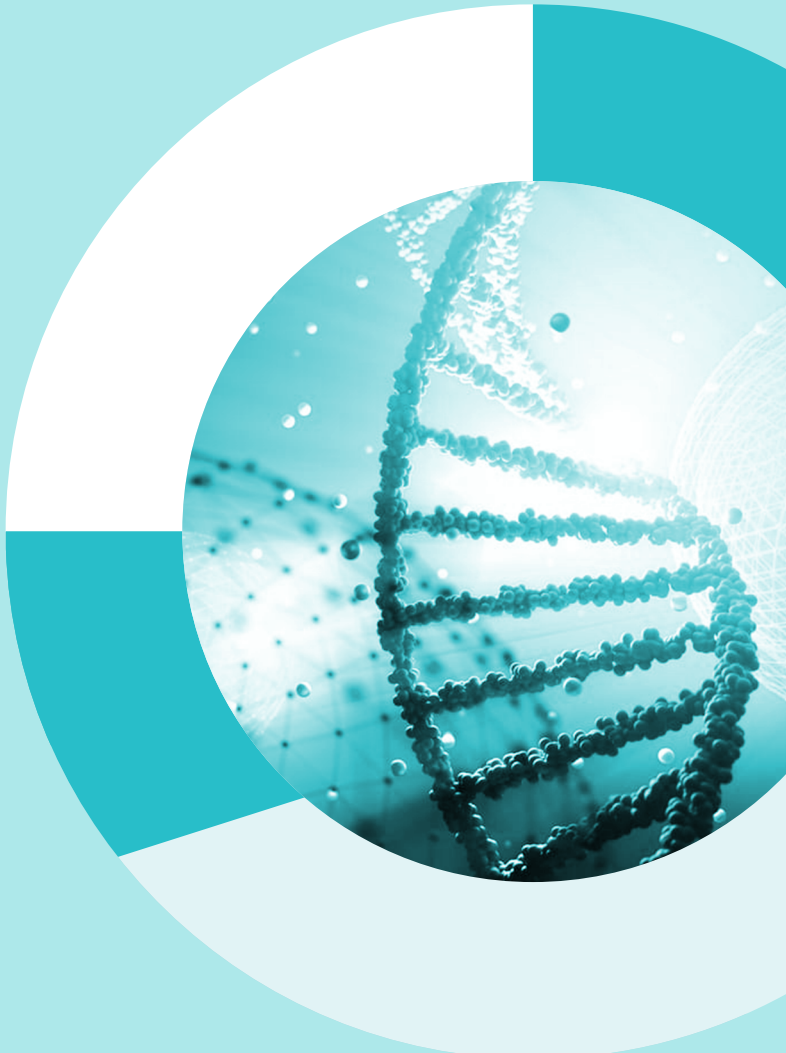
ISSN: 2149-7893 E-ISSN: 2536-507X

CYPRUS JOURNAL OF MEDICAL SCIENCES

Indexed in the Web of Science

Volume: 10 Issue: 5 October 2025



Official Journal of Cyprus Turkish Medical Association

galenos yayınevi

www.cyprusjmedsci.com

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

Publisher Contact
Address: Molla Gürani Mah. Kaçamak Sk. No: 21/1 34093 İstanbul, Türkiye
E-mail: info@galenos.com.tr/yayin@galenos.com.tr
Web: www.galenos.com.tr **Publisher Certificate Number:** 14521

Publication Date: October 2025
E-ISSN: 2536-507X
ISSN: 2149-7893
International scientific journal published bi-annually.

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

International Advisory Board

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

EDITORIAL BOARD

Please refer to the journal's webpage (**https://cyprusjmedsci.com/**) for "Aims and Scope", "Instructions to Authors" and "Ethical Policy".

The editorial and publication process of the Cyprus Journal of Medical Sciences are shaped in accordance with the guidelines of ICMJE, WAME, CSE, COPE, EASE, and NISO. The journal is in conformity with the Principles of Transparency and Best Practice in Scholarly Publishing.
Cyprus Journal of Medical Sciences is indexed in **Web of Science-Emerging Sources Citation Index, TUBITAK ULAKBIM TR Index, Embase, EBSCO, J-GATE, CABI, CNKI** and **Gale**.
The journal is published electronically.
Owner: Ahmet Özant on behalf of Cyprus Turkish Medical Association
Responsible Manager: Sonuç Büyük

CYPRUS
JOURNAL OF MEDICAL SCIENCES
Indexed in Web of Science
Volume: 10 | Issue: 5 | October 2025

CONTENTS

LETTER TO EDITOR

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-106
Cyprus J Med Sci 2025;10(5):293-294

Communication Strategies for Mechanically Ventilated Patients in the Emergency Department: A Letter to the Editor

Merve Ekşioğlu

Clinic of Emergency Medicine, University of Health Sciences Türkiye, Fatih Sultan Mehmet Training and Research Hospital, İstanbul, Türkiye

Dear Editor,

I read with interest the article published in the Cyprus Journal of Medical Sciences on communication with patients receiving mechanical ventilation in intensive care units.[1] The review clearly describes the challenges of communication and emphasizes the contribution of both low- and high-technology tools in supporting patient-healthcare worker interaction.

From an emergency medicine perspective, these issues are equally relevant. Both non-invasive mechanical ventilation (NIMV) and invasive mechanical ventilation are widely used in the emergency department.[2] Due to limited intensive care capacity, many patients remain in the emergency department for prolonged periods under the supervision of emergency physicians. However, communication is complicated by high patient flow, time pressure, limited staffing, and less controlled conditions compared with intensive care.

Agitation is common in patients receiving NIMV and may compromise treatment. Structured tools such as visual communication boards or tablet-based interfaces may reduce anxiety and agitation. This can improve compliance with NIMV. This could lower sedative requirements and decrease the transition rate to invasive ventilation. In intubated patients, effective communication may support lighter sedation, improve comfort, and contribute to better outcomes. A recent study showed that patients intubated in the emergency department face a higher risk of deep sedation and take longer to achieve lighter sedation than those intubated in intensive care.[3] Effective communication strategies may contribute to achieving lighter sedation in this context, and further research exploring this relationship would be valuable.

The literature describes various methods to facilitate communication, including illustrated materials, communication cards, visual guides, computer-based tools, and eye-tracking technologies.[4] For example, eye-tracking systems have been shown to enable intubated or tracheostomized patients to express basic needs, monitor complications, and respond to quality-of-life measures.[5] Such findings suggest that advanced technologies may play an important role in emergency care as well.

In this context, adapting structured communication interventions to the specific dynamics of emergency departments could address a notable gap in the literature. Pilot studies testing the feasibility of these strategies under conditions of high patient load and limited resources may help align emergency and intensive care practices and improve patient-centered outcomes.

Footnotes

Financial Disclosure: The author declared that this study had received no financial support.

REFERENCES

1. Çelebi C, Yeşilyurt KÖ. Ensuring effective communication with patients receiving mechanical ventilation support in intensive care units: current communication materials. Cyprus J Med Sci. 2025; 10(4): 228-35.
2. Göksu E, Kılıç D, İbze S. Non-invasive ventilation in the ED: whom, when, how? Turk J Emerg Med. 2018; 18(2): 52-6.
3. Sereeyotin J, Yarnell C, Mehta S. Sedation practices in patients intubated in the emergency department compared with those in patients in the intensive care unit. Crit Care Sci. 2025; 37: e20250247.

To cite this article: Ekşioğlu M. Communication strategies for mechanically ventilated patients in the emergency department: a letter to the editor. Cyprus J Med Sci. 2025;10(5):293-294

ORCID IDs of the author: M.E. 0000-0003-0108-9855.

Corresponding author: Merve Ekşioğlu
E-mail: mervekoyunoglu@gmail.com
ORCID ID: orcid.org/0000-0003-0108-9855

Received: 10.09.2025
Accepted: 11.09.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

4. Karlsen MW, Holm A, Kvande ME, Dreyer P, Tate JA, Heyn LG, et al. Communication with mechanically ventilated patients in intensive care units: a concept analysis. J Adv Nurs. 2023; 79(2): 563-80.

5. Ull C, Weckwerth C, Schildhauer TA, Hamsen U, Gaschler R, Waydhas C, et al. First experiences of communication with mechanically ventilated patients in the intensive care unit using eye-tracking technology. Disabil Rehabil Assist Technol. 2023; 18(1): 44-9.

REVIEW

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-103
Cyprus J Med Sci 2025;10(5):295-300

The Impact of Psychoactive Substances on Fatal Traffic Accidents

Ceyda Ergil Özbilge[1], İdris Deniz[2,3], Emel Hülya Yükseloğlu[1]

[1]Institute of Forensic Sciences and Legal Medicine, İstanbul University-Cerrahpaşa, İstanbul, Türkiye
[2]Clinic of Forensic Medicine, Dr. Burhan Nalbantoğlu State Hospital, Nicosia, North Cyprus
[3]Eastern Mediterranean University Faculty of Law, Famagusta, North Cyprus

Abstract

Deaths due to road traffic accidents continue to represent a pressing global public health challenge. Reports from the World Health Organization and other international agencies indicate that millions sustain injuries and hundreds of thousands lose their lives annually due to traffic collisions. Most fatalities occur in nations with limited economic resources, where inadequate road infrastructure, limited use of seatbelts and helmets, disregard for speed limits, and the prevalence of operating a vehicle while impaired by alcohol or other psychoactive substances substantially increase the risk of death. In the investigation of fatal traffic accidents, postmortem examinations combined with systematic toxicological analyses are indispensable for clarifying accident mechanisms and informing the development of targeted preventive strategies.

Keywords: Fatal traffic accident, alcohol, psychoactive substance, toxicology, autopsy

INTRODUCTION

Traffic accident-related fatalities are defined as deaths occurring either immediately at the crash site or within 30 days of the incident. Every year, road traffic accidents claim the lives of approximately 1.35 million individuals, translating to a fatality every few seconds. Furthermore, between 20 and 50 million individuals suffer non-fatal injuries, a significant portion of which results in long-term disabilities. Among these fatalities, 92% are reported in nations with restricted and intermediate levels of economic development; Africa experiences the highest incidence rates, while Europe experiences the lowest incidence rates. More than 50% of road traffic fatalities involve vulnerable road users, including pedestrians, cyclists, and motorcyclists. Infrastructure shortcomings were a major contributor: 80% of the evaluated facilities failed to meet the minimum three-star safety threshold for pedestrian protection and dedicated cycling lanes. Such deficiencies amplify collision risks and magnify the severity of injuries.[1]

From a demographic standpoint, road traffic accidents remain one of the primary causes of mortality among individuals aged 5 to 29 years. Males are almost three times more likely than females to be victims, and nearly two-thirds of fatalities occur among individuals aged 18-59 years, who are the economically productive segment of the population. This emphasises significant socioeconomic consequences as well as human costs.[1]

Urban Transportation: Injuries and Fatalities Surrounding Micro-Mobility Devices

Notably, new data show a significant increase in the number of traffic crashes involving bicycles, motorcycles, electric scooters, and other micromobility vehicles. According to a study conducted by Poulos et al.[2] and colleagues in Australia, there are 0.29 bicycle accidents per 1,000 km. In a study examining hospital admissions due to bicycle injuries in the Netherlands, a 5.7% mortality rate and 41% incidence of multiple traumas were identified.[3]

To cite this article: Ergil Özbilge C, Deniz İ, Yükseloğlu EH. The impact of psychoactive substances on fatal traffic accidents. Cyprus J Med Sci. 2025;10(5):295-300

ORCID IDs of the authors: C.E.Ö. 0000-0002-0509-6625; İ.D. 0000-0002-7986-4658; E.H.Y. 0000-0003-2009-6065.

Corresponding author: Ceyda Ergil Özbilge
E-mail: ceyda.ergil@gmail.com , ceyda.ergil@ogr.iuc.edu.tr
ORCID ID: orcid.org/0000-0002-0509-6625

Received: 01.09.2025
Accepted: 30.09.2025
Publication Date: 09.10.2025

In a study analysing data on the clinical and demographic characteristics, time of accident, injury conditions, and helmet use of emergency department patients involved in bicycle accidents in Rome, Italy, between 2019 and 2022, a mortality rate of 0.3% and multiple trauma frequency of 30.4% was found among 763 patients. The results of the investigation revealed that collisions with other automobiles led to higher trauma scores and intensive care unit (ICU) admission rates, whereas helmet use decreased head trauma severity and prevented more ICU admissions.[4]

The national database in the United States (US) reviewed 1,933,296 micromobility-related injuries (including electric scooters, electric bicycles, electric skateboards, and bicycles) from 2019 to 2022. The study results showed a large increase in e-bike (from 293%) and e-scooter (from 88%) injuries during the four-year period.[5]

Electric scooters are emerging as alternatives to bicycles and public transportation systems, particularly for short distances. Owing to their high availability from mobile applications and relatively small size, they have gained popularity in urban transportation as micromobility electric vehicles, that can be easily maneuvered between or alongside vehicles on roads or sidewalks. In Poland, an analysis of nine fatalities in traffic accidents involving electric scooters revealed that accidents primarily occurred during the summer, on weekdays, and during peak morning traffic hours. In only two of the cases examined, blood analysis indicated the presence of alcohol at the time of the incident.[6]

Substance Use and Traffic Risk

A person who drives a vehicle under the influence of alcohol or other psychoactive substances is subject to criminal liability if, as a result of impaired driving, there is an accident with serious or fatal consequences. Studies, which focus on alcohol and illegal drugs, show that such substances only lead to an increased probability of road events, as they impair the brain functions needed for driving.[7]

Forensic sciences are crucial in elucidating both the causes and the situational aspects of deaths resulting from road traffic accidents. In cases of fatal traffic accidents, autopsy examinations and systematic toxicological analyses are vital for determining the circumstances of the accident, as well as the physiological state of the driver or the victim's condition at the time of the incident, including potential influencing factors. Toxicological analyses are typically performed to determine whether the driver or victim was affected by alcohol, illicit drugs, or medications at the time of the incident. Blood, urine, stomach contents, brain tissue, liver, and lungs were collected for toxicological and biochemical analyses. Forensic toxicology analyses of biological samples were used to determine whether the driver exceeded the legal limits or was influenced by drugs (medications used for medical and/or recreational purposes). In addition, postmortem biological changes are considered to estimate the level of a substance at the time of the incident.[8]

Alcohol is the most commonly detected psychoactive substance in traffic accidents. After alcohol, the most commonly detected drug classes include cannabinoids (cannabis/marijuana), benzodiazepines, stimulants, and opioids.[9]

Ethanol, commonly referred to as alcohol, is a prevalent euphoric substance that exerts a depressant effect on the central nervous system. Beyond its impact on cognitive functions, it impairs judgment, induces memory deficits, reduces alertness, and causes disturbances in emotional regulation and physical coordination; this includes balance, speech, vision, hearing, and reaction time. At elevated concentrations, alcohol consumption can result in severe outcomes, such as vomiting, loss of consciousness, and even death. The absorption rate of alcohol from the gastrointestinal system varies depending on the amount consumed, ethanol concentration in the beverage, interactions with medications, presence of food in the stomach, and digestion time.[10]

Extensive research indicates that individuals impaired by alcohol consumption have a significantly higher propensity for involvement in traffic collisions compared to those who abstain from alcohol. Alcohol consumption affects drivers' speed preferences, increasing the risk, severity , and extent of injuries in accidents.[11]

The relationship between high blood alcohol concentration (BAC) and accident frequency has been demonstrated in numerous studies. These findings have led many countries to implement regulatory policies against drunk driving. A BAC of ≥0.50 g/L is typically considered the threshold at which driving capabilities are impaired, thereby posing a risk to road safety.[12] Canada, the US, and New Zealand are recognized as having the highest rates of traffic fatalities linked to alcohol consumption.[10]

Two longitudinal studies from Greece have shown that the proportion of drivers involved in traffic collisions who were impaired by alcohol was 37% during the period from 1995 to 1997. This percentage increased to 41% in the following years, from 1998 to 2004.[13]

Further research is required to clarify the long-term risk of traffic accidents due to alcohol consumption. Serum carbohydrate-deficient transferrin (CDT) levels have been measured by researchers observing correlations between CDT and post-accident BACs. This may provide evidence suggesting that CDT is a new biomarker for detecting road traffic crashes associated with chronic alcohol consumption.[12]

Over a five-year period (2017 to 2021), a retrospective study, performed in the Iraqi Nineveh province, revealed that most victims (injured or dead) of traffic accidents were male. This is believed because not as many women are driving. The research also found that motorcyclists had a greater tendency to be involved in crashes compared to drivers of other vehicles, and the rate of motorcyclist accidents was generally on the rise. The predominant causes of mortality were identified as head trauma and fractures of the lower extremities.[14]

A study comparing alcohol use among fatal and injured motorcycle and bicycle riders, using data from three national public databases, emphasized that the likelihood of fatal and non-fatal injuries being alcohol-related was higher among middle-aged adults and men. The findings indicated that over 38% of motorcycle riders who died each year from 2008 to 2020 and 20% of bicycle riders involved in traffic accidents were under the influence of alcohol.[15]

In Lithuania, an analysis of BAC from 2013 to 2023 was conducted concerning sex, user category, location of death, and time of death in 136 traffic accident cases. The analysis was based on the frequency of alcohol detected in blood specimens collected during autopsy. A total of 31% of the individuals who succumbed to fatal injuries suffered from alcohol intoxication. Specifically, alcohol consumption was identified in 32% of vehicle drivers, 41% of vehicle passengers, 37% of motorcycle riders, and 37% of bicycle riders at the time of the collision. BAC was

highest during the period from 9:00 PM to 5:00 AM, and over a slightly smaller time window of 4 h, from 5:00 PM to 9:00 PM.[16]

Studies conducted in Scotland[17], Portugal[18], and Greece[19] indicate that car and motorcycle drivers are the primary contributors to alcohol-related traffic fatalities, whereas research from Côte d'Ivoire, China, Russia, and Pakistan highlights higher mortality rates among pedestrians. Such cross-national differences may reflect variations in cultural norms and behaviors, the dominance of certain motorized transport modes, and the broader conditions for cycling and walking.[20-22]

While the effect of alcohol on impaired driving ability is the most frequently studied and documented factor, scientific data on the effects of illicit and prescription psychoactive substances on drivers are quite limited. Therefore, there is a lack of information on the frequency of substances other than alcohol in fatal traffic accidents worldwide.[23] Nevertheless, existing studies indicate that other substances that affect the central nervous system (e.g., medical and/or recreational drugs) also seriously impair driving ability and cause road traffic accidents. Extensive research has demonstrated that the intake of alcohol and mind-altering substances markedly increases the probability of fatal road traffic collisions.[24]

Papalimperi et al.[10] analyzed 1,841 autopsy cases from fatal traffic accidents to assess the role of alcohol and psychoactive substances. Toxicological tests showed that 40.7% of deaths were alcohol-related, while 18.9% involved drugs, including such as cannabis (46.6%), benzodiazepines (25.9%), opiates (16.4%), and cocaine (11.1%). Alcohol was combined with other substances in 4.5% of cases. Fatalities were most common among males (87.3%) aged 21-30 years with high blood alcohol levels.[10]

The misuse of illegal, naturally derived, or artificially synthesised, psychoactive compounds often leads to mood changes. The repeated use of such substances often causes addiction, resulting in health, social, and environmental problems. Today, drug use has increased at an unprecedented rate on a global scale, becoming a major public health issue that directly affects crime rates, social stability, and the economy.[25]

According to the World Drug Report, 284 million adults worldwide aged between 15 and 64 years used at least one illicit drug, with a majority being male.[26] Regarding the coronavirus disease-2019 pandemic, increased drug use due to social isolation, as well as concerns about mental health and heightened economic insecurity, have been further advanced can be set for the above reasons.[27]

Drugs are subject to various restrictions based on their origin, pharmacological effects, chemical structures, and legal status. Within this classification, substances are categorised as natural, semi-synthetic, or fully synthetic and further classified based on their legal status as either prescription, legal, or illegal. Illegal drugs are those drugs whose production, transportation, and sale are in contravention of laws.[28]

In recent years, the heterogeneity of drugs available to individuals has expanded, use pattern complexities have intensified, and the co-consumption of several substances simultaneously has increased. By 2022, the global estimated number of drug users was 292 million (5.6% of the population aged 15-64), representing a 20% increase from a decade ago. Illicit abuse is more frequent with opioids than any other substance except cannabis; the third most commonly abused substances are amphetamine-type stimulants, followed by cocaine and MDMA (ecstasy).[29]

In a study conducted in the US, toxicological test results for one or more psychoactive substances were positive in 71-99% of five different driver populations. Additionally, approximately 50% of drivers tested positive for multiple substances. The most commonly detected substances across all groups were alcohol and cannabis; alcohol emerged as the most commonly identified substance in isolation, whereas cannabis was most often detected in conjunction with alcohol and additional psychoactive agents.[30]

The rapid expansion of synthetic drugs within the illicit drug market is largely due to their uncomplicated production methods, use of inexpensive chemical components, and the ease of manufacturing irrespective of geographical constraints. This development presents intricate and substantial challenges to public health and safety, particularly in low- and middle-income nations. The detection and frequency of psychoactive substances are shaped by the country's patterns of drug misuse, its economic landscape, its regulatory stance on alcohol, and the use of both prescription and illegal drugs.[29]

Recent studies have highlighted that in some populations, the likelihood of vehicular accidents is higher when drivers are impaired by cannabis than when they are impaired by alcohol. This risk is predicted to increase in the coming years, and it is emphasised that this situation will have increasingly negative impact on road safety.[31]

Medications can have different effects depending on an individual's genetic makeup, physical characteristics, or current medical condition.[32] Driving a motor vehicle is a complex activity that requires attention, coordination, and the simultaneous execution of cognitive multitasking. Research investigating the impact of pharmaceuticals and various medications on driving performance has assessed multiple parameters, including lane changes or deviations, vehicle speed and variability, response time to environmental cues, and levels of attention. In most studies in this field, participants are administered controlled doses of drugs, after which their driving performance is measured in simulated environments or closed courses. While performance tests provide valuable information about the effects of a particular substance on driving, they also have limitations, such as the inability to experimentally test illegal substances due to legal and ethical restrictions and the fact that controlled environmental conditions do not fully reflect real-world drug use and driving conditions.[30,33]

The "Drug and Human Performance Fact Sheets" were published in 2004, encompassing 16 distinct drugs or categories of drugs. Developed by an international panel of experts on driving under the influence of drugs, these fact sheets contain scientific data on each drug's chemical properties, effects on the body, method of use and dosage, and its potential effects on driving performance. These updated information sheet provide scientific information on the substances most commonly involved in traffic accidents caused by alcohol and drugs.[34]

In the "Drug, Alcohol, and Medication Influence on Driving" (DRUID) project, which involved 36 institutions from 18 European countries and lasted five years (2006-2011), the frequency of use of various psychoactive substances and their risk levels on driving performance were assessed, and the general effects of different drug categories on performance were identified through meta-analyses.[35]

Recent studies have supported the findings of the DRUID project. McCartney and colleagues highlighted that cannabis consumption results in deficits across various driving-related abilities. These impairments are more pronounced in occasional users compared to habitual users.[36]

Simmons et al.[37] reported that the consumption of alcohol and cannabis, as well as their simultaneous use, significantly impaired driving performance. Moreover, the concurrent intake of these substances results in a more pronounced detrimental effect than the consumption of either substance individually.[37]

Additionally, impairments in driving performance have been observed in the morning following the use of certain hypnotic medications. The effects of sedative hypnotics such as zopiclone, flunitrazepam, and ramelteon are similar to the impairing effects of alcohol on driving performance.[38]

Toxicological Analysis of Biological Samples Collected from Drivers: Applications and Limitations

A law enforcement officer who arrests a driver suspected of operating a motor vehicle while impaired by alcohol and/or other psychoactive agents, will request that the driver provide a biological sample (breath, blood, urine, or oral fluid) for screening or testing for the presence of alcohol and other controlled substances. In some circumstances, the officer may compel the driver to do so. Toxicological analyses of biological samples are conducted as part of forensic investigations of living drivers and post-mortem investigations of individuals involved in fatal traffic accidents.[39]

Breath

In cases where drunk driving is suspected, portable breathalysers are routinely used to reliably estimate the BAC. However, because the current technology can only measure alcohol levels through breath, it is not suitable for the detection of other psychoactive substances.[40]

Urine

Urine is a commonly preferred biological specimen, particularly for assessing drug consumption. Urine analysis is a valuable method for detecting the history of drug use or exposure. There is debate about whether urine is a suitable test sample for driving under the influence of drugs,. Urinalysis is unable to determine the exact time of substance ingestion or the precise concentration of a substance affecting the body in relation to the timing of a traffic accident or driving violation.[41]

Blood

Blood is widely regarded as an optimal biological specimen for toxicological evaluation aimed at detecting psychoactive substances. However, for a blood sample to be obtained in a suspected driving violation, the driver must be transported to a healthcare facility. During this time, the medications in the driver system continue to be metabolised. Therefore, the findings from toxicological assessments may not accurately indicate the concentration of drugs in the driver's bloodstream at the time of the incident, as the substance could have been completely metabolized within the time elapsed since the event.[42]

Oral Fluid

Saliva is a biological sample, an oral fluid composed of substances such as cell debris found in the mouth and particles of swallowed materials, that can be easily and quickly collected at the time of the event compared to blood and urine. Currently, in some countries, oral fluid analysis devices are used during roadside checks to screen for specific drug groups. Rapid and qualitative (positive/negative) results regarding the presence of drugs can be obtained using these devices. Toxicology laboratories can use oral fluid specimens for confirmatory testing, resulting in a full drug panel and quantitative determination of drug concentration.[43]

Biological samples collected from living individuals often include blood (whole blood, plasma, or serum), urine, hair, nails, exhaled air, oral fluid (saliva), and stomach content. For post-mortem investigations, critical samples for toxicological analysis encompass arterial or venous femoral blood, cardiac blood, urine, vitreous fluid, stomach contents, and organ tissues, particularly liver and lungs. Furthermore, under specific circumstances, alternative samples, such as blood clots, blood from the thoracic or abdominal cavities, cerebrospinal fluid, brain tissue, spleen, bile, bone, synovial fluid, bone marrow, skeletal muscle, and larvae may be utilised if traditional samples are unavailable or compromised.[44]

Interpretation of Drug Concentrations in Postmortem Toxicology

Interpreting drug concentrations in postmortem biological samples presents several challenges. For example, urine is a simpler sample than blood or intraocular fluid; however, substance detection in urine is only an indicator of exposure. Concentrations found in urine are usually intermediate to high and may not yield useful information in terms of quantification because there is no correlation with blood levels or toxic effects.[45]

The postmortem alterations in drug concentrations complicate the assessment of a substance's role in fatal road traffic incidents. The chemical and biological degradation processes during human decomposition, however, bring about the fluctuation of drug levels. In addition, the chemical stability of drugs is an important factor to consider. For instance, some substances rapidly decompose other highly volatile compounds, including biological molecules, and are quickly broken down into various states of decomposition after death. In addition, improper handling or long-term storage deteriorates the structural preservation of active pharmaceuticals, leading to incorrect toxicological evaluation.[46]

A study in Wisconsin (2019-2021) examined the blood toxicology results of 8,923 drivers arrested for alcohol-impaired driving after traffic accidents. As drug levels vary with the onset, peak, and duration of action, delays between crashes, arrests, and blood sample collection can reduce accuracy. The findings showed that both blood alcohol (BAC) and delta-9-tetrahydrocannabinol concentrations decreased significantly with longer collection times. Accident severity and the time of day were linked to such delays. Researchers have stressed that measured concentrations may not reflect actual levels at the time of a crash due to ongoing drug metabolism and elimination.[47]

Effectiveness of Legal Regulations

Since the publication of the first global road safety report in 2004, countries have agreed on the adoption of numerous road safety policies, including lowering legal alcohol limits. The World Health Organization

and the European Transport Safety Council have recommended that countries lower their legal BAC limit to 0.05 g/dL to reduce drunk driving and its consequences.[48]

Empirical evidence from multiple studies demonstrates a reduction in the occurrence of alcohol-impaired driving subsequent to the introduction of legal measures and the imposition of statutory penalties. Reducing the BAC limit to 0.05 g/dL has been associated with a 48% decrease in road traffic deaths in Australia, a decrease in alcohol-related fatal accidents in Japan, a 9% decrease in Austria, and a 36% decrease in France (74). 25% A large-scale analysis that decreased the BAC value to 0.05 g/dL and was carried out in 27 European countries led to an 11% reduction in road traffic deaths.[49]

Legal interventions such as lowering BAC limits are considered one of the most effective strategies for reducing drunk driving. Indeed, lowering the BAC to below 0.05 in Japan and Sweden has led to significant decreases in alcohol-related traffic accidents. However, there are also findings that legal regulations are not always as effective as expected. According to a study conducted in Australia, licence restrictions for drunk driving do not provide an effective deterrent, and the tendency to drive under the influence of alcohol reaches its highest level when offenders expect sanctions.[50]

The United Nations aims to reduce deaths and injuries from traffic accidents by 2030 within the framework of the sustainable development goals and in this regard, encourages local governments to effectively implement traffic laws.[1]

CONCLUSION

To reduce the rates of deaths and injuries related to traffic accidents, it is important to develop legal regulations, strengthen inspection mechanisms, and increase awareness campaigns aimed at preventing impaired driving by alcohol and/or other psychoactive substances. In addition to legal intervention, equal importance should be given to other prevention strategies aimed at improving road safety. Implementing multifaceted, holistic policies, such as regulating alcohol sales, community-based education programs, and increasing access to alcohol treatment services, can help raise awareness about and discourage driving under the influence.

