
Intuitive eating score	0.189 **(<0.001)****	-								
Unconditional permission to eat	0.180 **(<0.001)****	0.330 **(<0.001)****	-							
Physical eating	0.102 (0.022)*	0.763 **(<0.001)****	-0.093 **(0.037)***	-						
Relying on hunger satiety signals	0.130 **(0.003)****	0.657 **(<0.001)****	0.128 (0.004)**	0.318 **(<0.001)****	-					
Harmony of body-nutrient selection	0.013 (0.775)	0.494 **(<0.001)****	-0.049 (0.271)	0.181 **(<0.001)****	0.458 **(<0.001)****	-				
Body self-compassion total score	0.100 **(0.025)***	0.298 **(<0.001)****	0.089 **(0.048)***	0.212 **(<0.001)****	0.255 **(<0.001)****	0.187 **(<0.001)****	-			
Dissociation	0.124 (0.005)**	0.276 **(<0.001)****	0.94 **(0.036)***	0.226 (<0.001)**	0.190 **(<0.001)****	0.137 (0.002)**	0.718 **(<0.001)****	-		
Bodily acceptance	0.126 (0.005)**	0.260 (0.001)**	0.110 **(0.014)***	0.173 (0.001)**	0.237 **(0.001)****	0.096 **(0.031)***	0.775 (0.001)**	0.419 (0.001)**	-	
Common human values	-0.026 (0.557)	0.076 (0.092)	0.10 (0.820)	0.002 (0.957)	0.111 **(0.013)***	0.165 **(<0.001)****	0.548 **(<0.001)****	-0.018 (0.692)	0.315 **(<0.001)****	-
BMI (kg/m^2)	0.006 (0.897)	-0.111 **(0.013)***	-0.147 **(<0.001)****	-0.040 (0.367)	-0.084 (0.059)	0.004 (0.932)	-0.124 (0.006)**	-0.100 **(0.025)***	-0.115 **(0.010)***	-0.038 (0.398)

*p<0.05, **p<0.001, Spearman rank correlation coefficient test was applied.
ORTO-11: Orthorexia Nervosa Risk Assessment Scale, BMI: Body mass index

Table 3. Linear regression analysis for prediction of young adult intuitive eating level

	Intuitive eating score				
Model	**Beta**	**t**	**95% CI Lower**	**95% CI Upper**	**p-value**
ORTO-11 total score	0.157	3.721	0.008	0.025	**<0.001**
Body self-compassion total score	0.262	6.163	0.006	0.012	**<0.001**
BMI (kg/m^2)	-0.106	-2.464	-0.028	-0.003	0.014
Gender	0.114	2.650	0.026	0.176	0.008
			R^2=0.129;p<0.001*		

*Significant at p-value <0.05.
ORTO-11: Orthorexia Nervosa Risk Assessment Scale, BMI: Body mass index, CI: Confidence interval

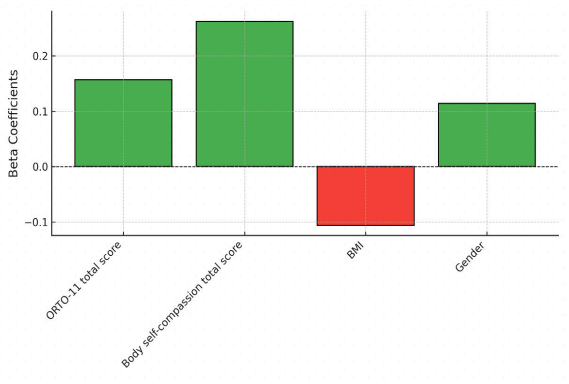

Figure 1. Regression analysis: factors affecting intuitive eating
ORTO-11: Orthorexia Nervosa Risk Assessment Scale, BMI: Body mass index

There are some studies examining the relationship between ON and negative body image perception (9,10). Accordingly, it has been observed that individuals with ON symptoms also have negative body image (10). When ON was first defined, it was seen as a disorder related only to healthy eating, but today it is now accepted that it may also include negative body image. Promotion of unrealistic body standards by social media and society has increased disordered eating behaviors in different age groups and genders (31). In addition to all these, self-compassion intervention is recommended as a protective factor against negative eating behavior and negative body image perception (11). Multiple studies have indicated a protective role of self-compassion against disordered eating and negative body image. A meta-analysis revealed a significant inverse relationship between self-compassion and both dysfunctional eating behaviors and negative body perceptions (12). Another comprehensive review emphasized that self-compassion can directly mitigate adverse outcomes related to body dissatisfaction and eating disorders by reducing underlying risk factors (13). Additionally, research examining the link between body-related self-compassion and eating behavior reported that higher levels of self-compassion indirectly contributed to a reduction in maladaptive eating patterns (14). These results suggest that individuals with higher levels of body self-compassion may be more likely to trust their physical hunger signals and approach food in a more relaxed and less anxious manner. In addition, responding to negative body image with self-compassion enables the individual to accept his/her physical appearance as it is and protects him/her from weight control efforts (32). In a study, as BMI increased, negative eating behavior and a negative body image increased, and a decrease in self-compassion was observed (33). In this study, consistent with previous findings, ON was negatively associated with self-compassion in young adults; BMI decreased as self-compassion increased.

Intuitive eating has been suggested as another protective factor in individuals with negative eating behaviors (19). A study showed that individuals with low ON scored higher on self-esteem and intuitive eating measures (21). A systematic review highlighted that intuitive eating is linked to a decreased risk of developing eating disorders, as well as enhanced body image and improved emotional well-being (18). Similarly, another study reported a positive correlation between intuitive eating and indicators of positive body image, while also noting a negative association with ON symptoms (4). Murray et al. (34) showed that women had poorer body image perception and lower levels of intuitive eating behavior, compared to men, due to body-related pressures leading to negative body image in women. It was also observed that BMI decreased with increasing intuitive eating. In our study, in line with other studies, our findings revealed that ON decreased intuitive eating; intuitive eating was higher in men than in women; and BMI decreased as intuitive eating score increased.

In this study, male participants demonstrated higher intuitive eating scores compared to females. At first glance, this finding appears to diverge from several studies reporting greater intuitive eating levels in women (35,36). However, recent evidence also suggests mixed gender patterns. A comprehensive meta-analysis synthesizing data from 36 independent samples (n=22.939) found that men reported significantly higher intuitive eating levels than women, with a moderate effect size, (d=0.35) (16). This gender difference may be explained by the more frequent and intense socio-cultural pressures on women to

conform to thin ideals, which may discourage reliance on internal hunger and satiety cues (37). Therefore, women's engagement in intuitive eating may be suppressed due to cultural norms and body image concerns. The present finding may reflect how these dynamics manifest in young adults within the cultural context of this study.

On the other hand, according to our regression model, ON and body self-compassion were observed to be factors affecting intuitive eating. These results reveal that ON and body image should not be ignored in intuitive eating interventions. These findings align with theoretical perspectives such as self-determination theory (38). Acceptance and commitment therapy (39), both of which emphasize the importance of autonomy, psychological flexibility, and self-awareness in promoting adaptive eating behaviors. We found a positive correlation between the intuitive eating score and the body self-compassion score.

This study has several strengths. First, this study is one of the few to comprehensively explore the interrelationships among intuitive eating, body self-compassion, and ON in a large sample of university students, providing valuable insights into the psychological and behavioral factors influencing nutrition-related disorders. Secondly, the use of validated scales, such as ORTO-11 and IES-2, alongside a robust sample size, enhances the reliability of the findings and ensures their applicability to similar populations. Thirdly, with a substantial sample size of 500 participants, this study offers robust statistical power and represents a diverse demographic of university students, enhancing the generalizability of the results. Finally, by demonstrating that intuitive eating and body self-compassion are negatively associated with ON and BMI, our findings may offer useful insights for developing future intervention strategies. Unlike existing research, this study not only identifies correlations but also emphasizes their clinical relevance. Integrating these psychological constructs into intervention programs may help mitigate ON risk and promote overall well-being. This innovative approach bridges the gap in existing literature by addressing the interconnected roles of intuitive eating and body self-compassion, paving the way for more holistic intervention strategies in the field of nutritional psychology.

From a public health perspective, these findings emphasize the need for preventive interventions focusing on intuitive eating and body self-compassion to reduce ON risk and improve dietary behaviors. Future research should explore these relationships in longitudinal and interventional studies to assess the long-term impact of intuitive eating and body self-compassion on disordered eating tendencies, and develop targeted strategies for at-risk populations. These findings may inform the development of student wellness programs by universities and health organizations, emphasizing intuitive eating and self-compassion to promote healthier relationships with food.

However, there are some limitations that should be considered in future research. First, dietary records were not collected. Dietary records should be obtained to assess diet quality and the relationship between diet quality and ON. The second limitation is that the cross-sectional design limits the ability to infer causal relationships among the variables studied, necessitating further longitudinal research to confirm these findings. Finally, future studies should include diverse age groups and settings to explore the long-term effects of intuitive eating and self-compassion on ON through longitudinal and interventional designs.

Conclusion

This study highlights the potential role of intuitive eating and body self-compassion as protective factors against ON among university students. The findings suggest that encouraging a more intuitive approach to eating, and promoting self-compassion might help reduce the risk factors associated with ON, particularly among individuals with higher BMI and gender-related differences in eating behaviors. Given the increasing prevalence of disordered eating behaviors, integrating psychological well-being approaches into nutrition-related public health strategies may contribute to healthier eating patterns among young adults.

Ethics

Ethics Committee Approval: This study was obtained from the Gülhane Scientific Research Ethics Committee of Health Sciences University (decision no.: 2024-22, date: 03.01.2024).

Informed Consent: Before data collection, participants were provided with detailed study information and asked to sign a written informed consent form.

Footnotes

Authorship Contributions

Concept: E.M.E., N.B., Design: E.M.E., N.B., Data Collection or Processing: E.M.E., N.B., Analysis or Interpretation: E.M.E., Literature Search: E.M.E., N.B., Writing: E.M.E., N.B.

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

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Assessment of routine hematological and biochemical parameters as markers of systemic inflammation in patients with pterygium

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ABSTRACT

Aims: This study aimed to evaluate whether routine hematological and biochemical indices reflect systemic inflammation in patients with pterygium and to compare these indices with healthy controls.

Methods: This retrospective study included patients with clinically diagnosed pterygium and age- and sex-matched healthy controls. Main inclusion criteria were documented ophthalmological examination and available complete blood count (CBC) and routine biochemistry results; patients with systemic diseases or conditions affecting laboratory parameters were excluded. The participants' CBC values, glucose, creatinine, and blood lipid profiles were reviewed. The primary endpoint was the comparison of systemic inflammatory markers—neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), monocyte-to-lymphocyte ratio (MLR), and monocyte-to-high-density-lipoprotein ratio (MHR)—between the two groups.

Results: A total of 107 patients with pterygium (mean age 56.57±14.47 years; 63.6% male) and 104 controls (mean age 56.05±13.28 years; 69.3% male) were included. Only hematocrit and white blood cell (WBC) count were significantly higher in patients with pterygium (p=0.044 and p=0.009, respectively). There were no significant differences in NLR (p=0.108), PLR (p=0.462), MLR (p=0.190), or MHR (p=0.134) between the groups. The patient group exhibited significantly higher total cholesterol and triglyceride (TG) levels (p=0.004 and p=0.007, respectively).

Conclusions: This study indicated that routine systemic inflammatory indices (NLR, PLR, MLR, MHR) did not differ significantly between patients with pterygium and healthy controls, whereas hematocrit, WBC, total cholesterol, and TG levels were higher in the pterygium group.

Introduction

Pterygium is a fibrovascular growth originating from the subconjunctival tissue and extending onto the corneal surface, typically occurring in the interpalpebral region and most commonly located nasally (1). The etiology of pterygium involves multiple risk factors, including immune system dysregulation, genetic predisposition, chronic environmental irritation caused by exposure to ultraviolet (UV) radiation, hot and dry air, and wind, and the duration of exposure to such conditions (2). One of the proposed pathogenic mechanisms is that UV radiation causes damage to limbal stem cells, leading to the activation of tissue growth factors, which subsequently induce angiogenesis and fibroblast proliferation (3). Human papillomavirus has also been implicated in the pathogenesis of pterygium (4). Although

several risk factors for pterygium are well documented, the precise mechanisms by which these factors promote cell proliferation remain incompletely understood. However, the prevailing hypothesis suggests that chronic exposure to UV radiation increases free radical production (5). Consequently, free radicals, oxidative stress, and inflammation are increasingly recognized as key contributors to the pathophysiology of pterygium (6).

Cytokines that play roles in the immune response and inflammation have been found to be overexpressed in pterygium tissue (7). Likewise, increased expression of the inflammatory cytokine tumor necrosis factor-alpha (TNF-α) has been observed in pterygium samples (8). Recently, there has been increasing interest in the role of systemic inflammatory mechanisms in the development of pterygium. Increased levels of both local and systemic endothelial progenitor cells (EPCs) have been documented (9). Because EPCs play a key role in postnatal neovascularization, it has been proposed that their increased levels—triggered by proinflammatory mediators—may contribute to angiogenic processes underlying pterygium pathogenesis (9). Additionally, patients with pterygium were found to have increased serum immunoglobulin E (IgE) levels and mast cell counts (10). IgE may play a role in promoting inflammation and angiogenesis during pterygium development by causing mast cell degranulation (10). Elevated concentrations of interleukin-6 (IL-6), IL-17A, and nitric oxide have likewise been detected in the tear fluid and serum of patients with pterygium (11). Additionally, accumulating evidence indicates that pterygium behaves as a tumor-like proliferative disorder in which abnormal cellular growth and deoxyribonucleic acid (DNA) replication are closely linked to disturbances in cholesterol metabolism and lipid peroxidation (12). Increased levels of both high-density lipoprotein (HDL) and low-density lipoprotein (LDL) have been reported to be potential risk factors for pterygium, particularly among individuals younger than 50 years or with a normal body mass index (13).

These findings, together with systemic inflammatory and immunological mechanisms, support the notion that some systemic metabolic pathways may contribute substantially to the underlying pathophysiological mechanisms of pterygium. Recent evidence has reinforced the involvement of inflammatory processes in the development of pterygium, irrespective of the initial trigger. While these complex molecular mediators have been shown to be involved in the development of pterygium, there is a need for accessible biomarkers that reliably indicate the presence of systemic inflammation.

This study aimed to assess systemic inflammatory biomarkers by examining complete blood count (CBC) and lipid profile measurements. For this purpose, the neutrophil-to-lymphocyte (NLR), platelet-to-lymphocyte (PLR), monocyte-to-lymphocyte (MLR), and monocyte-to-HDL (MHR) ratios were calculated. These readily available laboratory parameters have been recognized as markers of systemic inflammation in various conditions, particularly in cardiovascular conditions and eye diseases, including glaucoma, dry eye, age-related macular degeneration, pseudoexfoliation syndrome, and keratoconus (14-18). In their study evaluating systemic inflammatory biomarkers across multiple eye diseases, including pterygium, Shirvani et al. (19) found that patients with pterygium exhibited a significantly elevated NLR. The main objective of this study was to assess systemic inflammation in patients with pterygium through analysis of standard hematological and biochemical parameters derived from CBCs and lipid profiles. The study sought to determine whether these commonly available laboratory parameters could serve as reliable biomarkers of systemic inflammatory status and metabolic alterations associated with pterygium.

Methods

This retrospective analysis examined data from 107 eyes of patients diagnosed with pterygium at a tertiary teaching hospital over 11 months (January-November 2024). The study adhered to the ethical principles stated in the Declaration of Helsinki and received approval from the Gülhane Scientific Research Ethics Committee of the University of Health Sciences (approval no.: 2025-71, date: 11.02.2025).

All consecutive patients with pterygium who presented to our clinic during the defined study period were included, regardless of age or sex. Inclusion criteria included having undergone a comprehensive ophthalmological examination with fully documented findings and having CBC and routine biochemistry test results available. Exclusion criteria included refractive error with an absolute value greater than 5.00 diopters, intraocular pressure above 22 mmHg, incomplete medical records or laboratory results, history of ocular inflammatory disease, previous intraocular surgery, and history of a systemic condition. The control group included individuals matched for age and sex who had received a standard ophthalmological examination, a CBC, and biochemical testing. These individuals had no ophthalmological disease other than refractive error within the limits specified in the inclusion criteria and no history of systemic disease.

Laboratory parameters assessed in this study represent well-known indicators of systemic inflammation and may be influenced by age, sex, and various acute or chronic conditions. To minimize bias, comparisons were made with an age- and sex-matched control group. In the patient group, many factors that could affect these parameters were considered, such as acute infections, systemic diseases (e.g., diabetes mellitus, hypertension, dyslipidemia), and medication use (e.g., anti-inflammatory agents, lipid-lowering drugs). Individuals meeting these criteria were excluded from the study.