MAIN POINTS

- Traffic accidents are a serious global public health concern.
- Vulnerable road users (pedestrians, cyclists, and motorcyclists) accounted for more than half of the deaths.
- Alcohol is the most commonly encountered psychoactive substance in fatal traffic accidents.
- The combination of alcohol and other substances poses a higher risk than either alcohol alone.
- Lowering the blood alcohol concentration limit to 0.05 g/dL has resulted in a significant decrease in traffic fatalities in many countries (Australia, 48%; Japan, 25%; France, 36%).

Footnotes

Authorship Contributions

Concept: C.E.Ö., Design: C.E.Ö., Data Collection and/or Processing: C.E.Ö., Analysis and/or Interpretation: C.E.Ö., Literature Search: C.E.Ö., İ.D., E.H.Y., Writing: C.E.Ö., İ.D., E.H.Y.

DISCLOSURES

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

Financial Disclosure: The authors declared that this study had received no financial support.

REFERENCES

1. WHO. World Health Organization road traffic injuries. 2023. Available from: https://www. who.int/news-room/fact-sheets/detail/road-traffic-injuries
2. Poulos RG, Hatfield J, Rissel C, Flack LK, Murphy S, Grzebieta R, et al. An exposure based study of crash and injury rates in a cohort of transport and recreational cyclists in New South Wales, Australia. Accid Anal Prev. 2015; 78: 29-38.
3. de Guerre LEVM, Sadiqi S, Leenen LPH, Oner CF, van Gaalen SM. Injuries related to bicycle accidents: an epidemiological study in the Netherlands. Eur J Trauma Emerg Surg. 2020; 46(2): 413-8.
4. Cittadini F, Aulino G, Petrucci M, Raguso L, Oliveri ES, Beccia F, et al. Bicycle-related accidents in Rome: investigating clinical patterns, demographics, injury contexts, and health outcomes for enhanced public safety. Injury. 2024; 55(4): 111464.
5. Burford KG, Itzkowitz NG, Rundle AG, DiMaggio C, Mooney SJ. The burden of injuries associated with e-bikes, powered scooters, hoverboards, and bicycles in the United States: 2019-2022. Am J Public Health. 2024; 114(12): 1365-74.
6. Rzepczyk S, Pawlas K, Borowska-Solonynko A, Karnecki K, Cywka T, Moskała A, et al. Fatal traffic accidents involving electric scooters in Poland in 2019-2023. Injury. 2024; 55(11): 111836.
7. Gjerde H, Frost J. Prevalence of alcohol and drugs among drivers killed in road traffic crashes in Norway during 2011-2020. Traffic Inj Prev. 2023; 24(3): 256-61.
8. Kibayashi K, Shimada R, Nakao K-İ. Fatal traffic accidents and forensic medicine. IATSS Research. 2024; 38(1): 71-6.
9. Legrand SA, Gjerde H, Isalberti C, Van der Linden T, Lillsunde P, Dias MJ, et al. Prevalence of alcohol, illicit drugs and psychoactive medicines in killed drivers in four European countries. Int J Inj Contr Saf Promot. 2014; 21(1): 17-28.
10. Papalimperi AH, Athanaselis SA, Mina AD, Papoutsis II, Spiliopoulou CA, Papadodima SA. Incidence of fatalities of road traffic accidents associated with alcohol consumption and the use of psychoactive drugs: a 7-year survey (2011-2017). Exp Ther Med. 2019; 18(3): 2299-306.
11. Blandino A, Cotroneo R, Tambuzzi S, Di Candia D, Genovese U, Zoja R. Driving under the influence of drugs: correlation between blood psychoactive drug concentrations and cognitive impairment. A narrative review taking into account forensic issues. Forensic Sci Int Synerg. 2022; 4: 100224.
12. Porpiglia NM, Tagliaro F, Micciolo R, Canal L, Musile G, Bortolotti F. New evidence of high association between carbohydrate deficient transferrin (CDT) and alcohol-related road traffic accidents. A retrospective study on 929 injured drivers. Forensic Sci Int. 2022; 340: 111438.
13. Papadodima SA, Athanaselis SA, Stefanidou ME, Dona AA, Papoutsis I, Maravelias CP, et al. Driving under the influence in Greece: a 7-year survey (1998-2004). Forensic Sci Int. 2008; 174(2-3): 157-60.

14. Younis NM, Ahmed MM. Road traffic accidents in nineveh province (2017_2021): a retrospective study. J Current Med Res Opinion. 2024; 7(04): 2354-62.

15. Burford KG, Rundle AG, Frangos S, Pfaff A, Wall S, Adeyemi O, et al. Comparing alcohol involvement among injured pedalcycle and motorcycle riders across three national public-use datasets. Traffic Inj Prev. 2024; 25(8): 1023-30.

16. Kirstukaitė B, Paškauskienė A, Chmieliauskas S, Laima S, Vasiljevaitė D, Stasiūnienė J. Forensic assessment of alcohol intoxication in cases of fatal road traffic accidents in Lithuania. Acta Med Litu. 2024; 31(1): 169-76.

17. Hamnett HJ, Ilett M, Izzati F, Smith SS, Watson KH. Toxicological findings in driver and motorcyclist fatalities in Scotland 2012-2015. Forensic Sci Int. 2017; 274: 22-6.

18. Costa N, Silva R, Mendonça MC, Real FC, Vieira DN, Teixeira HM. Prevalence of ethanol and illicit drugs in road traffic accidents in the centre of Portugal: an eighteen-year update. Forensic Sci Int. 2012; 216(1-3): 37-43.

19. Papadopoulos IN, Bonovas S, Kanakaris NK, Konstantiadou I, Nikolopoulos G, Konstantoudakis G, et al. Motor vehicle collision fatalities involving alcohol and illicit drugs in Greece: the need for management protocols and a reassessment of surveillance. Addiction. 2010; 105(11): 1952-61.

20. Bénié Bi Vroh J, Tiembre I, Ekra DK, Ano Ama MN, Ka OM, Ncho Dagnan S, et al. Déterminants des accidents mortels de la circulation routière en côte d'ivoire de 2002 à 2011 [Determinants of fatal road traffic injuries in côte d'ivoire from 2002 to 2011]. Sante Publique. 2016; 28(5): 647-53. French.

21. Ding Y, Zhou J, Yang J, Laflamme L. Demographic and regional characteristics of road traffic injury deaths in Jiangsu Province, China. J Public Health (Oxf). 2017; 39(3): e79-87.

22. Kudryavtsev AV, Nilssen O, Lund J, Grjibovski AM, Ytterstad B. Road traffic crashes with fatal and non-fatal injuries in Arkhangelsk, Russia in 2005-2010. Int J Inj Contr Saf Promot. 2013; 20(4): 349-57.

23. Kelly E, Darke S, Ross J. A review of drug use and driving: epidemiology, impairment, risk factors and risk perceptions. Drug Alcohol Rev. 2004; 23(3): 319-44.

24. Simonsen KW, Linnet K, Rasmussen BS. Driving under the influence of alcohol and drugs in the eastern part of Denmark in 2015 and 2016: abuse patterns and trends. Traffic Inj Prev. 2018; 19(5): 468-75.

25. Fakude CT, Modise RP, Haruna AB, Pillay J, Ozoemena KI. Advances in the application of nanomaterials for the electrocatalytic detection of drugs of abuse. Advanced Sensor and Energy Materials. 2023; 2(2): 100056.

26. UNODC. World Drug Report. 2022. Available from: https://www.unodc.org/unodc/data-and-analysis/world-drug-report-2022.html

27. Bilge S, Dogan-Topal B, Gürbüz MM, Yücel A, Sınağ A, Ozkan SA. Recent advances in electrochemical sensing of cocaine: a review. TrAC Trends in Analytical Chemistry. 2022; 157: 116768.

28. Li Z, Shen F, Mishra RK, Wang Z, Zhao X, Zhu Z. Advances of drugs electroanalysis based on direct electrochemical redox on electrodes: a review. Crit Rev Anal Chem. 2024; 54(2): 269-314.

29. UNODC. World Drug Report. 2024. Available from: https://www.unodc.org/unodc/data-and-analysis/world-drug-report-2024.html

30. NTSB. Alcohol, other drug, and multiple drug use among drivers. (Safety Research Report SR-22-02). Marc B, Ramdani S. Road traffic: global overview of drug and alcohol statistics. 2025; 205-13.

31. Marc B, Ramdani S. Road traffic: global overview of drug and alcohol statistics. Encyclopedia of Forensic and Legal Medicine (Third Edition). 2025; 205-13.

32. L Devlin A, Odell M, L Charlton J, Koppel S. Epilepsy and driving: current status of research. Epilepsy Res. 2012; 102(3): 135-52.

33. Brown T, Milavetz G, Murry DJ. Alcohol, drugs and driving: implications for evaluating driver impairment. Ann Adv Automot Med. 2013; 57: 23-32.

34. Couper FJ, Huestis M, Fulford J, Perkinson N, Miller S, Raymond P, et al. Drugs and human performance fact sheets: 2024 (No. DOT HS 813 650). United States. Department of Transportation. National Highway Traffic Safety Administration. 2024.

35. Hels T, Bernhoft IM, Lyckegaard A, Houwing S, Hagenzieker M, Legrand SA, et al. Risk of injury by driving with alcohol and other drugs. Project No. TREN-05-FP6TR-S07.61320-518404- DRUID.

36. McCartney D, Arkell TR, Irwin C, McGregor IS. Determining the magnitude and duration of acute Δ9-tetrahydrocannabinol (Δ9-THC)-induced driving and cognitive impairment: a systematic and meta-analytic review. Neurosci Biobehav Rev. 2021; 126: 175-93.

37. Simmons SM, Caird JK, Sterzer F, Asbridge M. The effects of cannabis and alcohol on driving performance and driver behaviour: a systematic review and meta-analysis. Addiction. 2022; 117(7): 1843-56.

38. McElroy H, O'Leary B, Adena M, Campbell R, Tahami Monfared AA, Meier G. Comparison of the effect of lemborexant and other insomnia treatments on driving performance: a systematic review and meta-analysis. Sleep Adv. 2021; 2(1): zpab010.

39. Yıldırım EF, Gürler M, Gürbüz A. Determination of alcohol from biochemical perspective and its importance in forensic sciences. J Ankara Univ Fac Med. 2024; 77(1): 1-6.

40. Johnson OE, Miskelly GM, Rindelaub, JD. Testing for cannabis intoxication: current issues and latest advancements. WIREs Forensic Sci. 2021; 4(10): e1450.

41. D'Orazio AL, Mohr ALA, Chan-Hosokawa A, Harper C, Huestis MA, Limoges JF, et al. Recommendations for toxicological investigation of drug-impaired driving and motor vehicle fatalities-2021 update. J Anal Toxicol. 2021; 45(6): 529-36.

42. Ferrari D, Manca M, Premaschi S, Banfi G, Locatelli M. Toxicological investigation in blood samples from suspected impaired driving cases in the Milan area: possible loss of evidence due to late blood sampling. Forensic Sci Int. 2018; 288: 211-7.

43. Sarris GG, Abbott DL, Moreno TM, Maychack KJ, Limoges JF. Development and validation of a simple chromatographic method to screen oral fluid samples for drugs in DUID investigations. J Anal Toxicol. 2024; 48(8): 528-34.

44. Dinis-Oliveira RJ, Carvalho F, Duarte JA, Remião F, Marques A, Santos A, et al. Collection of biological samples in forensic toxicology. Toxicol Mech Methods. 2010; 20(7): 363-414.

45. Dinis-Oliveira RJ, Vieira DN, Magalhães T. Guidelines for collection of biological samples for clinical and forensic toxicological analysis. Forensic Sci Res. 2017; 1(1): 42-51.

46. Butzbach DM, Stockham PC, Kobus HJ, Sims DN, Byard RW, Lokan RJ, et al. Stability of serotonin-selective antidepressants in sterile and decomposing liver tissue. J Forensic Sci. 2013; 58(Suppl 1): S117-25.

47. Price JM, Smith RC, Miles AK, Kayagil TA. Delays in blood collection and drug toxicology results among crash-involved drivers arrested for impaired driving. Traffic Inj Prev. 2024; 25(5): 667-72.

48. Nazif-Munoz JI, Anakök GA, Joseph J, Uprajhiya SK, Ouimet MC. A new alcohol-related traffic law, a further reduction in traffic fatalities? Analyzing the case of Turkey. J Safety Res. 2022; 83: 195-203.

49. Castillo-Manzano JI, Castro-Nuño M, Fageda X. Can health public expenditure reduce the tragic consequences of road traffic accidents? The EU-27 experience. Eur J Health Econ. 2014; 15(6): 645-52.

50. Jung E, Ro YS, Park JH, Song KJ, Ryu HH, Shin SD. Implementation of the new acts on driving under the influence of alcohol and clinical outcomes for patients severely injured in road traffic crashes. Traffic Inj Prev. 2024; 25(7): 887-93.

RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-22
Cyprus J Med Sci 2025;10(5):301-307

Clinical Implications of the Celiac Artery Variations: MDCT Angiography Study on TRNC Population

Yasemin Küçükçiloğlu[1], Akinola Abraham Olonade[2], Mehtap Tiryakioğlu[2]

[1]Department of Radiology, Near East University Faculty of Medicine, Nicosia, North Cyprus
[2]Department of Anatomy, Near East University Faculty of Medicine, Nicosia, North Cyprus

Abstract

BACKGROUND/AIM: Variations in the origin, course, and branching pattern of the celiac trunk (CT) have been well-documented in various populations with clinical implications for surgical and radiological procedures in the abdomen. However, the prevalence and characteristics of CT variations in the Turkish Republic of Northern Cyprus population have not been well studied.

MATERIALS AND METHODS: Abdominal multi-detector computed tomography (MDCT) angiography examinations of 500 patients and were retrospectively evaluated by a radiologist in the radiology department of our hospital. The examinations were performed with a 256-detector CT scanner. A thorough evaluation of 108 patients was performed. Eighty-three of these patients were male (M), and twenty-five were female (F). The age ranges were from 19-78 (F: 26-78, M: 19-78).

RESULTS: Results showed that branching of the CT into the left gastric artery (LGA), common hepatic artery, and splenic artery is the predominant branching pattern in 74 patients 68.5%. However, variations in the branching pattern of the CT were observed in 34 patients 31.5% (30 M and 4 F). Furthermore, this study reported an unreported branching pattern of the CT, where a patient had the LGA originating from the right inferior phrenic artery; and this was associated with the gastrosplenic trunk.

CONCLUSION: Understanding the scope of these variations is of clinical importance in patients undergoing preoperative radiological evaluations, hepatic transplants, and open gastrostomies. Lack of awareness regarding these variations can significantly impact radiologic interventions and pre/post-operative planning of surgical procedures involving the gastrointestinal system.

Keywords: Celiac trunk, celiacomesenteric trunk, gastrosplenic trunk, hepatomesenteric trunk, anatomic variations, MDCT

INTRODUCTION

The celiac trunk (CT), which is the first anterior and often the largest visceral branch of the abdominal aorta (AA), arises immediately after the descending thoracic aorta passes through the aortic hiatus between the crura of the diaphragm at the level of the 12th thoracic vertebra posterior to the median arcuate ligament.[1,2] As noted by Marco-Clement et al.[3], an excellent understanding of the vascular anatomy of the abdominal cavity is crucial for surgical intervention on abdominal organs such as the liver, pancreas, spleen, etc. To underscore the importance of having a detailed awareness of vascular anatomy, Omar et al.[2] submitted that the presence of variations in the vascular supply of an organ impacts the surgical approach to intervention. Variations in the origin, course, branching pattern, and diameter of the CT have been well-documented in various populations with clinical implications for surgical and radiological procedures in the abdomen.[2] However, the prevalence and characteristics of CT variations in the Turkish Republic of Northern Cyprus (TRNC) population have not been well-studied.

To cite this article: Küçükçiloğlu Y, Olonade AA, Tiryakioğlu M. Clinical implications of the celiac artery variations: MDCT angiography study on TRNC population. Cyprus J Med Sci. 2025;10(5):301-307

ORCID IDs of the authors: Y.K. 0000-0002-1572-1375; A.A.O 0000-0002-2345-3630; M.T. 0000-0001-7176-2764.

Corresponding author: Yasemin Küçükçiloğlu
E-mail: yasemin.kucukcioglu@neu.edu.tr
ORCID ID: orcid.org/0000-0002-1572-1375

Received: 17.04.2025
Accepted: 10.09.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

During embryonic development, CT forms due to the union of three arterial roots: the dorsal aorta, the vitelline artery, and the dorsal pancreatic artery. The embryological development of the CT begins in the fourth week of gestation when the primitive gut tube develops by folding and fusion of the endoderm and mesoderm layers. The dorsal aorta arises from the posterior aspect of the primitive heart and extends caudally, giving off segmental branches to the somites and intermediate mesoderm.[4] The vitelline artery, on the other hand, arises from the yolk sac and enters the embryo through the umbilical ring parallel to the gut tube. The dorsal pancreatic artery arises from the dorsal aorta and grows toward the developing pancreas. The fusion of these three arteries gives rise to the CT, which typically branches into the left gastric artery (LGA), the splenic artery (SA), and the common hepatic artery (CHA).[5] The complex and dynamic process of angiogenesis, vasculogenesis, and remodeling in the early embryo can lead to various CT variations, which have significant clinical implications for surgical and radiological procedures in the abdomen, such as trans-arterial chemoembolization (TACE) of the hepatopancreatic area, organ transplantation, metastatic tumor management.[6,7]

To date, no published study has investigated the prevalence and types of CT variations in the TRNC population, which has a unique geographical location and ethnic diversity. These variations can have significant clinical implications, affecting surgical and radiological procedures, and can lead to various iatrogenic pathologies if not properly understood. Detailed knowledge of the vascular anatomy of the CT is crucial to the success of many liver-related procedures. This knowledge provides a guide to the topography of liver vasculature, including procedural interventions such as TACE, trans-arterial radioembolization (TARE), and tumor resection. It is therefore imperative to examine the CT variations in the TRNC population using multi-detector computed tomography (MDCT) angiography and to compare the findings with the literature.

MATERIALS AND METHODS

Abdominal MDCT angiographies of 500 Turkish Cypriot patients were retrospectively evaluated, in the radiology department by a radiologist of our hospital. The examinations were performed with a 256-detector CT scanner (Somatom Definition Siemens Healthcare, Erlangen, Germany) with 120 mL of iodinated contrast material (Iobitridol, 350/200 mL, Guebert, Villepinte, France); scanning from the level of the diaphragm to the iliac bifurcation, using a bolus tracking system at the level of the descending aorta. The scanning parameters were as follows: kVp: 140, mAs: 34, slice thickness: 1 mm.

After excluding examinations of nonlocal patients living in TRNC and cases with an abdominal mass or who have undergone any surgical procedure, a thorough evaluation of 108 patients was performed. Eighty-three of these patients were male (M). Twenty-five were female (F), and the age ranges were between 19-78 (F: 26-78, M: 19-78).

The study was approved by the Near East University Faculty of Medicine Institutional Review Board (approval number: 2019/73-906, date: 24.10.2019). All participants included in this study provided informed consent.

Statistical Analysis

To analyze the variations of the CT, observed in this study, the classification approach of Ethiraj et al.[5] was followed. Five main branching patterns grouped into five types were identified in all 108 cases reviewed. Variations of the CT and its branches were noticed in 34 (31.5%) patients (30 M, 4 F). In addition, sub-branching patterns were further classified according to the main branching pattern with which they occurred. Using the Statistical Package for the Social Sciences software, descriptive statistics were used to calculate the frequencies and percentages of the branching patterns. The result obtained from the statistical analysis was tabulated and presented in Table 1.

Table 1. Five types of the CT's main branching pattern as well as the branching pattern of the subbranches, reported in this study

Type	Sub-type	CT's main branching pattern	CT sub-branching pattern/variation	n	%
1	a	Trifurcation	No variations	74	68.5%
	b	Trifurcation	rRHA from SMA	10	9.3%
	c	Trifurcation	LHA from LGA	6	5.6%
	d	Trifurcation	rLHA from LGA, accRHA from GDA	1	0.9%
	e	Trifurcation	Long CT, rLHAfrom LGA, accRHA from SMA	1	0.9%
	f	Trifurcation	accLGA from LHA	1	0.9%
	g	Trifurcation	Lat branch of LHA originated from LGA	3	2.8%
2		CMT		1	0.9%
3	a	GST + rCHA from aorta		4	3.7%
	b	GST	rLHA from LGA, GDA separately from the aorta, rRHA from SMA	1	0.9%
	c	GST	rRHA from SMA, rLHA, and rGDA originate from SA with a common trunk (rGDA separates at the level of porta hepatis)	1	0.9%
	d	GST + HMT		3	2.8%
4		HGT + SMT		1	0.9%
5		HST + GPT		1	0.9%
Total				108	100

CT: Celiac trunk, CMT: Celiacomesenteric trunk, GST: Gastrosplenic trunk, HMT: Hepatomesenteric trunk, SMT: Splenomesenteric trunk, HST: Hepatosplenic trunk, GPT: Gastrophrenic trunk, SMA: Superior mesenteric artery, LHA: Left hepatic artery, rCHA: Replaced common hepatic artery, rLHA: Replaced left hepatic artery, rRHA: Replaced right hepatic artery, LGA: Left gastric artery, accLGA: Accessory left gastric artery, rGDA: Replaced gastroduodenal artery, SA: Splenic artery, accRHA: Accessory right hepatic artery.

RESULTS

In Type 1a, we observed classical branching of the CT into the LGA, CHA, and SA, with no further observable variation in the distribution of the end arteries in 74 (68.5%) patients (Figure 1A). In Type 1b, a normal CT showing the origin of a replaced right hepatic artery (rRHA) from the superior mesenteric artery (SMA) was observed in 10 (9.3%) patients (Figure 1B). Type 1c showed a normal CT of a replaced left hepatic artery (rLHA) from LGA in 6 (5.6%) cases. Type 1d showed normal CT with rLHA originating from LGA and accessory right hepatic artery (accRHA) from the gastroduodenal artery (GDA) in 1 (0.9%) case (Figure 1C). Type 1e showed a normal CT with rLHA originating from LGA, an accRHA from SMA, present in 1 case (0.9%). Type 1f showing a normal CT with accessory left gastric artery (accLGA) from LHA was observed in 1 (0.9%) patient (Figure 1D), while Type 1g describes an abnormally long classical CT with the lateral branch of LHA originating from LGA in 3 (2.8%) patients.

In Type 2, we observed that the CT and SMA originated as a single trunk to form the celiacomesenteric trunk (CMT) in one (0.9%) patient (Figure 2).

Type 3a shows a gastrosplenic trunk (GST) + replaced CHA originating directly from the aorta in 4 (3.7%) patients. Also seen in a patient with this type of branching, was a long distance between the aortic orifice of the AA and CT of 7.7 cm (Figure 3A). Type 3b shows GST + rLHA originating from the LGA, GDA originating separately from the aorta, and rRHA originating from the SMA in 0.9% of cases. In Type 3c, we observed a GST with rRHA originating from SMA, while rLHA and replaced gastroduodenal artery (rGDA), originating from SA, were with a common trunk in 1 (0.9%) case (Figure 3B). It was also observed that the rGDA separates itself from adjacent structures at the level of the porta hepatis. Type 3d shows GST with hepatomesenteric trunks in 3 (2.8%) cases (Figure 3C). Type 4 shows hepatogastric trunk (HGT) alongside splenomesenteric trunk in one (0.9%) patient (Figure 4). Type 5 describes a hepatosplenic trunk (HST) with a gastrophrenic trunk [GPT-LGA, and right inferior phrenic artery (RIPA)] seen in 1 (0.9%) case (Figure 5).

DISCUSSION

One of the most consequential factors that impacts the outcome of surgical procedures is the proper understanding of the vascular anatomy of the area surgical intervention. A lack of detailed knowledge of vascular variations could result in negative patient outcomes or iatrogenic

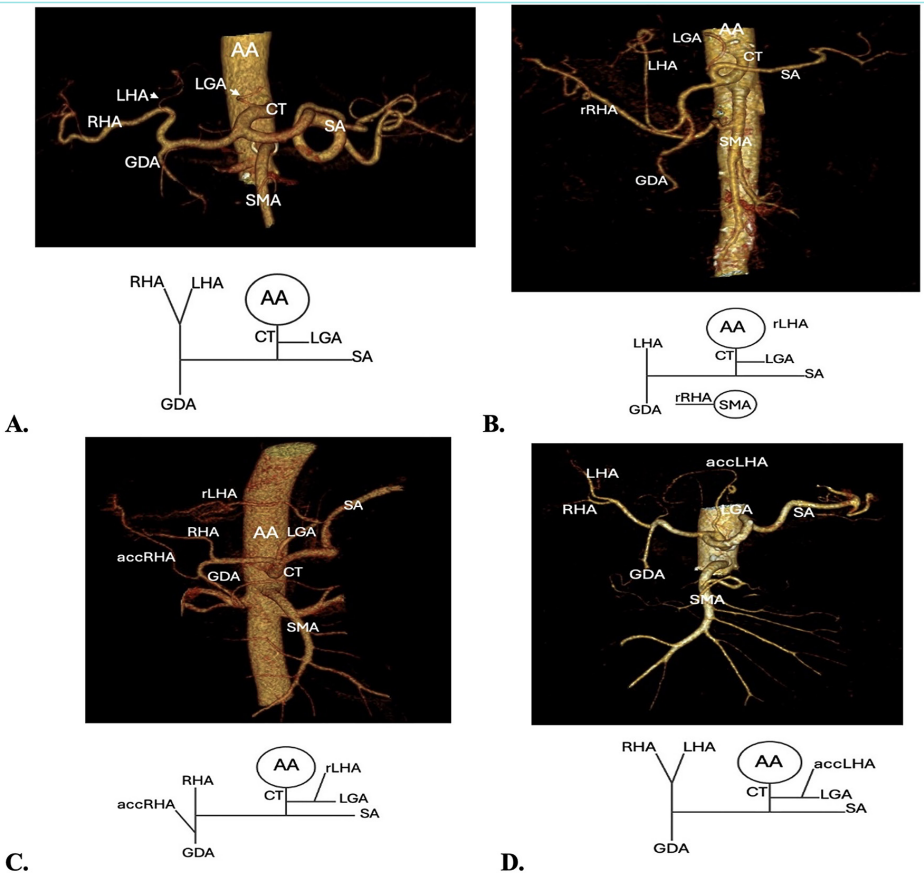


Figure 1. A. Type 1a shows abdominal aorta (AA), celiac trunk (CT), splenic artery (SA), left gastric artery (LGA), superior mesenteric artery (SMA), left hepatic artery (LHA), right hepatic artery (RHA), and gastroduodenal artery (GDA). **B.** Type 1b shows AA, CT, SA, LGA, SMA, LHA, replaced right hepatic artery (rRHA), and GDA. C. Type 1d shows AA, CT, SA, LGA, SMA, RHA, replaced left hepatic artery (rLHA), accessory right hepatic artery (accRHA), and GDA. D. Type 1f shows AA, CT, SA, LGA, accLGA, LHA, RHA, and GDA.

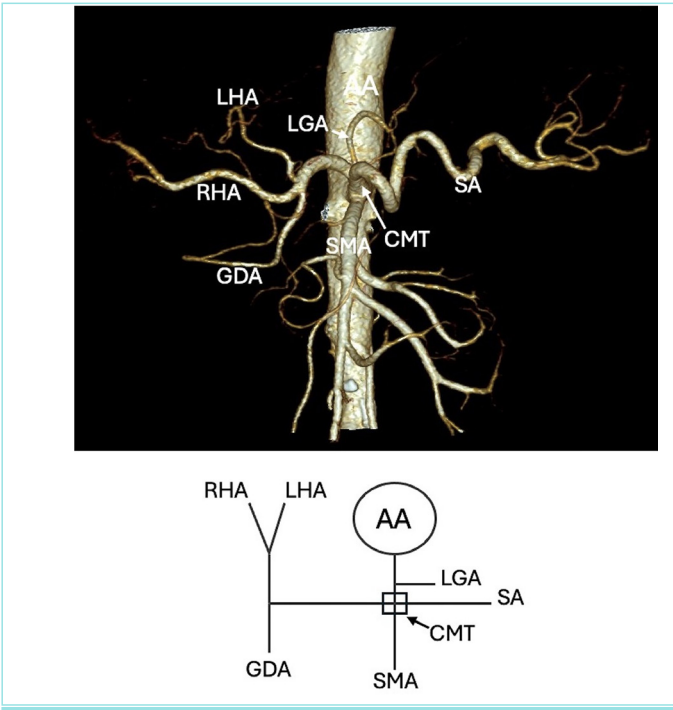


Figure 2. Type 2 shows abdominal aorta (AA), celiacomesenteric trunk (CMT), splenic artery (SA), left gastric artery (LGA), superior mesenteric artery (SMA), left hepatic artery (LHA), right hepatic artery (RHA), and gastroduodenal artery (GDA).

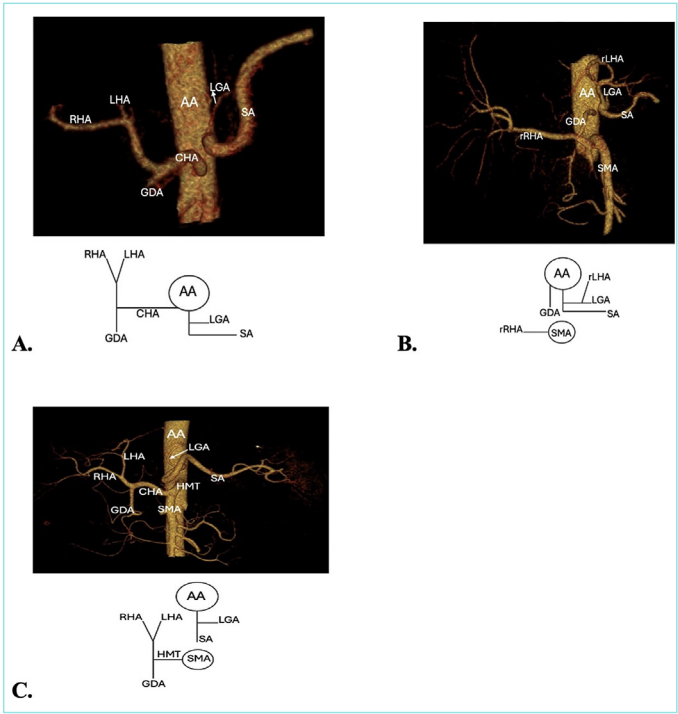


Figure 3. A. Type 3a shows abdominal aorta (AA), common hepatic artery (CHA), splenic artery (SA), left gastric artery (LGA), left hepatic artery (LHA), right hepatic artery (RHA), and gastroduodenal artery (GDA). **B.** Type 3c shows AA, SA, LGA, superior mesenteric artery (SMA), replaced left hepatic artery (rLHA), replaced right hepatic artery (rRHA), and replaced gastroduodenal artery (rGDA). C. Type 3d shows gastrosplenic trunk (GST) and hepatomesenteric trunk (HMT) originated from the AA.

injury to tissues and organs during surgical intervention.[8] According to Marco-Clement et al.[3], the clinical implications of having a thorough knowledge of the variations in the CT scans when planning for upper abdominal surgeries and radiological interventions are crucial to ensure a positive post-operative outcome in patients. Detailed awareness of the source, branching, and deviation from the norm of the CT is of utmost clinical importance when planning for surgical interventions such as digital subtraction angiography, as well as procedural interventions in the abdomen such as TACE, TARE, and tumor resection.[9] Omar et al.[2] acknowledged that precise knowledge of anatomical variations could determine surgical techniques and subsequent outcomes in patients. The study highlighted that lack of awareness regarding vascular variations can negatively impact surgical outcomes in patients. According to a case report by Roma et al.[10] published to elucidate the vascular anomalies of CT and its implications in the treatment of hepatocellular carcinoma using TACE, the importance of having detailed knowledge regarding the incidence, clinical and developmental significance of CT variations, particularly during invasive arterial procedures or abdominal surgeries, was highlighted. The study emphasized that precise identification of CT variations is germane for the success of surgical procedures such as endovascular treatment of unresectable malignant liver tumors and orthotopic liver transplantations. Ethiraj et al.[5] reported that an accurate understanding of the vascular anatomy and branching patterns of the CT in procedures involving splenectomy and gastrectomy using the Appleby technique can prevent iatrogenic injury of the CHA and mitigate the risk to surrounding vessels such as the mesenteric arteries.

The CT is a well-studied vessel due to its clinical and physiological importance in providing arterial blood to the foregut and its derivatives. As established in the literature, 15 variants of the CT have been identified.[8] Of all the variations of the CT, the trifurcation of the CT into CHA, LGA, and SA is considered the normal branching pattern.[5,9] Song et al.[11], in their study on CHA and CT variations in 5002 patients, observed 13 types of CT variations and reported the incidence of normal branching at 89.1%. Ugurel et al.[6] noted that the frequency of normal CT varies between 72% and 90%. In this study, as shown in Figure 1A, we observed that the normal branching of the CT in 74 patients (68.5%) was consistent with reports from numerous studies, which indicate that trifurcation of the CT into its classical branches remains the dominant branching type.[2,3] However, some studies have reported a lower incidence of this branching type.[5] Normal branching of the CT ensures adequate vascularization of abdominal organs, improves pre-operative and post-operative management techniques, and mitigates the risks of iatrogenic injuries that may occur during surgical manipulations in the abdomen.

Bifurcation of the CT has been observed and reported in the literature. According to Santos et al.[9], the incidence of bifurcation of the CT is 12%. However, in a retrospective study conducted on 100 patients by Ugurel et al.[6], 89% and 8% of the cases studied had trifurcation and bifurcation of the CT, respectively.[6] Their study also observed that accessory renal arteries increase the likelihood of variations in the CT and hepatic arteries.[6] Prakash et al.[12] reported the bifurcation of the CT into CHA and SA. Bifurcation of the CT can present enormous challenges to interventional radiologists and surgeons during preoperative procedural planning of transcatheter arterial chemoembolization in hepatic

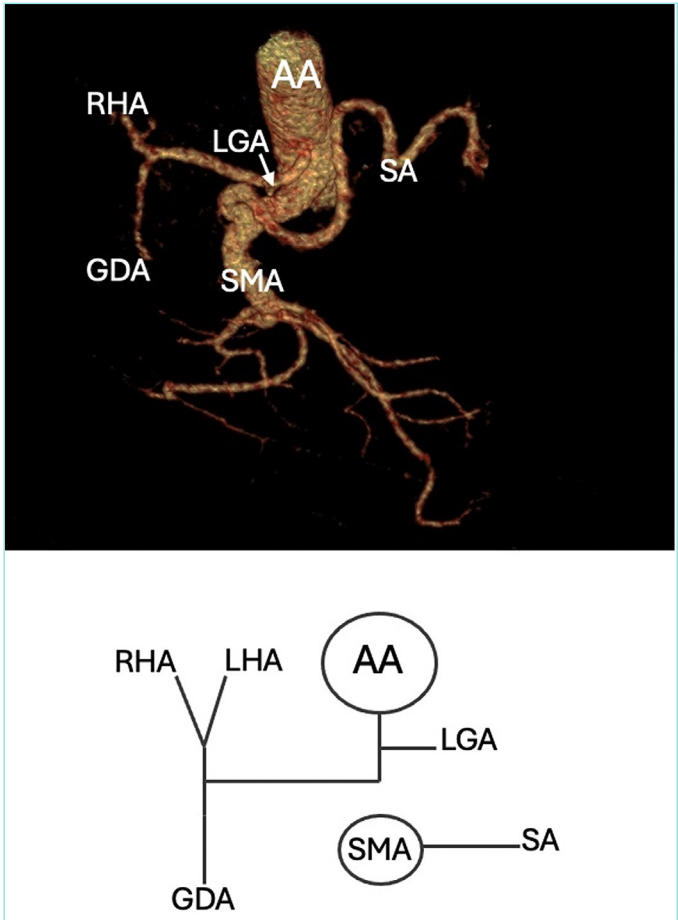


Figure 4. Type 4 shows abdominal aorta (AA), splenic artery (SA), left gastric artery (LGA), superior mesenteric artery (SMA), right hepatic artery (RHA), and gastroduodenal artery (GDA).

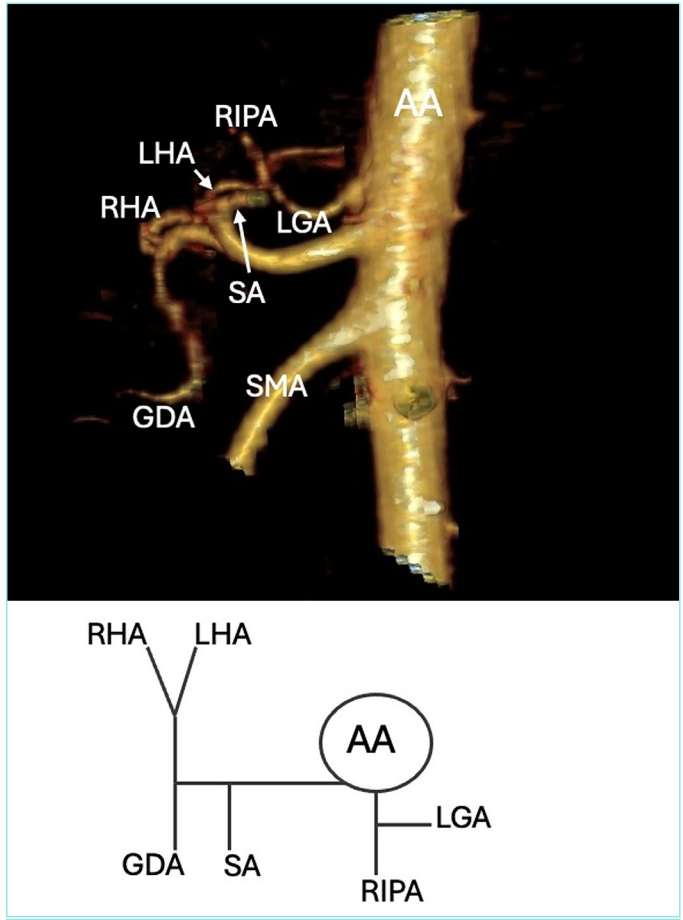


Figure 5. Type 5 showing abdominal aorta (AA), gastrophrenic trunk (GPT), hepatosplenic trunk (HST), splenic artery (SA), left gastric artery (LGA), superior mesenteric artery (SMA), left hepatic artery (LHA), right hepatic artery (RHA), replaced right inferior phrenic artery (rRIPA) and gastroduodenal artery (GDA).

tumors and liver transplants.[10] Iatrogenic injuries to abdominal viscera such as the liver, pancreas, spleen, and others due to postoperative complications of a bifurcated CT, have been reported.[6] According to a study by Pinal-Garcia et al.[13], the CT bifurcated in 7.1% of the cadaveric dissections. Bifurcation of the CT into the CHA and SA (HST), with the LGA originating from the AA, was seen in 33.3% of the cases observed. Bifurcation of the CT into SA and LGA (splenogastric trunk) was found in 25%, with the CHA arising from the SMA. Also, the study reported that the CT bifurcated into the CHA and LGA (HGT) while the SA arose from the SMA in 8.3% of the observed cases.[13]

In our study, we observed the bifurcation of the CT, which was named and classified according to the branches arising from the bifurcation point (Table 1). We observed the bifurcation of the CT into the HST with the LGA arising from RIPA as a GPT in 0.9% of the cases (Figure 5). To our knowledge, this branching variant has not been reported in the literature. In comparison, bifurcation of the CT into the GST was observed in 3.7% of the cases, with the CHA arising from the AA (Figure 3A). In a patient (0.9%), with the incidence of a GST, as shown in Figure 3B, we observed that the rRHA originated from the SMA, with an rLHA and rGDA originating from the SA. Complex sub-branching patterns, such as this, increase the challenges faced by surgeons and interventional radiologists during surgical procedures such as hepatobiliary carcinoma resection, liver resections, and hepato-pancreatico-duodenal interventional surgeries. Also, bifurcation of the CT, into the HGT with the SA arising from the SMA was observed in 1 patient (0.9%) (Figure 4).

The absence of an artery can impact the development and functioning of an organ if there is a lack of or insufficient collateral supply to that organ.[14] According to Marco-Clement et al.[3], the absence of CT does not have an embryologic explanation. It can present major clinical complications in patients with hepatocellular carcinomas, among other pathologies involving the abdominal region. This is especially concerning when there is poor collateral supply to compensate for the missing vessel, as the arterial supply to major organs is significantly altered.[2,9,15] Başar et al.[16] reported agenesis of the CT in which all the major organs that receive arterial blood from the CT and its branches were vascularized by a single artery. According to Van den Broecke et al.[17], CT is considered absent if the CHA, LGA, and SA arise independently from the AA. This study did not observe the complete absence of the CT in any of the patients evaluated. While rare, as noted by Omar et al.[2], the lack of CT can result in significantly altered blood supply to the stomach, pancreas, liver, spleen, and parts of the duodenum vascularized by its terminal branches. This type of variation can lead to the disruptive physiological functioning of these organs, complicating surgical interventions, and can result in fatal complications due to malnutrition and avascular necrosis of the affected organs.

The HST, described as the union of the CHA with the SA to form a common trunk with a separate LGA origin, was reported by Song et al.[11] as the most common variation of the CT. However, Ugurel et al.[6] found that the GST was the most observable variation (4%), followed by the HST (3%).

The GST as a variation of the CT is well reported: for example, Lipshutz[18] reported a GST with CHA arising from AA at an incidence of 4%, while Adachi reported a 2% incidence of a GST with CHA arising from the SMA.[19] Also, Song et al.[11] reported the incidence of GST as 0.22%. However, in our study, three patients had SMA originating from CHA (hepatomesenteric trunk) with GSTs, comprising 2.8% (Figure 3C).

There are reports of variants formed by the union of the CT with other branches of AA, in the literature. For instance, Adachi, in his study on 252 cadaveric specimens, reported a CMT, the union of CT and the SMA to form a single trunk, with an incidence of 2.4%.[19] Sangster et al.[14] reported that the presence of this type of variation deprives a patient of the dual vascular supply to the abdominal viscera: the liver, gall bladder, stomach, and parts of the small intestine, thereby elevating the risk of atherosclerosis or other vascular complications to the abdominal viscera. Marco-Clement et al.[3] attributed the development of this branching pattern to the persistence of large primitive ventral anastomoses between the developing superior mesenteric groups and the CT despite the regression of the 10th and 12th vitelline arteries. The scholarly report of Omar et al.[2] attests to this claim. Furthermore, a study by Matusz et al.[20] reported an unusual case in a small percentage of individuals where the CT originated from SMA. As shown in Figure 2, we observed the CMT in 1 patient (0.9%). Awareness of this variation among clinicians and interventional radiologists is of utmost importance during preparations for surgical interventions in the abdominal region, as it can significantly affect the blood supply to critical digestive organs.

Various classifications of CT variations, including types and subtypes, have been proposed, with some widely accepted among scholars and clinicians.[3,18] However, with the introduction of improved imaging techniques, the emergence and detailed observation of new variants that do not conform to established descriptions in the literature are on the rise. A study by Ugurel et al.[6] attributed the existence of such variants to complex embryogenesis involved in the development of the branches of the AA. In this study, the CHA originated directly from the aorta, while the LGA and SA branched off from the AA as the GST in four cases (3.7%) (Figure 3A). This variant supports the report of a study conducted by Lipshutz.[18] Ugurel et al.[6] highlighted the shared origin of branches of the AA to form a trunk. This variation is clinically significant due to the altered patterns of blood supply to the liver and intestines, which may influence procedural strategies for treating diseases in these organs.

Observations and reports of anomalous or accessory branches arising from the main branches of the CT have been documented. Our study observed and documented several variations in the branching pattern of the hepatic artery proper, one of the terminal branches of the CHA. In one patient, a rRHA arose as a branch of the SMA (Figure 1B), and an rLHA originated from the LGA. As shown in Figure 1C, a rLHA arose from LGA, while an accRHA branched from the SMA in a patient (0.9%). We also observed an abnormally long CT with an AA-CT distance of 7.7 cm. The incidence of this branching type can present a complex challenge to surgeons and interventional radiologists who lack awareness of it. In this case, the risk of iatrogenic injury to the CT is significantly elevated. In three patients, the anterior branch of the LHA originated from the LGA. Accessory LGA, is a rare variation of the LGA that should be kept in mind during the surgical interventions in the region particular to the aneurysms. It may originate either from the LGA or LHA.[21] In one case (Figure 1D), we observed the accLGA originating from the LHA (0.9%).

In some patients (10%), the rRHA originated from the SMA, while in others, 7% of the rLHA originated from the LGA. The percentage of appearance of rLHA was reported between 10-12% in Walker's[22] scholarly work, and Joshi et al.[23], and Kavitha[24] reported a 5% presence of rLHA in their studies. Ethiraj et al.[5] explained that branching of the right lateral hepatic artery (rLHA) from the LGA to supply segments 2 and 3 in left lobe donors is advantageous as it reduces the risk of injury to the remaining liver. However, Asif et al.[25] found that a rRHA can significantly increase the risk of thrombosis and hepatic artery stenosis in liver transplant recipients. This can increase the likelihood of iatrogenic injuries during surgical procedures like hepatobiliary hilar surgery, cholecystectomy, and pancreaticoduodenectomy.

Understanding the existence and extent of aberrant or accessory arteries in the body. A recent report by Cirocchi et al.[26] found that some patients undergoing preoperative radiological evaluations, hepatic transplants, and open gastrostomies had accessory or aberrant left hepatic arteries that originated from the left gastric arteries.

Failure to recognize these variations can have a significant impact on radiologic interventions and surgical procedures involving the gastrointestinal system, both before and after the operation.

Study Limitations

Our study has some limitations. The most important limitation is the small size of the study group. We believe that further studies with larger study groups may reveal previously unreported variations of CTA. The second limitation is the low quality of some figures, which can be attributed to patient or technical issues.

CONCLUSION

MDCT angiography enabled accurate and detailed observation of the vascular anatomy with CT. This study elucidated the variability of the celiac artery in the TRNC population and established the presence of previous unreported variations of clinical importance. CT variations can pose challenges for radiologists when interpreting imaging studies. Misinterpreting these variations may lead to inaccurate diagnoses of diseases and impaired treatment planning, underscoring the necessity of radiologists' familiarity with these anatomical anomalies. In the literature, a case exists where a rare CT variation played a crucial role in identifying an unknown deceased person. Therefore, understanding these variations can aid forensic experts in reconstructing the individual's identity and determining the cause of death.

Furthermore, surgical procedures involving the organs supplied by the CT are particularly affected by variations. Therefore, extensive knowledge of these variations of the CT is crucial in procedures such as liver transplantation and other surgical interventions, as it allows for better surgical planning and decreased postoperative complications.

MAIN POINTS

- The use of multi-detector computed tomography angiography enabled accurate and detailed observation of the vascular anatomy of the celiac trunk.

- This study elucidated the variability of the celiac artery in the Turkish Republic of Northern Cyprus population and established the presence of previously unreported variations of clinical importance.
- Misinterpreting these variations may lead to inaccurate diagnoses of diseases and impaired treatment planning, underscoring the necessity of radiologists' familiarity with these anatomical anomalies.

ETHICS

Ethics Committee Approval: The study was approved by the Near East University Faculty of Medicine Institutional Review Board (approval number: 2019/73-906, date: 24.10.2019).

Informed Consent: Patients signed informed consent regarding publishing their data.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Y.K., Concept: Y.K., A.A.O., M.T., Design: Y.K., A.A.O., M.T., Data Collection and/or Processing: Y.K., A.A.O., M.T., Analysis and/or Interpretation: Y.K., A.A.O., M.T., Literature Search: Y.K., A.A.O., M.T., Writing: Y.K., A.A.O., M.T.

DISCLOSURES

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

Financial Disclosure: The authors declared that this study had received no financial support.

REFERENCES

1. Bajzer CT. Abdominal aorta and mesenteric arteries. In: Bhatt DL, editor. Guide to Peripheral and Cerebrovascular Intervention. London: Remedica; 2004.
2. Omar R, Kisansa M, Dehnavi AD. The prevalence of anatomical variants of the coeliac trunk and renal arteries on contrast-enhanced abdominal computed tomography scans at Dr George Mukhari Academic Hospital. SA J Radiol. 2021; 25(1): 1990.
3. Marco-Clement I, Martinez-Barco A, Ahumada N, Simon C, Valderrama JM, Sanudo J, et al. Anatomical variations of the celiac trunk: cadaveric and radiological study. Surgical Radiol Anat. 2016; 38(4): 501-10.
4. Sadler TW. Langman's Medical Embryology. 14th edition. Wolters Kluwer. Philadelphia: 2019.
5. Ethiraj D, Kalyanasundaram S, Indiran V, Varadan B, Subbiah K, Srinivas S, et al. Newly proposed classification of celiac artery variations based on embryology and correlation with computed tomography angiography. Pol J Radiol. 2022; 18(87): 563-73.
6. Ugurel MS, Battal B, Bozlar U, Nural MS, Tasar M, Ors F, et al. Anatomical variations of hepatic arterial system, coeliac trunk and renal arteries: an analysis with multidetector CT angiography. Br J Radiol. 2010; 83(992): 661-7.
7. Yüksel M, Yalin A, Weinfeld AB. Concurrentanomalies of the abdominal arteries: an extremelylongcoeliactrunk, an inferiorphrenictrunk, and an aberrantrighthepaticartery. Kaibogaku Zasshi. 1998; 73(5): 497-503.
8. Thangarajah A, Parthasarathy R. Celiac axis, common hepatic and hepatic artery variants as evidenced on MDCT angiography in South Indian Population. J Clin Diagn Res. 2016; 10(1): 1-5.
9. Santos PVD, Barbosa ABM, Targino VA, Silva NA, Silva YCM, Barbosa F, et al. Anatomical variations of the celiac trunk: a systematic review. Arq Bras Cir Dig. 2018; 31(4): 1403.
10. Roma S, D'Amato D, Ranalli T, Nardone V, Pace C, Lenci I, et al. Vascular anomalies of the celiac trunk and implications in treatment of HCC with TACE. Description of a case and review of the literature. Radiol Case Rep. 2019; 14(10): 1221-7.
11. Song SY, Chung JW, Yin YH, Jae HJ, Kim HC, Jeon UB, et al. Celiac axis and common hepatic artery variations in 5002 patients: systematic analysis with spiral CT and DSA. Radiology. 2010; 255(1): 278-88.
12. Prakash, Rajini T, Mokhasi V, Geethanjali BS, Sivacharan PV, Shashirekha M. Coeliac trunk and its branches: anatomical variations and clinical implications. Singapore Med J. 2012; 53(5): 329-31.
13. Pinal-Garcia DF, Nuno-Guzman CM, Gonzalez-Gonzalez ME, Ibarra-Hurtado TR. The Celiac trunk and its anatomical variations: a cadaveric study. J Clin Med Res. 2018; 10(4): 321-29.
14. Sangster G, Ramirez S, Previgliano C, Al Asfari A, Hamidian Jahromi A, Simoncini A. Celiacomesenteric trunk: a rare anatomical variation with potential clinical and surgical implications. J La State Med Soc. 2014; 166(2): 53-5.
15. Badagabettu SN, Padur AA, Kumar N, Reghunathan D. Absence of the celiac trunk and trifurcation of the common hepatic artery: a case report. J Vasc Bras. 2016; 15(3): 259-62.
16. Başar R, Onderoğul S, Cumhur T, Yüksel M, Olçer T. Agenesis of the celiac trunk: an angiographic case. Kaibogaku Zasshi. 1995; 70(2): 180-2.
17. Van den Broecke M, Leenknegt B, Delrue L. Absence of the celiac trunk. J Belg Soc Radiol. 2019; 103(1): 15.
18. Lipshutz B. A composite study of the coeliac axis artery. Ann Surg. 1917; 65(2): 159-69.
19. Adachi B. Das Arteriensystem der Japaner. Vol. 2, Verlag der Kaiserlich-JapanischenUniversitatzuKyoto. 1928.
20. Matusz P, Miclaus GD, Ples H, Tubbs RS, Loukas M. Absence of the celiac trunk: case report using MDCT angiography. Surg Radiol Anat. 2012; 34(10): 959-63.
21. Tomosugi T, Takahashi T, Kawase Y, Yoshida K, Hayashi S, Sugiyama T, et al. Accessory left gastric artery aneurysms in granulomatosis with polyangiitis: a case report and literature review. Nagoya J Med Sci. 2017; 79(1): 75-83.
22. Walker TG. Mesenteric vasculature and collateral pathways. Semin Intervent Radiol. 2009; 26(3): 167-74.
23. Joshi A, Deshpande S, Firke V, Andhalgaonkar T, Rathod P. Replaced left hepatic artery: clinical significance and review of the literature. International Journal of Science and Research. 2020; 9(4): 828-30. https://www.ijsr.net/archive/v9i4/SR20410224441.pdf.
24. Kavitha KB. A study of variant hepatic arterial anatomy and its relevance in current surgical practice. Int J Anat Res. 2015; 3(1): 947-53.
25. Asif M, Anewenah LS, Reddy N, Khan FA. Replaced right and left hepatic arteries: a variation in origin and course. BMJ Case Reports. 2017; 2017: 2016218345.
26. Cirocchi R, D'Andrea V, Amato B, Renzi C, Henry BM, Tomaszewski KA, et al. Aberrant left hepatic arteries arising from left gastric arteries and their clinical importance. Surgeon. 2020; 18(2): 100-12.

RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-57
Cyprus J Med Sci 2025;10(5):308-313

Effect of Serum 25-OH D Levels on Vitamin B12 and Folic Acid Levels in Healthy Preschool Age (3-6 Years Old) Children

Özlem Kemer Aycan

Department of Pediatrics, Balıkesir University Faculty of Medicine, Balıkesir, Türkiye

Abstract

BACKGROUND/AIMS: This prospective research aimed to evaluate the effect of serum 25-OH D levels on vitamin B12 and folic acid levels in healthy preschool age (3-6 years old) children.

MATERIALS AND METHODS: The research was conducted as a cross-sectional and descriptive study. In this context, 130 healthy children, aged 3-6, who applied to the Balıkesir University Health Practice and Research Hospital Child Health and Diseases General Pediatrics polyclinic, were included during working hours. Children who came for routine healthy child examination, and had blood taken for control purposes were included in the study.

RESULTS: The frequency of smoking at home, vitamin B12 levels greater than 200, the rate of mothers' diets primarily consisting of meat and vegetables during pregnancy, and the frequency of the child going outside every day were statistically significantly higher in the group with vitamin D levels greater than 20 ($p<0.05$). The mean folic acid level was significantly higher in the vitamin D (>20) group, whereas the mean homocysteine level was significantly lower ($p<0.05$). All other laboratory parameter differences between vitamin D groups were not statistically significant ($p>0.05$). 77.8% of participants with <20 ng/mL vitamin D had a vitamin B12 level between 0-200 pg/mL, whereas 22.2% in the vitamin D >20 ng/mL group had a vitamin B12 level between 0-200 pg/mL, with a statistically significant difference ($p<0.05$). Correlation analysis results showed that vitamin D was significantly correlated with homocysteine ($r=-0.2$; $p<0.05$), vitamin B12 ($r=0.3$; $p<0.01$), and folic acid ($r=0.3$; $p<0.01$).