Blood analyses were performed at the Biochemistry Department of Gülhane Training and Research Hospital. An automated hematology analyzer (Sysmex XN-1000, Sysmex Corporation, Kobe, Japan) was used for CBC testing. Red blood cells, white blood cells (WBC), neutrophils, monocytes, lymphocytes, and platelet (PLT) counts, as well as hemoglobin, mean platelet volume (MPV), platelet distribution width (PDW), red cell distribution width (RDW), and plateletcrit (PCT) values were obtained. Biochemical measurements, including glucose, creatinine, serum lipids [HDL, LDL, triglyceride (TG), and total cholesterol], were conducted using a biochemistry analyzer (Cobas e602, Roche Diagnostics GmbH, Mannheim, Germany). Subsequently, MLR, NLR, PLR, and MHR values were calculated. All CBC and biochemical measurements were collected from venous blood samples drawn after at least 8 hours of fasting. All procedures were performed after patients had been provided with detailed information and their written informed consent had been obtained.

Statistical Analysis

Statistical analyses were conducted using Jamovi software (v.1.6). Continuous variables are summarized as mean ± standard deviation, while categorical variables are presented as frequency (n) and percentage (%). The normality of the data distribution was assessed using the Shapiro-Wilk test. Based on the results of the normality test, comparisons of continuous variables (age, CBC, and biochemical parameters) between the two groups were conducted using the Student's t-test for normally distributed data or the Mann-Whitney U test for non-normally distributed data. Pearson's chi-square test was used to assess differences in the distribution of categorical variables between the groups. A p-value of <0.05 was considered statistically significant.

Due to the exploratory design of the study involving multiple comparisons, effect sizes (such as Cohen's d) and 95% confidence intervals were also provided to aid in interpreting the magnitude of the observed effects. Additionally, the adequacy of the sample size was assessed using G*Power software (version 3.1.9.7). A post-hoc power analysis was performed for an Independent samples t-test including 107 patients and 104 control subjects. Under the assumption of a conventional medium effect size (Cohen's d=0.5) and a Type I error rate (α) of 0.05, the analysis revealed that statistical power (1-β) was 95%. This high statistical power indicates that the sample size was sufficient to detect significant between-group differences, should such differences exist.

Results

The medical records of 134 patients diagnosed with pterygium were retrospectively reviewed. A total of 27 patients were excluded due to incomplete ophthalmological records (n=5), missing CBC and biochemistry results (n=7), systemic conditions such as diabetes, hypertension, or collagen vascular disease (n=7), use of topical cyclosporine for dry eye (n=5), or a diagnosis of pseudoexfoliation syndrome (n=3). Accordingly, the analysis incorporated data from 107 patients with pterygium and 104 healthy individuals as the control group.

The mean age of the patients with pterygium was 56.57±14.47 years, and that of healthy controls was 56.05±13.28 years (p=0.708). Demographic characteristics and CBC test results of the patients are shown in Table 1. No significant differences were found between the two groups in terms of age, sex, and MLR, NLR, PLR, and MHR values. However, hematocrit and WBC count were significantly higher among patients with pterygium (p=0.044 and 0.009, respectively). Biochemical analysis showed that total cholesterol and TG levels were significantly higher in patients with pterygium (p=0.004 and p=0.007, respectively). A detailed comparison of biochemical parameters is provided in Table 2.

Discussion

In this study assessing systemic inflammatory markers in patients with pterygium, the patient group had significantly higher levels of WBC, hematocrit, total cholesterol, and TG compared with controls. However, all other parameters were comparable between the groups.

UV radiation and environmental factors are recognized as significant contributors to the development of pterygium (2). UV exposure, in particular, has been shown to damage limbal stem cells, resulting in the activation of growth factors, angiogenesis, and fibroblast proliferation (3,4). Additionally, prolonged exposure to UV radiation has been linked to increased production of free radicals (5). Lipid peroxidation produces aldehydes, which are markedly elevated in pterygium specimens (19). Mitochondrial DNA is highly susceptible to oxidative damage due to limited repair mechanisms, making it a vulnerable target in ocular cells. Its instability contributes to mitochondrial dysfunction, cellular damage, and the development of age-related and chronic eye diseases. Increased mitochondrial reactive oxygen species (ROS) levels have been strongly associated with ophthalmological disorders affecting both the anterior and posterior segments (6). Pyroptosis—a form of programmed inflammatory cell death—is triggered by ROS via *NLRP3*/caspase-1 activation, thereby amplifying inflammation, fibrosis, and epithelial-mesenchymal transition in pterygial tissues (19).

Several studies have demonstrated that an imbalance between oxidative stress and antioxidant defenses, together with local inflammation, is a central factor in the development of pterygium (6,20). Patients with pterygium exhibit decreased antioxidant capacity, and UV radiation, a primary risk factor, has been demonstrated to induce oxidative DNA damage, leading to apoptosis and unregulated cell proliferation (19). It has also been

Table 1. Demographic characteristics and complete blood count data of patients with pterygium and control group

	Patients (n=107) Mean ± SD	Controls (n=104) Mean ± SD	95% CI of difference (Lower)	95% CI of difference (Upper)	p
Age (years)	56.57±14.47	56.05±13.28	-3.251	4.295	0.708
Sex, n (%) Female Male	 39 (36.4) 68 (63.6)	 32 (30.7) 72 (69.3)			0.467
Hemoglobin (g/dL)	14.07±1.77	13.72±1.63	-0.11933	0.80935	0.090
Hematocrit (%)	42.37±4.56	41.28±4.40	-0.12684	2.31099	**0.044***
MPV (fL)	10.14±0.90	10.31±1.07	-0.44661	0.09237	0.436
PDW (%)	11.75±2.00	11.65±1.90	-0.42350	0.63741	0.632
RDW (%)	13.49±1.73	13.60±1.53	-0.55210	0.33869	0.324
Plateletcrit (%)	0.24±0.06	0.24±0.05	-0.01759	0.01442	0.782
White blood cell (x10³/µL)	7.70±2.21	7.01±2.07	0.10255	1.26822	**0.009***
Neutrophil count (x10³/µL)	4.79±2.02	4.30±1.80	-0.03939	1.00525	0.050
Monocyte count (x10³/µL)	0.61±0.27	0.57±0.20	-0.02296	0.10719	0.272
Lymphocyte count (x10³/µL)	2.13±0.66	2.17±0.71	-0.23026	0.14577	0.916
Platelet count (x10³/µL)	240.03±54.37	235.14±61.20	-10.80860	20.59490	0.431
MLR	0.33±0.23	0.28±0.13	-0.00500	0.10004	0.190
NLR	2.52±1.66	2.12±1.07	0.02415	0.78636	0.108
PLR	124.71±53.59	117.79±44.88	-6.52206	20.35015	0.462
MHR	0.012±0.006	0.011±0.006	-0.00075	0.00280	0.134

*p<0.05
SD: Standard deviation, CI: Confidence interval, MPV: Mean platelet volume, PDW: Platelet distribution width, RDW: Red cell distribution width, MLR: Monocyte to lymphocyte ratio, NLR: Neutrophil to lymphocyte ratio, PLR: Platelet to lymphocyte ratio MHR: Monocyte to high-density ratio

Table 2. Biochemical data of patients with pterygium and control group

	Patients (n=107) Mean ± SD	Controls (n=104) Mean ± SD	95% CI of difference (Lower)	95% CI of difference (Upper)	p
Glucose (mg/dL)	114.39±47.50	87.53±9.10	17.49126	36.21687	0.528
Creatinine (mg/dL)	0.74±0.21	0.73±0.18	-0.04544	0.06475	0.889
Total cholesterol (mg/dL)	192.85±45.72	174.29±28.69	8.15722	28.94757	**0.004***
LDL (mg/dL)	116.21±38.70	94.87±26.81	12.27945	30.40046	0.463
HDL (mg/dL)	50.64±11.68	52.87±14.78	-5.84619	1.37657	0.549
Triglyceride (mg/dL)	144.41±94.40	111.3±55.77	11.98302	54.22402	**0.007***

*p<0.05
SD: Standard deviation, CI: Confidence interval, LDL: Low-density lipoprotein, HDL: High-density lipoprotein

shown that nitric oxide levels are elevated and that superoxide dismutase (SOD) and catalase levels are decreased in primary pterygium (8). Chronic UV exposure leads to depletion of enzymatic antioxidants (SOD, catalase, glutathione peroxidase) and increased oxidative stress in pterygial tissue. Although the cell may upregulate defense mechanisms (e.g., glutathione S-transferase, ALDH3A1), this compensation is often insufficient under sustained UV stress (19). ROS activate mitogen-activated protein kinase pathways including extracellular signal-regulated kinase, c-Jun N-terminal Kinase, and p38, which in turn induce expression of matrix metalloproteinase-1 (MMP-1) and pro-inflammatory cytokines IL6 and IL8. ROS and signaling pathways induce MMPs that degrade Bowman's layer, thereby facilitating fibrovascular tissue invasion onto the cornea. UV also activates the nuclear factor kappa B pathway in conjunctival and keratocyte cells, promoting transcription of genes related to inflammation, cell survival, and angiogenesis (e.g., TNFα, IL1, IL6, cyclooxygenase-2) (21).

Histopathological research has emphasized the important contribution of local inflammation to pterygium development (22). Exposure to UVB radiation elevates IL-6 and IL-8 levels in the epithelial layers of pterygium tissue (23). These pro-inflammatory cytokines contribute to pterygium development by sustaining local chronic inflammatory processes. Overall, this evidence strongly supports the contribution of local inflammation to the development of pterygium.

Research on systemic inflammation in pterygium remains limited. Various hematological parameters serve as indicators of systemic inflammatory status, and in this study, we assessed these markers using patients' peripheral blood. Ratios such as NLR, PLR, and MHR have been used to indicate inflammation in systemic disorders, including cardiovascular conditions (24). These markers have also been studied in eye disorders, including glaucoma, dry eye syndrome, age-related macular degeneration, pseudoexfoliation syndrome, and keratoconus (14-18, 25,26). A meta-analysis by Shirvani et al. (19) found that NLR values were notably elevated in individuals with pterygium compared with the control group. Gokmen and Gokmen (27) also observed elevated NLR in patients with pterygium and attributed this finding to chronic inflammation and neovascularization. However, Gokmen and Gokmen (27) found no significant changes in MPV, PCT, or PDW in these patients, and suggested that this observation can be explained by the predominance of the fibrous component and fibroblast activity over neovascularization process in pterygium pathology. Two studies from Türkiye evaluated NLR and PLR in individuals with pterygium and found that these values did not differ significantly from those in healthy controls (27-29). Our results align with these observations, as we found no significant differences in MPV, PLT, PCT, PDW, PLR, NLR, or MLR between the patient group and controls.

Heterogeneous findings have been reported for these inflammatory markers in patients with pterygium, particularly for NLR, which is frequently emphasized in the literature. These discrepancies may be related to variability in inclusion criteria; however, the exclusion criteria across studies were generally quite strict and similar, considering these laboratory parameters can be influenced by many conditions. In their meta-analysis, Shirvani et al. (19) noted that most of the included studies were from Türkiye and China, which they cited as a limitation. To determine whether variations in ethnicity or other demographic characteristics influence the results, it is essential to conduct comparative studies involving patient groups representing diverse ethnicities under standardized conditions. Additionally, the severity and size of pterygium may impact systemic inflammatory parameters. However, existing studies lack consistent classification, grading, or standardization of these factors. Moreover, methodological differences—such as variations in laboratory techniques and in the timing of blood sample collection—may contribute to the discrepancies observed in the literature.

Monocytes are key players in inflammation, with elevated counts observed in several inflammatory disorders. HDL cholesterol exerts antioxidant and anti-inflammatory effects; hence, MHR is commonly used to reflect inflammatory status in both systemic and ocular conditions. Belviranli et al. (30) observed that MHR levels did not differ notably between the pterygium cohort and the control group, whereas NLR was higher in the pterygium cohort, potentially reflecting systemic inflammation. Similarly, our study detected no significant difference in MHR between the groups. Kilic Toprak et al. (31) provided evidence of systemic oxidative stress in patients with pterygium. HDL participates in antioxidant and detoxification processes, whereas elevated TG levels may counteract these protective effects (31,32). Kilic and Guven (28) suggested that an imbalance between oxidative and antioxidative processes in patients with pterygium may be attributable to decreased HDL levels and elevated TG levels. In our study, TG levels were significantly higher in patients with pterygium, supporting this hypothesis. However, no significant between-group difference in HDL levels was observed. Moreover, findings from prior studies examining the association between pterygium and serum lipids have been inconsistent (33). For instance, the Singapore Malay Eye Study found a positive link between pterygium and serum total cholesterol, whereas a multiethnic Asian cohort showed no such association (34). Additionally, a cross-sectional investigation of Han and Manchu populations in Hebei, China (35) suggested HDL as a risk factor for pterygium in men, while a separate retrospective case-control study found no connection between HDL and pterygium (36). In another case-control study, LDL levels were notably elevated in individuals with advanced pterygium (36). Although the mechanisms linking low HDL cholesterol to pterygium formation have not been fully elucidated, it has been suggested that intracellular alterations in cholesterol homeostasis may be involved in pterygium formation (37,38). While the elevated TG and total cholesterol levels observed in our study lend support to this theory, additional research is needed to clarify whether these results stem from lifestyle factors (such as diet) or are directly linked to underlying biochemical mechanisms. Kilic and Guven (28) proposed that the observed reduction in HDL levels, accompanied by elevated TG levels, in individuals with pterygium may warrant further exploration of HDL's potential role as a novel antioxidant therapy. Interestingly, the same study found no notable differences in NLR, PLR, or MHR between the pterygium group and controls, consistent with our findings. RDW, which reflects variations in the size of red blood cells, serves as an indicator of inflammation and oxidative stress. Elevated RDW levels have been reported in various ocular diseases, including retinopathy and allergic conjunctivitis (39,40). Kurtul et al. (29) observed increased RDW values in patients with pterygium, although the precise mechanism linking RDW to pterygium remains unclear. They proposed that elevated expression of inflammatory cytokines in pterygium tissue may impair erythrocyte maturation, resulting in the release of immature erythrocytes into the circulation, thereby increasing erythrocyte size heterogeneity and RDW values. In contrast, our study did not find significant changes in RDW. As noted for other inflammatory parameters, factors such as ethnicity, demographic characteristics, and pterygium

size may influence RDW results. Achieving methodological standardization across studies is essential for generating more reliable and comparable results.

The study's retrospective nature and the exclusion of patients with incomplete medical records or laboratory data may introduce selection bias. Furthermore, primary and recurrent pterygium may exhibit distinct inflammatory profiles, which are not differentiated in the current analysis. Prospective studies incorporating detailed assessments of UV exposure duration, occupational risks, and dietary habits, which may affect systemic inflammatory status and oxidative balance, are necessary to better understand the fundamental biochemical pathways involved. Additionally, the evaluation of a broader panel of inflammatory and oxidative stress biomarkers, including proinflammatory cytokines (e.g., IL-6, TNF-α), would provide more comprehensive insight into the inflammatory process associated with pterygium. However, these biomarkers are not specific to pterygium and may be influenced by many inflammatory conditions. Therefore, it is important to consider that systemic markers may not directly indicate the presence of pterygium-related inflammation. A main statistical constraint of this research is the heightened possibility of committing a Type I error, since separate analyses were conducted on multiple biomarkers without applying corrections for multiple testing. While this approach increases the chance of spurious findings, it was considered appropriate given the exploratory and hypothesis-generating nature of this research. Consequently, our results should be interpreted as preliminary, requiring confirmation through future hypothesis-driven studies with adequate statistical power specifically designed to validate these specific associations.

Conclusion

The results of our study revealed that systemic inflammatory markers did not differ notably between individuals with pterygium and healthy subjects. Currently, there is no clear consensus regarding the correlation between systemic inflammatory markers and pterygium. These results suggest that systemic inflammation, unlike the local inflammatory response, might make a minor contribution to the mechanisms underlying pterygium. However, focusing on more sensitive and specific oxidative stress markers, such as nitric oxide, SOD, and catalase, which play roles in the oxidant-antioxidant balance, would help elucidate biochemical mechanisms. Additionally, validation of elevated TG levels as an indicator of systemic oxidative stress in a larger patient cohort could inform future research on antioxidant therapeutic strategies for the management of pterygium.

Ethics

Ethics Committee Approval: The study adhered to the ethical principles outlined in the Declaration of Helsinki, and ethics approval for our study was obtained from the ethics committee at the Gülhane Scientific Research Ethics Committee of the University of Health Sciences (approval no.: 2025-71, date: 11.02.2025).

Informed Consent: All patients provided written informed consent to participate in the study after receiving a detailed explanation of the study procedures.

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Footnotes

Author contributions

Surgical and Medical Practices: A.C.Y., Ö.A., Concept: A.C.Y., Ö.A., Design: A.C.Y., H.Y., Ö.A., Data Collection or Processing: A.C.Y., H.Y., B.A.Ç.İ., Analysis or Interpretation: A.C.Y., H.Y., B.A.Ç.İ., Literature Search: A.C.Y., B.A.Ç.İ., Writing: A.C.Y.

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Implementation of a predictive model to improve early detection of stroke in patients with comorbidities

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ABSTRACT

Aims: This study aims to develop and implement a predictive model to enhance the early detection of stroke in patients with comorbidities, thereby enabling clinicians to identify high-risk patients more quickly and effectively.