CONCLUSION: There was a significant positive relationship between vitamin D levels and blood B12 and folic acid levels in healthy preschool children. In cases of B12 and folate deficiency in healthy children, measuring serum 25-OH-D levels and correcting the deficiency, if present, may have positive effects on serum B12 and folate levels. New supportive studies are needed on this subject.

Keywords: Vitamin D, vitamin B12, folic acid, children

INTRODUCTION

Vitamins are essential for various biochemical functions in the body.[1] Vitamins are molecules that the body must obtain from the outside, and a deficiency in them leads to hypovitaminosis.[2] Among them are vitamin D, a fat-soluble secosteroid prohormone produced in the skin as a result of exposure to sunlight, as well as ergocalciferol, which is found in plants, and cholecalciferol, which is more common in animal sources.[3-5] It is converted into a hormone known as calcitriol, which plays an important role in the metabolism of calcium and phosphorus

To cite this article: Kemer Aycan Ö. Effect of serum 25-OH D levels on vitamin B12 and folic acid levels in healthy preschool age (3-6 years old) children. Cyprus J Med Sci. 2025;10(5):308-313

ORCID IDs of the authors: Ö.K.A. 0000-0002-2462-0939.

Corresponding author: Özlem Kemer Aycan
E-mail: ozlem.aycan@balikesir.edu.tr
ORCID ID: orcid.org/0000-0002-2462-0939

Received: 14.06.2025
Accepted: 25.08.2025
Epub: 01.10.2025
Publication Date: 09.10.2025

through various metabolic changes in the body.[6] There are three main target organs for vitamin D. These are the intestine bone, and the parathyroid gland. In the intestine, vitamin D enters enterocytes and induces the synthesis of calbindin, an intestinal calcium-binding protein.[7-9] In the bone, it was shown that the 24R,25-dihydroxyvitamin D_3 is an essential hormone in the healing process of bone fractures.[1] In the parathyroid, the levels of parathyroid hormone, blood levels of 1,25 dihydroxyvitamin D, and serum calcium and phosphorus all tightly control the bioconversion of 25-OH D to 1,25 dihydroxyvitamin D_3. Parathyroid hormone and 1,25 dihydroxyvitamin D are major hormonal regulators of Ca homeostasis.[8]

Vitamin B12 is derived primarily from cobalamins found in animal products. Cobalamins are released in the acidic environment of the stomach, and enter the duodenum by binding to R and intrinsic factor (IF) proteins, and the B12-IF complex is absorbed via the cubilin receptor in the distal ileum.[10] This process is calcium-dependent. Megalin binds several structurally unrelated ligands, and the IF-vitamin B12 complex enters the intestine via receptor-mediated endocytosis.[11,12] The complex first binds to a receptor anchored in the outer layer of the plasma membrane, followed by endocytosis of the cargo mediated by cubilin and megalin.[13] Megalin deficiency indirectly results in cubilin deficiency and impaired vitamin B12 absorption.[14]

1,25 dihydroxyvitamin D and serum ionized calcium regulate calcium transport at the bone, gut, and kidney.[6] In addition, vitamin D is necessary for adequate bone growth.[8] Folic acid and vitamin B12 have essential roles in cellular processes, and prevent megaloblastic anemia.[14] Vitamin B12 as a hydrogen receptor, regulates metabolic processes.[12] Some studies have reported a relationship between vitamin D, vitamin B12, and folate, and these studies suggest that vitamin D_3 influences the absorption of B12 and folate.[15-17] This effect may be mediated directly through vitamin D receptors or indirectly through calcium-dependent absorption, but no clinical studies have examined this relationship in children. This research aimed to evaluate the effect of serum 25-OH D levels on vitamin B12 and folic acid levels in healthy preschool age (3-6 years old) children.

MATERIALS AND METHODS

Research Model

The research was designed as a cross-sectional, descriptive study. In this context, 130 healthy children aged 3-6 years, who visited the General Pediatric Pathology and Child Health Outpatient Clinic of Balıkesir University Health Practice and Research Hospital during working hours, were included. The study included children who came for a routine healthy child examination and from whom blood samples were collected as controls. Detailed information was provided to the children's parents, and informed consent was obtained. The parents were informed that no additional blood sampling would be performed for this research.

Patients

Children aged 3-6 years without any diagnosed chronic diseases who applied to the Child Health and Diseases Outpatient Clinic of Balıkesir University Health Practice and Research Hospital with specific complaints between October 2019 and August 2020 were included in the thesis research. The number of participants included in the study was determined using G-Power analysis. The aim was to include at least 127 participants with a confidence level of 95%, a power of 80%, and an effect size of 0.[15] A total of 130 children participated in our study. The total number of applications over a 10-month period was 12,015 children, approximately 6% of whom were aged 3-6 years. The participants to be included in the study were randomly determined at the beginning of each week. Complaints of the study participants included: 53% loss of appetite, 15% short stature, 12% constipation, 4% rash, and 16% cough.

Criteria for inclusion of volunteers in the study:

- Age 3 to 6 years
- No chronic diseases and/or irregular medication intake
- Do not take any medications that affect the metabolism of vitamins D, B12, and folic acid

Inclusion criteria for the study:

- Excluding children aged 3 to 6 years
- Presence of a chronic disease and regular medication intake

During the selection phase of the children, random numbers were generated in the SPSS program, and children were selected based on this order.

Of the children who presented to our clinic, 127 were deemed sufficient based on a power analysis; however, 130 were included in the study. During this process, 145 children who met the inclusion criteria and applied within a week were randomly contacted, and 15 of these were excluded because they met the exclusion criteria.

Laboratory

A 6 mL blood sample was taken from the patient for routine biochemical and hormonal analyses. The blood samples were centrifuged at 3000 rpm to separate serum and plasma. Folic acid, vitamin B12, and 25-OH vitamin D from these sera were analyzed by the chemiluminescence immunoassay method in the biochemistry laboratory of Balıkesir University Health Practice and Research Hospital using the Beckman Coulter DXI 600/800 instrument. Excess serum, which could become medical waste, was stored at -40 degrees until analysis in three separate Eppendorf tubes. Homocysteine level, which is directly related to vitamin B12 and folate metabolism, was measured by electrochemiluminescence immunoassay method, on the Abbott ARCHITECT instrument, in the microbiology laboratory of Balıkesir University Health Practice and Research Hospital.

Normal values for folate were determined to be in the range of 2.33-17.24 ng/mL. Normal values for vitamin B12 were determined to be 126.5-505 pg/mL and for 25-OH vitamin D to be 30-70 ng/mL.

After taking samples for calcium, phosphorus, sodium, potassium, alkaline phosphatase, aspartate aminotransferase and alanine aminotransferase, the samples were analyzed spectrophotometrically on the same day using a Beckman Coulter DXI 800 instrument in the biochemistry laboratory of Balıkesir University Health Practice and Research Hospital.

Statistical Analysis

SPSS, version 23.0 (IBM INC., Armonk, NY, USA). The SPSS 23.0 software package was used for statistical analysis of the study. Descriptive statistics of continuous variables are displayed using mean, standard deviation, median, minimum and maximum values, while categorical variables are displayed using frequency and percentage. The suitability of continuous variables for normal distribution was tested using the Shapiro-Wilk test. One-way analysis of variance was used when comparing three or more groups of continuous variables with normal distribution. For variables that do not have a normal distribution, the Mann-Whitney U test was used to compare two groups, and the Kruskal-Wallis test was used to compare three or more groups. Pearson's chi-square test, Yates's chi-square test, and Fisher's exact chi-square test were used for group comparisons of categorical variables.[18,19] In all statistical comparisons in the study, a p-value below 0.05 was considered statistically significant.

Ethical Approval

The study was conducted at the Ethics Committee Balıkesir University Health Practice and Research Hospital between October 2019 and August 2020 (approval number: 2019/44, date: 09.10.2019).

RESULTS

Participants were 47% female and 53% male. 92.3% of the couples in the families were married, and the majority of the mothers and fathers had primary school education or below. The majority of mothers (75.4%) were unemployed, while the majority of fathers (98.5%) were employed. Monthly income was mostly at a medium level, and the majority of participants were predominant in the central category. The rate of chronic disease was 11.5%; the number of family members was generally 4 or fewer. The rate of families stating that the mother and father smoked was 54.6%, 48.5% of families had heart disease; and 13.8% used vitamins. The majority of children were outside fewer than 4 days a week, and 69.2% of mothers had a diet rich in meat and vegetables during pregnancy (Table 1).

Statistically significant factors for the vitamin D >20 group ($p<0.05$) included smoking at home, vitamin B12 levels >200, mothers' adherence to a diet mainly of meat and vegetables during pregnancy, and the child's daily outdoor activities (Table 2).

Folic acid mean was significantly higher in vitamin D >20 group, whereas homocysteine mean was significantly lower ($p<0.05$). All other laboratory parameter differences between vitamin D groups were insignificant ($p>0.05$) (Table 3).

77.8% of participants in the <20 ng/mL vitamin D group had vitamin B12 levels between 0-200 pg/mL, whereas 22.2% in the >20 ng/mL vitamin D group had vitamin B12 levels between 0-200 pg/mL, and a statistically significant difference was observed ($p<0.05$) (Table 4).

Correlation analysis results showed that vitamin D was significantly correlated with homocysteine ($r=-0.2$; $p<0.05$), vitamin B12 ($r=0.3$; $p<0.01$), and folic acid ($r=0.3$; $p<0.01$) (Table 5). Although correlations were significant, correlation coefficients were low.

DISCUSSION

According to the socio-demographic factors that influence vitamin D levels, there were found to be weak associations with ethnicity, maternal age, married parents, education, and employment status. In a study in the Netherlands, 4167 children were examined, and vitamin D deficiency was found to be more common in children of Western descent.[20] It was also found to be associated with birth weight and maternal age. In another study, maternal employment status was associated with vitamin D.[21-24] In our study, no association was found between vitamin D levels and parental employment status, education level, and number of people living with the study participants.

Table 1. Baseline characteristics of patient groups

Parameters		n %
Gender	Female	47.0 (61)
	Male	53.0 (69)
Marital status	Married	92.3 (120)
	Separated	7.7 (10)
Mother education	Primary school or no education	41.5 (54)
	High school	40 (52)
	Bachelor's/master's degree	18.5 (24)
Father education	Primary school or no education	41.6 (54)
	High school	38.5 (50)
	Bachelor's/master's degree	20 (26)
Mother working status	Working	24.6 (32)
	Not working	75.4 (98)
Father working status	Working	98.5 (128)
	Not working	1.5 (2)
Income	0-4999 TL	36.9 (48)
	5000-9999 TL	40.8 (53)
	10000 TL and above	22.3 (29)
Location	Central	86.2 (112)
	Rural	13.8 (18)
Chronic illness	Yes	11.5 (15)
	No	88.5 (115)
Number of people living in the house	3 or less than 3	34.6 (45)
	4	47.7 (62)
	5 and above	17.7 (23)
Smoking at home	Mother and father	54.6 (71)
	Mother and father	10 (13)
	Never smokes	35.4 (46)
Heart disease in the family	Yes	48.5 (63)
	No	51.5 (67)
Vitamin usage history	Yes	13.8 (18)
	No	86.2 (112)
The duration of the child's stay outside	Everyday	16.2 (21)
	4-5-6 days a week	32.3 (42)
	Less than 4 days a week	51.5 (67)
Mother's diet during pregnancy	Meat and vegetable based	69.2 (90)
	Meat based	2.3 (3)
	Vegetable based	28.5 (37)

TL: Turkish lira.

Vitamin D plays a role in calcium transfer within the body for the kidneys, gut, and bones.[2-4] Vitamin B12, along with folic acid, is vital for cellular processes.[10-12] These vitamins play a vital role in the body's homeostasis, growth, and basic functions. Many studies have highlighted the importance of diet as a source of vitamin D, especially in countries with little sunlight, such as the Scandinavian countries. In our study, we examined the frequency of consumption of red meat, milk and dairy products, and vegetables, in relation to vitamin D levels and found a particular association with the consumption of red meat, eggs, milk and dairy products with vitamin D levels. When we created a dietary index, we showed again that diet was associated with vitamin D.

Table 2. Comparison of sociodemographic data with vitamin D

Parameters		Vitamin D ≤20 ng/mL	Vitamin D >20 ng/mL	p value
Age	36-48 months	14 (41.2)	20 (58.8)	0.480
	49-60 months	13 (56.5)	10 (43.5)	
	61-83 months	37 (50.7)	36 (49.3)	
Gender	Female	30 (49.2)	31 (50.8)	0.990
	Male	34 (49.3)	35 (50.7)	
Marital status	Married	60 (50.0)	60 (50.0)	0.540
	Divorced	4 (40.0)	6 (60.0)	
Mother education	Uneducated or primary	27 (50)	27 (50)	0.930
	High school	26 (50)	26 (50)	
	College/ undergraduate	11 (45.8)	13 (54.2)	
Father education	Uneducated or primary	27 (50)	27 (50)	0.970
	High school	24 (48)	26 (52)	
	College/ undergraduate	13 (50)	13 (50)	
Mother job	Not working	47 (48)	51 (52)	0.610
	Working	17 (53.1)	15 (46.9)	
Father job	Not working	1 (50)	1 (50)	0.980
	Working	63 (49.2)	65 (50.8)	
Income	0-4999 TL	25 (52.1)	23 (47.9)	0.750
	5000-9999 TL	24 (45.3)	29 (54.7)	
	10000 TL and above	15 (51.7)	14 (48.3)	
Location	Rural	9 (50)	9 (50)	0.940
	Central	55 (49.1)	57 (50.9)	
Smoking at home	Yes	14 (30.4)	**32 (69.6)**	**0.020**
	No	50 (59.5)	34 (40.5)	
Chronic disease	Yes	9 (56.3)	7 (43.8)	0.540
	No	55 (48.2)	59 (51.8)	
B12 groups	≤200	21 (77.8)	6 (22.2)	**0.010**
	>200	43 (41.7)	**60 (58.3)**	
Hearth disease in family	Yes	39 (61.9)	24 (38.1)	0.050
	No	25 (37.3)	42 (62.7)	
Mother's diet during pregnancy	Meat-vegetables**	37 (41.1)	**53 (58.5)**	**0.020**
	Meat	2 (68.7)	1 (33.3)	
	Vegetables	25 (67.6)	12 (32.4)	
The duration of the child's stay outside	Everyday	4 (19)	17 (81.0)	**0.000**
	4-5-6 days a week	8 (19)	34 (81.0)	
	Less than 4 times	52 (77.6)	15 (22.4)	

**Difference group.
TL: Turkish lira.

Table 3. Mean values of laboratory parameters and comparison with vitamin D groups

Parameters	Vitamin D	$\bar{x}\pm SD$	p
ALP	<20	240.37±92.84	0.490
	>20	250.69±78.76	
Fosfor	<20	4.79±0.59	0.060
	>20	4.97±0.53	
Hemoglobin	<20	12.15±0.75	0.060
	>20	12.42±0.92	
RBC	<20	4.68±0.31	0.290
	>20	4.75±0.43	
Hematocrit	<20	37.09±2.36	0.790
	>20	37.21±2.77	
Folic acid	<20	11.10±4.34	**0.002**
	>20	13.41±4.13	
Calcium	<20	9.78±0.40	0.250
	>20	9.86±0.41	
Magnesium	<20	1.94±0.33	0.660
	>20	1.96±0.30	
MCV	<20	79.34±4.21	0.590
	>20	79.73±4.34	
Homocysteine	<20	**7.48±2.55**	**0.030**
	>20	6.57±1.66	
Ferritin	<20	19.24±16.26	0.630
	>20	18.23±13.54	
Age	<20	62.80±15.18	0.520
	>20	61.12±15.66	
WBC	<20	8.11±2.39	0.970
	>20	8.17±2.44	
PLT	<20	337.10±113.07	0.160
	>20	350.39±88.22	
MCV	<20	79.34±4.21	0.730
	>20	79.73±4.34	
AST	<20	30.30±11	0.980
	>20	31.40±13.63	
ALT	<20	15.35±5.97	0.140
	>20	17.24±7.37	
TSH	<20	2.87±1.26	0.370
	>20	2.67±1.19	
sT4	<20	0.93±0.22	0.070
	>20	1.04±0.41	

ALP: Alkaline phosphatase, RBC: Red blood cell, MCV: Mean corpuscular volume, WBC: White blood cell, PLT: Platelet, AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, TSH: Thyroid stimulating hormone, sT4: Free thyroxine (Free T4), SD: Standard deviation.

Table 4. Comparison of grouped B12 levels with dichotomized vitamin D

		Vitamin D		Total
		<20 ng/mL	>20 ng/mL	
B12	0-200 pg/mL	21 (77.8%)	6 (22.2%)	27 (100%)
	200 pg/mL and over	43 (41.7%)	60 (58.3%)	103 (100%)
p=0.010.				

Table 5. Correlation between participants' vitamin D, B12, homocysteine and folic acid levels

Parameters	Homosistein	B12	Folic acid
Vitamin D	r=-0.2 (p=0.03)	r=0.3 (p=<0.001)	r=0.3 (p=<0.001)
B12	r=-0.5	-	r=0.3
Folic acid	r=0.3	r=0.3	-
Homocysteine	-		r=0.2

The study found that mothers' knowledge of vitamin D and of which foods contain vitamin D was poor.[25-27]

Upon comparing dietary patterns in our study, we found that the effect of red meat, egg, milk, and dairy consumption on vitamin D levels was statistically significant ($p<0.05$). However, the frequency of chicken, vegetable dishes, and fish consumption did not have a statistically significant effect on vitamin D levels ($p>0.05$). Fatty fish is mentioned in the literature as one of the best dietary sources of vitamin D.[28] However, in our study, we did not find an association between the frequency of fish consumption and vitamin D. We explained this by the fact that 60% of our patients had not developed the habit of eating fish. Although nutrition is important, the majority of children were outside less than 4 days a week, and this may affect their vitamin D levels. Thus, this may be a confounding factor. Further research may be needed on sunlight to understand this factor.

The mean vitamin B12 in our study participants was 303.7±134.4 pg/mL, and the mean folate were 12.2±4.3 ng/mL. Looking at the study, the levels of vitamin B12 and folate were similar in a study conducted among an adolescent group.[27] In the study by Öncel et al.[27], the levels of vitamin B12 and folate were studied in 889 students aged 12 to 22 years, and vitamin B12 deficiency was 2.2% and folate deficiency was 21.8%.

In a study involving 280 children aged 3-17 years who attended the Child Health and Diseases Outpatient Clinic of Bağcılar Training and Research Hospital, 25-OH vitamin D levels were defined as follows: deficiency <15 ng/mL, insufficiency 15-20 ng/mL, and >20 ng/mL as normal values. Insufficiency was found in 80.36% (n=225) of the patients and deficiency in 11.79% of the patients. In this study, 25-OH vitamin D levels were found to be lower in late winter than those in late summer. Age was negatively correlated with both 25-OH vitamin D levels in late winter ($r=-0.203$, $p=0.001$) and 25-OH vitamin D levels in late summer ($r=-0.184$, $p=0.008$). When comparing levels in late summer and late winter, a positive correlation was found between vitamin D and Ca ($r=0.508$, $p=0.001$).[28]

In a study, 171 patients (83 girls, 88 boys) aged 3-18 years who attended the pediatric endocrinology outpatient clinic had 25-OH vitamin D levels assessed as <12 ng/mL, deficiency; 12-20 ng/mL, insufficiency; and >20 ng/mL, normal.[29] Of the patients included in the study, 40 had type 1 diabetes mellitus, 47 were obese, and 84 were observed for other endocrine diseases. The study found that vitamin D deficiency was 51.5%, and insufficiency was 35.1%.[29]

In a study where serum 25-OH D levels were examined in 640 healthy primary school children aged 6-9 years, the median level was found to be 25.95 ng/mL.[27] Vitamin D deficiency was defined as serum 25-OH D levels less than 12 ng/mL, and such deficiency was found in 36 children (5.62%).[30]

There was not a significant difference between children whose family uses vitamins and those whose family does not. The main reason may be that the usage level of vitamins varies and may cause variation in effects. Further research may be conducted on the effect of family vitamin usage.

Study Limitations

Our study is important because it is the first to report that vitamin D is associated with B12 and folate levels in healthy children of this age range. For this reason, comparisons were made with other studies that were partially similar to our study, but the interpretation of the results was very limited. Prospective studies in this area involving larger patient groups, with more detailed information on seasonal characteristics, daily food intake, daily sun exposure, and other sociodemographic characteristics, are needed. In addition, we believe that further large-scale studies are needed to examine polymorphisms in vitamin D hydroxylase and receptor enzymes, which could help clarify the details of the associations we found. Since the study is cross-sectional, results cannot prove a cause-effect relationship. On the other hand, it may be a source for further research. This is another limitation of the study.

CONCLUSION

It is evident that there is a significant positive association between vitamin D levels and serum B12 and folate levels in healthy preschool children. This association is consistent with the notion that vitamin D affects the absorption of both vitamins, as reported in some studies. We believe that in cases of vitamin B12 and folate deficiency in healthy children, measuring serum 25-OH D levels and correcting the deficiency, if any, may have a positive effect on serum vitamin B12 and folate levels. Further confirmatory studies are needed on this issue.

It is evident that vitamin D has calcemic and noncalcemic effects, as well as pleiotropic effects in many tissues. At the same time, there are many studies indicating that the common genetic polymorphism observed in the vitamin D receptor is important in determining the effects of vitamin D on the body. This may have influenced the associations found in our study between vitamin D, B12, and folate levels.

MAIN POINTS

- Consumption of red meat, eggs, milk, and dairy products in particular was associated with vitamin D levels.
- There is a significant positive association between vitamin D levels and serum B12 and folate levels in healthy preschool children.
- Vitamin D affects the absorption of certain vitamins in children.
- Vitamin D has calcemic and noncalcemic effects, as well as pleiotropic effects in many different tissues.

ETHICS

Ethics Committee Approval: The study was conducted at the Ethics Committee Balıkesir University Health Practice and Research Hospital between October 2019 and August 2020 (approval number: 2019/44, date: 09.10.2019).

Informed Consent: Detailed information was provided to the children's parents, and informed consent was obtained.

Note: Produced from author's thesis data.

Financial Disclosure: The author declared that this study received no financial support.

REFERENCES

1. Bendik I, Friedel A, Roos FF, Weber P, Eggersdorfer M. Vitamin D: a critical and essential micronutrient for human health. Front Physiol. 2014; 5: 248.
2. Awuchi CG, Igwe VS, Amagwula IO, Echeta CK. Health benefits of micronutrients (vitamins and minerals) and their associated deficiency diseases: a systematic review. International Journal of Food Sciences. 2020; 3(1): 1-32.
3. Jäpelt Rie B, Jette Jakobsen. Vitamin D in plants: a review of occurrence, analysis, and biosynthesis. Front Plant Sci. 2013; 4: 136.
4. Khan MU, Gautam G, Jan B, Zahiruddin S, Parveen R, Ahmad S. Vitamin D from vegetable VV sources: hope for the future. Phytomedicine Plus. 2022; 2(2): 100248.
5. Nigwekar SU, Bhan I, Thadhani R. Ergocalciferol and cholecalciferol in CKD. Am J Kidney Dis. 2012; 60(1): 139-56.
6. Peacock M. Calcium metabolism in health and disease. Clin J Am Soc Nephrol. 2010; 5(Suppl 1): 23-30.
7. Christakos S, Li S, De La Cruz J, Shroyer NF, Criss ZK, Verzi MP, et al. Vitamin D and the intestine: review and update. J Steroid Biochem Mol Biol. 2020; 196: 105501.
8. Fleet JC. Vitamin D-mediated regulation of intestinal calcium absorption. Nutrients. 2022; 14(16): 3351.
9. Bouillon R, Van Cromphaut S, Carmeliet G. Intestinal calcium absorption: molecular vitamin D mediated mechanisms. J Cell Biochem. 2003; 88(2): 332-9.
10. Guéant JL, Guéant-Rodriguez RM, Alpers DH. Vitamin B12 absorption and malabsorption. Vitam Horm. 2022; 119: 241-74.
11. Kozyraki R, Verroust P, Cases O. Cubilin, the intrinsic factor-vitamin B12 receptor. Vitam Horm. 2022; 119: 65-119.
12. Moestrup SK, Birn H, Fischer PB, Petersen CM, Verroust PJ, Sim RB, et al. Megalin-mediated endocytosis of transcobalamin-vitamin-B12 complexes suggests a role of the receptor in vitamin-B12 homeostasis. Proc Natl Acad Sci U S A. 1996; 93(16): 8612-7.
13. De S, Kuwahara S, Saito A. The endocytic receptor megalin and its associated proteins in proximal tubule epithelial cells. Membranes. 2014; 4(3): 333-55.
14. Castellanos-Sinco HB, Ramos-Peñafiel CO, Santoyo-Sánchez A, Collazo-Jaloma J, Martínez-Murillo C, Montaño-Figueroa E, et al. Megaloblastic anaemia: folic acid and vitamin B12 metabolism. Revista Médica Del Hospital General De México. 2015; 78(3): 135-43.
15. Rogenhofer N, Mischitz D, Mann C, Gluderer J, von Schönfeldt V, Jeschke U, et al. Correlation of vitamin D3 (calcitriol) serum concentrations with vitamin B12 and folic acid in women undergoing in vitro fertilisation/intracytoplasmatic sperm injection. Gynecol Obstet Invest. 2019; 84(2): 128-35.
16. Watson J, Lee M, Garcia-Casal MN. Consequences of inadequate intakes of vitamin a, vitamin B 12, vitamin D, calcium, iron, and folate in older persons. Curr Geriatr Rep. 2018; 7(2): 103-13.
17. Butola LK, Kanyal D, Ambad R, Jha RK. Role of omega 3 fatty acids, vitamin D, vitamin B12, vitamin B6 and folate in mental wellbeing-a short review of literature. Indian Journal of Forensic Medicine Toxicology. 2021; 15(2): 283-8.
18. Yilmaz K, Turanlı M. A multi-disciplinary investigation on minimizing linearization deviations in different regression models. Change & Shaping The Future, IV. ASC-2022/Fall Congress.
19. Yılmaz K, Turanlı M. A multi-disciplinary investigation of linearization deviations in different regression models. Asian Journal of Probability and Statistics. 2023; 22(3): 15-9.
20. Voortman T, van den Hooven EH, Heijboer AC, Hofman A, Jaddoe VW, Franco OH. Vitamin D deficiency in school-age children is associated with sociodemographic and lifestyle factors. J Nutr. 2015; 45(4): 791-8.
21. Wang H, Xiao Y, Zhang L, Gao Q. Maternal early pregnancy vitamin D status in relation to low birth weight and small-for-gestational-age offspring. J Steroid Biochem Mol Biol. 2018; 175: 146-50.
22. Ni M, Zhang Q, Zhao J, Shen Q, Yao D, Wang T, et al. Relationship between maternal vitamin D status in the first trimester of pregnancy and maternal and neonatal outcomes: a retrospective single center study. BMC Pediatr. 2021; 21(1): 330.
23. Amberntsson A, Papadopoulou E, Winkvist A, Lissner L, Meltzer HM, Brantsaeter AL, et al. Maternal vitamin D intake and BMI during pregnancy in relation to child's growth and weight status from birth to 8 years: a large national cohort study. BMJ Open. 2021; 11(10): 048980.
24. Aji AS, Lipoeto NI, Yusrawati Y, Malik SG, Kusmayanti NA, Susanto I, et al. Impact of maternal dietary carbohydrate intake and vitamin D-related genetic risk score on birth length: the vitamin d pregnant mother (VDPM) cohort study. BMC Pregnancy Childbirth. 2022; 22(1): 690.
25. Şolt A, Dolgun G. Pregnants awareness of the use of vitamin D for themselves and their infants. Journal of Anatolia Nursing and Health Sciences. 2018; 21(1): 18-24.
26. Fink C, Peters RL, Koplin JJ, Brown J, Allen KJ. Factors affecting vitamin D status in infants. Children. 2019; 6(1): 7.
27. Öncel K, Özbek MN, Onur H, Söker M, Ceylan A. B12 vitamin and folat prevelance of children and adolescents in Diyarbakır. Dicle Medical Journal. 2006; 33(1): 163-9.
28. Erol M, Yiğit Ö, Küçük SH, Bostan Gayret Ö. Vitamin D deficiency in children and adolescents in Bağcılar, İstanbul. J Clin Res Pediatr Endocrinol. 2015; 7(2): 134-9.
29. Demiral M, Sırmagül B, Kirel B. Vitamin D levels in children admitted to the endocrine outpatient clinic. Güncel Pediatr. 2016; 14(2): 60-6.
30. Hocaoğlu-Emre FS, Sarıbal D, Oğuz O. Vitamin D deficiency and insufficiency according to the current criteria for children: vitamin d status of elementary school children in Turkey. J Clin Res Pediatr Endocrinol. 2019; 11(2): 181-8.

RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-15
Cyprus J Med Sci 2025;10(5):314-320

Alcohol, Tobacco, and Sedative Drug Consumption in North Cyprus; Before and During the Early COVID-19 Pandemic

Amber Eker[1], Nimet İlke Akçay[2], Ashour M. Farag Shallof[3], Ayçin Buse İzzettin[3], Dhergham Alshawawreh[3], Leyla Çiğdem[3], Mobina Hivehchi[3], Mourad Mohamed Ahmed Abousamaan[3], Mustafa Omar Hasan Abuhamra[3], Rukiye Tolgay[3], Soheil Foroughian[3]

[1]Department of Neurology, Eastern Mediterranean University Faculty of Medicine, Famagusta, North Cyprus
[2]Department of Biostatistics, Eastern Mediterranean University Faculty of Medicine, Famagusta, North Cyprus
[3]Eastern Mediterranean University Faculty of Medicine, Famagusta, North Cyprus

Abstract

BACKGROUND/AIMS: The coronavirus disease-2019 (COVID-19) pandemic resulted in the implementation of restrictions and caused lifestyles to change; the economy to decline; and psychiatric problems to arise. These factors might have influenced the consumption of alcohol, tobacco, and sedative drugs. This study aims to investigate the consumption trends of alcohol, tobacco, and sedative drugs before and during the early period of the COVID-19 pandemic in North Cyprus.

MATERIAL AND METHODS: A cross-sectional study was conducted using an online questionnaire targeting residents of North Cyprus aged 18 years and above. A sample of 270 people was selected using the snowball sampling method to represent the population with 90% confidence. The alcohol, smoking, and substance involvement screening test (ASSIST) scale was employed to evaluate alcohol, tobacco, and sedative drug use before and during the first three months of the COVID-19 pandemic.

RESULTS: A total of 280 residents participated in this study. 50.7% of the participants reported the use of tobacco before the pandemic. 86.8% had moderate risk before COVID-19, while 65% had low-risk usage in the pandemic's first three months. 62.9% of the participants indicated no tobacco use during the first three months of the pandemic. Tobacco consumption severity significantly decreased with the COVID-19 pandemic ($p<0.001$), which was observed in both sexes and all age groups. However, no significant changes were found in alcohol and sedative drug consumption.

CONCLUSION: The findings indicate a substantial reduction in tobacco use during the early phase of the pandemic in North Cyprus. No significant changes were observed in alcohol or sedative drug consumption during the early pandemic period, and both substances showed consistently low-risk levels based on ASSIST classifications.

Keywords: COVID-19, alcohol, tobacco, sedative drugs, ASSIST scale, Cyprus

To cite this article: Eker A, Akçay Nİ, Shallof AMF, İzzettin AB, Alshawawreh D, Çiğdem L, et al. Alcohol, tobacco, and sedative drug consumption in North Cyprus; before and during the early COVID-19 pandemic. Cyprus J Med Sci. 2025;10(5):314-320

ORCID IDs of the authors: A.E. 0000-0001-9997-4662; N.İ.A. 0000-0001-5096-069X; A.M.F.S. 0009-0002-6254-4823; A.B.İ. 0009-0001-0425-5778; D.A. 0009-0003-3412-3092; L.Ç. 0009-0005-0164-7409; M.H. 0009-0008-2837-8925; M.M.A.A. 0009-0004-2910-9699; M.O.H.A. 0009-0000-2042-5936; R.T. 0009-0004-4134-4341; S.F. 0009-0000-7346-789X.

Corresponding author: Amber Eker
E-mail: amber.eker@emu.edu.tr
ORCID ID: orcid.org/0000-0001-9997-4662

Received: 17.02.2025
Accepted: 20.08.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

INTRODUCTION

In late 2019, a pandemic of cases with severe acute respiratory syndrome coronavirus 2 spread from Wuhan, China, to the rest of the world, resulting in a global coronavirus disease-2019 (COVID-19) pandemic. COVID-19 is known to be a severe acute respiratory syndrome, showcasing symptoms such as fever, cough, sore throat, breathlessness, fatigue, and malaise. The disease, however, can be mild in most people; it can be fatal in others, particularly the elderly and immunocompromised.[1] The high transmission rate of COVID-19 led countries to implement a serious set of rules for all citizens. Social distancing, wearing masks, restrictions on going out, and the closure of all restaurants, entertainment places, and schools were just a few of the measures implemented during the COVID-19 pandemic. These restrictions led to rapid changes in people's lifestyles and quality of life. Combined with unemployment, the effects of certain factors they also negatively affected the economy. This, in turn, had further adverse effects on health and social life. Cumulative factors of the COVID-19 outbreak create anxiety and fear for people's health and jobs, and force them to live an unfamiliar lifestyle, and be deprived of relationships. These emotions affected every individual; however, conditions among people with pre-existing psychological issues may have worsened during the pandemic. Additionally, the problem of the recent era, infodemic on social media, also induces psychiatric problems. Anxiety, depression, sleep problems, obsessive behaviors, and post-traumatic stress disorder are mainly reported psychiatric problems during COVID-19.[2-6] All these mental health problems and a stressful lifestyle are known to be risk factors for increased use of alcohol, tobacco, and sedative drugs. Sedative drugs are also commonly used for the treatment of anxiety and insomnia.[7] It is reasonable to expect COVID-19 to affect the use of these substances. Starting from the first months of the pandemic, research articles on the changing usage patterns of these substances began to appear in the literature. COVID-19 has affected addictions in different ways due to the stressful times during the pandemic and lockdown, impacting consumption patterns. Restrictions might have also limited product availability and healthcare access for patients undergoing treatment for addictions, increased the withdrawal syndromes during the pandemic.[8,9]

With the first imported case in North Cyprus at the beginning of March 2020, strict restrictions were suddenly implemented, including the closure of all areas except the sectors that provide health, safety, and basic life needs.[10]

This study aimed to determine the effect of the early COVID-19 pandemic and lockdown period on alcohol, tobacco, and sedative drug consumption among North Cyprus residents, to identify the risk factors for high-risk usage.

MATERIALS AND METHODS

This study was conducted between November 2019 and June 2020, covering the first three months of the COVID-19 pandemic (March-June 2020) and the preceding three-month period (December 2019-February 2020). The study was approved by the Eastern Mediterranean University Research and Publication Ethics Committee Health Subcommittee before data collection (approval number: ETK00-2021-0083/ETK00-2021-009, date: 07.04.2021).

The target population consisted of adults aged 18 years and above residing in North Cyprus. The sample size was calculated as 270 participants based on the adult population of Region[11] and a confidence level of 90%, using Cochran's formula for sample size estimation. A total of 280 participants were ultimately included. Recruitment was carried out via Facebook groups with large local memberships, using a snowball sampling method. An anonymous online questionnaire, hosted on a secure platform, was distributed via private messages. Participants were encouraged to share the link with other eligible individuals. Informed consent was obtained electronically before survey participation.

The survey included demographic questions (age, gender, marital status, living location, education, employment, household type, income change during the pandemic, and psychiatric diagnosis history) and the validated Turkish version of the alcohol, smoking, and substance involvement screening test (ASSIST) that was developed by the World Health Organization (WHO).[12] The ASSIST questionnaire evaluates substance involvement risk levels for tobacco, alcohol, and sedative/hypnotic drugs. In this questionnaire, the risk level is based on the frequency of use of the relevant substance and its effects on daily life. Scores are assigned for each frequency. Frequencies are grouped as "Never, once or twice in 3 months, monthly, weekly, and daily/almost daily", and the score increases with increasing frequency of occurrences. The total score for each substance is calculated by adding all scores, and varies between 0 and 39. According to the ASSIST scoring guidelines, for tobacco and sedative drugs, scores of 0-3 indicate low risk, 4-26 indicate moderate risk, and 27 or above indicate high-risk. For alcohol, scores of 0-10 indicate low risk, 11-26 indicate moderate risk, and 27 or above indicate high-risk. Participants were asked to complete the ASSIST questionnaire for two distinct time points: the three months before the pandemic and the first three months during the pandemic, including the initial lockdown period.

Statistical Analysis

All data were analyzed using IBM SPSS Statistics version 22.0. To compare the differences in substance use before and during the pandemic, McNemar's chi-square test was applied for paired categorical data. Comparative analyses of ASSIST scores before and during the pandemic were conducted using Paired Samples t-tests. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 280 individuals took part in the study. The majority were female (61.8%), and the mean age was 46.5 years. Most participants were between 18 and 45 years old (85%), single (50%), university graduates (69.6%), and employed (61.1%). A large proportion lived in urban areas (71.8%) and in nuclear family settings (87.1%). Nearly half reported a decrease in household income during the pandemic. Additionally, 8.6% had a previously diagnosed psychiatric condition. Descriptive statistics for the study sample are presented in (Table 1).

According to responses to the first item of the ASSIST questionnaire, whether the participant had ever used the listed substances, self-reported use decreased across all substance categories during the early COVID-19 period. For alcohol, 236 participants (84%) reported lifetime use before the pandemic, which dropped to 206 participants (74%) during the first three months of the pandemic (McNemar $p<0.001$). Tobacco use similarly decreased from 142 participants (51%)

before the pandemic to 117 participants (42%) during the same period (McNemar p<0.001). For sedative drugs, reported use declined from 37 participants (13%) to 16 participants (6%) (McNemar p<0.001). These results demonstrate statistically significant reductions in substance use during the early phase of the pandemic (Table 2).

As indicated by the ASSIST questionnaire responses, the tobacco involvement risk score significantly decreased during the COVID-19 period, as the mean risk score for tobacco involvement was 9.90±7.549 before the pandemic and 5.81±8.723 during the pandemic (p<0.001). In contrast, there was no significant change in alcohol, (5.81±5.653 vs. 5.75±6.404), or sedative drug involvement risk scores, (1.09±0.316 vs. 1.07±0.309), before and during the pandemic (Table 3).

Based on the ASSIST substance involvement risk classification, alcohol involvement risk remained predominantly low both before (89.6%) and during (88.6%) the pandemic (Table 4). Tobacco involvement risk was categorized as moderate for 86.8% of participants before the pandemic, whereas 65% were classified as low risk during the pandemic (Table 4). Sedative drug involvement risk levels before the pandemic were high in 1%, moderate in 6%, and low in 93% of participants, while during the COVID-19 period, these levels were high in 1%, moderate in 4%, and low in 95% (Table 4).

Comparative analyses revealed that substance involvement risk levels for alcohol and tobacco did not significantly differ across any demographic categories, either before or during the pandemic. In contrast, the risk of sedative drug involvement was significantly higher among participants with lower education levels and those with a psychiatric diagnosis in both periods (Table 5).

Table 6 presents tobacco use frequency before and during the COVID-19 period, by gender and age groups. In the pre-pandemic period, the majority of both females and males across all age groups reported using tobacco 5-7 days a week (approximately 85%). In contrast, during the first three months of the pandemic, around 60% of both females and males across all age groups reported not smoking at all. This difference was most pronounced among males and participants aged 25-45.

DISCUSSION

In this study, which examines the early effects of the pandemic, a significant decrease was observed in cigarette use within North Cyprus. There was no significant change in the frequency of alcohol and sedative use. Different results on smoking have been reported in publications from all over the world, and even among participants included in the same study. Alongside those reporting an increase in use, an increase in attempts to cut has also been reported. In the study conducted by Klemperer et al.[13] from the United States, it was determined that there was an increase in the number and frequency of use among those who use cigarettes and electronic cigarettes with a degree of addiction. Conversely, 1/3 of the participants turned this period into an opportunity to quit.[13] A study examining the early stages of the pandemic in the United States found that many people attempted to cut down on smoking due to concern that they would be more affected by COVID-19; however, more people reported an increase in smoking.[14]

Table 1. Sociodemographic characteristics of the participants

Variable	Categories	Frequency percentage
Gender	Male	107 (38.2%)
	Female	173 (61.8%)
Age	18-25	111 (39.6%)
	26-45	127 (45.4%)
	46-65	39 (13.9%)
	66-75	3 (1.1%)
Marital status	Single	140 (50%)
	Married	123 (43.9%)
	Divorced	16 (5.7%)
	Widow	1 (0.4%)
Birth place	Cyprus	228 (81.4%)
	Turkey	35 (12.5%)
	Other	17 (5,4)
Living region	City	201 (71.8%)
	Village	79 (28.2%)
Working status	Yes	171 (61.1%)
	No	109 (38.9%)
Educational status	No education	1 (0.4%)
	Primary school	2 (0.7%)
	Secondary school	7 (2.5%)
	High school	75 (26.8%)
	University	195 (69.6%)
Household type	Alone	22 (7.9%)
	Nuclear family	244 (87.1%)
	Extended family	14 (5%)
Salary change with COVID	Decreased	136 (48.6%)
	Increased	9 (3.2%)
	Not changed	135 (48.2%)
Pre-COVID psychiatric diagnosis	Yes	24 (8.6%)
	No	256 (91.4%)

COVID: Coronavirus disease.

Table 2. Alcohol, tobacco and sedative drug use before and during COVID-19

	At least one time usage, before COVID-19		At least one time usage, during COVID-19		p-value†
Alcohol	Yes	236 (84%)	Yes	206 (74%)	<0.001
	No	44 (16%)	No	74 (26%)	
Tobacco	Yes	142 (51%)	Yes	117 (42%)	<0.001
	No	138 (49%)	No	163 (58%)	
Sedative drugs	Yes	37 (13%)	Yes	16 (6%)	<0.001
	No	243 (87%)	No	264 (94%)	

†p-value from Mc Nemar chi-square test. COVID-19: Coronavirus disease-2019.

Table 3. Alcohol, tobacco and sedative drug involvement risk scores in the pre-COVID-19 and COVID-19 period

	Pre-COVID-19 period mean score ± std. dev.	Early COVID-19 period mean score ± std. dev.	p-value‡
Alcohol involvement risk level	5.81±5.653	5.73±6.404	0.851
Tobacco involvement risk level	9.90±7.549	5.81±8.723	<0.001
Sedative drug involvement risk level	1.09±0.316	1.07±0.309	0.372

‡p-value from paired sample t-test. COVID-19: Coronavirus disease-2019, std. dev.: Standard deviation.

Table 4. Alcohol, tobacco and sedative drug involvement risk classification in the pre-COVID-19 and COVID-19 periods

	Pre-COVID-19 period n (%)			COVID-19 period n (%)		
	Low	**Moderate**	**High**	**Low**	**Moderate**	**High**
Alcohol involvement risk category	25 (89.6%)	24 (8.6%)	5 (1.8%)	248 (88.6%)	25 (8.9%)	7 (2.5%)
Tobacco involvement risk category	21 (7.5%)	243 (86.8%)	16 (5.7%)	182 (65%)	84 (30%)	14 (5%)
Alcohol involvement risk category	260 (92.9%)	18 (6.4%)	2 (0.7%)	265 (94.7%)	13 (4.6%)	2 (0.7%)

COVID-19: Coronavirus disease-2019.

Table 5. Pre-COVID-19 and COVID-19 period sedative involvement risk scores according to demographics

Variable	Categories	Pre-COVID-19 period sedative involvement risk scores		COVID-19 period sedative involvement risk scores	
		Mean ± SD	p-value	Mean ± SD	p-value
Gender	Male	1.09±5.09	0.763§	1.07±5.41	0.976§
	Female	1.27±4.06		1.09±4.46	
Age	18-25	1.39±5.40	0.222ɬ	1.56±6.14	0.095ɬ
	26-45	1.39±4.96		0.97±4.23	
	46-65	0.28±0.57		0.12±0.57	
	66-75	0.00±0		0±0	
Marital status	Single	1.15±4.63	0.198ɬ	1.26±5.33	0.517ɬ
	Married	0.79±3.40		0.40±2.20	
	Divorced	4.87±10.86		4.81±10.62	
	Widow	0.00±0.00		0±0	
Household type	Alone	2.13±6.17	0.34ɬ	2.13±6.99	0.186ɬ
	Nuclear family	1.14±4.75		1.05±4.74	
	Extended family	0.71±2.67		0±0	
Educational status	Less than 9 year education	5.80±11.06	**0.018**§	6.00±12.72	**0.006**§
	More than 9 year education	1.03±4.34		0.90±4.23	
Pre-COVID psychiatric diagnosis	Yes	7.12±0.94	**<0.001**§	7.62±11.55	**<0.001**§
	No	0.64±3.54		0.47±3.02	

§p-value from Independent Samples t-test. ɬ p-value from One-Way ANOVA test. COVID-19: Coronavirus disease-2019, SD: Standard deviation.

Studies from the Netherlands and Poland reported an increase in cigarette use at similar rates and a decrease in some participants.[15,16] A study from Belgium reported an increase in smoking and alcohol use during the pandemic period.[17]

Much of the evidence on this issue has come from developed countries. The limited articles from developing countries show that although it is thought, that the degree of development of the countries may affect the attitude towards smoking, the results are similar to those of developed countries. In a study from Pakistan, which reported different results in the same study group, Siddiqi et al.[18] mentioned that 14% of the participants quit smoking, while 68% of those who continued showed a decreasing trend in smoking, and an increase of 18% was observed. However, it is unclear what the increase referred to.

Studies rapidly added to the literature during the pandemic, along with systematic reviews and meta-analyses that compiled these studies indicated that the disease was more severe in smokers and had a less serious course in non-smokers.[19-24] With the arrival of information about the negative effects of smoking, on COVID-19 spread and course, some countries have introduced very strict bans to prevent the spread among the public throughout the country. For example, during the pandemic, sales of tobacco products were banned in India and South Africa.[25]

Table 6. Tobacco usage frequency in the pre-COVID-19 and COVID-19 period

How often did you use tobacco products?	Gender n (%)		Age n (%)				Total
	Female	Male	18-25	26-45	46-65	66-75	
In the last three months before the COVID pandemic,							
None	6 (3.5)	5 (4.7)	9 (8.1)	1 (0.8)	1(2.6)	0	11 (3.9)
Once or twice	1 (0.6)	2 (1.9)	0 (0.0)	2 (1.6)	1 (2.6)	0	3 (1.1)
1-3 times a month	17 (9.8)	8 (7.5)	7 (6.3)	15 (11.8)	3 (7.7)	0	25 (8.9)
1-4 days a week	2 (1.2)	2 (1.9)	1 (0.9)	2 (1.6)	1 (2.6)	0	4 (1.4)
5-7 days a week	147 (85.0)	90 (84.1)	94 (84.7)	107 (84.3)	33 (84.6)	3 (100)	237 (84.6)
In the first three months after the lockdown of the COVID pandemic,							
None	103 (59.5)	73 (68.2)	63 (56.8)	87 (68.5)	24 (61.5)	2 (66.7)	176 (62.9)
Once or twice	13 (7.5)	14 (13.1)	10 (9.0)	14 (11.0)	3 (7.7)	0	27 (9.6)
1-3 times a month	13 (7.5)	6 (5.6)	9 (8.1)	8 (6.3)	2 (5.1)	0	19 (6.8)
1-4 days a week	10 (5.8)	4 (3.7)	7 (6.3)	3 (2.4)	4 (10.3)	0	14 (5.0)
5-7 days a week	34 (19.7)	10 (9.3)	22 (19.8)	15 (1.8)	6 (15.4)	1 (33.3)	44 (15.7)

COVID-19: Coronavirus disease-2019.

The result of our study in our developing country reflects a significant decrease in smoking. Studies reporting an increase, primarily blamed stress triggered by the pandemic. Our study evaluated the first 3 months of the COVID-19 pandemic and the early phase of the shutdown. In our study examining the early period, concerns about COVID-19 disease may be more prominent than the stressors that accumulate over time. For this reason, in the early period of the pandemic, a decrease may have been observed in the study. Although there are no special restrictions on cigarette products due to the pandemic in our country, economic difficulties and the lockdown may also have affected the purchase of these products. In addition, it has been observed that even in those with high-risk use, the intense usage did not prevent attempts to quit or reduce smoking. With the findings of studies containing similar observations, researchers emphasized that these findings should be reflected in public health practices and smoking cessation. The WHO also stated this in its public announcements.[22,23,26]

Studies on alcohol came mostly from Europe. This study is one of the few studies on this subject in our region. In our study, no significant change in alcohol use was found during the pandemic. Information from countries, on alcohol use, is similar to that on smoking. In the study conducted on the Polish population, it was stated that while there was an increase in certain characteristics among some participants, there was a decreasing trend in the use were observed at a similar rate.[16] Studies from Norway and Belgium examining the early period of the pandemic have found increased alcohol consumption. In these studies, increased use was associated with economic concerns related to lockdowns.[17,27]

The socioeconomic challenges brought by the COVID-19 pandemic have triggered many mental health problems. This may lead patients to be more prone to taking benzodiazepine medication in a manner similar to alcohol consumption. Additionally, it could in many cases result in addiction or misuse. According to a study conducted in the United States, there has been, during the COVID-19 pandemic, an increase of about thirty-four percent in the prescription of anxiolytics and other sedative drugs.[7] On the contrary, another study from the United States of America showed that there has been a significant decrease in sedative drug usage, that has been later correlated with the fact that this decrease was due to a decrease in prescription fillings by patients due to the lockdown during the pandemic.[28]

However, in our study, the ASSIST score of sedative usage before and during the COVID-19 pandemic has not indicated a significant difference; only a very slight decrease was observed in the first three months of the pandemic, possibly due to restrictions. Since the evaluation is made over a short period, it can be expected that there will be no change. In the long term, the effect of COVID-19 on psychiatric diseases and sedative use may be more variable.

In addition, the study revealed that smoking in Cyprus was quite prevalent before the pandemic. The study was conducted with 280 North Cyprus residents and revealed that in the pre-COVID-19 period, the prevalence of tobacco usage was 96.1% and alcohol usage was 84.3% in North Cyprus. According to the first study conducted on this topic in North Cyprus among the age group of 18-65, the prevalence of consumption from 2003 to 2015 ranged from 62.1-66% for tobacco and 68.5-82.3% for alcohol.[29] Our study results show that the measurements were higher for alcohol consumption and especially for tobacco usage. In a recent study conducted in Northern Cyprus with a large number of participants, the smoking rate was reported as 40.7%, above the world average.[30] Studies conducted at medical faculties in the same region also revealed similar results for smoking.[31,32] The first study also revealed that the lifetime prevalence of sedative/hypnotic drug use was about 5.7% between the years 2003 and 2015.[31] Similarly, we have recorded about 6.4% misuse of sedative drugs and about 0.7% addiction among the population of the study. The results prove that sedative drug misuse is still a problem in North Cyprus. Relatively, in our study, we recorded that people older than twenty-five had more frequent use of these drugs before the pandemic, but this trend reversed, showing that younger people had the highest frequency of using these drugs after the pandemic. Our study also revealed that individuals with psychiatric problems, lower levels of education, as well as divorced or lonely individuals, had higher scores for sedative usage in the ASSIST score system.

Study Limitations

The study includes certain limitations. The researcher has little control over the sampling method. The snowball sampling technique may cause some sampling bias. Additionally, this study was performed using an online questionnaire during the pandemic. Researchers cannot be sure, that the subject and questions are fully understood in online research on such survey topics. In addition, the participants may not have felt very confident because of questions about psychiatric conditions and substance use.

CONCLUSION

To conclude, the decrease in tobacco usage is significant in our study, and this decrease is obviously due to the COVID-19 pandemic. The decrease was not limited to any of the genders or the age groups; other life circumstances might have had an effect as well. Our results may also support that it is the best time for North Cyprus to initiate efforts for quitting smoking. This pandemic-induced action may protect the population from common smoking-related health problems. Lastly, although there was no change in the use of alcohol and sedatives in the early period of the pandemic, it was noted that alcohol use was common among the participants, and the prevalence of sedatives at high-risk levels could not be underestimated.

MAIN POINTS

- Tobacco consumption significantly decreased with the coronavirus disease-2019 pandemic.
- No significant changes were observed in alcohol and sedative drug use.
- According to the alcohol, smoking, and substance involvement screening test scale, tobacco use was classified as moderate risk among a large proportion of participants in North Cyprus before the pandemic.

ETHICS

Ethics Committee Approval: The study was approved by the Eastern Mediterranean University Research and Publication Ethics Committee Health Subcommittee (approval number: ETK00-2021-0083/ETK00-2021-009, date: 07.04.2021).

Informed Consent: Informed consent was obtained from each participant.

Footnotes

Authorship Contributions

Concept: A.E., N.İ.A., A.M.F.S., A.B.İ., D.A., L.Ç., M.H., M.M.A.A., M.O.H.A., R.T., S.F., Design: A.E., N.İ.A., A.M.F.S., A.B.İ., D.A., L.Ç., M.H., M.M.A.A., M.O.H.A., R.T., S.F., Data Collection and/or Processing: A.E., N.İ.A., A.M.F.S., A.B.İ., D.A., L.Ç., M.H., M.M.A.A., M.O.H.A., R.T., S.F., Analysis and/or Interpretation: A.E., N.İ.A., A.M.F.S., A.B.İ., D.A., L.Ç., M.H., M.M.A.A., M.O.H.A., R.T., S.F., Literature Search: A.E., A.M.F.S., A.B.İ., D.A., L.Ç., M.H., M.M.A.A., M.O.H.A., R.T., S.F., Writing: A.E., N.İ.A., A.M.F.S., A.B.İ., D.A., L.Ç., M.H., M.M.A.A., M.O.H.A., R.T., S.F.

DISCLOSURES

Conflict of Interest: The authors declare that they have no conflicts of interests.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Wang C, Horby PW, Hayden FG, Gao GF. A novel coronavirus outbreak of global health concern. Lancet. 2020; 395(10223): 470-3.
2. Dubey S, Biswas P, Ghosh R, Chatterjee S, Dubey MJ, Chatterjee S, et al. Psychosocial impact of COVID-19. Diabetes Metab Syndr. 2020; 14(5): 779-88.
3. Morin CM, Carrier J. The acute effects of the COVID-19 pandemic on insomnia and psychological symptoms. Sleep Med. 2021; 77: 346-7.
4. Solomou I, Constantinidou F. Prevalence and predictors of anxiety and depression symptoms during the COVID-19 pandemic and compliance with precautionary measures: age and sex matter. Int J Environ Res Public Health. 2020; 17(14): 4924.
5. Alzueta E, Perrin P, Baker FC, Caffarra S, Ramos-Usuga D, Yuksel D, et al. How the COVID-19 pandemic has changed our lives: a study of psychological correlates across 59 countries. J Clin Psychol. 2021; 77(3): 556-70.
6. Yuksel D, McKee GB, Perrin PB, Alzueta E, Caffarra S, Ramos-Usuga D, et al. Sleeping when the world locks down: correlates of sleep health during the COVID-19 pandemic across 59 countries. Sleep Health. 2021; 7(2): 134-42.
7. Agrawal R. Careful prescribing of benzodiazepines during COVID-19 pandemic: a review. J Ment Health Clin Psychol. 2020; 4(4): 13-16.
8. Dubey MJ, Ghosh R, Chatterjee S, Biswas P, Chatterjee S, Dubey S. COVID-19 and addiction. Diabetes Metab Syndr. 2020; 14(5): 817-23.
9. Zaami S, Marinelli E, Varì MR. New trends of substance abuse during COVID-19 pandemic: an international perspective. Front Psychiatry. 2020; 11: 700.
10. Sultanoglu N, Baddal B, Suer K, Sanlidag T. Current situation of COVID-19 in Northern Cyprus. East Mediterr Health J. 2020; 26(6): 641-5.
11. KKTC İstatistik Kurumu. Temel İstatistikler: Nüfus ve Demografi İstatistikleri. Available from: https://istatistik.gov.ct.tr/TEMEL-%C4%B0STAT%C4%B0ST%C4%B0KLER/N%C3%9CFUS-VE-DEMOGRAF%C4%B0-%C4%B0STAT%C4%B0ST%C4%B0KLER%C4%B0.
12. Altın D, Coşkunol H. Turkish validity and reliability of the alcohol, smoking and substance involvement screening test. Addicta. 2020; 6(4): 67-86.
13. Klemperer EM, West JC, Peasley-Miklus C, Villanti AC. Change in tobacco and electronic cigarette use and motivation to quit in response to COVID-19. Nicotine Tob Res. 2020; 22(9): 1662-3.
14. Kowitt SD, Cornacchione Ross J, Jarman KL, Kistler CE, Lazard AJ, Ranney LM, et al. Tobacco quit intentions and behaviors among cigar smokers in the United States in response to COVID-19. Int J Environ Res Public Health. 2020; 17(15): 5368.
15. Bommele J, Hopman P, Walters BH, Geboers C, Croes E, Fong GT, et al. The double-edged relationship between COVID-19 stress and smoking: implications for smoking cessation. Tob Induc Dis. 2020; 18: 63.
16. Chodkiewicz J, Talarowska M, Miniszewska J, Nawrocka N, Bilinski P. Alcohol consumption reported during the COVID-19 pandemic: the initial stage. Int J Environ Res Public Health. 2020; 17(13): 4677.
17. Vanderbruggen N, Matthys F, Van Laere S, Zeeuws D, Santermans L, Van den Ameele S, et al. Self-reported alcohol, tobacco, and cannabis use during

COVID-19 lockdown measures: results from a web-based survey. Eur Addict Res. 2020; 26(6): 309-15.

18. Siddiqi K, Siddiqui F, Khan A, Ansaari S, Kanaan M, Khokhar M, et al. The impact of COVID-19 on smoking patterns in Pakistan: findings from a longitudinal survey of smokers. Nicotine Tob Res. 2021; 23(4): 765-9.
19. Alqahtani JS, Oyelade T, Aldhahir AM, Alghamdi SM, Almehmadi M, Alqahtani AS, et al. Prevalence, severity and mortality associated with COPD and smoking in patients with COVID-19: a rapid systematic review and meta-analysis. PLoS One. 2020; 15(5): 0233147.
20. Vardavas CI, Nikitara K. COVID-19 and smoking: a systematic review of the evidence. Tob Induc Dis. 2020; 18: 20.
21. Zhao Q, Meng M, Kumar R, Wu Y, Huang J, Lian N, et al. The impact of COPD and smoking history on the severity of COVID-19: a systemic review and meta-analysis. J Med Virol. 2020; 92(10): 1915-21.
22. Patanavanich R, Glantz SA. Smoking is associated with COVID-19 progression: a meta-analysis. Nicotine Tob Res. 2020; 22(9): 1653-6.
23. Berlin I, Thomas D, Le Faou AL, Cornuz J. COVID-19 and smoking. Nicotine Tob Res. 2020; 22(9): 1650-2.
24. Simons D, Shahab L, Brown J, Perski O. The association of smoking status with SARS-CoV-2 infection, hospitalization and mortality from COVID-19: a living rapid evidence review with Bayesian meta-analyses (version 7). Addiction. 2021; 116(6): 1319-68.
25. Ahluwalia IB, Myers M, Cohen JE. COVID-19 pandemic: an opportunity for tobacco use cessation. Lancet Public Health. 2020; 5(11): 577.
26. World Health Organization. WHO statement: Tobacco use and COVID-19. HYPERLINK https://www.who.int/news/item/11-05-2020-who-statement-tobacco-use-and-covid-19.
27. Alpers SE, Skogen JC, Mæland S, Pallesen S, Rabben ÅK, Lunde LH, et al. Alcohol consumption during a pandemic lockdown period and change in alcohol consumption related to worries and pandemic measures. Int J Environ Res Public Health. 2021; 18(3): 1220.
28. Downs CG, Varisco TJ, Bapat SS, Shen C, Thornton JD. Impact of COVID-19 related policy changes on filling of opioid and benzodiazepine medications. Res Social Adm Pharm. 2021; 17(1): 2005-8.
29. Çakıcı M, Karaaziz M, Babayiğit A, Eş A. Lifetime prevalence and risk factors of drug use in North Cyprus: 2003-2015. Cogent Psychology. 2020; 7(1): 1772630.
30. Asut O, Vaizoglu S, Abuduxike G, Khader E, Ramadan NG, Cali S. Consumption of tobacco products and associated factors among outpatient visitors of two healthcare facilities in Northern Cyprus: a descriptive cross-sectional study. J Addict Dis. 2024: 1-8.
31. Asut O. Tobacco use and attitudes on tobacco control among faculty members of a medical school in Northern Cyprus (tobacco use among medical teachers). J Addict Dis. 2020; 38(2): 153-63.
32. Aslan D, Ay P, Raymond K, Aşut Ö, Abuduxike G, Şengelen M, et al. Medical students' tobacco consumption status and experiences with smoke-free law violations in enclosed spaces in Türkiye and Northern Cyprus. Thorac Res Pract. 2025; 26(2): 48-54.

RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-1
Cyprus J Med Sci 2025;10(5):321-325

Evaluation of Quality of Life, Anxiety and Depression in Patients with Alopecia Areata: A Prospective Case-Control Study

Pınar Özdemir Çetinkaya[1], Ömer Kutlu[2]

[1]Department of Dermatology and Venereology, University of Health Sciences Türkiye, Şişli Hamidiye Etfal Training and Research Hospital, İstanbul, Türkiye
[2]Department of Dermatology and Venereology, Tokat Gaziosmanpaşa University Faculty of Health Sciences, Tokat, Türkiye

Abstract

BACKGROUND/AIMS: Alopecia areata (AA) is an immune response-driven, scarless hair disease specified by the destruction of hair follicles by an inflammatory response resulting from the loss of immune privilege. Apart from posing a cosmetic concern, it is a condition that impacts patients due to its chronic, unpredictable course and the lack of a definitive treatment. This study sought to explore the psychosocial state of patients with AA during its acute phase and compare them with a control group.

MATERIALS AND METHODS: This multicenter, prospective case-control study contained 70 patients with AA and 70 voluntary controls. The AA group included patients with recent onset or recurrent AA with a disease duration of under one year. After the demographic information and clinical traits of the patients were recorded, the study group was asked to complete the hospital anxiety and depression scale (HADS) and the dermatology life quality index (DLQI) to appraise their psychological well-being and quality of life.

RESULTS: In this study, the psychosocial characteristics of 140 participants were evaluated. The AA cohort comprised 70 patients, while the control cohort included 70 individuals matched for age and gender. Of the 70 patients with AA, 45 (64.3%) were men, and 25 (35.7%) were women, with a median age of 29 (interquartile range =12.25) years. The median anxiety and depression scores according to HADS (HADS-Anxiety and HADS-Depression) were markedly elevated in the patient group compared to controls. Additionally, the median DLQI score of the patient group was substantially greater than that of the control group, which was statistically significant.

CONCLUSION: The outcomes of our study indicated that anxiety and depression scores were elevated in patients with acute AA compared to the controls. Therefore, it is essential for clinicians to recognize and address psychiatric comorbidities in patients with AA, even during the early period of the condition.

Keywords: Alopecia areata, anxiety, depression, quality of life

INTRODUCTION

Alopecia areata (AA) is an immune response-driven, scarless hair disease specified by destruction of hair follicles by an inflammatory response resulting from the loss of immune privilege.[1] It may manifest as one or more alopecic patches on the scalp, as well as alopecia totalis or alopecia universalis. It can also involve the facial region, leading to hair loss in the eyebrows, eyelashes, and beard.[2,3] The progression of AA is unpredictable, as it may either resolve spontaneously or persist for a long time, even a lifetime. Given that the duration of the current episode is a key prognostic factor, AA was classified as acute (≤12 months) or chronic (>12 months).[4] The condition poses a cosmetic concern and impacts

To cite this article: Özdemir Çetinkaya P, Kutlu Ö. Evaluation of quality of life, anxiety and depression in patients with alopecia areata: a prospective case-control study. Cyprus J Med Sci. 2025;10(5):321-325

ORCID IDs of the authors: P.Ö.Ç. 0000-0001-5286-3260; Ö.K. 0000-0002-9665-015X.

Corresponding author: Pınar Özdemir Çetinkaya
E-mail: pinarozdemir44@gmail.com
ORCID ID: orcid.org/0000-0001-5286-3260

Received: 02.02.2025
Accepted: 21.07.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

patients due to its chronic and unpredictable course, compounded by the absence of a curative treatment.

To date, the psychological symptoms and comorbidities associated with AA have been thoroughly investigated, with several meta-analyses conducted on the topic. In their meta-analysis, Lee et al.[5] assessed all comorbidities associated with AA. According to the findings of 87 studies, an adjusted odds ratio (OR) of 1.72 for anxiety and an adjusted OR of 1.49 for depression were reported. Okhovat et al.[6] conducted a meta-analysis focused on the link between anxiety, depression, and AA. Analyzing the data from 8 studies, the meta-analysis found pooled ORs of 2.5 for anxiety, and 2.71 for depression. Finally, Lauron et al.[7] assessed the prevalence of depression and anxiety disorders in a meta-analysis that included 29 studies on depression and 26 studies on anxiety. They reported that the prevalence of depression was 9% (OR: 1.38), while the prevalence of depressive symptoms was 37% (OR: 2.70). Similarly, the prevalence of unspecified anxiety disorders was 13% (OR: 1.51), and the prevalence of anxiety symptoms was 34% (OR :3.07). Overall, it is evident that there are varying levels of association between AA and depression as well as anxiety.

In AA, stressful life events can trigger the onset of the disease, while the condition itself may lead to psychological symptoms, creating a bidirectional relationship. This study aimed to investigate the psychological stress associated with the disease during its acute phase. Given the chronic nature of the condition and the prolonged treatment process, patients experience a disease burden along with associated psychiatric comorbidities. However, in this study, we sought to appraise anxiety and stress symptoms in patients with a disease duration of one year or less who were seeking hospital care for the first time, and to compare these symptoms with a control group.

MATERIALS AND METHODS

This multicenter, prospective case-control study was carried out from March 2020 to March 2021, involving 70 patients with AA and 70 voluntary controls, all recruited from the dermatology outpatient clinics of two state hospitals. The research acquired endorsement from the Erciye University's Ethics Committee (approval number: 2020/119, date: 12.02.2020). Participants were provided with complete information, and written consent was obtained.

The AA group included 70 patients aged 18 to 65 years, diagnosed with AA based on clinical history and dermatological examination. The study included patients with new onset or recurrent AA with a disease duration under one year. Patients with new onset disease were admitted to the outpatient clinic for the first time, while patients with recurrent AA were admitted due to their current relapse. Patients with a diagnosed psychiatric disorder were excluded from the AA group. The control group comprised 70 volunteers who had no history of dermatological or psychiatric conditions. The demographic information, family history, and clinical characteristics of the patients, including disease duration, presence of concomitant autoimmune diseases, pattern of disease involvement, and nail changes, were recorded. the severity of alopecia tool (SALT) was calculated to determine disease severity in patients with AA. The total score of SALT is used to evaluate the extent of hair loss. The scalp is divided into vertex, right lateral side, left lateral side, and the back. The percentage of hair loss in each region is then multiplied by specific weight factors-0.4 for the vertex, 0.18 for the right and left lateral sides, and 0.24 for the back. The SALT score is calculated by summing the weighted scores from all four regions. Areata Investigational Assessment Guidelines, the SALT score is categorized into the following subgroups: S0 = no hair loss, S1 = <25% hair loss, S2 = 25-49% hair loss, S3 = 50-74% hair loss, S4 = 75-99% hair loss, and S5 = 100% hair loss.

The AA and control group were asked to complete the hospital anxiety and depression scale (HADS) and the dermatology life quality index (DLQI) to assess their mental well-being and quality of life (QoL). The validated Turkish edition of the HADS was used to evaluate manifestations of anxiety/depression. The HADS is a 14-item self-administered inventory, with each item scored on a 4-level Likert scale (0-3 points). It includes subscales of HADS-anxiety (HADS-A) and HADS-depression (HADS-D), with seven questions dedicated to each subscale. The cut-off scores for identifying anxiety and depression were set at 10 and 7, respectively. The QoL of the study groups was evaluated with the Turkish version of the DLQI. The DLQI is a 10-question self-reported instrument with a 4-level Likert scale (0-3), with total scores varying from 0 to 30. Elevated scores reveal a worse QoL, and scores greater than 10 suggest that it is moderately or severely affected.

Statistical Analysis

IBM SPSS Statistics for Windows, version 20.00 (Armonk, New York, USA: IBM Corp) was used to analyze the study, and a p-value of under 0.05 was interpreted as indicating statistical significance. The Shapiro-Wilk test was employed to analyze the normality of the data. The median and interquartile range (IQR) are used to express continuous variables with a non-parametric distribution. Categorical variables were stated as frequencies/percentages. The Mann-Whitney U test was utilized for independent samples. Pearson's chi-square test was applied for categorical variables, and, if any cell contained an expected count below five, Fisher's exact test was utilized instead.

RESULTS

In this study, the psychosocial characteristics of 140 participants were evaluated. The AA group consisted of 70 patients, and the control group consisted of 70 age- and sex-matched volunteers (p=0.424, p=0.275, respectively). Of the 70 patients with AA, 45 (64.3%) were men, and 25 (35.7%) were women with a median age of 29 (IQR=12.25) years. Disease duration varied from 10 days to 12 months; and the median duration of AA was 1 month (IQR=1). Ten patients (14.3%) with AA had a family history; and 1 (1.4%) patient also had an accompanying autoimmune disease, Hashimoto's thyroiditis. Clinically, 7 (10%) patients had nail changes that indicated nail involvement, 5 (7.1%) patients had ophiasis, and the SALT scores of all the patients were <25%, categorizing them in the S1 subgroup. Forty-four (62.9%) of the patients stated that they had a history of life stressors before the onset of the disease (Table 1).

The median anxiety and depression scores according to HADS (HADS-A and HADS-D) were statistically significantly higher in the patient group than the control group (p=0.019, p=0.041, respectively). In addition, the median DLQI scores of the AA group were statistically significantly higher than the scores of the control group (p<0.001). The comparison of HADS and DLQI scores between the AA and control groups is given in Table 2.

Table 1. Demographic characteristics and clinical findings of patients with AA

	Patient group (n=70)
Sex (n/%)	
Female	25 (35.7%)
Male	45 (64.3%)
Age [Median, (IQR), years]	**29 (12.25)**
Duration of AA [Median, (IQR), months]	**1 (1)**
Family history of AA (n/%)	10 (14.3%)
Accompanying autoimmune diseases (n/%)	
Hashimoto's thyroiditis	1 (1.4%)
Clinical findings of AA (n/%)	
Nail involvement	7 (10%)
Ophiasis	5 (7.1%)
S1 subgroup according to SALT scores	70 (100%)
History of life stressors	44 (62.9%)

Data were expressed as the median and the IQR in continuous variables, and the n (%) in categorical variables.
AA: Alopecia areata, IQR: Interquartile range, SALT: Severity of alopecia tool.

Table 2. Comparison of HADS and DLQI scores between the alopecia areata and control group

	AA group (n=70)	Control group (n=70)	p
HADS [median, (IQR)]			
Anxiety	8 (6.25)	7 (4)	0.019*m
Depression	7 (5.25)	4.5 (6)	0.041*m
HADS classification (n/%)			
Anxiety			
Absent	40 (57.1%)	58 (82.9%)	0.001*X²
Present	30 (42.9%)	12 (17.1%)	
Depression			
Absent	33 (47.1%)	44 (62.9%)	0.062X²
Present	37 (52.9%)	26 (37.1%)	
Presence of stressful life events (n/%)			
Absent	26 (37.1%)	37 (52.9%)	0.062X²
Present	44 (62.9%)	33 (47.1%)	
DLQI [median, (IQR)]	2 (6)	0.5 (2)	<0.001*m
DLQI classification (n/%)			
Mildly-moderately affected	63 (90%)	70 (100%)	0.013*f
Severely affected	7 (10%)	0	

Data were expressed as median (IQR) for continuous variables and n (%) for categorical variables.
Independent samples were compared with the Mann-Whitney U and chi-square tests.
If one or more cells had an expected count of less than 5, Fisher's exact test was used.
*p<0.05, mMann-Whitney U test, X²chi-square test, fFisher's exact test.
AA: Alopecia areata, DLQI: Dermatology life quality index, HADS: Hospital anxiety and depression scale, IQR: Interquartile range.

DISCUSSION

An increasing body of evidence suggests a connection between psychiatric comorbidities and inflammatory diseases such as psoriasis, atopic dermatitis, rheumatoid arthritis, and inflammatory bowel disease.[8-11] Among these, AA, an autoimmune condition that results in hair loss, has garnered growing interest due to its potential psychological impact. CD8 + T cells are thought to play a central role in mediating hair loss in AA, and there are higher levels of IL-6, IL-1β, tumor necrosis factor (TNF), along with cytokines of type 2 and type 17 immune pathways.[12] Several meta-analyses revealed that IL-6, IL-1β, and TNF have been closely linked to depression.[13,14] Bain et al.[12] reported that increased levels of IL-17E and IL-22 were positively associated with depression scores of patients with AA.

In our study, we intended to evaluate the psychosocial parameters of patients with AA admitted to outpatient clinics for the first time during the acute phase. While 62.9% of the patients reported a history of significant stress prior to the onset of the disease, the median anxiety and depression scores of the AA group were significantly higher compared to the control group. However, only the frequency of anxiety was significantly higher based on the HADS' defined cut-off values. While the psychosocial effects of AA have been studied in detail in the literature, our study uniquely focuses on the HADS scores in patients at the first hospital admission at disease onset or relapse. Unlike previous studies that may focus on longer disease durations, our focus on early-stage patients offers a unique perspective on the initial emotional challenges faced by individuals with AA. Thus, our findings underscore the importance of addressing mental health early in the course of AA.

The new international classification of psychodermatological disorders categorizes AA as a "primary skin disorder related to mental health", similar to conditions like urticaria, vitiligo, and psoriasis.[15,16] This implies that AA is a skin condition influenced by stress and linked to secondary psychiatric conditions.[15] It is commonly believed, based on anecdotal evidence, that psychological stress triggers AA. While some case-control studies support this link, other publications have found no evidence to support it.[17-20] Kutlu et al.[17] highlighted the increase in AA cases during the coronavirus disease-2019 pandemic compared to the preceding year and proposed that AA may be more closely linked to short-term stress (less than 2 months) rather than long-term stress. Ferentinos et al.[18] conducted a case-control study involving 52 patients with new-onset or recurrent AA and 51 matched controls. They found that patients with AA experienced a significantly higher number of stressful life events in the previous year (number of events: 4 vs. 3) compared to the controls. Although there was no significant difference in HADS scores between the two groups, the study revealed that stressful life events were linked to higher HADS-A scores in patients with AA. Additionally, Taheri et al.[19] investigated the potential role of stressful life events as a trigger for AA in a study involving 61 patients and 61 controls. The results revealed no significant differences in the number or mean scores of physical and sexual stress events between the two groups. However, patients experienced more emotional stress events with higher mean scores compared to the control group. In our study, we found that 62.9% of patients had experienced stressful life events, 52.9% had symptoms of depression, and 42.9% had symptoms of anxiety. Among these, only the prevalence of anxiety was significantly higher than in the control

group. Since no differences were found in stressful life events, it may be concluded that high anxiety may be a comorbidity of the disease rather than a trigger. Although the exact role of stress in triggering AA remains unclear, the possibility that stress could act as a trigger in susceptible individuals still exists and warrants further investigation.

AA often causes cosmetic disfigurement rather than severe physical symptoms, yet it still has a considerable effect on mental well-being. Thus, the psychosocial impact of AA has been studied over an extended period. In their study assessing the psychological profile and QoL in 126 patients (94 adults) with AA, Vélez-Muñiz et al.[21] found that the majority of patients had patchy alopecia, and 77.6% of the adults had an impaired QoL. Additionally, 71.2% displayed symptoms of depression and anxiety, according to the HADS, and 60% of the referred patients were prescribed pharmacological treatment. The impact of the disease on patients also varies. In a study by Bain et al.[12] involving 39 patients with AA, depression was found in 18% of patients and anxiety in 51% of patients, as measured by the HADS. Interestingly, the frequency of depression and anxiety was higher in patients who had experienced patchy hair loss for less than 10 years compared to those with more advanced stages and longer durations of the condition. Furthermore, Bewley et al.[22] conducted a multicenter, cross-sectional survey involving 747 patients with a history of or current hair loss severity of ≥50% to assess the disease burden. They reported that 26.1% of patients were diagnosed with anxiety and 18.1% with depression. Additionally, 86.2% of patients had severely affected DLQI scores (>10). Further analysis showed that the DLQI score was lower in patients with less than 50% hair loss compared to those with equal to or more than 50% hair loss, as expected. However, DLQI scores were still lower (but above 10) in patients with a disease duration of >4 years, compared to those with 0-4 years. Improved depression, anxiety, and QoL scores in long-term or severe illness may be attributed to the development of greater disease acceptance and the establishment of effective coping mechanisms. Finally, using several questionnaires, including HADS, Clemmesen et al.[23] studied the psychosocial and mental impact of AA with 376 patients. They reported that Skindex-16 and AA symptom impact scale could distinguish disease severity. They found that moderate to severe disease, female sex, and eyebrow involvement contributed to a higher score and had a detrimental effect on the patient's QoL. They also emphasized that the DLQI is not an ideal tool for evaluating the Qol related to AA, as it mainly focuses on skin symptoms rather than those linked to hair loss.[23] In the studies summarized above, despite variations in disease duration, severity, and the scales used, it is evident that the QoL was impacted, and patients displayed symptoms of depression and anxiety. Although our patient group consisted of individuals with patchy alopecia and a disease duration under one year, 42.9% exhibited symptoms of anxiety, 52.9% exhibited symptoms of depression, and 10% had a severely affected QoL. From these findings, it can be concluded that patients with newly onset disease are more likely to experience psychological impacts, irrespective of the disease's severity. Additionally, it is important to acknowledge that the DLQI may not fully capture the QoL in patients with AA. Moreover, QoL is likely to be more significantly affected in cases of severe disease or during the acute phase, regardless of the disease's overall severity. Therefore, even in cases of mild disease, clinicians should prioritize assessing the psychological well-being and QoL of patients at the onset of the condition.

Study Limitations

Our study has several limitations. While the study design was prospective and the sample size was moderate, it was a case-control study, which limits the ability to draw conclusions about causal relationships. Additionally, the psychological status of the study population was assessed using self-reported questionnaires commonly used in clinical practice. However, neither the patients nor the controls underwent psychiatric evaluations by clinicians. Another limitation of the study was that the patient group consisted of individuals in the S1 group of SALT, with scalp involvement below 25%, despite the inclusion criteria not specifying restrictions based on disease severity. As a result, HADS scores could not be assessed in relation to disease severity. Additionally, because the disease duration was short in this study, we were unable to assess the correlation between disease duration and HADS scores.

CONCLUSION

The findings of our study indicated that anxiety and depression scores were higher in patients with acute AA compared to the control group. Therefore, it is essential for clinicians to recognize and address psychiatric comorbidities in patients with AA, even during the early phase of the condition. In this way, they can ensure a comprehensive approach to the patient's overall well-being and refer them for further evaluation if psychological symptoms are observed.

MAIN POINTS

- 62.9% of the patients reported a history of significant stress before the onset of the disease.
- Although our patient group consisted of individuals with patchy alopecia and a disease duration of under one year, 42.9% exhibited symptoms of anxiety and 52.9% of depression, and 10% had a severely affected quality of life (QoL).
- Even in cases of mild disease, clinicians should prioritize assessing the psychological well-being and QoL patients at the onset of the condition.

ETHICS

Ethics Committee Approval: The research acquired endorsement from the Erciye University's Ethics Committee (approval number: 2020/119, date: 12.02.2020).

Informed Consent: Participants were provided with complete information and written consent was attained.

Acknowledgements: The authors state that they have no relationships that provided financial or editorial assistance for the study, which could potentially lead to a conflict of interest regarding the submission.

Footnotes

Authorship Contributions

Surgical and Medical Practices: P.Ö.Ç., Ö.K., Concept: P.Ö.Ç., Ö.K., Design: P.Ö.Ç., Ö.K., Data Collection and/or Processing: P.Ö.Ç., Ö.M., Analysis and/or Interpretation: P.Ö.Ç., Ö.K., Literature Search: P.Ö.Ç., Ö.K., Writing: P.Ö.Ç., Ö.K.

DISCLOSURES

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

Financial Disclosure: The authors declared that this study had received no financial support.

References

1. Strazzulla LC, Wang EHC, Avila L, Lo Sicco K, Brinster N, Christiano AM, et al. Alopecia areata: disease characteristics, clinical evaluation, and new perspectives on pathogenesis. J Am Acad Dermatol. 2018; 78(1): 1-12.
2. Hon KL, Leung AK. Alopecia areata. Recent Pat Inflamm Allergy Drug Discov. 2011; 5(2): 98-107.
3. Olsen EA, Hordinsky MK, Price VH, Roberts JL, Shapiro J, Canfield D, et al. Alopecia areata investigational assessment guidelines--Part II. National Alopecia Areata Foundation. J Am Acad Dermatol. 2004 Sep; 51(3): 440-7.
4. Prinsen CA, Vohra S, Rose MR, King-Jones S, Ishaque S, Bhaloo Z, et al. Core outcome measures in effectiveness trials (COMET) initiative: protocol for an international Delphi study to achieve consensus on how to select outcome measurement instruments for outcomes included in a 'core outcome set'. Trials. 2014; 15: 247.
5. Lee S, Lee H, Lee CH, Lee WS. Comorbidities in alopecia areata: a systematic review and meta-analysis. J Am Acad Dermatol. 2019; 80(2): 466-77.e16.
6. Okhovat JP, Marks DH, Manatis-Lornell A, Hagigeorges D, Locascio JJ, Senna MM. Association between alopecia areata, anxiety, and depression: a systematic review and meta-analysis. J Am Acad Dermatol. 2023; 88(5): 1040-50.
7. Lauron S, Plasse C, Vaysset M, Pereira B, D'Incan M, Rondepierre F, et al. Prevalence and odds of depressive and anxiety disorders and symptoms in children and adults with alopecia areata: a systematic review and meta-analysis. JAMA Dermatol. 2023; 159(3): 281-8.
8. Kurd SK, Troxel AB, Crits-Christoph P, Gelfand JM. The risk of depression, anxiety, and suicidality in patients with psoriasis: a population-based cohort study. Arch Dermatol. 2010; 146(8): 891-5.
9. Almutawa YM, AlGhareeb M, Bhattarai E, Aljalahma J. Investigation of the impact of atopic dermatitis (AD) on stress, depression, anxiety, and suicidal ideation: a systematic review and meta-analysis. Cureus. 2024; 16(6): e63376.
10. Nerurkar L, Siebert S, McInnes IB, Cavanagh J. Rheumatoid arthritis and depression: an inflammatory perspective. Lancet Psychiatry. 2019; 6(2): 164-73.
11. Martin-Subero M, Anderson G, Kanchanatawan B, Berk M, Maes M. Comorbidity between depression and inflammatory bowel disease explained by immune-inflammatory, oxidative, and nitrosative stress; tryptophan catabolite; and gut-brain pathways. CNS Spectr. 2016; 21(2): 184-98.
12. Bain KA, McDonald E, Moffat F, Tutino M, Castelino M, Barton A, et al. Alopecia areata is characterized by dysregulation in systemic type 17 and type 2 cytokines, which may contribute to disease-associated psychological morbidity. Br J Dermatol. 2020; 182(1): 130-7.
13. Haapakoski R, Mathieu J, Ebmeier KP, Alenius H, Kivimäki M. Cumulative meta-analysis of interleukins 6 and 1β, tumour necrosis factor α and C-reactive protein in patients with major depressive disorder. Brain Behav Immun. 2015; 49: 206-15.
14. Liu Y, Ho RC, Mak A. Interleukin (IL)-6, tumour necrosis factor alpha (TNF-α) and soluble interleukin-2 receptors (sIL-2R) are elevated in patients with major depressive disorder: a meta-analysis and meta-regression. J Affect Disord. 2012; 139(3): 230-9.
15. Ferreira BR, Vulink N, Mostaghimi L, Jafferany M, Balieva F, Gieler U, et al. Classification of psychodermatological disorders: proposal of a new international classification. J Eur Acad Dermatol Venereol. 2024; 38(4): 645-56.
16. Karaosmanoğlu N, Özdemir Çetinkaya P, İmren IG, Kıratlı Nalbant E, Karaaslan E. Childhood and adolescence vitiligo: clinicoepidemiological profile and its impact on quality of life. Cyprus J Med Sci. 2020; 5(1): 41-6.
17. Kutlu Ö, Aktaş H, İmren IG, Metin A. Short-term stress-related increasing cases of alopecia areata during the COVID-19 pandemic. J Dermatolog Treat. 2022; 33(2): 1177.
18. Ferentinos P, Kalogeropoulou E, Pappa G, Antoniou A, Bozi E, Kyprianou M, et al. Assessing the role of stressful life events in the induction and recurrence of alopecia areata: a case-control study. J Am Acad Dermatol. 2022; 87(5): 1215-7.
19. Taheri R, Behnam B, Tousi JA, Azizzade M, Sheikhvatan MR. Triggering role of stressful life events in patients with alopecia areata. Acta Dermatovenerol Croat. 2012; 20(4): 246-50.
20. Russiello F, Arciero G, Decaminada F, Corona R, Ferrigno L, Fucci M, et al. Stress, attachment and skin disease: a case-control study. J Eur Acad Dermatol Venereol. 2006; 5(3): 234-9
21. Vélez-Muñiz RDC, Peralta-Pedrero ML, Jurado-Santa Cruz F, Morales-Sánchez MA. Psychological profile and quality of life of patients with alopecia areata. Skin Appendage Disord. 2019; 5(5): 293-98.
22. Bewley A, Figueras-Nart I, Zhang J, Guerreiro M, Tietz N, Chtourou S, et al. Patient-reported burden of severe alopecia areata: first results from the multinational alopecia areata unmet need survey. Clin Cosmet Investig Dermatol. 2024; 17: 751-61.
23. Clemmesen MER, Gren ST, Frøstrup AG, Thomsen SF, Egeberg A, Thein D. Psychosocial and mental impact of alopecia areata: analysis of the Danish Skin Cohort. J Eur Acad Dermatol Venereol. 2025; 39(3): 688-97.

RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-48
Cyprus J Med Sci 2025;10(5):326-334

Assessment of the Postoperative Recovery: A Mixed Methods Study

Nurdan Sarmusakcı[1], Deniz Şanlı[2]

[1]Neurology Intensive Care Unit, İzmir Katip Çelebi University Atatürk Traning and Research Hospital, İzmir, Türkiye
[2]Department of Surgical Nursing, Division of Nursing, İzmir Katip Çelebi University Faculty of Health Sciences, İzmir, Türkiye

Abstract

BACKGROUND/AIMS: Assessing the postoperative recovery is crucial for expediting healing and optimizing care. The study aims to assess patients' postoperative recovery levels.

MATERIALS AND METHODS: This mixed-methods study was executed in the surgery clinic from March 2022 to February 2023. The study sample consisted of 140 patients for the quantitative method and 12 for the qualitative method. Study data were collected using the postoperative recovery index (PoRI) and a semi-structured interview form. The data were further analyzed utilizing the independent sample t-test and one-way analysis of variance for quantitative analysis, alongside content analysis for qualitative analysis.

RESULTS: For the quantitative analysis section of the study, the mean scores in the sub-dimensions of the PoRI were 3.54±0.80 for the physical activities, 2.38±0.87 for the bowel symptoms, 2.41±0.93 for the appetite symptoms, 2.35±0.74 for the general symptoms, and 3.03±0.84 for the psychological symptoms, whereas the overall index was 2.85±0.55. Differences were determined in patients' sub-dimension and total index scores according to age, body mass index, tobacco use, chronic diseases, and prior surgery, as well as the clinic in which they were hospitalized, type of surgery, and type of anesthesia received ($p<0.05$). The themes developed for the qualitative analysis of the study were perspectives on postoperative complaints and changes, recovery status, factors affecting recovery, perspectives on the results of surgery, and the significance of recovery.

CONCLUSION: Patients experienced considerable difficulty in the overall index throughout the postoperative recovery. Patients reported positive and negative perceptions and perspectives regarding postoperative recovery.

Keywords: Postoperative care, postoperative period, postoperative recovery, recovery

INTRODUCTION

Postoperative recovery is a multidimensional process that influences various conditions, including physical, psychological, social, and economic status. Owing to its multifaceted nature, it is considered a complex process.[1,2] Postoperative recovery involves restoring capacity and homeostasis, leading to normalization.[2]

Therefore, evaluating the level of postoperative recovery is essential for assessing and enhancing perioperative care.[3] Assessing patient outcomes and symptoms via postoperative recovery measurement methods is crucial for expediting postoperative recovery and optimizing nursing care.[4] Incomplete postoperative recovery indicates potential long-term adverse outcomes. The prompt and precise identification of these symptoms facilitates the timely application of interventions that can avert adverse outcomes.[2]

Historically, significant emphasis has been placed on physical symptoms in assessing recovery.[2] Current trends focus on determining the multidimensional aspects of recovery. The study evaluated physical, psychological, and functional dimensions, and has recently

To cite this article: Sarmusakcı N, Şanlı D. Assessment of the postoperative recovery: a mixed methods study. Cyprus J Med Sci. 2025;10(5):326-334

ORCID IDs of the authors: N.S. 0000-0002-9352-7754; D.Ş. 0000-0001-6076-0317.

Corresponding author: Deniz Şanlı
E-mail: deniz.sanli@ikc.edu.tr
ORCID ID: orcid.org/0000-0001-6076-0317

Received: 21.05.2025
Accepted: 15.07.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

included cognitive dimensions.[1] Including patient-oriented outcomes in the recovery assessment is critical to evaluating the postoperative recovery.[5]

The multifactorial nature of postoperative treatment and recovery necessitates a multidisciplinary approach to reduce complications and shorten the duration of hospitalization.[6] Nursing care seeks to identify complications and promptly administer appropriate treatment, a crucial aspect of the process.[7] Thus, nurse efficacy in postoperative recovery commences with accurate problem diagnosis, progresses through the delivery of suitable care, and involves implementing diverse recovery techniques.[6]

Throughout the postoperative recovery process, which is influenced by many variables, it is crucial to systematically evaluate the patient using accurate and reliable measurement methods to monitor the patient accurately and diagnose problems early. It is essential to assess the recovery process from the patient's perspective, considering all its dimensions. The study was believed to have the potential to contribute to this process.

Purpose

The study aims to assess patients' postoperative recovery levels. For this purpose, the postoperative recovery status of the patients and changes in their condition based on sociodemographic characteristics and clinical factors were examined through quantitative methods. Subsequently, patients' perceptions and perspectives regarding postoperative recovery were elucidated through qualitative analysis.

MATERIALS AND METHODS

Study Design/Setting

The study was conducted using mixed methods. Thus, a holistic understanding was achieved by combining quantitative and qualitative analysis methods. The mixed method was a concurrent design.[8]

The study was conducted between March 2022 and February 2023 in the surgery clinics of a training and research hospital. These clinics covered various surgeries.

Sample

The study sample consisted of patients who had undergone surgery in the surgical clinics throughout the study term and who satisfied specific inclusion criteria. These criteria included being 18 or older, being on the postoperative first day, and having undergone elective surgery. The stratified sampling method was employed in the quantitative analysis.

The sample size for the quantitative analysis was determined using the G*Power software.[9] The minimum sample size was 130, with an effect size of 0.50, a Cronbach's alpha of 0.05, and a power of 0.80. The quantitative analysis of the study involved 140 patients. The sample size of the qualitative analysis is determined based on the amount of information to be collected from the sample. It is the point at which data saturation occurs.[10] The qualitative analysis of the study was finalized with 12 patients.

Data Collection Tools

Personal information form: The researchers developed the form from the literature. It has 17 items addressing the sociodemographic and clinical characteristics of the patients, including anthropometric traits, health and disease history, and current surgery details.

Postoperative recovery index: Postoperative recovery index (PoRI) was developed by Butler et al.[4] in 2012. The index comprises 37 items and five sub-dimensions. These are physical activities (basic, advanced), bowel symptoms (lower, upper), appetite symptoms (pleasure, digestion), general symptoms (physical/neuropsychological, sleep), and psychological symptoms (internal, interpersonal). The arithmetic mean calculates the sub-dimension and overall index scores. PoRI has been adapted into Turkish by Cengiz and Aygin[11] with 25 items and five sub-dimensions. Cengiz and Aygin[11] determined Cronbach's alpha values as 0.978 for physical activities, 0.977 for bowel symptoms, 0.971 for general symptoms, 0.983 for craving symptoms, 0.930 for psychological symptoms, and 0.967 for the whole index. The Cronbach's alpha coefficient for the index in the study varies from 0.658 to 0.905 across the sub-dimensions and 0.886 for the overall index.

Semi-structured interview form: The interview technique requires a written form.[9] Consequently, this form was used. Qualitative analysis necessitates trustworthiness. The criteria used to demonstrate the study's trustworthiness are established through credibility, transferability, dependability, and confirmability.[8] The form was structured based on expert opinions. Expert opinions were obtained from three academicians from the field of nursing and two specialist physicians from the field of surgery. The definitive version of the form was established during a pilot interview with two patients. The form consists of an introduction, process steps, interview questions, and the closing sections. The interview questions include what postoperative recovery means to the patient, what they think about postoperative recovery, what changes they experienced after surgery compared to their preoperative condition, how the surgery affected the patient, and whether they had any complaints or problems after the surgery.

Data Collection

For quantitative analysis, a researcher visited all patients in the sample on the first postoperative day to administer the data collection tools. Patients were requested to be assessed in the next 24 hours. The procedure required 10 to 15 minutes.

Qualitative data were collected through in-depth interviews, necessitating a thorough analysis of sensitive subjects. The in-depth interviews aimed to elucidate patients' perceptions, opinions, and experiences concerning their postoperative recovery. The interviews were performed in person based on the questions developed by the researchers. Digital voice recorders were employed to capture the interviews. Furthermore, the researchers documented their observations throughout the interview. The interviews were conducted by the first researcher. There was no observer during the interview. It was determined that the patients participated voluntarily in the interview. An interview plan, including the date and time, was created for the patients who consented to participate. The interviews took place in a tranquil room at the clinics where the patients were and lasted 30 to 45 minutes.

Statistical Analysis

Data analysis using the quantitative method was performed with statistical package for the social sciences 22.0 software. The skewness and kurtosis metrics, Q-Q plot, and normality assessments were used to evaluate whether the data were normally distributed. Given that

the normal distribution assumption was satisfied, an independent samples t-test and one-way analysis of variance (accompanied by the Bonferroni test to determine the group responsible for the difference) were employed. The significance level was established at $p<0.05$.

Content analysis was employed for qualitative analysis. Two researchers coded and documented the data, which was collected through the interviews, on the voice recorder. The data were further statistically analyzed using MAXQDA. Accordingly, the themes, categories/sub-dimensions, and codes were established. Frequency values (f) and patient numbers (p) were used to present the data. Patients were anonymized with codes H1-H12.

Ethical Considerations

Ethical approval for this study was obtained from the Non-Interventional Clinical Studies Institutional Review Board of İzmir Katip Çelebi University (approval number: 0092, date: 24.02.2022). Informed consent was obtained from all participants. Each patient participating in the interview was assigned a numerical code to ensure confidentiality, which was in line with the aims of the qualitative analysis.

RESULTS

Qualitative Analysis Results

37.8% of the patients were 65 years of age and older, 57.9% were male, 41.4% were overweight, 34.3% used tobacco, and 68.6% had chronic diseases. 62.1% of the patients had undergone prior surgery. The distribution of patients by clinic is balanced, with each clinic having 14.3% of the total patients. 89.3% of the patients, had undergone open surgery, while 72.9% had received general anesthesia (Table 1).

The mean scores of the patients on the sub-dimensions and overall of the PoRI was presented in Table 2.

Physical activity scores of patients aged between 55 and 64 (3.80±0.67) and 65 years and over (3.58±0.81) were higher than patients under 45 years of age (3.05±0.68) ($f=5.024$, $p=0.002$). Bowel symptom scores of patients aged between 55 and 64 (2.71±0.81) were higher than patients under 45 years of age (2.05±0.84) ($f=3.437$, $p=0.019$). Overall index scores of patients aged between 55 and 64 (3.08±0.47) and 65 years and over (3.58±0.51) were higher than patients under 45 years of age (3.05±0.53) ($f=5.397$, $p=0.002$). No significant difference was observed in the patients' scores based on their gender. Appetite symptom scores of obese patients (2.63±1.06) were found to be higher than overweight patients (2.19±0.84) ($f=3.437$, $p=0.019$). Psychological symptom scores of patients who used tobacco (3.23±0.88) were found to be higher than patients who did not use tobacco (2.92±0.79) ($t=2.092$, $p=0.038$). Psychological symptom scores of patients with chronic diseases (3.13±0.83) were found to be higher than those of patients who did not have a chronic disease (2.81±0.80) ($t=2.076$, $p=0.040$). Psychological symptom scores of patients who had undergone a prior surgery (3.14±0.82) were higher to than patients who had not undergone a prior surgery (2.83±0.83) ($t=2.145$, $p=0.034$).

Significant differences were observed in all sub-dimensions except one and overall index scores of the patients depending on the surgery clinics in which the patients were hospitalized ($p<0.05$) (Table 3).

Table 1. Sociodemographic and clinical characteristics of the patients

Characteristics	n	%
Age ($\tilde{X}$ ± SD=57.75±15.51)		
<45	26	18.6
45-54	25	17.9
55-64	36	25.7
>65	53	37.8
Gender		
Female	59	42.1
Male	81	57.9
Education		
Illiterate	7	5.0
Literate	12	8.6
Primary/secondary school	69	49.3
High school	42	30.0
University and post-graduate education	10	7.1
Marital status		
Married	113	80.7
Single	27	19.3
Body mass index		
Normal	50	35.7
Overweight	58	41.4
Obese	32	22.9
Tobacco use		
Yes	48	34.3
No	92	65.7
Chronic diseases		
Yes	96	68.6
No	44	31.4
Prior surgery		
Yes	87	62.1
No	53	37.9
The patient was hospitalized		
Neurosurgery	20	14.3
General surgery	20	14.3
Cardiovascular surgery	20	14.3
Otolaryngology	20	14.3
Urology	20	14.3
Orthopedics and traumatology	20	14.3
Plastic, reconstructive, and aesthetic surgery	20	14.3
Type of surgery		
Open	108	77.1
Laparoscopic	32	22.9
Type of anesthesia received		
General	102	72.9
Spinal	36	25.7
Nerve block	2	1.4

n=140. SD: Standard deviation.

Physical activities scores (3.64±0.75, 3.20±0.85, t=2.791, p=0.006), general symptoms scores (2.42±0.71, 2.11±0.75, t=2.117, p=0.036), psychological symptoms scores (3.11±0.85, 2.75±0.70, t=2.158, p=0.033) and overall index scores (2.93±0.53, 2.60±0.56, t=3.076, p=0.003) of the patients who had undergone open surgery were higher than the patients who had undergone a laparoscopic surgery. Physical activities scores (3.66±0.81, 3.21±0.64, t=2.994, p=0.003), general symptoms scores (2.45±0.70, 2.10±0.77, t=2.507, p=0.013), psychological symptoms scores (3.15±0.83, 2.69±0.75, t=2.916, p=0.004), and overall index scores (2.94±0.54, 2.63±0.52, t=3.029, p=0.003) of the patients who had received general anesthesia were higher compared to patients who had received spinal anesthesia.

Qualitative Analysis Results

Six of the patients were younger than 45 years, six were women, six were overweight, five used tobacco, and two had chronic diseases. Three of the patients had undergone prior surgery. The clinics where patients were hospitalized were most commonly neurosurgery (n=4) and general surgery (n=4). Eleven patients had undergone open surgery, and nine received general anesthesia.

Table 4 presents the themes, categories/sub-themes, and codes developed for the study's purposes.

Theme 1. Perspectives on postoperative complaints (f=63): Four categories were developed under this theme. These are physical, psychological, social, and habitual complaints. This theme has been the most cited by patients. Patients were predominantly referred for the group for physical complaints (f=46). Patients' perspectives have predominantly concentrated on the themes of pain (f=12), limitation of mobility (f=11), and fear (f=8). The patients' remarks concerning these codes are delineated below:

"I suffer very severe pain during the exercises designed to enhance my leg mobility and joint function. There were even moments when I feared my leg would detach." (P10: 52 years of age, female, orthopedics and traumatology clinic).

"On the evening of the surgery, the nurses informed me that I should have already gotten up and started walking. The attempt to get up induced such agony that I recall saying, "Perhaps I will be unable to leave my bed for a week." I have sutures; hence, I should avoid exertion. For this reason, my movements are sluggish and restricted. I progress at

Table 2. Patients' mean scores and median scores in pori sub-dimensions

Sub-dimension	X̄	SD	Median	Minimum-maximum
Physical activities	3.54	0.80	3.50	1.50-5.00
Bowel symptoms	2.38	0.87	2.40	1.00-4.80
Appetite symptoms	2.41	0.93	2.25	1.00-5.00
General symptoms	2.35	0.74	2.25	1.00-4.00
Psychological symptoms	3.03	0.84	3.00	1.00-5.00
Overall index	2.85	0.55	2.82	1.68-4.16

n=140. SD: Standard deviation.

Table 3. Comparison of patients' mean scores in pori sub-dimensions based on the clinics they were hospitalized in

Sub-dimension	Clinic							f	p	Bonferroni
	Neurosurgery (a)	General surgery (b)	Cardiovascular surgery (c)	Otolaryngology (d)	Urology (e)	Orthopedics (f)	Plastic surgery (g)			
	X̄ ± SD	X̄ ± SD	X̄ ± SD	X̄ ± SD	X̄ ± SD	X̄ ± SD	X̄ ± SD			
Physical activities	3.70±0.79	3.99±0.63	3.64±0.75	3.31±0.84	3.24±0.46	3.75±0.84	3.12±0.86	3.525	0.003*	b>e b>g
Bowel symptoms	2.08±0.53	3.10±1.11	2.50±0.74	2.34±0.76	2.42±0.78	2.49±0.74	1.71±0.75	5.735	0.000*	b>a b>g c>g f>g
Appetite symptoms	1.94±0.80	2.85±0.88	2.05±0.62	3.20±1.17	2.09±0.76	2.51±0.59	2.26±0.88	6.198	0.000*	b>a c>a d>c d>e d>g
General symptoms	2.44±0.74	2.34±0.61	2.53±0.69	2.50±0.71	1.94±0.67	2.43±0.65	2.28±0.93	1.527	0.174	-
Psychological symptoms	3.34±0.67	3.10±0.80	3.03±0.73	3.18±0.79	2.90±0.90	2.45±0.79	3.20±0.93	2.553	0.023*	a>f
Overall index	2.83±0.49	3.22±0.55	2.88±0.35	2.95±0.64	2.63±0.51	2.88±0.45	2.58±0.63	3.252	0.005*	b>e b>g

n=140, *p<0.05. SD: Standard deviation.

Table 4. Themes, categories/sub-dimensions, and codes of the study

Themes	Categories/sub-dimensions	Codes
Perspectives on postoperative complaints (f=63)	Physical complaints (f=46)	Limitation of mobility (f=11)
		Gas/intestinal dysfunction (f=2)
		Urinary retention (f=3)
		Loss of appetite/weight loss (f=3)
		Nausea (f=3)
		Difficulty in breathing (f=3)
		Loss of sensation/numbness (f=3)
		Pain (f=12)
		Weakness/fatigue (f=2)
		Insomnia (f=4)
	Psychological complaints (f=14)	Fear (f=8)
		Anxiety (f=6)
	Social complaints (f=2)	Avoiding crowds/going out (f=2)
	Habitual complaints (f=1)	Anxiety about not being able to return to work (f=1)
Postoperative changes (f=16)	Treatment (f=12)	Medication (f=3)
		Dieting/weight loss (f=3)
		Physiotherapy (f=2)
		Using assistive equipment (f=4)
	Changes in lifestyle (f=2)	Making changes in life (f=2)
	Health awareness (f=2)	Self-care (f=2)
Postoperative recovery status (f=19)	Physical recovery (f=7)	Feeling physical recovery (f=2)
		Relief from pain (f=5)
	Psychological recovery (f=8)	Alleviation of fear (f=4)
		Being happy (f=4)
	Social recovery (f=1)	Socialization (f=1)
	Habitual recovery (f=3)	Ability to return to everyday life/work (f=3)
Factors affecting postoperative recovery (f=29)	Patient-related factors (f=13)	Prior surgery (f=4)
		Contact with people who had undergone prior surgery (f=3)
		Paying attention to postoperative care (f=5)
		Believing in recovery (f=1)
	Factors related to patient relatives (f=7)	Support from family/friends (f=7)
	Factors related to healthcare professionals (f=9)	Information provided by health care professionals (f=3)
		Support from health care professionals (f=6)
Perspectives on the results of surgery (f=25)	Service quality (f=18)	Success of the surgery (f=11)
		Satisfaction (f=7)
	Feeling better (f=7)	Feeling good (f=7)
Significance of postoperative recovery (f=20)	Being healthy (f=11)	Relief from difficulties (f=4)
		Regaining health (f=4)
		Returning to everyday life (f=1)
		Ability to take care of oneself (f=2)
	New beginnings (f=9)	Restarting life (f=9)

a slow rate. I am uncertain how much longer I can sustain this." (P11: 37 years of age, male, neurosurgery clinic).

"There were instances when I wept profusely and experienced profound sadness. I was exceedingly apprehensive of what would occur to me. I contemplated extensively regarding my spouse and children. I nearly experienced the fear of death." (P6: 42 years of age, female, general surgery clinic).

Theme 2. Postoperative changes (f=16): Three categories were developed under this theme. These include receiving treatment, changes in lifestyle, and health awareness. Patients' perspectives have predominantly concentrated on the use of assistive equipment (f=4), medications (f=3), and dieting/weight loss (f=3). A patient articulated the perspective on using assistive equipment as follows:

"As I mentioned before, my whole life has been transformed by a new way of living. Now and then, I have to manage a colostomy bag. This induces a sense of melancholy. I have concerns about how I will look, use the bag, and so on. My nurse and physician supplied me with information regarding the use of the bag. Nonetheless, I remain cognizant that a formidable journey is ahead." (P8: 56 years of age, female, general surgery clinic).

Theme 3. Postoperative recovery status (f=19): The categories delineated within this theme are physical recovery, psychological recovery, social recovery, and habitual recovery. Patients' perspectives have predominantly concentrated on the codes of relief from pain (f=5), alleviation of fears (f=4), and being happy (f=4). A patient's statements concerning relief from pain are as follows:

"The most significant outcome of the surgery was the alleviation of the excruciating pain I endured before the procedure. "Currently, I occasionally experience discomfort at the surgical site; however, it is not comparable to the first pain I endured." (P7: 24 years of age, male, general surgery clinic).

Theme 4. Factors affecting postoperative recovery (f=29): Three categories were developed under this theme. These are patient-related factors, patients' relatives, and health care professionals. Patients' perspectives have predominantly concentrated on the codes of support from family/friends (f=7), support from health care professionals (f=6), and paying attention to postoperative care (f=5). Below are patient testimonials concerning these codes:

"My family never left me alone, even for a single day. My physicians always emphasized the significance of mental resilience and drive throughout this procedure. Consequently, my family and friends tried to enhance my well-being." (P6: 42 years of age, female, general surgery clinic).

"The assistance of the physicians, nursing staff, and caregivers sustained my existence and intensified my will to live." (P4: 58 years of age, male, orthopedics and traumatology clinic).

Theme 5. Perspectives on the surgery results (f=20): The categories developed under this theme were service quality and feeling better. Patients articulated remarks highlighting the success of the surgery (f=11), satisfaction (f=7), and feeling good (f=7). One patient remarked on the successful surgery:

"I did not expect such a miracle. It is incredible. Let me say Mashallah." (P10: 52 years of age, female, orthopedics and traumatology clinic).

Theme 6. Significance of postoperative recovery (f=20): The first category recognized under this theme was being healthy, and the subsequent category was new beginnings. Patients said they frequently perceived themselves as having restarted life (f=9). Patients have articulated this vividly as follows:

"Postoperative recovery for me resembles being reborn, crawling anew, walking again, and commencing a new life." (P4: 58 years of age, male, orthopedics and traumatology clinic).

"Surgery is an event that transforms an individual's entire existence. It, however perilous due to the numerous associated risks, is essential for recovery, instilling fear. Life contains pivotal moments, akin to the distinctions before and after a surgical procedure." (P12: 32 years of age, male, neurosurgery clinic).

DISCUSSION

For the study's quantitative analysis, the patient's postoperative recovery status, as well as changes in this recovery status, and the changes in depending on various factors were examined. Patients reported that they experienced extreme difficulty in physical activities, considerable difficulty in psychological symptoms, and the overall index, and moderate difficulty in bowel symptoms, appetite symptoms, and general symptoms.

The conclusion that the patients experienced considerable difficulty in the overall index is similar to the results of studies reporting that the patients experienced considerable difficulty.[11,12] or extreme difficult[13] in general postoperative recovery and partial recovery after surgery.[14] On the other hand, these results contradict those of different studies reporting an overall postoperative recovery above the moderate level.[15-18] The study was conducted in a tertiary training and research hospital. This result may suggest that the problems of patients admitted to the hospital for surgical procedures are complex and that their general health condition is poor. The theme under which the highest number of codes were developed was postoperative complaints, and the patients' views were mainly focused on this within qualitative data analysis. It was concluded that the qualitative and quantitative findings obtained in the study overlapped.

The only sub-dimension in which patients experienced extreme difficulty was physical activities. Surgical procedures may temporarily restrict patients' mobility. The patient's mobility is intentionally limited for a designated term to expedite healing during the inflammatory phase of wound recovery.[7] The study's findings coincide with the information compiled in the literature review. For the qualitative analysis, the second code, under the physical complaints category of theme 1, was a mobility limitation focused on in the patients' views. Qualitative findings supported quantitative findings in this sub-dimension.

The perception of recovery is customized and related to several factors, such as demographic characteristics, preoperative health status, the information provided before the surgery, expectations regarding the surgical procedure's results, and postoperative support.[19,20]

Significant differences were found in all sub-dimensions except for general symptoms and overall index scores, depending on the clinic where the patients are hospitalized. Patients hospitalized in the general surgery clinic experienced more difficulties in physical activities, bowel symptoms, sub-dimensions, and overall index, than those hospitalized in the plastic surgery clinic. The literature review revealed that patients hospitalized in orthopedic clinics recovered significantly more slowly than general surgery patients.[21] Orthopedic patients also recovered more slowly than general surgery patients.[22] The quality of recovery is poorer in patients who have undergone ileostomy, colostomy closure, mastectomy, and splenectomy compared to patients who have undergone hernioplasty, cholecystectomy, and appendectomy.[23] The clinic with the lowest comfort is the urology clinic, whereas the clinic with the highest comfort is the plastic and aesthetic surgery clinic.[24] While recovery takes a few days or weeks after minor surgical procedures, it may take a year or more following major surgical procedures.[3] It can be concluded that the general surgery clinic patients who participated

in the study underwent major procedures, while the plastic surgery patients underwent a minor procedures.

Six themes were identified in the qualitative analysis: perspectives on postoperative complaints, postoperative changes, postoperative recovery status, factors affecting postoperative recovery, perspectives on the surgery results, and significance of postoperative recovery. Postoperative recovery is examined in the literature in four dimensions: physical recovery, psychological recovery, social recovery, and habitual improvement.[19,25] These dimensions referred to in the literature are similar to the categories of physical, psychological, social, and habitual complaints under theme 1, and physical, psychological, social, and habitual recovery under theme 3. The PoRI sub-dimensions used as data collection tools in the quantitative analysis are compatible with the themes, categories, and codes developed within the framework of qualitative analysis. The physical activities sub-dimension is correlated with limitation of movements, nausea, weakness/fatigue codes under theme 1, feeling of physical recovery codes under theme 3, and being able to take care of one's care code under theme 6; the bowel symptoms sub-dimension is correlated with gas/intestinal dysfunction code under theme 1; appetite symptoms sub-dimension is correlated with loss of appetite/weight loss code under theme 1; general symptoms sub-dimension is correlated with weakness/fatigue and insomnia codes under theme 1; psychological symptoms sub-dimension is correlated with anxiety and anxiety about not being able to return to work under theme 1, ability to return to everyday life/work under theme 3 and belief in recovery under theme 4.