Methods: This study used a prospective cohort design involving 235 patients treated in the stroke care unit. Data were collected over six months through direct interviews, physical examinations, and laboratory analyses. Statistical analysis was conducted using multivariate logistic regression to identify the main predictive factors of stroke. The evaluation model was conducted using the area under the curve (AUC) to measure predictive accuracy.

Results: A total of 235 patients were included in the analysis, with a mean age of 56.4±12.7 years; 76.6% were male and 23.4% female. Significant predictive factors for stroke occurrence included diabetes mellitus, hypertension, rheumatoid arthritis, physical activity, family health history, random blood sugar levels, uric acid levels, and salt consumption ($p<0.05$). The developed model achieved an AUC of 98.7%, which—based on comparisons with established models such as the Framingham Stroke Risk Profile (AUC~0.78) and the QStroke algorithm (AUC~0.80)—demonstrates substantially higher discriminative ability in distinguishing between patients with and without stroke risk.

Conclusions: This predictive model has demonstrated a high capacity for detecting stroke risk in patients with comorbidities. The implementation of this model in clinical practice is expected to enhance the effectiveness of stroke screening and accelerate early intervention.

Introduction

Stroke remains one of the leading causes of death and disability worldwide, with patients who have comorbidities such as hypertension, diabetes mellitus, and heart disease facing significantly higher risk (1). In Indonesia, stroke prevalence has increased markedly, from 7 per 1,000 in 2018 to 10.9 per 1,000 in 2023—a 56% rise over five years—highlighting the urgent need for more effective prevention and early detection strategies (2-6). The increasing prevalence indicates that existing approaches are insufficient, particularly among high-risk patients with multiple comorbidities. Developing predictive models is therefore essential to strengthen early detection in this population (7,8).

Although advances in diagnostic tools exist, the timely identification of high-risk patients remains challenging. Most prior studies have examined individual risk factors in isolation, such as hypertension or diabetes, without adequately integrating multiple comorbidities and lifestyle factors into comprehensive models (9-11). As a result, existing tools often lack adaptability for diverse patient populations with concurrent conditions. This study addresses that gap by developing and implementing a predictive model that incorporates a broader range of clinical and lifestyle predictors. By combining multiple risk factors, the model is expected to improve early stroke detection and support more targeted, efficient decision-making in clinical practice (12-15).

The present study develops and implements such a model, aiming to integrate both clinical and lifestyle predictors to enhance stroke risk assessment in patients with comorbidities and support more targeted, efficient clinical decision-making.

Methods

Study design and participants

This study used a prospective cohort design. The research participants included stroke patients treated in three hospitals with specialized stroke care units. A total of 235 patients were included in this study, and they were observed for 6 months to collect data related to stroke risk factors and clinical outcomes. The sample size using G*Power version 3.1 calculation is shown in Figure 1. Patients who meet the criteria are designated as respondents. Inclusion criteria were patients who have been diagnosed with stroke (ischemic or hemorrhagic) based on clinical examination and imaging with computed tomography scan or magnetic resonance imaging, aged ≥18 years, patients with one or more comorbidities such as diabetes mellitus, hypertension, heart failure, atrial fibrillation, rheumatoid arthritis (RA), chronic kidney disease, or a history of heart attack, willing to participate in the study and sign a written consent form, and patients who can undergo observation for a full 6 months. Meanwhile, the exclusion criteria were patients with terminal conditions estimated to have a life expectancy of less than 6 months, patients with severe cognitive or mental disorders that prevent them from providing the necessary information or following the research protocol, patients who have undergone brain surgery less than 1 month before data collection, patients with active infectious diseases that affect laboratory results (e.g., severe sepsis), and patients who do not complete data during the observation period or withdraw from the study for personal or medical reasons.

Ethical consideration

This research has obtained written consent from the patients involved in the study. The research protocol complies with the ethical guidelines of the Helsinki Declaration of 1975, as revised in 2013. The research protocol was approved by the Health Research Ethics Committee of Universitas Muhammadiyah Gombong (approval no.: 003.6/II.3.AU/F/KEPK/I/2025, date: 07.01.2025). To ensure data confidentiality, all collected data were anonymized by removing personal identifiers and stored in password-protected electronic files accessible only to the principal investigators. Paper records, if any, were kept in locked cabinets. All data handling procedures complied with institutional and national guidelines for research involving human subjects.

Data collection

Data were collected through direct interviews, physical examinations, and laboratory data analysis. The sources of research data were as follows: interviews and questionnaires, medical data, and direct measurements. Direct interviews were used to collect demographic information (age, gender) as well as medical history, physical activity, stress levels, fruit and/or vegetable consumption, salt consumption levels, and parental medical history. Medical data were taken from patient medical records to obtain information on comorbid disease history, such as diabetes mellitus, hypertension, heart failure, atrial fibrillation, RA, chronic kidney disease, and heart attacks. Direct measurements were conducted to assess body mass index (BMI), random blood sugar levels, uric acid levels, and blood pressure. This data was collected periodically during the observation period to ensure the completeness and accuracy of the information. Not all stroke respondents followed the study protocol. Sample size calculation was performed using G*Power version 3.1, assuming a medium effect size [odds ratio (OR) =1.8], significance level $\alpha=0.05$, and desired power $(1-\beta)=0.95$, with an allocation ratio of 1:1. The minimum required sample size was estimated to be 207 participants, as shown in Figure 1. The final sample of 235 participants exceeded this requirement, thus providing sufficient power to detect clinically meaningful effects. There was an initial selection of 25 patients who did not meet the criteria. Additionally, 13 patients did not participate in the study and were observed for 6 months due to deteriorating conditions until they passed away, as shown in Figure 2. Of the 235 initially

included participants, 13 patients did not complete the six-month observation period due to deterioration or death. These patients had incomplete data and were therefore excluded from the final analysis using a complete case analysis approach. No data imputation or sensitivity analysis was performed, given the small proportion of missing cases and the focus on maintaining data accuracy.

Before the main research was conducted, validity and reliability tests were performed on the observation sheet used for data collection. This test is conducted on 30 respondents who have similar characteristics to the research sample but are not included in the main research population. The results of the validity test indicate that all items on the observation sheet have a correlation coefficient value of more than 0.3 ($p<0.05$); thus, it can be concluded that all items on the instrument are valid for the research. Meanwhile, the results of the reliability test show a Cronbach's alpha value of 0.85, which indicates that the instrument has high internal consistency and is suitable for use in data collection for the research.

Statistical Analysis

Data analysis is conducted using a quantitative approach with statistical software. The stages of analysis include descriptive analysis, bivariate analysis, multivariate analysis, and model validation. Bivariate tests were conducted to identify the relationship between each independent variable (risk factor) and the occurrence of recurrent stroke. The chi-square test was used to examine the relationship between two categorical variables, the occurrence of recurrent stroke (yes/no), and others, such as gender (male/female). Multivariate tests using logistic regression were conducted to identify the main predictors of recurrent stroke events by controlling for other variables. The model's predictive accuracy was measured using the area under the curve (AUC) on the receiver operating characteristic curve to measure the model's predictive accuracy. To assess the robustness of the model and mitigate the risk of overfitting, a 5-fold cross-validation approach was applied using the same dataset. The model was trained and tested across different subsets, and the mean AUC achieved across all folds was 96.3% (standard deviation ±1.8%), supporting the reliability of the model's predictive power. For the multivariate logistic regression, all variables with $p<0.25$ in the bivariate analysis were considered as candidate predictors. A backward stepwise elimination method was applied, and variables were sequentially removed based on likelihood ratio testing and significance level $p>0.05$. Additionally, multicollinearity was assessed using the variance inflation factor (VIF), and any variable with a VIF >5 was excluded. This ensured that only independent and statistically significant predictors were retained in the final model.

Before finalizing the logistic regression model, multicollinearity was assessed using the VIF. Variables with VIF >5 were excluded to ensure independent contributions of predictors. All variables retained in the final model showed acceptable VIF values (all <5), indicating no critical multicollinearity. For binary variables such as hypertension, diabetes mellitus, and others, we used a coding system of 1=presence and 0=absence. Regression coefficients and ORs were interpreted accordingly. Statistical test using SPSS version 27.

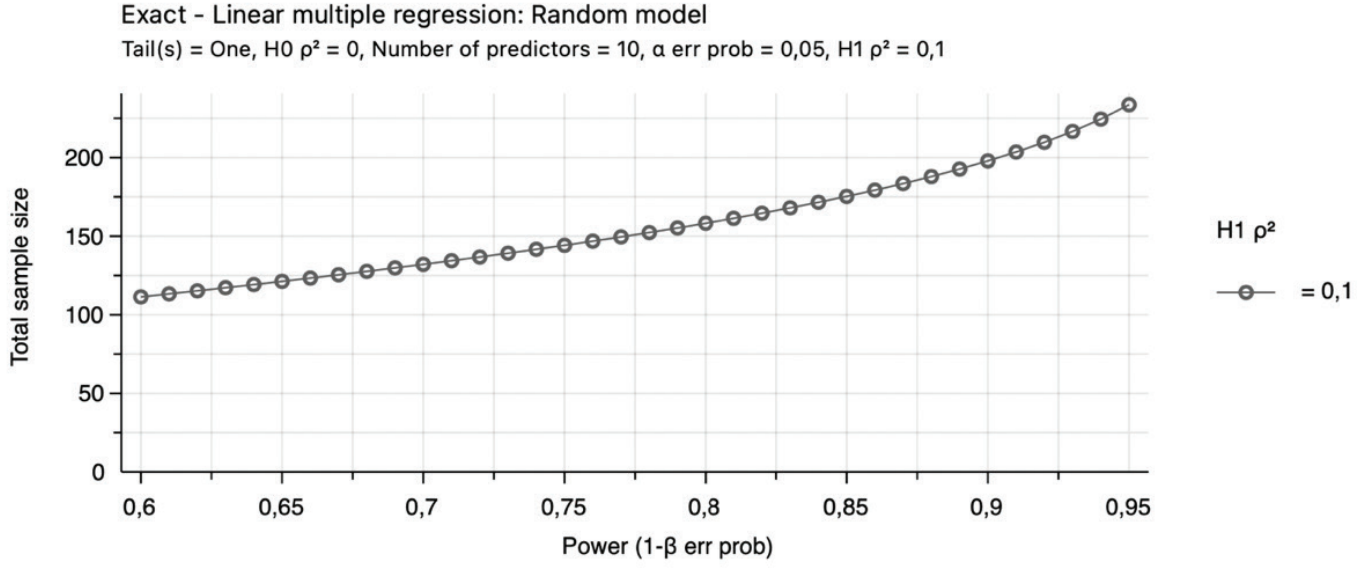

Figure 1. Power plot sample size using G*Power version 3.1

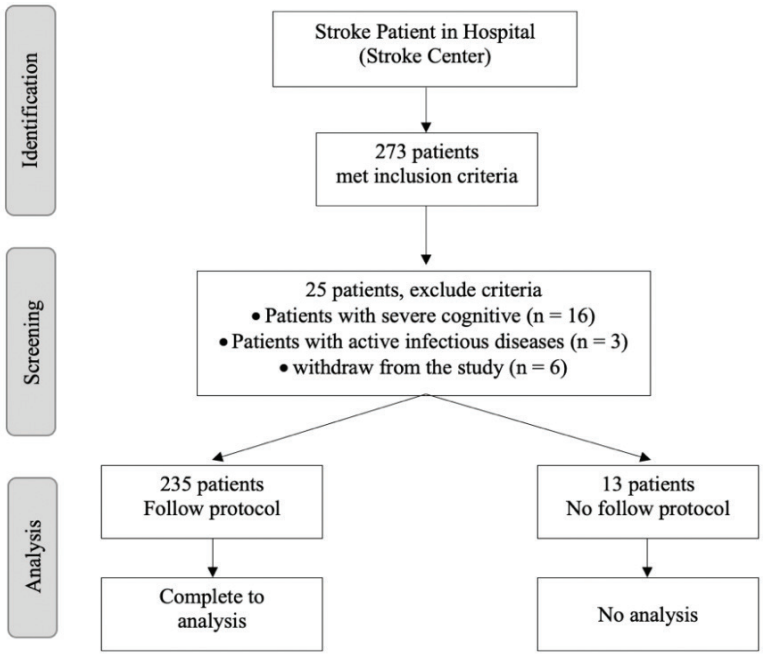

Figure 2. A flow diagram of study selection

Results

A total of 235 patients were included in the final analysis. The mean age was 56.4±12.7 years, with 76.6% of participants being male and 23.4% female. Most patients had at least one comorbidity, with diabetes mellitus (42.1%) and hypertension (58.3%) being the most prevalent. Additional baseline characteristics, including BMI, physical activity, stress level, family medical history, and laboratory findings, are summarized in Table 1. Following the baseline description, logistic regression analysis was performed to identify significant predictors of stroke occurrence. Table 2 shows that diabetes mellitus, hypertension, RA, physical activity, family health history, random blood sugar, uric acid levels, and salt consumption were retained as significant predictors ($p<0.05$). Next, a logistic regression analysis was conducted with a p-value criterion of >0.05, resulting in the variables of age, gender, previous health history such as diabetes mellitus, hypertension, heart failure, RA, BMI, physical activity, family health history, stress level, random blood sugar, uric acid level, and salt consumption. Logistic regression analysis (Table 2) identified diabetes mellitus, hypertension, RA, physical activity, family health history, random blood sugar, uric acid levels, and salt consumption as significant predictors of stroke incidence.

AUC 98.7% which indicates a very strong interpretation. However, this high AUC raised concerns about potential overfitting. To address this, internal validation using 5-fold cross-validation was conducted. The average AUC from cross-validation was 96.3% with a standard deviation of ±1.8%, indicating that while it is slightly lower than previous results, the model still demonstrates strong discriminative ability. This suggests that the model's performance is stable and not overly fitted to the training data.

The Hosmer and Lemeshow test indicates the model has a good fit or is suitable for the data, as shown in Figure 3. The predictive model demonstrated strong discriminative performance, showing high accuracy in distinguishing between patients with and without stroke risk. Internal validation confirmed model stability, and calibration analysis indicated a good fit to the observed data.

Discussion

This study identified eight key predictors of stroke: diabetes mellitus, hypertension, RA, low physical activity, family health history, elevated random blood sugar, high uric acid, and excessive salt intake. The predictive model incorporating these factors demonstrated excellent discriminative ability, with an AUC of 98.7% and stable performance on cross-validation (mean AUC 96.3%). These findings suggest that integrating multiple comorbidities and lifestyle variables can significantly improve early stroke risk detection compared to existing models. In our study population, diabetes mellitus and hypertension emerged as the strongest predictors, consistent with their established role in vascular pathology. RA also contributed significantly, reflecting the impact of systemic inflammation on cerebrovascular risk. Meanwhile, lifestyle-related factors such as physical activity and salt intake highlighted the importance of behavioral modification for prevention (14-16). Research also showed that although men are more likely to suffer from strokes, women

Table 1. Clinical and demographic characteristics of the study population

Variable	n (%)	Mean±SD	OR	p
Age (year)				
<40	112 (47.7)	2.42±0.86	3.61	**<0.001**
40-60	122 (51.9)			
>60	34 (14.4)			
Sex				
Male	180 (76.6)	1.23±0.42	2.56	**0.001**
Female	55 (23.4)			
Medical history				
Diabetes mellitus				
Yes	145 (61.7)	1.38±0.48	2.61	**0.014**
No	90 (38.3)			
Hypertension				
Yes	205 (87.2)	1.12±0.33	32.71	**0.000**
No	30 (12.8)			
Heart failure				
Yes	60 (25.5)	1.74±0.43	1.92	**0.040**
No	175 (74.5)			
Atrial fibrillation				
Yes	40 (17.0)	1.82±0.37	1.49	0.272
No	195 (83.0)			
Rheumatoid arthritis				
Yes	70 (29.8)	1.70±0.49	8.91	**0.028**
No	165 (70.2)			
Chronic kidney disease				
Yes	100 (42.6)	1.57±0.49	0.89	0.783
No	135 (57.4)			
Heart attack				
Yes	90 (38.3)	1.61±0.48	1.38	0.263
No	145 (61.7)			
Body mass index (kg/m²)				
Underweight (<18.5)	20 (8.5)	2.42±0.65	18.91	**<0.001**
Normal (18.5-24.9)	95 (40.4)			
Overweight (≥25)	120 (51.1)			
Physical activity (minutes/week)				
Active (exercise ≥150)	85 (36.2)	1.63±0.48	12.81	**<0.001**
Inactive (exercise <150)	150 (63.8)			
Stress level				
Low	50 (21.3)	2.06±0.69	10.89	**<0.001**
Medium	120 (51.1)			
High	65 (27.7)			
Family history of disease				
Yes (history of stroke/heart disease in parents)	155 (66.0)	1.34±0.47	13.91	**<0.001**
No	80 (34.0)			
Random blood sugar level (mg/dL)				
Normal (<140)	60 (25.5)	2.19±0.81	6.95	**<0.001**
Prediabetes (140-199)	70 (29.8)			
Diabetes (≥200)	105 (44.7)			

Table 1. Continued

Variable	n (%)	Mean±SD	OR	p
Uric Acid Levels (mg/dL)				
Normal	120 (51.1)	1.48±0.51	2.07	**0.009**
High	115 (48.9)			
Salt consumption level				
Normal (<5 grams/day)	70 (29.8)	1.71±0.45	22.43	**0.003**
High (≥5 grams/day)	165 (70.2)			

SD: Standard deviation, OR: Odds ratio

Table 2. Multivariate logistic regression analysis of stroke risk predictors

	B	S.E.	Wald	df	p	OR	95% CI	
							Min	Max
DM	-1.510	1.257	1.443	1	**0.025**	3.65	0.18	74.14
Hypertension	-5.055	1.215	17.322	1	**0.000**	0.21	0.01	0.69
RA	2.239	0.909	6.061	1	**0.014**	0.2.2	0.02	0.63
Heart attack	2.142	0.897	5.710	1	**0.017**	0.21	0.02	0.68
PA	1.775	0.800	4.924	1	**0.026**	5.88	1.23	28.29
FHD	4.205	0.930	20.467	1	**0.000**	0.12	0.01	0.92
Stress	8.074	2.510	10.344	1	**0.001**	32.08	3.41	43.91
BS	2.625	0.952	7.604	1	**0.006**	12.81	2.13	29.11
Constant	1.814	2.578	0.496	1	**0.001**	0.00		

Note: Coding for binary variables was 1=absence, 0=presence of condition. Interpretation of ORs is based on this coding direction.
Some odds ratios initially appeared inconsistent with their corresponding confidence intervals due to reporting errors. These have been corrected to reflect accurate relationships between the regression coefficients, OR values, and confidence intervals, ensuring coherence with standard logistic regression output.
DM: Diabetes mellitus, RA: Rheumatoid arthritis, PA: Physical activity, FHD: Family history disease, BS: Blood sugar, OR: Odds ratio, CI: Confidence interval, S.E.: Standard error, B: Regression coefficient, df: Degrees of freedom

have a higher risk of hemorrhagic strokes (17,18). Among these predictors, diabetes mellitus and hypertension were the most dominant, supporting previous evidence of their central role in vascular pathology. RA also emerged as an important risk factor, highlighting the contribution of systemic inflammation to stroke risk. Lifestyle-related variables such as low physical activity, salt intake, and high uric acid further emphasize the value of preventive strategies targeting modifiable behaviors (19,20).

High BMI has been associated with increased ischemic stroke risk and severity, though its impact may vary depending on comorbidities such as diabetes and hypertension. Low physical activity further amplifies stroke risk, highlighting the importance of lifestyle modification (21). Research shows that a lack of physical activity can increase the risk of hypertension, diabetes mellitus, and obesity, all of which contribute to the occurrence of strokes (22,23). Regular exercise can help control weight and blood pressure as well as improve overall heart health (24).

Psychological stress also plays a role in increasing the risk of stroke (25). Stress can cause an increase in blood pressure and trigger unhealthy behaviors such as poor eating habits and lack of physical activity. Research shows that individuals who experience high levels of stress tend to have higher cardiovascular risk factors (26,27). Stress was a significant predictor of stroke in this study, though the effect size appeared higher than previous reports, likely due to self-reported measurement and unmeasured confounders. Future research should use validated stress scales and account for mental health comorbidities to confirm this association. A positive family history of stroke or heart disease increases an individual's risk, as genetic predisposition to conditions like hypertension and diabetes contributes significantly to stroke susceptibility (28,29). High blood sugar levels, especially in individuals with diabetes mellitus, are strongly associated with an increased risk of stroke (30). Research shows that diabetic patients have a higher likelihood of experiencing a stroke compared to those who do not have diabetes. Uncontrolled random blood sugar can cause damage to blood vessels and increase the risk of atherosclerosis (31,32). Hyperuricemia has been linked to vascular inflammation and damage that elevate stroke risk, while excessive salt intake promotes hypertension; reducing dietary salt can therefore lower blood pressure and help prevent strokes (33,34).

Logistic regression identified diabetes mellitus, hypertension, RA, physical activity, family history, blood sugar, uric acid, and salt intake as significant stroke predictors. Among these, diabetes is a major risk factor, as elevated blood sugar damages vessels and accelerates atherosclerosis, increasing ischemic

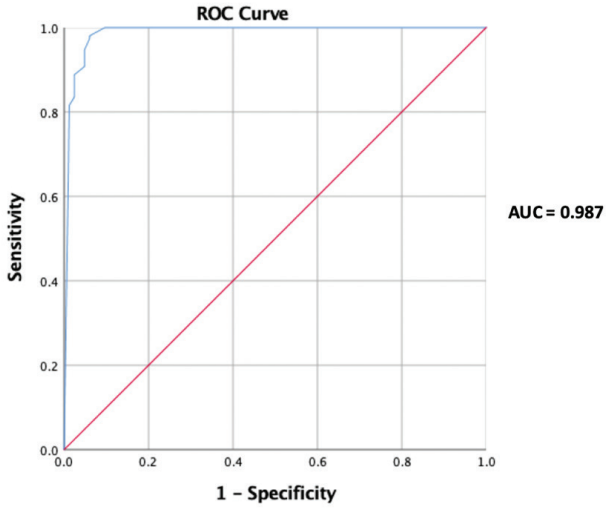

Figure 3. ROC curve
Area under the curve 98.7% this indicates a very strong interpretation. The Hosmer and Lemeshow test yielded a p-value of 0.493, indicating that the p-value >0.05 means the model has a good fit or is suitable for the data. A p-value greater than 0.05 indicates that there is no significant difference between the values predicted by the model and the observed values, which means the model has a good fit, as shown in Figure 3.
ROC: Receiver operating characteristic, AUC: Area under the curve

stroke risk (11,18). Hypertension is the most dominant risk factor for stroke. High blood pressure can cause damage to the brain's blood vessels and increase the likelihood of haemorrhagic and ischemic strokes. Research results show that a history of hypertension has an elevated OR in predicting the occurrence of stroke.

RA can increase the risk of stroke through prolonged systemic inflammation. This inflammation can affect cardiovascular health and increase the risk of blood clots, which can ultimately lead to a stroke (35,36). Low physical activity is directly related to an increased risk of stroke. Lack of physical activity can lead to obesity, hypertension, and diabetes, all of which are risk factors for stroke (37,38). Individuals with an active lifestyle have a lower risk of stroke, while a positive family history significantly increases susceptibility due to genetic and environmental influences on cardiovascular health (39). RA also emerged as a significant predictor of stroke. RA is a chronic autoimmune disease characterized by persistent systemic inflammation, which has been increasingly recognized as a risk factor for cardiovascular events, including stroke (36). High random blood sugar levels also contribute to the risk of stroke, especially in individuals with diabetes. Uncontrolled blood sugar can cause damage to blood vessels and increase the incidence of ischemic stroke (40). High uric acid levels contribute to inflammation and vascular damage, which increase stroke risk, while excessive salt intake raises blood pressure and worsens cardiovascular health, thus making both important modifiable risk factors (41,42).

This model achieved high accuracy with a sensitivity of 92.1% and specificity of 94.6%, surpassing many existing models. Its enhanced performance is likely due to the inclusion of diverse risk factors and the use of easily accessible clinical and behavioral variables, making it practical for populations with high comorbidity burdens.

This study has several limitations that should be considered when interpreting the findings. First, the research was conducted at a single-center hospital, which may limit the generalizability of the results to other populations or healthcare settings. Second, although the predictive model demonstrated a high AUC, we acknowledge the lack of external validation with an independent dataset. Internal validation using cross-validation was conducted, but further multi-center studies are needed to confirm model stability and reproducibility. Third, the study did not incorporate comprehensive socio-economic or dietary variables (e.g., income level, education, dietary habits beyond salt intake), which are known to influence stroke risk. Finally, some of the data, particularly regarding physical activity, stress, and medical history, were collected through self-reported questionnaires, which are subject to recall and reporting bias. Addressing these limitations in future studies will help strengthen and refine the predictive model.

Conclusion

This study identified eight key predictors of stroke—diabetes mellitus, hypertension, RA, low physical activity, family health history, elevated random blood sugar, high uric acid, and excessive salt intake—using a predictive model with strong discriminative ability (AUC 98.7%). The model offers potential to enhance early stroke detection in high-risk patients, but its single-center design and lack of external validation warrant caution. Future multi-center studies are recommended to confirm generalizability and strengthen their clinical applicability.

Ethics

Ethics Committee Approval: The research protocol was approved by the Komisi Etik Penelitian Kesehatan Health Research Ethics Committee (decision no.: 003.6/II.3.AU/F/KEPK/I/2025, date: 07.01.2025).

Informed Consent: This research has obtained written consent from the patients involved in the study.

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Footnotes

Authorship Contributions

Concept: P.A.W.S., B.W., E.E., E.S., Design: P.A.W.S., B.W., E.E., Data Collection or Processing: P.A.W.S., B.W., E.S., Analysis or Interpretation: P.A.W.S., E.E., Literature Search: P.A.W.S., B.W., E.E., E.S., Writing: P.A.W.S.

Conflict of Interest: The author declared no conflict of interest.

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Metaphors of diabetes nurse educators regarding "diabetes education": a qualitative study

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ABSTRACT

Aims: Nurses play a vital role in diabetes education, and their involvement has a positive impact on patient outcomes. To date, no research has specifically investigated the metaphors used by diabetes nurse educators in diabetes education. This study aimed to explore the perceptions of nurses who provide care for diabetic patients by analysing the metaphors they use to describe diabetes education.

Methods: A qualitative research design and purposive sampling were used. Data were collected using a data collection form developed by the researchers based on the literature, which included descriptive characteristics of diabetes nurse educators and their metaphorical expressions. The nurses' responses were analysed using content analysis.

Results: The study included 52 diabetes nurse educators. The mean age of nurse educators was 41.51±7.31 years, and the mean duration of working as diabetes nurse educators was 8.96±7.98 years. Analysis of their responses to the metaphorical expression identified 38 metaphors, which were grouped into four themes based on shared characteristics: a tool to empower the patient, an indispensable process, a thorny path that requires patience and effort, and a tool to touch the lives of others. These themes reflect both positive and negative perceptions of diabetes education.

Conclusions: Diabetes nurse educators were found to have both positive and negative perceptions of diabetes education. They described it as an indispensable tool – it strengthens patients, helps them navigate a new path in life, and enables effective disease management – and as a long, challenging, and labour-intensive process.

Introduction

Diabetes, which is increasingly prevalent worldwide and in Türkiye, is a significant public health issue associated with a risk of microvascular and macrovascular complications (1). Optimum glycaemic control and effective self-management are essential to prevent or delay these complications (2). For this reason, diabetes management includes medical nutrition therapy, physical activity, blood glucose monitoring, medication, and diabetes education (3). Evidence-based guidelines emphasise diabetes education as a core component of diabetes management, and the literature consistently highlights the active role nurses play in this process (4-6). Nurse-led education has been shown to positively influence hemoglobin A1c levels, blood pressure, body weight, and self-management behaviours

(2,7-9). In addition, structured and individualised education provided by primary care nurses enhances patients' knowledge, emotional regulation, and quality of life (9). However, while many studies focus on diabetes-related treatment adherence (10,11), self-management (12), and self-care (13), few studies have investigated nurses' perceptions of diabetes (14-17).

Metaphors are powerful cognitive and communicative tools that allow individuals to define an experience or concept by likening its characteristics to a familiar object, event, or phenomenon (18,19). Metaphors offer novel perspectives that foster a deeper understanding, serving as valuable rhetorical tools not only for communicating a phenomenon but also for analysing and comprehending it (20,21). Additionally, metaphors can shed light on broader cultural frameworks and on how we perceive the world (22). In the context of nursing, metaphors are powerful teaching and learning resources that facilitate the understanding of nursing experiences and help establish creative connections between existing conceptual frameworks and new knowledge (23). They help reveal the perceptions of society or of members of the profession (23). Understanding nurse educators' metaphorical perceptions is essential because their conceptualisations can influence their teaching approaches, their communication with patients, and the motivational climate they create in educational settings (24,25). Negative metaphors may hinder the educational process, whereas positive metaphors can empower both educators and patients (26). By analysing these metaphors, it becomes possible to identify underlying beliefs, replace limiting perceptions with more constructive ones, and guide the development of more engaging curricula (24).

A review of metaphor studies showed that researchers have examined nurses' experiences regarding the nursing profession, provision of care, COVID-19, professional communication, and clinical practice (24,27-31). However, no studies have examined how nurses perceive diabetes education through metaphors. In studies conducted among patients, Ardahan et al. (32) reported that diabetes was described using negative, threatening metaphors (e.g., cancer, virus, burnt house, cigarette, dangerous path, broken machine) and more manageable metaphors (e.g., flower, watch, diet). Tok Özen et al. (26) found that individuals with diabetes often described their disease using negative metaphors such as "darkness," "prison," "microbe," "captivity," and, less frequently, using positive metaphors such as "friend," "traffic sign," and "driving a car." However, these patient-centered studies do not reveal how nurse educators perceive and define the process. The present study aimed to explore the perceptions of nurses caring for patients with diabetes by analysing the metaphors they use to describe diabetes education. Gaining a deeper understanding of nurses' beliefs can enrich teaching strategies and strengthen both nurse-led education and patients' self-management.

Methods

Study design and participants

This study employed a qualitative research design. A qualitative research approach is effective for investigating complex phenomena and uncovering participants' underlying perspectives (33). Metaphor analysis is a technique based on the phenomenological research method within qualitative research. Metaphor analysis serves as a qualitative technique that facilitates the comprehension of abstract and complex ideas by comparing them with more familiar concepts (34). Consistent with these explanations, this study utilised the metaphor analysis technique within a phenomenological framework to explore how diabetes nurse educators' metaphors reflect their perspectives and help make sense of the complex nature of diabetes education.

Participants were selected through purposive sampling, targeting individuals who could offer rich, relevant, and diverse insights related to the research question (35). The inclusion criteria were: being a diabetes nurse educator, providing diabetes education, and agreeing to participate in the study. Exclusion criteria were the following: (1) not currently working as a diabetes nurse educator; and (2) providing incomplete or meaningless answers on the data collection form.

In qualitative studies, saturation is the commonly recommended criterion for determining when a sufficient sample size has been reached. Data collection was terminated once saturation was reached (36,37). Therefore, we intentionally included a larger sample of diabetes nurse educators to enrich the diversity of metaphors and achieve conceptual saturation. Thus, we expanded our sample size until conceptual saturation was achieved, a standard consistent with qualitative research. Initially, a total of 55 nurses were recruited. Since three participants provided incomplete or meaningless responses to the open-ended metaphor prompt, their data were excluded from the final analysis to ensure data integrity. The study included 52 participants.

The research was approved by the Çankırı Karatekin University Ethics Committee (decision no.: 26, date: 28.06.2022). Participants were informed about the study at the beginning of the online survey and provided their consent electronically. The research was conducted in accordance with the Helsinki Declaration. To ensure confidentiality and anonymity, the letter "N" was used to represent nurses, along with Arabic numerals indicating their sequence.

Data collection form

Researchers developed a two-part form based on existing literature (19,20,28-30,38). The first part included questions about the descriptive characteristics of diabetes nurse educators. The second part featured an open-ended metaphor prompt:

"Diabetes education is like ..., because ..." Participants were also free to provide more than one metaphor if they wished.

Data collection

The data were collected through a web-based data collection form between July 2022 and March 2023. The Informed consent statement on the first page of the online survey explained the study's purpose and participants' rights. Nurse educators were informed that their data would remain confidential, and that all information obtained would be analysed anonymously and used solely for scientific purposes. Participants were contacted via social media and WhatsApp groups that diabetes nurse educators actively use. An online link directing them to the data collection form was shared with the nurses. Voluntary participants individually completed the first part of the data collection form, which included questions about the descriptive characteristics of the diabetes nurse educators. Afterwards, participants completed the second section of the form, which included an open-ended metaphor prompt: "Diabetes education is like …, because ..." The "like" section determined how nurse educators perceived diabetes education, while the "because" section revealed the reasoning behind it. They were asked to write their metaphorical expressions and explanations directly in response to the open-ended prompt. Participants were also free to generate more than one metaphor and to repeat the given sentence structure "Diabetes education is like …, because …" if they wished.

Data analysis

Data analysis was conducted using IBM SPSS Statistics for Windows, Version 21.0 (IBM Corp., Armonk, NY: USA). Descriptive statistics were presented as counts, percentages, means, and standard deviations. The responses to the open-ended metaphor question were analysed through content analysis in three steps. First, the diabetes nurse educators' responses were repeatedly reviewed to identify metaphors and indicators such as repetition, elaboration, relatedness, contrast, and emotion. All metaphors were then listed, and participants who did not produce any were excluded from the study. In the second step, a general metaphor analysis was conducted. The meanings of selected metaphors were examined in isolation from their sentence contexts, focusing on comparisons, associations, dimensions, categories, concepts, and idioms. Distinct categories were then developed manually based on the compiled list and the group classifications. In the third step, a text-immanent metaphor analysis was conducted by revisiting the original sentences to examine each metaphor in context. The final grouping was determined based on participants' explanations beginning with "because …" (39).

The study was conducted in accordance with the principles of credibility, dependability, confirmability, and transferability. To ensure participant diversity, purposive sampling was employed. The data collection procedures were described in detail, and a specific routine was followed. The stages of data analysis were explained step by step, and the researchers had prolonged engagement with the data, reading and rereading it multiple times. The analysis included direct quotations, and the researchers reviewed the categories several times (27). In this study, 38 metaphors were categorised into four themes based on their shared characteristics. Sample expressions representing the general views of the nurse educators were selected and presented to provide deeper insights.

Results

Socio-demographic characteristics

As shown in Table 1, the mean age of the nurse educators was 41.51±7.31 years. All participants were female, with 71.2% being married, 67.3% having children, and 42.3% reporting a chronic disease. The average duration of professional experience among the nurse educators was 19.34±8.35 years, while their expertise as diabetes nurse educators averaged 8.96±7.98 years.

An analysis of the metaphors provided about diabetes education revealed four main themes. These themes are: a tool to empower the patient, an indispensable process, a thorny path requiring patience and effort, and a tool to touch other lives (Table 2).

Theme 1: A tool to empower the patient

When the metaphors used by nurse educators were examined in the research, the first identified theme was "diabetes education as a tool to empower the patient." Within

Table 1. The descriptive characteristics of nurses (n=52)

Characteristics	Value
Age (years), mean ± SD	41.51±7.31
Working time in the profession (years)	19.34±8.35
Working time as a diabetes nurse educator (years)	8.96±7.98
Marital status, n (%)	
Married	37 (71.2)
Single	15 (28.8)
Having children, n (%)	
Yes	35 (67.3)
No	17 (32.7)
Number of children*, n (%)	
One	16 (45.7)
Two	16 (45.7)
Three	3 (8.6)
Having chronic disease, n (%)	
Yes	22 (42.3)
No	30 (57.7)

*Calculated for nurses with children (n=35)
SD: Standard deviation

this theme, nurse educators used eight different metaphors. Two subthemes emerged: "managing the disease" and "drawing a new path in life." The metaphors within this theme commonly emphasised that diabetes education helps patients understand that they can manage their disease, reminding them that they are not alone and that they can chart a new path in their lives. Overall, the metaphors found in this theme reflected positive perceptions of diabetes education.

The first subtheme identified in the study is "managing the disease." Within this subtheme, nurse educators employed metaphors such as "teaching how to fish," "key," "compass," and "rain in the desert" to describe diabetes education.

- *"Diabetes education is analogous to teaching individuals how to fish. It eliminates dependency and empowers individuals to sustain themselves throughout their lives."* (N 29)
- *"Diabetes education shifts patients from the passenger seat to the driver's seat. It teaches patients how to manage and take control of their disease."* (N 33)
- *"Diabetes education serves as a guide for individuals with diabetes. Without education, patients feel lost and struggle to find a healthy lifestyle."* (N 46)

"Diabetes education is analogous to rain in a desert. It provides clarity and relief to newly diagnosed patients or those facing treatment changes, helping them understand that they are not alone and can navigate a new path." (N 38)

Table 2. Metaphors generated by nurse educators regarding diabetes education

Core themes	Subthemes	n	%	Metaphor
A tool to empower the patient	Drawing a new path in life	10	13.0	• A rising sun/light (n=5) • A new path (n=3) • Opportunity for self-expression (n=1) • A port in a storm (n=1)
	Managing the disease	6	7.8	• Teaching how to fish (n=2) • Key (n=2) • Compass (n=1) • Rain in the desert (n=1)
An indispensable process		15	19.5	• Necessity (n=9) • Honeycomb (n=1) • Foundation of a building (n=1) • Traffic rules (n=1) • Four-legged table (n=1) • Seat belt (n=1) • Life partner (n=1)
A thorny path that requires patience and effort	Process and labor	24	31.2	• Growing flowers (n=8) • School (n=7) • Time-consuming (n=5) • Bringing up a child (n=4)
	Difficulty and challenge	8	10.4	• Flog a dead horse (n=2) • A difficult path (n=1) • Tunnel of horror (n=1) • Funeral home (n=1) • House arrest for a relative (1) • Sometimes battle of nerves (n=1) • Removing watermelon seeds (n=1)
	Complexity and depth	6	7.8	• Endless sea (n=2) • The tip of the iceberg (n=1) • Puzzle (n=1) • A dark road (n=1) • Ocean (n=1)
	Value and potential	3	3.9	• Diamond (n=1) • Internet connection (n=1) • Boomerang (n=1)
A tool to touch other lives		5	6.5	• Achieving satisfaction in the profession (n=2) • Holding on to life (n=1) • Discovering the unseen (n=1) • Achieving a new turning point in life (n=1)

n= It indicates the number of nurses who provided the metaphor.

The second subtheme, "drawing a new path in life," uses metaphors such as a new path, a rising sun or light, an opportunity for self-expression, and a port in a storm.

- *"Diabetes education enhances patients' understanding by clarifying specific details."* (N 41)
- *"Diabetes education serves as a source of illumination and empowerment for patients with diabetes. They can learn comprehensive information about managing the disease from that source."* (N 3)
- *"Diabetes education provides a setting in which the patient can express himself/herself and serves as a port in a storm. This is because he/she can tell the nurse about his/her problems."* (N 3)

Theme 2: An indispensable process

When examining the metaphors used by nurse educators, the next theme identified was "diabetes education as an indispensable process." The central idea conveyed by the metaphors in this theme is that diabetes education is essential and non-negotiable in patients' lives. Nurse educators emphasised that without a solid educational foundation, effective disease management would not be possible. Overall, the metaphors within this theme emphasized positive views.

The most frequently used metaphor within this theme was "necessity." Examples of nurse educators' expressions highlighting this metaphor include;

- *"Diabetes education, like air, water, or oxygen, is essential—life cannot continue without it."* (N 19)
- *"Just as a bee cannot live on flowers without a honeycomb, the disease cannot be managed without education."* (N 26)
- *"It is the cornerstone of diabetes treatment."* (N 52)
- *"A person should know everything they should and should not do."* (N 35)

Theme 3: A thorny path that requires patience and effort

When the metaphors created by the nurse educators were examined as part of the research, another significant theme emerged: "diabetes education as a thorny path that requires patience and effort." Within this theme, nurse educators described education as a challenging process that demands persistence, proceeds in stages, and requires substantial time and dedication. The metaphors within this theme conveyed both positive and negative perceptions of the challenges of education.

Within this theme, four subthemes were identified: "process and labor," "difficulty and challenge," "complexity and depth," and "value and potential." Among these, the "process and labor" subtheme stood out as particularly important. The metaphors most frequently used in this subtheme were "growing flowers," "school," "bringing up a child," and "time-consuming." These metaphors share a common thread; they emphasise the patience and effort required in the educational process.

- *"It is like a child; it requires endless responsibility."* (N 17)
- *"It is like caring for flowers; it requires constant attention and follow-up. Education should be conveyed patiently, according to the needs of the patient."* (N 42)
- *"It is like time: when used correctly, it changes lives; when wasted, it is nothing."* (N 1)
- *"It is like school; there is always something to learn."* (N 24)

Another subtheme identified in the study is "difficulty and challenge." This subtheme captures the challenges and hardships experienced by both patients and nurses in the education and monitoring process. The metaphors in this subtheme, such as "flog a dead horse" and "funeral home," highlight the emotional and practical difficulties involved.

The common thread in these metaphors is the acknowledgement that this process can be highly demanding and, at times, discouraging. Examples of nurse educators' expressions reflecting this subtheme include;

- *"Sometimes it is like flogging a dead horse, because no matter how much education you give, the patient still does what he/she knows."* (N 49)
- *"It is like writing on water because what is important is not what you say, but how well the other person understands you."* (N 16)
- *"Sometimes it resembles a funeral home because it is characterized by rebellion, denial, and non-acceptance. Patients often have questions such as, 'Why did this happen to me?'"* (N 11)
- *"At times, the patient experiences a tunnel of horror, appearing fearful and asking, 'How will I do this?' How many rules must I follow? Every subject is perceived by them as a tunnel of horror."* (N 11)

Another subtheme identified in the study is "complexity and depth." This subtheme highlights the intricate nature of diabetes and its management, emphasising the need to integrate various aspects of the disease into the educational process. Metaphors such as "endless sea," "the tip of the iceberg," and "puzzle" were frequently used to describe this complexity.

- *"It is like an endless sea because the explanations and topics never end."* (N 32)
- *"It is like an endless sea because there is no limit to knowledge."* (N 47)

Another notable subtheme is "value and potential." This subtheme highlights the importance of achieving valuable results through persistent effort, maintaining continuity and connection, and recognizing that the outcomes of actions often come full circle. Metaphors such as "diamond," "internet connection," and "boomerang" were used to illustrate these ideas.

- *"It is like a diamond because it is valuable; this stone emerges through effort. We know that there is no cure for the disease without effort."* (N 28)

- *"It is like an internet connection: when the patient–education connection is broken, education must start from scratch." "It is necessary to ensure continuity of the patients' education."* (N 13)
- *"It is like a boomerang because the patient comes back to you again and again."* (N 20)

Theme 4: A tool to touch other lives

Another theme identified in the study was "diabetes education as a tool to touch other lives." Within this theme, nurses emphasised that education helps patients navigate their ups and downs and uncover deeper issues beyond what patients openly share, and that it enables nurses to find fulfillment in their professional roles. The metaphors under this theme reflected positive perceptions.

The most frequently mentioned metaphor within this theme was "achieving satisfaction in the profession," reflecting how diabetes education allows nurses to make meaningful connections with their patients. Examples of nurse educators' expressions include:

- *"It provides professional satisfaction because it allows one to touch people's lives and to transfer information. The feedback I receive from patients makes me very happy."* (N 32)
- *"It provides support in life because sometimes you get stuck on the road and you need someone to help you get back on your feet."* (N 50)
- *"It is like discovering the unseen because in addition to what the patient tells you, you also need to reach the essence by asking questions."* (N 50)
- *"Diabetes education represents a turning point in life because the patient must recreate their entire life to accommodate this disease."* (N 10)

Discussion

This study found that diabetes nurse educators view patient education as a tool to empower patients and create new opportunities, believing that this can enhance disease management. Metaphors such as "teaching to fish," "key," and "compass" reflected positive perceptions, emphasising self-management, independence, and guidance. Similarly, previous studies have demonstrated that diabetes education motivates and empowers patients, leading to improved self-care behaviours and overall well-being (15,40-43). At the same time, it helps reduce complications and healthcare utilisation (44). However, in this study, alongside expressing positive views, some nurse educators described negative views using metaphors such as "funeral home," "tunnel of fear," or even "house arrest for a relative." These metaphors reflected frustration, emotional strain, and a sense of restriction. These findings highlight the critical role of diabetes education in empowering patients to manage their condition more effectively, to reduce diabetes-related complications, and to adopt healthy lifestyles.

In the sub-theme of charting a new path in life, nurse educators often liken diabetes education to the "sun," symbolising its role in illuminating knowledge and empowering patients for effective self-management. Just as the sun is an essential source of energy for sustaining life, diabetes education is viewed as indispensable for developing patients' self-management abilities and improving their quality of life. Moreover, the use of this metaphor by nurse educators is meaningful in emphasising that education is a continuous, dynamic, and lifelong process. Similarly, Ardahan et al. (32) emphasised the metaphors of guidance and wayfinding, which are consistent with this study. In the sub-theme of disease management, the metaphor of "teaching how to fish" reflects that patient education goes beyond merely providing information. It develops self-management skills, represents the shift from dependency to independence, and embodies the concept of empowerment. Additionally, the metaphor of the "key" symbolises access to knowledge and tools needed to control and manage the disease. It conveys the idea of facilitating treatment and self-care processes by providing essential skills and information. Together, these metaphors emphasise that diabetes education should go beyond information-sharing to build patients' self-management abilities.

National and international guidelines support our study findings, emphasising diabetes education as a core element of treatment (3-6). O'Brien et al. (15) examined diabetes nurse educators' experiences of diabetes self-management, identifying knowledge as a key factor in effective self-management. Similarly, Ndjaboue et al. (44) found that patients consider learning about the disease essential. In this study, diabetes nurse educators consistently described patient education as an indispensable part of disease management, frequently using the metaphor of "necessity" to underline its fundamental role. In addition, the "four-legged table" metaphor emphasises that effective diabetes management requires balance and stability. In contrast, the metaphor of a "life partner" reflects the lifelong nature of diabetes education. When evaluated together, the metaphors highlight the core messages that diabetes education is mandatory, foundational, protective, vital, and that it requires ongoing commitment.

In this study, nurse educators acknowledged that diabetes education, while essential, is also a laborious, time-consuming, and demanding process. Similarly, patients have expressed comparable perspectives. Consistent with Ndjaboue et al. (44), patients often view managing diabetes as a challenging task requiring ongoing effort and support. Individuals with diabetes face various challenges, including treatments required to control blood glucose levels and self-management practices

to prevent complications (45). Gardsten et al. (45) highlighted that patients recently diagnosed with diabetes often struggle most with accepting the diagnosis and finding motivation to adopt lifestyle changes. In contrast, more experienced patients emphasise difficulties related to complications and medication management. These findings underscore the multidimensional nature of diabetes education, which must address a wide range of challenges across different stages of the disease. Nurse educators frequently used metaphors such as "growing a flower," "a school," and "bringing up a child" to describe the ongoing, patient, and nurturing nature of the educational process. These metaphors highlight both the long-term commitment required and the potential for positive growth and meaningful outcomes. Despite these positive perspectives, negative metaphors such as "funeral home" and "tunnel of horror" reflect the emotional toll and sense of hopelessness that may arise during this journey. In contrast, positive metaphors such as "diamond" and "boomerang" underscore that persistence, effort, and support can eventually lead to success and transformation. Altogether, these metaphors reflect the challenging yet promising nature of diabetes education. These findings are also consistent with those reported by Tok Özen et al. (26), in which patients described diabetes using restrictive and coercive metaphors. However, unlike in patient-centered studies, our participants also highlighted positive, empowering metaphors such as "compass" or "diamond," reflecting the dual perspective of educators who both witness challenges and aim to inspire hope.

This study emphasises that nurse-led diabetes education has a meaningful impact on patients' lives by helping them cope with their condition, manage it more effectively, and improve their overall well-being. At the same time, it contributes to nurse educators' professional satisfaction, confidence, and self-esteem. Supporting studies indicate that completing diabetes education programs enhances patients' motivation and that educator support is important in navigating the challenges of the disease (45,46). For example, Findlay-White et al. (16) found that nurses involved in empowerment-based education reported greater confidence, role satisfaction, and self-esteem. These metaphors illustrate the richness and multidimensional nature of diabetes education, reflecting nurses' personal experiences. The metaphors suggest that diabetes education is not merely the transfer of information but also a complex process that requires empathy, patience, continuity, and professional expertise. Ultimately, it offers mutual benefits. While patients gain self-management skills and an improved quality of life, nurses experience professional satisfaction, increased self-esteem, and enhanced role confidence. However, these findings should be considered in light of Türkiye's cultural and contextual factors, and caution is warranted when comparing them to different healthcare settings.

This study has some strengths and limitations. One of the main strengths of this study is its focus on a relatively neglected topic: how diabetes nurse educators perceive diabetes education through metaphors. A qualitative research design with purposive sampling provided rich insights into nurse educators' views of their roles, and a relatively large, diverse group of participants strengthened the credibility of the findings. However, some limitations should be noted. Although the data were collected online and nurse educators from different parts of Türkiye were able to participate, the sample may not fully represent the diversity of healthcare and educational settings. Participation may have been more feasible for nurses with better access to technology and the internet, higher digital literacy, or stronger professional networks, which could have limited the diversity of perspectives captured. Furthermore, as the data were obtained through self-reported written responses, the results reflect participants' subjective perceptions rather than directly observed practices. As with most qualitative studies, the findings are not intended to be generalised, but to provide a deeper understanding and generate new insights for future research.

Conclusion

The research revealed that nurse educators' perceptions of diabetes education were diverse, ranging from positive to negative. Nurse educators described diabetes education as both a powerful tool empowering patients to take control of their lives, manage their disease, and view it as indispensable, and a process that is long, challenging, and labor-intensive.

Understanding nurse educators' experiences and perceptions is key to the development and improvement of diabetes education programs. Future research should explore the challenges educators face and the support systems needed to address them. This can help reduce nurses' workload and enhance the benefits of patient education.

Ethics

Ethics Committee Approval: The research was approved by Çankırı Karatekin University Ethics Committee (decision no.: 26, date: 28.06.2022).

Informed Consent: Informed consent was obtained from all participants before the study.

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Footnotes

Authorship Contributions

Concept: F.İ.Ç., D.A., A.D., Design: F.İ.Ç., D.A., A.D., Data Collection or Processing: F.İ.Ç., D.A., A.D., E.Ü., Analysis or Interpretation: F.İ.Ç., D.A., A.D., E.Ü., Literature Search: F.İ.Ç., D.A., A.D., E.Ü., Writing: F.İ.Ç., D.A., A.D., E.Ü.

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Social jetlag increases energy intake independent of ultra-processed food consumption in young adults

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Keywords: Diet, energy intake, social jetlag, ultra-processed foods

ABSTRACT

Aims: The aim of this study was to investigate the relationship between social jetlag (SJL), ultra-processed food (UPF) consumption, and total energy intake in young adults.

Methods: This cross-sectional study included 648 healthy individuals aged 18-30 years. SJL was assessed using the Munich Chronotype Questionnaire and categorized into three groups: <1 hour, 1-2 hours, and >2 hours. Dietary intake was evaluated using a 24-hour dietary recall. UPF consumption was determined using a NOVA-based food frequency questionnaire. Multiple linear regression analyses were performed to evaluate the associations, adjusting for age, sex, body mass index, physical activity, smoking status, and total energy intake.

Results: Total energy intake was significantly higher in the SJL ≥2 hours group (1698.7±34.8 kcal/day) compared to the SJL <1 hour (1474.3±44.1 kcal/day) and the 1≤ SJL <2 hours (1582.3±33.9 kcal/day) groups ($p<0.001$). Participants with SJL ≥2 hours had significantly higher macronutrient intake, including fat, saturated fat, carbohydrate, and protein, compared with those with SJL <1 hour ($p<0.05$). No significant association was found between SJL duration and UPF consumption when modeled as a continuous variable (B=-0.0024; 95%, CI:-0.0124 to 0.0076; $p=0.636$). Age was inversely associated with UPF consumption (B=-0.0097; 95%, CI:-0.0154 to -0.0040; $p=0.001$), indicating lower UPF intake with increasing age. No other variables were significantly associated with UPF consumption ($p>0.05$).

Conclusions: SJL is associated with increased energy and macronutrient intake in young adults, independent of UPF consumption.

Introduction

Social jetlag (SJL), defined as the discrepancy between an individual's biological and social clocks, arises from differences in sleep timing between workdays and free days (1). This misalignment is prevalent in modern society, particularly among young adults; approximately 50% experience at least two hours of SJL and 70% report a misalignment of at least one hour (1,2). SJL has been linked to various adverse health outcomes, including obesity, depression, diabetes, and cardiovascular disease, suggesting its potential role in metabolic dysfunction (3-5). In addition to these metabolic and physiological risks, SJL has been associated with psychosocial consequences, including increased stress, impaired academic performance, reduced subjective well-being, and poor mental health outcomes, particularly in young populations (4,6). While the mechanisms underlying these associations remain an area of ongoing

investigation, recent studies suggest that one such mechanism may involve dietary behaviors. Individuals experiencing greater SJL have been observed to consume more ultra processed food (UPF) and sugar-sweetened beverages and to have lower intakes of nutrient-dense foods such as fruits, vegetables, whole grains, and legumes (6-9). These dietary patterns are of particular concern given their well-established links to obesity, insulin resistance, and other metabolic disorders (3). However, evidence on this topic remains limited, with some studies failing to establish a consistent association between SJL and dietary intake (10-12). Given that SJL is influenced by cultural, occupational, and societal structures, its prevalence and impact may differ across regions. In Türkiye, a limited number of studies have addressed the relationship between SJL and dietary habits in young adults, suggesting similar patterns to those observed in Western societies (13). However, comparisons across different socio-cultural contexts highlight the need for region-specific evidence, as variations in lifestyle, work schedules, and social norms may influence the expression and consequences of SJL (14-16). Given their accessibility, palatability, and tendency to be consumed during irregular or late-night eating episodes, UPFs may serve both as a consequence of and as a contributor to the irregular dietary patterns associated with circadian misalignment. These characteristics make UPFs particularly relevant in the context of SJL. Moreover, UPFs are consistently associated with poor dietary quality and increased metabolic risk. Despite these potential links, the relationship between SJL and UPF intake remains unclear, with mixed findings reported in different populations (10,17,18). Therefore, this study aims to examine the relationship among SJL, UPF consumption, and total energy intake in young adults.

Methods

Study design, participants and ethics

This cross-sectional study included healthy adults aged 18-30 years living in Ankara. Based on prior studies (13,17), eligible participants were those who were within the specified age range, had no chronic disease or psychological disorders, were not using regular medications or dietary supplements, were not pregnant or breastfeeding, and were not students of the department of nutrition and dietetics. Individuals who did not meet these criteria were excluded.

The sample size was determined using statistical power analysis. The analysis was conducted with a Type I error (α) of 0.05, a statistical power (1-β) of 0.85, and a medium effect size (0.20). Based on these parameters, at least 640 participants were required. The study was approved by the Ankara University Ethics Committee (approval no.: 06/53, date: 16.04.2024), and all procedures were conducted in accordance with the Declaration of Helsinki.

Data collection

Participants were recruited between April and June 2024 through announcements posted on bulletin boards across various faculties at Ankara University. Those who expressed interest were contacted and invited to the department of nutrition and dietetics outpatient clinic. After providing written informed consent, eligible individuals completed all assessments during a single visit under the supervision of trained research staff. Each data collection session lasted approximately 30-45 minutes.

Assessment of social jetlag

The Munich Chronotype Questionnaire (MCTQ), developed by Roenneberg et al. (18), was used to assess SJL in participants. This questionnaire includes items measuring biological clock characteristics, morning and evening activity levels, weekday and weekend sleep patterns, exposure to daylight, and SJL. The Turkish adaptation of the MCTQ was validated by Erdoğan et al. (19), who confirmed its reliability and applicability in the Turkish adult population.

SJL was calculated as the absolute difference between mid-sleep on free days and mid-sleep on workdays; mid-sleep was defined as the midpoint between sleep onset and wake time, and all measures were derived from responses to the MCTQ (1,19). Participants were then categorized into three groups: <1 hour, 1-2 hours, and >2 hours, according to previous studies (20,21).

Dietary intake assessment and determination of ultra-processed food consumption

A 24-hour dietary recall was conducted by researchers to assess participants' food and beverage consumption. To improve accuracy in estimating portion sizes, the food and beverage photo catalog was used (22). The Nutrition Information System (BEBIS) software was used to analyze participants' energy, macronutrient, and micronutrient intake. BEBIS is a computerized dietary analysis program widely used in Türkiye by dietitians and researchers to assess nutrient intake and plan dietary interventions. The software contains an extensive Turkish food composition database with over 20,000 food items and more than 130 nutrient components, including macronutrients, vitamins, minerals, amino acids, and fatty acids (23). Additionally, a food-frequency questionnaire was developed to assess the consumption of UPF over the past month based on the NOVA classification, in which category 4 includes UPF (Appendix 1) (24). These were further categorized into ultra-processed snacks, ultra-processed beverages, and other UPFs. The NOVA classification categorizes foods according to the extent and purpose of industrial processing. It includes four groups: unprocessed or minimally processed foods, processed culinary ingredients, processed foods, and UPFs. UPFs, which correspond to group 4, are industrial formulations typically made from five or more ingredients. These foods often contain

additives such as colorants, flavorings, emulsifiers, sweeteners, and preservatives that are not commonly found in domestic kitchens. Examples include packaged snacks, sugar-sweetened beverages, instant noodles, reconstituted meat products, and ready-to-eat frozen meals. The NOVA system is widely used in nutritional epidemiology to investigate the associations between food processing levels and various health outcomes (25).

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics version 25 (IBM.Corp., Armonk, NY, USA). The normality of continuous variables was assessed using both the Kolmogorov-Smirnov and Shapiro-Wilk tests, supported by visual inspection of histograms and quantile-quantile plots. Extreme outliers, particularly in nutrient intake variables, were examined carefully. Implausible values identified as data entry errors were corrected or excluded, and sensitivity analyses were performed with and without these outliers. After these adjustments, the assumption of normality was reasonably met, and parametric tests were applied. Pearson correlation analyses were performed to identify potential covariates for regression modeling and to assess collinearity among continuous variables. Group differences were analyzed using the independent samples t-test, while comparisons across three or more groups were conducted using one-way analysis of variance (ANOVA). For variables with a statistically significant ANOVA ($p<0.05$), Bonferroni post-hoc tests were applied to identify differences between groups. For multivariable analyses, linear regression models were applied, with a significance level set at $p<0.05$.

To account for total energy intake when evaluating UPF consumption, the residual method was applied. A linear regression model was constructed with UPF consumption as the dependent variable and total energy intake (kcal) as the independent variable. The residual values obtained from this model represented deviations from expected UPF consumption based on energy intake, allowing an energy-independent comparison. Since residual values could be negative, min-max normalization was applied to standardize all values to the range (0,1). The resulting variable was used as the dependent variable in further analyses. Model fit was evaluated by reporting R^2 and adjusted R^2 as indicators of the regression models' explanatory power.

To evaluate the impact of SJL on UPF consumption, multiple linear regression analyses were performed. SJL was analyzed as a continuous variable (measured in hours). To control for potential confounders, the model included total energy intake (kcal), age, sex, smoking status, body mass index (BMI), and physical activity level (PAL). To improve comparability with research and minimize the influence of any residual confounding, total energy intake (kcal) was retained as a covariate in the regression models, even though UPF consumption had already been adjusted for energy intake using the residual method

Results

Demographic characteristics of participants

The demographic characteristics of the participants are presented in Table 1. There were no statistically significant differences among the groups with respect to age, sex, smoking status, BMI, BMI categories, or PAL ($p>0.05$ for all comparisons).

However, significant differences were observed in nutrient intake across the SJL groups. Total energy intake was significantly higher in the SJL ≥2 hours group (1698.7±34.8 kcal/day) compared to the SJL <1 hour (1474.3±44.1 kcal/day) and the 1≤ SJL <2 hours (1582.3±33.9 kcal/day) groups ($p<0.001$). Similarly, protein intake was highest in the SJL ≥2 hours group (65.6±1.7 g/day), showing a significant difference between groups ($p=0.046$).

Fat intake and saturated fatty acid (SFA) intake also increased with increasing SJL duration, with the SJL ≥2 hours group having the highest intakes ($p=0.025$ and $p=0.011$, respectively). Carbohydrate (CHO) intake was significantly lower in the SJL <1 hour group and increased across groups, reaching the highest values in the SJL ≥2 hours group ($p<0.001$). In contrast, fiber intake showed a decreasing trend, with significantly lower levels in the SJL ≥2 hours group ($p=0.022$). Although sodium intake appeared higher in the SJL ≥2 hours group, the difference was not statistically significant ($p=0.122$).

Energy and nutrient intake from ultra-processed foods by social jetlag group

Energy and nutrient intakes from UPFs across SJL categories are presented in Figure 1. Analysis of energy intake from UPFs indicates that packaged snacks, chips, cookies, cakes, protein bars, and ice cream contribute most to total UPF-derived energy. A clear increase in energy intake from these food groups was observed with increasing SJL duration (Figure 1a). Regarding protein intake from UPFs, the highest contributions were from chocolate-flavored drinks, protein bars, and processed meats. In particular, participants with SJL duration ≥2 hours had higher protein intake from processed meats than other groups (Figure 1b). In terms of fat intake, the primary UPF sources were chips, cakes, ice cream, and processed meat products. Fat intake, particularly from processed meats and margarines, increased with longer SJL duration (Figure 1c). For CHO intake, the most significant contributions came from chips, cakes, sweetened beverages, and chocolate-flavored drinks. CHO intake from chocolate-flavored drinks and sugary beverages increased substantially with increasing SJL duration (Figure 1d). Regarding sodium intake, processed meats, chips, and fast-food items were the primary UPF sources. Notably, participants with an SJL duration of 2 hours had higher sodium intake from processed meats and instant soups compared with other groups (Figure 1e). Finally, an evaluation of SFA intake from UPFs showed that the largest contributors were ice cream, cakes, margarine, and

Table 1. Demographic characteristics of participants

Characteristic	SJL <1 hour (n=129)	1< SJL <2 hours (n=212)	SJL >2 hours (n=307)	p-value
Age (years)	21.1±2.3	21.1±2.7	21.1±2.5	0.985
Sex				
Female	105 (81.4)	157 (74.1)	241 (78.5)	0.253
Male	24 (18.6)	55 (25.9)	66 (21.5)	
Smoking status				
Smoker	44 (34.1)	51 (24.1)	89 (29.0)	0.130
Non-smoker	85 (65.9)	161 (75.9)	218 (71.0)	
BMI (kg/m²)	22.2±3.4	22.1±3.2	22.0±3.2	0.328
BMI category				
Underweight	15 (11.6)	25 (11.8)	39 (12.7)	0.929
Normal weight	89 (69.0)	152 (71.7)	219 (71.3)	
Overweight/obese	25 (19.4)	35 (16.5)	49 (16.0)	
PAL	1.4±0.1	1.4±0.1	1.4±0.1	0.886
Nutrients				
Energy intake (kcal/day)	1474.3±44.1[a] (645.1-2436.5)	1582.3±33.9[a] (639.6-2934.4)	1698.7±34.8[b] (841.1-3692.4)	**<0.001**
Protein intake (g)	58.6±2.3[a] (16.5-161.5)	62.3±1.6[a] (20.0-162.4)	65.6±1.7[b] (16.4-248.1)	**0.046**
Fat intake (g)	66.0±2.3[a] (14.0-139.0)	68.9±1.8[a] (14.8-146.5)	73.6±1.8[b] (15.2-214.0)	**0.025**
Saturated fatty acids (g)	23.6±0.9[a] (3.7-52.1)	24.97±0.70[a] (2.6-63.1)	27.0±0.7[b] (6.5-78.3)	**0.011**
Carbohydrate intake (g)	157.4±5.8[a] (35.1-400.0)	174.1±4.7[a] (32.7-468.5)	188.6±4.4[b] (32.9-455.5)	**<0.001**
Fiber intake (g)	13.8±0.7[a] (1.4-40.2)	15.5±0.5[b] (0.9-42.7)	15.9±0.4[b] (3.9-59.8)	**0.022**
Sodium intake (mg)	2121.1±111.6 (161.6-7991.9)	2512.5±84.6 (375.4-7177.0)	2801.4±253.9 (355.1-7619.7)	0.122

Values are presented as mean ± standard deviation (minimum–maximum) or frequency (percentage), as appropriate.
Different superscript letters ([a, b]) indicate statistically significant differences between groups (p<0.05), determined by one-way ANOVA followed by Bonferroni post-hoc test for continuous variables, and chi-square test for categorical variables
SJL: Social jetlag, BMI: Body mass index, PAL: Physical activity level

processed meats. As SJL duration increased, SFA intake from margarines increased notably, while a smaller increase was observed for processed meats (Figure 1f).

Effect of social jetlag duration on ultra-processed food consumption

Table 2 presents the multiple linear regression results evaluating the effect of SJL duration (in hours) on UPF consumption. The model was adjusted for total energy intake (using the residual method), age, sex, smoking status, BMI, and PAL and included 95% confidence intervals for all predictors.

The results show that SJL duration was not significantly associated with UPF consumption (B=-0.0024; 95% CI: -0.0124 to 0.0076; p=0.636). Among all predictors, age was the only variable significantly associated with UPF intake (B=-0.0097; 95% CI: -0.0154 to -0.0040; p=0.001), indicating that UPF consumption decreases with increasing age. No other variables, including sex, smoking status, BMI, or PAL, were significantly associated with UPF consumption (p>0.05 for all). The final sample size for the regression analysis was n=648. The model explained approximately 3.5% of the variance in UPF consumption (R^2=0.035; adjusted R^2=0.025).

These findings suggest that while SJL does not appear to influence UPF consumption directly, age-related factors may play a more prominent role in shaping dietary patterns, particularly with respect to UPF intake.

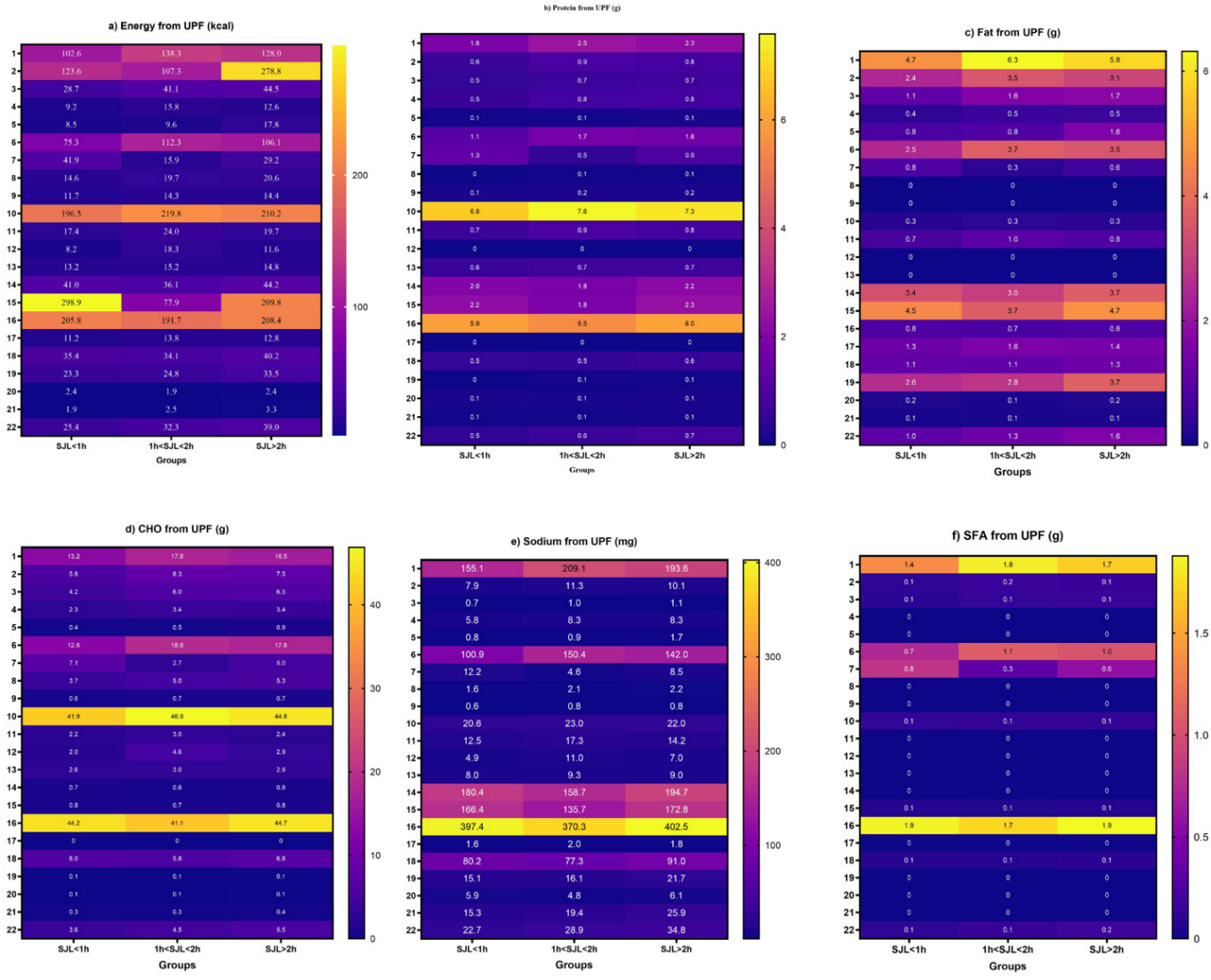

Figure 1. Heatmaps of energy and nutrient intake from ultra-processed foods across social jetlag categories

Panels represent intake levels of (a) energy (kcal), (b) protein (g), (c) fat (g), (d) carbohydrate (g), (e) sodium (mg), and (f) saturated fatty acids (g) from ultra-processed foods, stratified by social jetlag groups (SJL <1 hour, 1-<2 hours, ≥2 hours). Color intensity indicates relative intake levels, with higher values shown in warmer tones. Rows represent individual ultra-processed food items listed in Appendix 1.

CHO: Carbohydrate, UPF: Ultra processed food, SFA: Saturated fatty acid, SJL: Social jetlag

Table 2. Multiple linear regression results for the effect of social jetlag (continuous) on ultra-processed food consumption

Variable	B (Beta)	SE	95% CI	p-value
Constant	0.6748	0.1078	0.4635, 0.8861	**<0.001**
SJL duration (hours)	-0.0024	0.0051	-0.0124, 0.0076	0.636
Energy (kcal)	-0.000001	0.000013	-0.0000, 0.0000	0.937
Age	-0.0097	0.0029	-0.0154, -0.0040	**0.001**
Gender	-0.0295	0.0189	-0.0665, 0.0075	0.120
Smoking	0.0247	0.0237	-0.0217, 0.0711	0.304
BMI	0.0031	0.0044	-0.0055, 0.0117	0.486
PAL	-0.0325	0.0189	-0.0695, 0.0045	0.092

Values represent unstandardized regression coefficients (B), standard errors, 95% confidence intervals, and p-values. Social jetlag was included as a continuous variable (in hours). The model was adjusted for total energy intake (using the residual method), age, gender, smoking status, BMI, and PAL. The final sample size for the regression analysis was n=648. Model fit statistics: R^2=0.035; adjusted R^2=0.025

SE: Standard error, CI: Confidence interval, SJL: Social jetlag, BMI: Body mass index, PAL: Physical activity level

Discussion

The study found that SJL is associated with dietary intake, particularly higher total energy and macronutrient intake. However, no significant association was observed between SJL and UPF consumption after adjusting for confounders.

Daily energy intake was higher among individuals with longer SJL duration. This suggests that misalignment between internal circadian timing and external social obligations may disrupt energy homeostasis and adversely affect metabolic health. These are consistent with previous studies linking SJL to components of the metabolic syndrome, including abdominal obesity and insulin resistance (5,16). With increasing duration of SJL, the intake of protein, total fat, SFA, and CHOs increased significantly. This suggests that circadian disruption affects not only energy intake but also other aspects of dietary intake. Of specific concern is the increased intake of SFA, given its role as a risk factor for cardiovascular disease (10). Furthermore, dietary fibre intake was significantly higher among individuals with SJL ≥2 hours ($p=0.022$). This finding contrasts with several previous studies reporting reduced fibre intake among those experiencing SJL and may reflect context-specific dietary patterns among young adults in Türkiye (14,15). This contrasts with findings by Al Khatib et al. (6), who reported reduced fibre consumption among individuals experiencing SJL. The difference may be attributable to cultural and dietary factors or to methodological variations. Collectively, these results suggest that SJL is associated not only with greater energy intake but also with poorer diet quality. Although descriptive analyses indicated increased energy intake from UPFs with greater SJL duration, the multiple regression analysis showed no statistically significant direct association between SJL and UPF consumption. This is consistent with other studies, although results have been inconsistent (26,27). While the present study did not directly examine the influence of SJL on UPF consumption, younger individuals consumed significantly more UPFs, consistent with previous reports (28,29).

Age appeared to have a protective effect on UPF consumption, as older participants reported lower intake levels. The observed age-related difference in UPF consumption supported the hypothesis that younger age groups may be more susceptible to unhealthy dietary behaviours, possibly due to socio-temporal constraints associated with education and employment (28,29).

While SJL was not identified as an independent determinant of UPF consumption, its indirect associations with diet quality suggest that SJL may influence dietary patterns rather than specific food choices (14,15). Compared with previous research, this study demonstrates the complexity of the relationship between SJL and dietary behaviour. The variability observed across cultural contexts, age demographics, and methodological approaches may be a contributing factor to the inconsistencies reported in the literature (15,27). In high-income countries, UPF consumption shows substantial heterogeneity based on socio-demographic indicators such as education, income, and immigration status (26).

The present study has some strengths and limitations. Firstly, the relatively large sample size enhances the statistical power and generalizability of the findings to young adult populations. Second, a comprehensive set of validated instruments was used to assess key study variables, including the MCTQ for SJL, a 24-hour dietary recall to assess nutrient intake, and a NOVA-based food frequency questionnaire for UPF consumption. The residual method was used to adjust UPF intake for total energy intake, thus minimising confounding and enabling a more accurate interpretation of UPF consumption patterns. Furthermore, the implementation of multiple regression models, controlling for potential confounders such as age, sex, smoking status, BMI, and PAL, increases the robustness of the results. Despite these strengths, several limitations should be considered. The cross-sectional design limits causal inference regarding the association between SJL and dietary behaviours. The potential for recall bias and under- or overestimation of food intake is a further limitation arising from the use of self-reported dietary data. The single-day dietary recall may not accurately show habitual intake, particularly for nutrients with high day-to-day variability. SJL was assessed using self-reported questionnaires rather than objective sleep measures (e.g., actigraphy), which may reduce measurement precision. The study population was restricted to healthy adults aged 18-30 years, which may limit the generalizability of the findings to other age groups or clinical populations. Finally, the study did not assess temporal eating patterns or meal timing, which may mediate the relationship between SJL and dietary quality. Given that individuals with prolonged SJL tend to delay their sleep and wake times, it is plausible that their food intake may also shift toward later hours. Future studies should investigate the timing of meals in relation to SJL, as evening and night-time eating have been associated with poorer diet quality and metabolic risk.

Conclusion

In conclusion, the study shows that SJL is significantly associated with increased energy intake and macronutrient consumption, particularly total fat, SFA, and CHOs, and increased fibre intake. However, no significant association was observed between SJL and UPF consumption after adjusting for confounders. These results suggest that circadian misalignment may contribute to reduced dietary quality independent of UPF consumption. The cross-sectional nature of the study indicates a need for further longitudinal and interventional research to clarify the causal pathways linking SJL with dietary behaviours and to explore the potential role of meal timing and chrononutrition strategies in reducing these effects.

Ethics

Ethics Committee Approval: The study was approved by the Ankara University Ethics Committee (approval no.: 06/53, date: 16.04.2024).

Informed Consent: After providing written informed consent, eligible individuals completed all assessments during a single visit under the supervision of trained research staff.

Footnotes

Authorship Contributions

Concept: M.B., E.N.S., G.D.A., Design: M.B., Data Collection or Processing: M.B., E.N.S., G.D.A., Analysis or Interpretation: M.B., Literature Search: M.B., E.N.S., G.D.A., Writing: M.B.

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

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Appendix 1. List of Ultra-Processed Food Items

No	Ultra-processed food item
1	Packaged chips or crackers
2	Cookies
3	Cakes and cake mixes
4	Protein bar
5	Ice creams and frozen desserts
6	Chocolate bar
7	Breakfast cereals
8	Soft drinks
9	Sweetened juices
10	Powdered and other “instant” soups
11	Chocolate drinks
12	Tea-based drinks
13	Sweetened yoghurts
14	Burgers, hot dogs, sausages
15	Processed meat products
16	Packaged breads
17	Margarines and spreads
18	French fries
19	Mayonnaise, ketchup and mustard
20	Salad sauces
21	Noodles
22	Pizza

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Metastatic malignant melanoma with obstructive jaundice: a case report

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Keywords: Metastatic malignant melanoma, obstructive jaundice, pembrolizumab, immunotherapy, anti-PD-1 antibodies

ABSTRACT

Metastatic malignant melanoma, which presents as obstructive jaundice due to common bile duct (CBD) involvement, is exceedingly rare. We present a case of a 36-year-old woman with metastatic malignant melanoma involving multiple organs including the lungs, pancreas, gallbladder, chest wall, and cervix, complicated by obstructive jaundice of unknown primary origin. Diagnostic evaluation revealed widespread metastases confirmed by histopathology and immunohistochemistry, positive for human melanoma black 45 and S-100. Treatment included placement of a self-expanding metallic stent in the CBD and initiation of pembrolizumab immunotherapy. This case highlights the diagnostic challenges and therapeutic considerations in managing metastatic melanoma with unusual biliary tract involvement.

Introduction

Malignant melanoma is a highly aggressive cutaneous malignancy known for its metastatic potential, yet spread to extracutaneous sites is relatively infrequent. Melanoma of unknown primary (MUP) is a rare entity, accounting for approximately 3.2% of all melanomas, and presents with metastasis to lymph nodes, subcutaneous tissues, and visceral organs (1). Metastasis to the bile duct is extremely rare, with very few cases involving the common bile duct (CBD) reported in the literature (2-6). Patients may present with painless jaundice and face diagnostic and therapeutic challenges due to the rarity and severity of the condition (2). We report a unique case of metastatic malignant MUP presenting with obstructive jaundice and extensive systemic involvement.

Case Presentation

A 36-year-old woman presented with abdominal pain and yellowish discoloration of the eyes for one month. On examination, she was icteric. Two palpable masses were noted: One measuring approximately 5×6 cm in the right hypochondrium and another 8×6 cm in the pelvic region. A 6×4 cm hard, fixed swelling was palpable over the right posterior

chest wall. Bilateral breast examination revealed increased nodularity. Per rectal and per vaginal examinations were unremarkable. No suspicious lesions were noted on the skin or mucosa upon evaluation by a multidisciplinary team including a dermatologist, oncologist, gynecologist, and general surgeon.

Blood work-up showed abnormal liver function with a total bilirubin level of 13.37 mg/dL (indirect 11.85 mg/dL) and an elevated alkaline phosphatase level of 575 U/L. Contrast-enhanced computed tomography (CT) of the abdomen and pelvis revealed enhancing lesions in the right lower lobe of the lung, gallbladder fundus, and a hypodense lesion in the pancreas, along with multiple periportal and peripancreatic lymph nodes. Bilateral adnexal lesions, heterogeneous cervix, and subcutaneous and intermuscular nodules were also noted.

Due to obstructive jaundice, endoscopic ultrasound with endoscopic retrograde cholangiopancreatography was performed, revealing a CBD stricture. A self-expanding metallic stent was placed after brush cytology and biopsy from the liver-adjacent lesion. Histopathology confirmed malignant melanoma. Fine needle aspiration cytology from the posterior chest wall mass and cervical biopsy, also confirmed metastatic melanoma. Immunohistochemistry was positive for human melanoma black 45 and S-100, and negative for chromogranin and GATA-3, supporting the diagnosis.

Positron emission tomography-CT revealed widespread metastases to the brain, bronchus (causing right middle lobe collapse), chest wall, left breast, adrenal glands, gallbladder, pancreas, right iliac fossa, left ischial tuberosity, adnexa, and cervix (Figure 1).

The patient was diagnosed with metastatic malignant MUP and initiated on immunotherapy treatment with pembrolizumab (every 3 weeks). After three cycles, treatment was continued in her hometown. Unfortunately, she showed a poor response to the therapy and discontinued it because of extensive disease burden.

Discussion

Malignant biliary obstruction is typically caused by primary tumors of the pancreas, bile ducts, liver, gallbladder, or ampulla of Vater. However, metastatic lesions from distant sites, such as the lungs, breasts, colon, and melanoma, can also lead to biliary obstruction (7). Melanoma metastases are often asymptomatic and widespread at diagnosis, with visceral metastases associated with poor prognosis (8).

Melanoma involving the pancreas and bile ducts may present in various forms: primary biliary melanoma, MUP involving the pancreas, secondary metastasis to the pancreas or bile ducts, or external compression of bile ducts by adjacent metastatic lymph

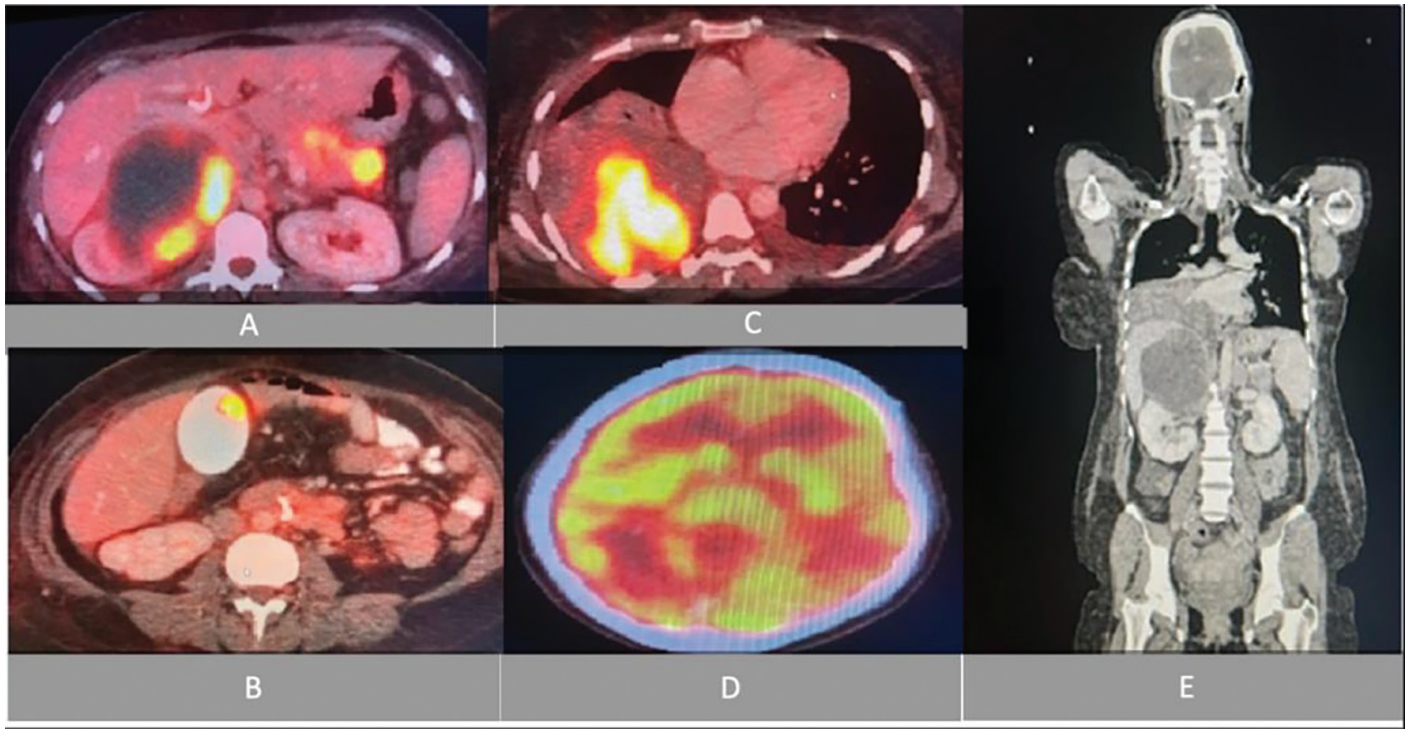

Figure 1. Positron emission tomography-computed tomography findings. (A) Increased FDG uptake in the right adrenal gland. (B) Distended gallbladder with contrast enhancement. (C) Increased FDG uptake in the basal segment of the lower lobe of the right lung. (D) Multiple metastatic deposits in the brain. (E) Coronal view showing widespread metastases

FDG: Fluorodeoxyglucose

nodes or liver lesions (7). Only around 18 cases of melanoma metastasizing to the CBD have been reported (3). Clinical presentation commonly includes painless jaundice, although hematobilia, cholangitis, or abdominal pain can occasionally occur (8).

MUP incidence ranges between 1.2% and 18% (9). First described by Das Gupta in 1963, MUP is defined as melanoma found in lymph nodes, subcutaneous tissues, or internal organs without any identifiable primary lesion on the skin, eyes, or mucosa (2). Theories explaining MUP include immune-mediated regression of the primary lesion, misdiagnosis of previously excised melanocytic nevi, or true primary development in internal organs or lymph nodes (2,9). Importantly, patients with MUP generally have prognoses comparable to those with known primary melanoma at the same stage (2).

While isolated bile duct metastasis may be surgically resectable, extensive systemic involvement, as in our patient, necessitates palliative interventions such as stenting to relieve obstructive jaundice (3). Systemic therapy is the cornerstone of management for unresectable advanced melanoma. Combining immunotherapy with other modalities, such as chemotherapy, radiotherapy, or targeted therapy, improves efficacy (10). Our patient also had multi-systemic involvement; therefore, surgical resection was not possible, and she was started on immunotherapy.

Melanoma's high immunogenicity makes it particularly responsive to immunotherapy. However, immune-related adverse events may occur due to immune system dysregulation (10,11). Several studies have demonstrated the efficacy of anti-programmed death-1 (PD-1) antibodies in melanoma. Topalian et al. (11), Brahmer et al. (12), Postow et al. (13), and Gambichler et al. (14) reported favorable clinical outcomes with PD-1 blockade. In addition, decreased levels of circulating PD-1+ regulatory T cells have been associated with reduced disease progression and better response to treatment (4).

Conclusion

This case highlights the importance of considering metastatic melanoma, even without a visible primary lesion, in patients presenting with obstructive jaundice and disseminated metastatic disease. Diagnosis of MUP requires thorough examination and exclusion of cutaneous, ocular, and mucosal primary sites. Immunotherapy remains a promising treatment, even in advanced disease, though challenges in management and prognosis persist. Multidisciplinary collaboration is crucial for optimizing care, improving outcomes, and ensuring comprehensive palliative and systemic treatment for such complex cases.

Ethics

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Footnotes

Authorship Contributions

Design: A.D.S., S.H.J., Data Collection or Processing: A.D.S., S.H.J., Y.C.S., Analysis or Interpretation: Y.C.S., C.D.S., Literature Search: A.D.S., S.H.J., Y.C.S., V.S., Writing: A.D.S., S.H.J., Y.C.S., C.D.S., V.S.

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

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Significance of diminished hormone expression in nulligravida woman presenting with triad of uterine pathologies

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ABSTRACT

Genital tract tuberculosis (TB) occurring together with adenomyosis and leiomyoma is rarely observed. A 40-year-old nulligravida woman was clinically diagnosed with the fibroid uterus. Histopathological examination revealed leiomyoma with adenomyosis and TB. Immunohistochemistry for oestrogen and progesterone receptors was performed to determine their expression, which was found to be moderate, although it was expected to be strongly positive. This case is being reported because of its rare coexistence of these conditions; moreover, it suggests that reduced hormone expression, particularly of oestrogen, may enhance the severity of TB, ultimately resulting in adverse reproductive outcomes.

Introduction

Female genital tract tuberculosis (TB) is a variant of extrapulmonary tuberculosis (EPTB) (1). It causes a negative impact on female fertility. TB's effects on female hormone alterations and menstrual cycles are overlooked. TB outcomes on hypothalamus, pituitary gland, and ovaries result in disordered menstruation. Simultaneously change in hormone profile and antigonadotrophic effects of *Mycobacterium* TB results in hypogonadism which accounts for infertility and menstrual irregularities. TB has been associated with lower serum oestrogen levels, and serum oestrogen levels are raised during TB treatment (2). It had been reported that in the TB patients, there were reduction in female sex hormone which leads to diminished ovarian function (3). This leads to

spontaneous abortions, which result in infertility. Leiomyoma is benign smooth muscle uterine tumour whereas adenomyosis is the presence of ectopic endometrial tissue in the myometrium. Both leiomyoma and adenomyosis are hormone-dependent tumors; that is, their size and activity increase with elevated of oestrogen and progesterone levels (4,5). The coexistence of genital TB with leiomyoma and adenomyosis is extremely rare. They also exhibit antagonistic hormone effects. This case is being reported because of its rare occurrence and to highlight the possible association between these pathologies.

Case Presentation

A 40-year-old nulligravida woman presented with complaints of pain and mass in the abdomen. She was also suffering from dysfunctional uterine bleeding, and her laboratory investigations revealed anemia, which represented her only clinical manifestation. Hormone levels could not be accessed earlier. A gynaecology examination was suggestive of fibroid uterus. The medications were not supportive in controlling dysfunctional uterine bleeding, so considering the dysfunctional uterine bleeding and the increased size of the fibroid uterus, hysterectomy was decided to be performed. Hysterectomy with bilateral (B/L) salpingo-oophorectomy was sent for histopathology examination. The specimen was measured 14 x 9 x 6 cm. Fibroids obliterated the endometrial cavity. It measured 8 cm and 4 cm in its largest and smallest diameters, respectively. On further sectioning, they were grey-white in colour with whirling.

The right-sided ovary measured 3 x 2 x 1 cm and the left-sized ovary measured 6 x 3 x 2 cm. Cut section of B/L ovaries showed solid and cystic areas.

The right-sided fallopian tube measured 3 cm in length, whereas left-sided fallopian tube measured 4 cm.

Tissues were stained with hematoxylin and eosin. Ziehl-Neelsen (ZN) stain was applied to confirm TB (6), simultaneously immunohistochemistry (IHC) for estrogen and progesterone was also applied.

Histopathology examination showed smooth muscle fibers with elongated blunt-ended nucleus and eosinophilic cytoplasm running at various angles with whirling. These finding confirmed leiomyoma.

Plenty of endometrial glands with stroma deep in myometrium (more than one low power field from endo myometrial junction) were appreciated. This histomorphology microscopic findings were suggestive of leiomyoma coexisting with adenomyosis and caseous necrosis [Figure 1 (a)].

These findings were accompanied by multiple epithelioid granulomas with caseous necrosis in myometrium [Figure 1 (b)]. ZN stain was also applied to isolate tubercular bacilli but could not be found contributory [Figure 1 (c)].

Based on these morphologies, the present case was reported as leiomyoma with adenomyosis and extra pulmonary TB. Tubercular features were also reported in other sections of the uterus.

IHC was applied for estrogen and progesterone receptors expression. Immunoreactive score (IRS) method was used. Nuclear positivity was confirmed. It was calculated as follows: IRS=staining intensity (SI) x percentage of positive (PP) stained cells (PP), where SI was the optical SI (graded as 0=no, 1=weak, 2=moderate, and 3=strong staining) and PP was the PP. The PP is mentioned as 0=no staining, 1=10%, 2=11-50%, 3=51-80% and 4=>80. The aggregation of these both finally result in IRS score categorization into negative, mild, moderate and strong expression.

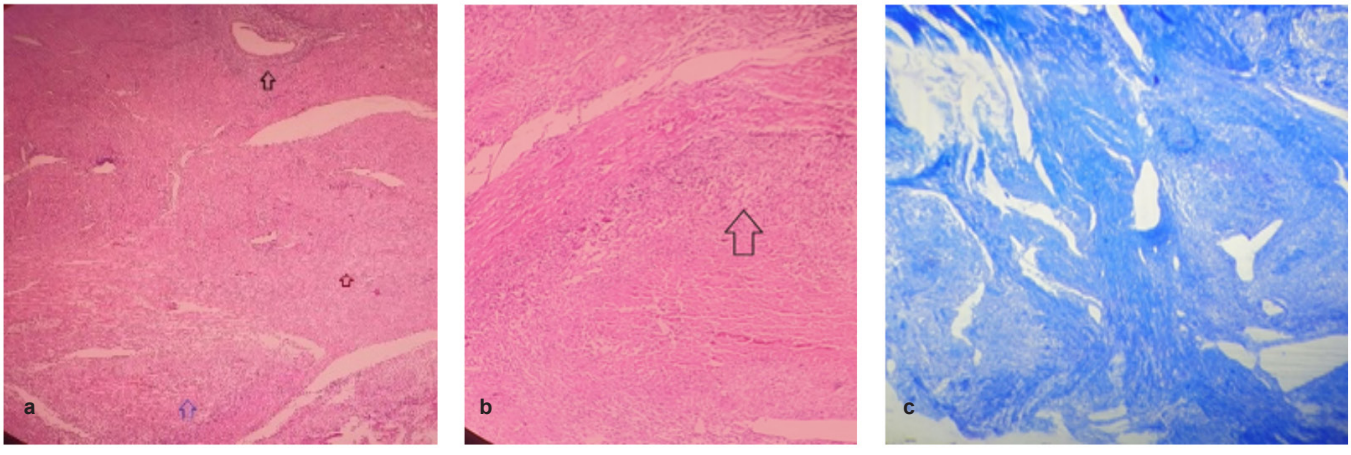

Figure 1. (a) H&E stained section showing adenomyosis (black arrow) leiomyoma (red) and caseous necrosis (blue). (b) H&E stained section showing caseous necrosis. (c) ZN stained section showing non-contributory staining
H&E: Hematoxylin and Eosin, ZN: Ziehl-Neelsen

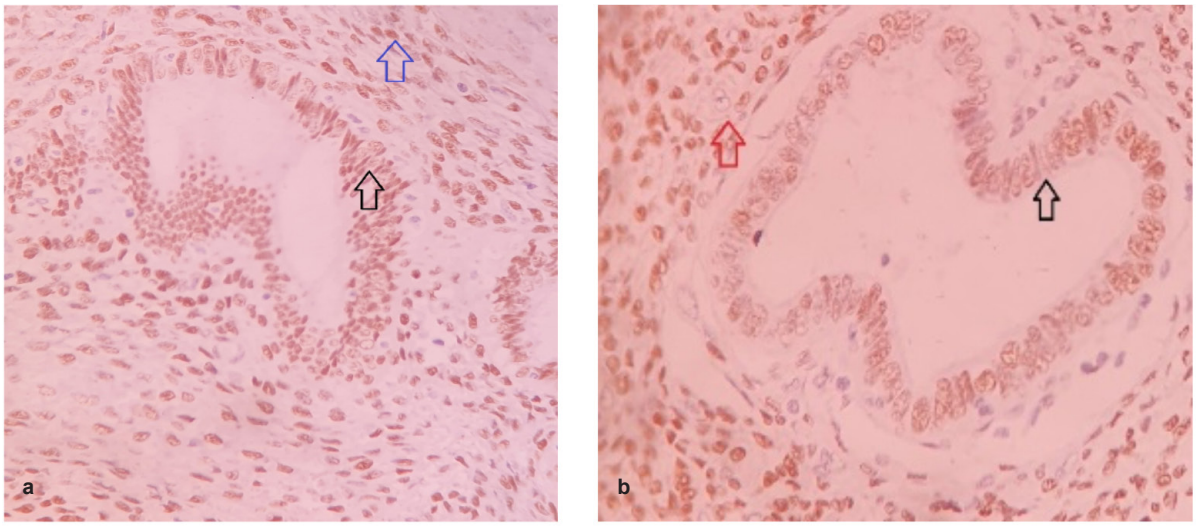

Figure 2. (a) Figure showing moderate positive immunoreactivity for estrogen receptor (black-gland, blue-stroma). (b) Figure showing moderate positive immunoreactivity for progesterone receptor (black-gland, red-stroma)

The results showed moderate immunoexpression of estrogen [Figure 2 (a)] and progesterone [Figure 2 (b)].

Informed consent was obtained from participants.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Discussion

This case presents a rare coexistence of leiomyoma, adenomyosis, and genital TB in a reproductive-age woman, highlighting the complex interaction between hormonal and infectious factors affecting the uterus.

Female genital tract TB causes adverse effect on reproduction. Tubercular bacilli infect the genital tract by four routes–haematogenous, descending direct spread, lymphatic, and sexual transmission. It may cause damage to fallopian tube leading to blockage or adhesions, reduced endometrial receptivity or ovarian damage. It is seen in patients of age range between 20 to 45 years. Clinically, it may be asymptomatic or present with symptoms diversity of symptoms like infertility and chronic pelvic inflammatory disease, dysfunctional uterine bleeding, pelvic pain and abnormal vaginal discharge (1) .These clinical features are not specific to female genital tract TB and may mimic other pathologies (6).

In current study, patient was 40-year-old nulligravida woman who presented with pain, mass in the abdomen and dysfunctional uterine bleeding.

The diagnosis of female genital tract TB are made on basis of culture positive specimen, or positive histopathology or strong clinical evidence consistent with active EPTB. Chest X-ray, complete blood count, erythrocyte sedimentation rate, and tuberculin test should be applied to rule out systemic spread. The two imaging techniques hysterosalpingography and sonography are also useful, as hysterosalpingography evaluates internal structure and tubal patency whereas ultrasonography carried out simultaneous evaluation of ovarian, uterine and extra pelvic involvement (1).

Radiology investigations such as ultrasonography shows thickened fallopian tubes with or without endometrial thickening, tubo-ovarian masses or adhesion. It is often may be misleading and mimic other intra uterine pathologies like leiomyoma specifically degenerated one, ovarian tumors etc (7). So, the awareness of sonographic changes associated with TB infection should be specifically known which may improve diagnostic accuracy and avoid clinical mismanagement and surgical explorations (8).

In the present case study, the ultrasonography findings were also suggestive of leiomyoma uteri.

On histopathology examination, TB is characterized by the presence of epithelioid cell granulomas along with caseous necrosis. The confirmation of TB is done by identification of *Mycobacterium* TB with ZN stain (7), but is difficult to diagnose the bacteria in the extrapulmonary sites because the organism are sparse in number at extra pulmonary locations (1).

In these cases, the ZN stain was also not contributory; however, the patient improved after antitubercular treatment.

Researches had already reported that ovarian steroids, oestradiol and progesterone promote leiomyoma growth (5). Intramural is the commonest variants (9). In present study, there were two intramural leiomyoma visualized obliterating the cavity. The symptoms depend on location, size of tumour and hormonal effect. Here, the patient was presented with mass, pain in abdomen and dysfunctional uterine bleed.

Leiomyoma on histopathology is characterised by spindle-shaped tumor cells with an elongated, blunt-ended nuclei and

eosinophilic cytoplasm forming bundles with whorls (9,10). We also found these features.

Adenomyosis is characterized by the presence of endometrial glands and stroma in the myometrium (11). We also observed these findings in our case.

Adenomyosis may coincide with leiomyoma, endometriosis, endometrial hyperplasia, endometrial polyp, and endometrial carcinoma, which occur due to unopposed estrogen (9,11). The present case consisted of adenomyosis with leiomyoma and myometrial TB.

Estrogen and progesterone receptors are the members of hormone receptor family of ligand dependent transcription factors. Hormone expression rises in leiomyoma and adenomyosis (4,5). Rosenthal et al. (12) mentioned that a lack of estrogen results in wide dissemination of TB. Ukibe et al. (13) assessed the hormonal changes in women suffering from TB and reported that progesterone and estrogen were found significantly low.

The benefit of the IRS score is that it includes both epithelial and stromal elements for expression (14). In the current study, the estrogen and progesterone receptor expression was found to be moderate.

Conclusion

The coexistence of leiomyoma with adenomyosis and TB is rare. Leiomyoma and adenomyosis depends on sex hormones for proliferation, whereas TB is associated with lower hormone expression. The reduced level of hormone expression, especially estrogen, increases the severity of TB and negatively affects reproduction. We emphasize that hormone receptor analysis should be included as a supplementary investigation in young and nulliparous or gravida tubercular patients.

Ethics

Informed Consent: Informed consent was obtained from participants.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.K., K.K., Concept: S.D., Design: S.D., Data Collection or Processing: K.S., Analysis or Interpretation: S.D., Literature Search: A.S., Writing: S.D.

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