Further themes revealed in the qualitative analysis were feeling unwell and feeling well[26]; recovery conditions at home, returning to everyday life and taking part in the care process[27]; the importance of being informed about treatment and recovery, the ability of patients who need assistance to find coping techniques at home, and the difficulty of rehabilitation for patients who receive limited rehabilitative support.[28]

The first theme is the perspectives on postoperative complaints. Two categories were identified under the theme of not feeling well in another study conducted with mixed methods: physical and psychological problems.[26] Throughout the postoperative period, patients may experience issues with respiratory, cardiovascular, urinary, gastrointestinal, musculoskeletal, and neurological functions, pain, discomfort, hypothermia, wound site-related problems, and problems with psychological and social functions.[7,29] This theme being most frequently mentioned in patient statements indicates that patients still experience postoperative problems today despite advances in surgical treatment and care.

Pain is a widespread and vital problem encountered in the postoperative period.[7] The fact that pain is the most frequently mentioned code may indicate that it continues to be a problem today. Relief from pain being the most commonly cited code under theme 3 confirms this conclusion. Effective pain management allows early mobilization.[30] Pain, which is the most frequently expressed complaint in the study, is the cause of movement limitation.

Postoperative recovery status is another theme referred to herein. The following themes were identified within the scope of qualitative analysis: recovery challenges and their impact on physical activity, factors that facilitate and prevent returning to physical activity, physical challenges of assuming pre-surgery social roles, and interventions in health care that may accelerate the return to physical activity.[31] There is consistency in the study between the most frequently mentioned codes pain, limitation of movements, and fear, in the first theme, and relief from pain and decrease in fear level in another theme.

Another theme developed herein are the factors affecting postoperative recovery. The themes identified within the scope of qualitative analysis were the provision of information, customized treatment, standard care, balancing the symptoms and expectations of rapid recovery, and a sense of security at discharge.[32] Patient-related and healthcare professional-, anesthesia-, and procedure-specific factors may also affect postoperative recovery.[19,20] It is concluded that the categories developed under this theme are compatible with the literature. Information support from health care professionals' codes reveals the nurse's role in postoperative recovery.

Surgical outcome is another theme developed herein. Within a mixed-method study, a category of adaptation to the situation was developed under the theme of feeling good, and a code of general well-being was created under it.[26] Patient satisfaction, a multidimensional concept, is paramount in recovery[1], is considered a component of the quality of recovery[33], and is considered a measure of surgical care outcomes.[34] Although not among the interview questions, this thematic content was developed by considering the patients' statements. Thus, the patient's satisfaction with the surgical process was revealed, as suggested in the literature.

The significance of postoperative recovery is the final theme developed herein. During qualitative studies, patients described postoperative recovery as a state that included internal and external pre-requisites that express changes in ordinary life with varying levels of support[27] and a return to core values for all issues in every field, or better.[35] Postoperative recovery is defined as the individual's ability to return to the pre-surgery level or better, regain all functions, and achieve a state of well-being.[3,19,20] The definitions of postoperative recovery mentioned by the patients participating in the study support the definitions in the literature. Patients' definitions of postoperative recovery have been expanded to include nociceptive, psychological, social, cognitive, and satisfaction domains.[36]

Study Limitations

The study has some methodological limitations. It was conducted on patients undergoing surgical procedures in a training and research hospital; therefore, the study results are limited to the specified patients. The findings are also limited to data from patients undergoing surgery throughout the study.

CONCLUSION

Patients reported that they experienced extreme difficulty in physical activities, considerable difficulty in psychological symptoms, and the overall index, and moderate difficulty in bowel symptoms, appetite symptoms, and general symptoms throughout the postoperative recovery process. There are differences in the postoperative recovery status of patients depending on their age, body mass index, tobacco use, chronic diseases, prior surgery, hospitalized clinic, type of surgery, and type of anesthesia received. The themes developed for the study included perspectives on postoperative complaints and surgery results, postoperative changes, recovery status, factors affecting recovery, the significance of postoperative recovery.

In line with these results, it is recommended that clinical nurses address all aspects of recovery in the postoperative period, including physical, psychological, and social improvement, with a holistic approach. It is imperative to support patients in physical activities. Elderly and obese patients who use tobacco, have chronic diseases, have had prior surgery, and have undergone general open surgery under general anesthesia, need to be supported more in relevant aspects. It is further recommended that patients' pain levels be controlled, provided support for mobility, encouraged to cope with their fear, trained on using assistive equipment, and social support systems be activated.

MAIN POINTS

- Patients reported that they experienced considerable difficulty with the overall index throughout the postoperative recovery process. In particular, they experienced extreme difficulty with physical activity.
- It was determined that postoperative recovery varies according to many variables.
- Patients had positive as well as negative perceptions about postoperative recovery.

ETHICS

Ethics Committee Approval: Ethical approval for this study was obtained from the Non-Interventional Clinical Studies Institutional Review Board of İzmir Katip Çelebi University (approval number: 0092, date: 24.02.2022).

Informed Consent: Informed consent was obtained from all participants.

Acknowledgements

The authors thank the patients who participated in the study.

Footnotes

Authorship Contributions

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

DISCLOSURES

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

Financial Disclosure: The authors declared that this study had received no financial support.

REFERENCES

1. Borrell-Vega J, Humeidan ML, Bergese SD. Defining quality of recovery - what is important to patients? Best Pract Res Clin Anaesthesiol. 2018; 32(3-4): 259-68.
2. Ferraz SM, Moreira JP, Mendes LC, Amaral TM, Andrade AR, Santos AR, et al. Evaluation of the quality of recovery and the postoperative health status after elective surgery. Braz J Anesthesiol. 2018; 68(6): 577-83.
3. Jaensson M, Nilsson U, Dahlberg K. Methods and timing in the assessment of postoperative recovery: a scoping review. Br J Anaesth. 2022; 129(1): 92-103.
4. Butler SF, Black RA, Techner L, Fernandez KC, Brooks D, Wood M, et al. Development and validation of the postoperative recovery index for measuring quality of recovery after surgery. J Anesth Clin Res. 2012; 3(12): 1-8.
5. Bowyer A, Royse C. The future of recovery - integrated, digitalised and in real time. Best Pract Res Clin Anaesthesiol. 2018; 32(3-4): 295-302.
6. Nilsson U, Gruen R, Myles PS. Postoperative recovery: the importance of the team. Anaesthesia. 2020; 75(1): e158-64.
7. Hinkle JL, Cheever KH, Overbaugh K. Brunner & Suddarth's textbook of medical-surgical nursing. 15th ed. Philadelphia: Wolters Kluwer; 2021.
8. Creswell JW, Creswell JD. Research design: qualitative, quantitative, and mixed methods approaches. 6th ed. Thousand Oaks, CA: Sage; 2022.
9. Polit DF, Beck CT. Nursing research: generating and assessing evidence for nursing practice. 10th ed. Philadelphia: Lippincott Williams & Wilkins; 2016.
10. Collins T, Onwuegbuzie AJ, Jiao QG. Prevalence of mixed methods sampling designs in social science research. Eval Res Educ. 2009; 19(2): 83-101.
11. Cengiz H, Aygin D. Validity and reliability study of the Turkish version of the postoperative recovery index of patients undergoing surgical intervention. Turk J Med Sci. 2019; 49(2): 566-73.
12. Ozmen T. Investigation of postoperative recovery conditions of patients undergoing surgical intervention [master's thesis]. Izmir: Ege University; 2020.
13. Digin F, Kizilcik Ozkan Z. Determination of postoperative recovery status of elderly patients. Online Turk J Health Sci. 2021; 6(3): 413-8.
14. Allvin R, Kling AM, Idvall E, Svensson E. Patient-reported outcome measures (PROMs) after total hip and knee replacement surgery evaluated by the postoperative recovery profile questionnaire (PRP)-improving clinical quality and person-centeredness. Int J Person Cent Med. 2012; 2(3): 368-76.
15. Kara U, Şimşek F, Kamburoğlu H, Özhan MÖ, Alakuş Ü, İnce ME, et al. Linguistic validation of a widely used recovery score: quality of recovery-15 (QoR-15). Turk J Med Sci. 2022; 52(2): 427-35.
16. Karaman S, Arici S, Dogru S, Karaman T, Tapar H, Kaya Z, et al. Validation of the Turkish version of the Quality of Recovery-40 questionnaire. Health Qual Life Outcomes. 2014; 12: 8.
17. Shida D, Wakamatsu K, Tanaka Y, Yoshimura A, Kawaguchi M, Miyamoto S, et al. The postoperative patient-reported quality of recovery in colorectal cancer patients under enhanced recovery after surgery using QoR-40. BMC Cancer. 2015; 15: 799.
18. Yolcu S, Akin S, Durna Z. Evaluation of patients' recovery status and care needs after orthopedic, cardiac, and general surgery. Health Soc. 2015; 25(3): 33-45.
19. Forsberg A, Vikman I, Wälivaara BM, Engström Å. Patterns of changes in patients' postoperative recovery from a short-term perspective. J Perianesth Nurs. 2018; 33(2): 188-99.
20. Jaensson M, Dahlberg K, Nilsson U. Factors influencing day surgery patients' quality of postoperative recovery and satisfaction with recovery: a narrative review. Perioper Med (Lond). 2019; 8: 3.
21. Forsberg A, Vikman I, Wälivaara BM, Engström Å. Patients'perceptions of their postoperative recovery for one month. J Clin Nurs. 2015; 24(13-14): 1825-36.
22. Berg K, Kjellgren K, Unosson M, Arestedt K. Postoperative recovery and its association with health-related quality of life among day surgery patients. BMC Nurs. 2012; 11(1): 24.
23. Suerdem B, Totur Dikmen B. Preoperative care dependency and postoperative quality of recovery of the surgical patients. Acta Paul Enferm. 2024; 37.
24. Kubat Bakir G, Yurt S. Evaluation of the comfort level of patients undergoing surgical operations. J Health Soc. 2020; 20(3): 158-65.

25. Allvin R, Berg K, Idvall E, Nilsson U. Postoperative recovery: a concept analysis. J Adv Nurs. 2007; 57(5): 552-8.

26. Nilsson U, Jaensson M, Dahlberg K, Hugelius K. Postoperative recovery after general and regional anesthesia in patients undergoing day surgery: a mixed methods study. J Perianesth Nurs. 2019; 34(3): 517-28.

27. Berg K, Arestedt K, Kjellgren K. Postoperative recovery from the perspective of day surgery patients: a phenomenographic study. Int J Nurs Stud. 2013; 50(12): 1630-8.

28. Phelps EE, Tutton E, Griffin X, Baird J; TrAFFix research collaborators. A qualitative study of patients' experience of recovery after a distal femoral fracture. Injury. 2019; 50(10): 1750-55.

29. Harding MM, Kwong J, Hagler D, Reinisch C. Lewis's medical-surgical nursing. 12th ed. St. Louis: Elsevier; 2023.

30. Kehlet H. Enhanced postoperative recovery: good from afar, but far from good? Anaesthesia. 2020; 75(1): e54-61.

31. O'Neill L, Bennett AE, Guinan E, Reynolds JV, Hussey J. Physical recovery in the first six months following oesophago-gastric cancer surgery. Identifying rehabilitative needs: a qualitative interview study. Disabil Rehabil. 2021; 43(10): 1396-403.

32. Sibbern T, Bull Sellevold V, Steindal SA, Dale C, Watt-Watson J, Dihle A. Patients' experiences of enhanced recovery after surgery: a systematic review of qualitative studies. J Clin Nurs. 2017; 26(9-10): 1172-88.

33. Heidegger T, Saal D, Nübling M. Patient satisfaction with anaesthesia - Part 1: satisfaction as part of outcome - and what satisfies patients. Anaesthesia. 2013; 68(11): 1165-72.

34. Bruder N, Auquier P. Integration of satisfaction and quality of recovery. Best Pract Res Clin Anaesthesiol. 2018; 32(3-4): 277-86.

35. Royse CF, Chung F, Newman S, Stygall J, Wilkinson DJ. Predictors of patient satisfaction with anaesthesia and surgery care: a cohort study using the postoperative quality of recovery scale. Eur J Anaesthesiol. 2013; 30(3): 106-10.

36. Bowyer A, Royse C. The importance of postoperative quality of recovery: influences, assessment, and clinical and prognostic implications. Can J Anaesth. 2016; 63(2): 176-83.

RESEARCH ARTICLE

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-38
Cyprus J Med Sci 2025;10(5):335-342

A Cross-Sectional Study of Malarial Patients in District Faisalabad, Pakistan: Frequency of Infection, Species Distribution, and Diagnostic Efficiency Comparison

Rashid Ali, Muhammad Asrar, Salma Sultana, Amna Sajjad

Department of Zoology, Government College University Faisalabad, Punjab, Pakistan

Abstract

BACKGROUND/AIMS: Malarial infection, caused by *Plasmodium* parasites transmitted by female Anopheles mosquito, is still a serious public health concern, especially in endemic areas such as Sub-Saharan Africa and Pakistan. The study aims to investigate the frequency of malarial infection in district Faisalabad.

MATERIALS AND METHODS: A cross-sectional study was conducted across the district Faisalabad to study the frequency of malarial infection. Blood samples were collected from 1460 suspected malaria cases between May 2023 and April 2024 at various government sector hospitals across the six administrative units (tehsil) of district, Faisalabad. For the purpose of the diagnosis of malarial patients, rapid diagnostic tests (RDTs), microscopy, and polymerase chain reaction (PCR) methods were employed.

RESULTS: RDTs detected 649 (44.4%) positive cases, while microscopy and PCR detected 452 (30.6%) and 459 (31.4%) cases, respectively. Among *Plasmodium* species, *P. vivax* was the most frequently detected, followed by *P. falciparum* and mixed infections. Significant differences were observed in diagnostic outcomes across the three methods. Notably, 55 RDT-positive cases were found to be negative by both microscopy and PCR, indicating potential false positives due to antigen persistence. The highest positivity rate was observed in the 1-15 years age group among males as well as in the months of June and July. These findings highlight the need for confirmatory diagnostics alongside RDTs to improve accuracy and support malaria surveillance and control efforts in endemic regions. Positivity rates varied across municipalities, with Faisalabad city showing the highest burden.

CONCLUSION: This study demonstrates that while RDTs offer rapid malaria detection, they are prone to false positives due to persistent parasite antigens, especially in mixed infections. PCR and microscopy provided more accurate results and revealed significant differences in diagnostic outcomes. Moreover, the study highlights a significant frequency of malaria in district Faisalabad, with *P. vivax* being the dominant species. The data indicate higher susceptibility among males and children aged 1-15 years, particularly during the peak months of June and July. These findings highlight the need for confirmatory diagnostics to accompany further investigations. RDTs to improve accuracy and support malaria surveillance and control efforts in endemic regions.

Keywords: *Plasmodium*, rapid diagnostic test, microscopy, polymerase chain reaction, Faisalabad

To cite this article: Ali R, Asrar M, Sultana S, Sajjad A. A cross-sectional study of malarial patients in district Faisalabad, Pakistan: frequency of infection, species distribution, and diagnostic efficiency comparison. Cyprus J Med Sci. 2025;10(5):335-342

ORCID IDs of the authors: R.A. 0009-0006-3732-6479; M.A. 0000-0002-4083-964X; S.S. 0000-0002-5153-3523; A.S. 0000-0001-8478-8138.

Corresponding author: Muhammad Asrar
E-mail: asrar@gcuf.edu.pk
ORCID ID: orcid.org/0000-0002-4083-964X

Received: 22.04.2025
Accepted: 08.07.2025
Publication Date: 09.10.2025

INTRODUCTION

Malarial infection is a serious medical issue caused by the *Plasmodium* parasite and spread by the female Anopheles mosquito. Malaria causes widespread death in endemic places, killing 62,700 individuals in 2021, the majority of whom were less than 5 years old, in Sub-Saharan Africa.[1] Pakistan reported 74,860 cases of malaria in March 2023 and 75,185 in April 2023, as compared to 14,371 cases in March 2022 and 23,562 in April 2022.[2] *P. vivax, P. falciparum, P. malariae, P. ovale* are the most common species found worldwide, and the fifth species is *P. knowlesi*, which has been recently discovered in several countries.[3,4] The malarial fever has a severe impact on human health and causes significant decreases in hemoglobin, red blood cells, lymphocytes, basophils, monocytes, sodium, potassium, chloride ions, creatinine, cholesterol, bilirubin and increases the serum glutamic pyruvic transaminase.[5]

The diagnosis of malaria is a critical step in managing the disease and preventing its spread, and accurate diagnosis is essential for effective treatment and control.[6,7] Malarial fever is typically diagnosed using rapid diagnostic test (RDT) kits based on antigens in a blood sample, by making both thick and thin blood films for microscopy, or efficiently detected through polymerase chain reaction (PCR).[8-10] Pakistan is a tropical agricultural country where 64% of the population lives in rural areas with inadequate water infrastructure, which are suitable habitats for mosquito egg laying.[11] Malarial infection is endemic throughout Pakistan and is becoming more prevalent, particularly in Baluchistan and Khyber Pakhtunkhwa.[12] In the Multan district of Punjab, Pakistan, 905 *P. vivax*, 425 *P. falciparum*, and 148 mixed cases were recorded.[13] Previous research has found significant endemicity in regions such as Rawalpindi and Islamabad, with *P. vivax* predominating.[14] Similarly, another previous study reveals that *P. vivax* (90.6%) was more common during the summer months as compared to any other *Plasmodium* species in Khyber Pakhtunkhwa, with the highest incidence recorded in southern regions.[15]

Furthermore, a study in the Khyber Pakhtunkhwa province revealed a malarial prevalence of 13.8%, with *P. vivax* accounting for 92.4% of cases.[16] In Quetta, Baluchistan, about 18.4% of clinically suspected people tested positive for malaria, with *P. vivax* responsible for 81.6% of these cases.[17] The prevalence of malaria and species distribution might differ dramatically across districts, seasons, and age groups, with some places exhibiting higher rates and others showing lower rates than the expected prevalence.[18] The previous studies based on region, district, age, and gender, overall reveal that *P. vivax* was mostly prevalent.[19-22] Despite numerous studies on malaria prevalence in various Pakistani districts, the epidemiology of malaria infection in Faisalabad district has not been thoroughly investigated. This study is designed to analyze the frequency of malaria infection in different administrative units of the district of Faisalabad, Punjab, Pakistan.

MATERIALS AND METHODS

Types of Study

A cross-sectional study was conducted to determine the frequency of malaria infection in the district Faisalabad, Punjab, Pakistan. The present study was conducted from May 2023 to April 2024.

The study was approved by the Ethics Review Committee of Government College University Faisalabad, Punjab, Pakistan (approval number: GCUF/ERC/460, date: 15.05.2023). Verbal informed consent was obtained from all participants prior to inclusion in the study.

Study Area

Faisalabad district (73°74 E; 30°31.5N) is approximately 604 feet above sea level; during summer, the maximum (max.) and lowest temperatures are 41 °C and 27 °C respectively. In winter, the temperatures fluctuate between 21 °C to 6 °C. Faisalabad district comprises six administrative units (tehsils) shown in Figure 1 Faisalabad Saddar, Faisalabad city, Tandilianwala, Jaranwala, Samundri, and Chak Jhumra.[23] Blood samples were collected from only Government Sector Hospitals likewise Tehsil Headquarter Hospital Chak Jhumra (31°33'56.8"N73°11'17.1"E), Tehsil Headquarter Hospital Tandilianwala (31°02'04.0"N 73°07'52.6"E), Tehsil Headquarter Hospital Jaranwala (31°20'26.2"N 73°25'27.2"E), Tehsil Headquarter Hospital Samundri (31°03'41.8"N 72°57'21.9"E), Allied Hospital Faisalabad (31°26'55.3"N 73°04'48.7"E), Civil Headquarter Hospital Faisalabad (31°25'16.9"N 73°05'40.9"E), Government General Hospital Ghulam Muhammad Abad Faisalabad (31°26'34.4"N 73°02'45.9"E) Government General Hospital Samanabad Faisalabad (31°23'06.8"N 73°04'00.7"E) and Social Security Hospital Faisalabad (31°25'09.5"N 73°06'59.6"E).

Laboratory Analysis

Blood samples were taken from 1,460 suspected cases that had symptoms of malaria, such as headache, chills, fever, and nausea; and subjected them to RDT, microscopy, and PCR. For RDT commercially available test kits (Abbot **Malaria** Ag P.f/Pan kit, LOT NO: 05EDI010C) were used.

Microscopic and Polymerase Chain Reaction Analysis

The slides were prepared for the identification of *Plasmodium* species and their stages. Thick and thin films were prepared on a clean glass slides, fixed and stained with Giemsa stain. Slides were observed under the 100x objective lens according to guidelines.[24] For PCR analysis, blood samples were brought to Integrated Genomics, Cellular Developmental and Biotechnology Laboratory University of Agriculture, Faisalabad (31°43'51.9" N, 73°07'16.9" E). DNA was extracted from 3 mL of an infected person's blood using a commercially available DNA extraction kit according to the manufacturer's instructions. For the extraction of DNA from blood samples, the QIAamp DNA Mini Kit (Catalogue No. 51304, Qiagen, Hilden, Germany) was used. This kit provides efficient extraction of high-purity DNA, commonly used in molecular diagnostics, including malaria studies. A nested PCR approach, of the small subunit RNA (ssrRNA) was used for the identification of *Plasmodium* species.[25] The *ssrRNA*

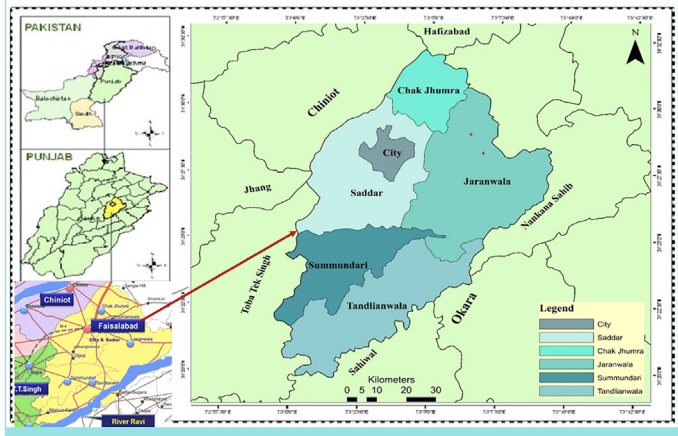


Figure 1. Map of study area.

gene specific to malaria parasites[26] was amplified using primers for *P. falciparum* (Forward primer: 5′-CTTTTGAGAGGTTTTGTTACTTTGAGTAA-3′; Reverse primer: 5′-TATTCCATGCTGTAGTATTCAAACACAA-3′) and for *P. vivax* (Forward primer: 5′-ACGCTTCTAGCTTAATCCACATAACT-3′; Reverse primer: 5′-ATTTACTCAAAGTAACAAGGACTTCCAAGC-3′), used in conjunction with the Taq PCR Core Kit (Catalogue No. 201223, Qiagen, Hilden, Germany). This kit facilitates accurate and efficient amplification of target genes and is widely used for molecular detection of *Plasmodium* species. The amplified PCR products were run alongside a 100 base pair DNA ladder on 1.5% agarose gel stained with ethidium bromide. DNA was visualized on an ultraviolet trans illuminator and photographed, as shown in Figure 2, using a gel documentation system.

Statistical Analysis

The data were analyzed using Microsoft Excel to determine the percentage infection rate. Categorical data were expressed as percentage and chi-square statistical analyses were applied. The performance of diagnostic methods was assessed by calculating sensitivity, specificity, and predictive values, with confidence intervals reported for each estimate. Formulas are used to calculate the diagnostic accuracy of RDT and microscopy compared to PCR as the reference standard.

Sensitivity (%): [true positives/(true positives + false negatives)] × 100

Specificity (%): [true negatives/(true negatives + false positives)] × 100

Positive predictive value (%): [true positives/(true positives + false positives)] × 100

Negative predictive value (%): [true negatives/(true negatives + false negatives)] × 100

RESULTS

A total of 1,460 blood samples were obtained from these nine Government Hospitals such as Tehsil Headquarter Hospital Chak Jhumra, Tehsil Headquarter Hospital Tandilianwala, Tehsil headquarter hospital Jaranwala, Tehsil Headquarter Hospital Samundri, Allied Hospital Faisalabad, Civil Headquarter Hospital Faisalabad, Government General Hospital Ghulam Muhammad Abad Faisalabad, Government General Hospital Samanabad Faisalabad, and Social Security Hospital Faisalabad. Out of 1,460 samples, 649 (44.4%) were positive, with 384 *P. vivax* (59.1%), 134 *P. falciparum* (20.6%), and 131 mixed (20.1%) cases recorded. The patients that were diagnosed with malaria show symptoms of chills, headache, weakness, and elevated temperature.

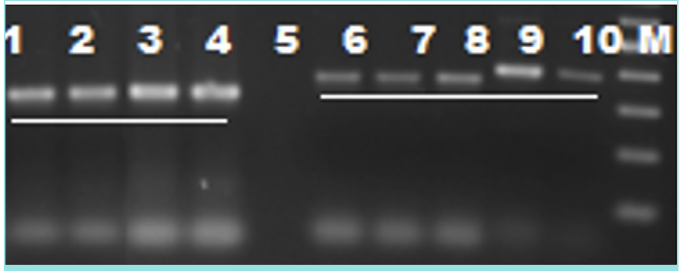


Figure 2. Gel image showing diagnosis of *Plasmodium* species. Lane M: DNA ladder (molecular marker), (Lane 1-3: Positive for *P. vivax*), (Lane 6-8: Positive for *P. falciparum)*, (Lane 10: showed Mixed infection), (Lane 5: Negative control as well as lane 4 and 9 are positive for *P. vivax* and *P. falciparum* respectively).

The month-wise frequency of malarial patients in Faisalabad city (Figure 3A) shows cases peaked in August 2023 (48), with *P. vivax* being the most frequent parasite (83.3%) in November and positivity rates highest in June 2023 (63.8%). Data from Faisalabad Saddar (Figure 3B) show that suspected cases were at their max. in September 2023 (48), with the positivity rate highest in July 2023 (68.5%) and *P. vivax* dominance (95.5%) in September. Figure 3C shows that Jaranwala city was under the highest attack in September 2023 (34 cases), with the highest positivity rate in June 2023 (85.1%) and notable *P. vivax* rates (47.8%). Samundri (Figure 3D) showed the highest case ratio in June 2023 (22 cases) with a max. positivity rate (86.3%), dominated by *P. vivax* (68.7%). Tandilian Wala (Figure 3E) showed peaks in June and July 2023, with mixed infections and *P. vivax* most prevalent, while Chak Jhumra (Figure 3F) showed moderate positivity rates, peaking at 65.3% in June, with mixed infections and *P. vivax* common. The species distribution among the positive cases highlighted *P. vivax* as the most prevalent species with 384 cases (61.1%), followed by mixed infections with 131 cases (20.64%), and *P. falciparum* with 118 cases (18.17%). The data indicate significant seasonal and regional variations in malaria prevalence, with peaks observed during the summer months, particularly in June and July. This underscores the importance of targeted public health interventions and continuous monitoring to effectively manage and control malaria transmission in the region.

Age-Based Frequency of Malarial Infection

Table 1 shows data on malaria cases categorized by age groups. In the 1-15 years age group, 111 individuals tested positive for malaria, accounting for 62.3% of suspected cases. Among these positive cases, 71.1% were attributed to *P. vivax,* 11.7% were attributed to *P. falciparum*, and 16.2% were mixed infections. In the 16-30 age group, 335 suspected cases were tested, with 104 (65.0%) being *P. vivax,* 21.2% being *P. falciparum*, and 13.7% being mixed infections. In the 31-45 age group, 204 (43.4%) tested positive, with 109 (53.4%) being for *P. vivax*, 26.0% for *P. falciparum,* and 20.5% for mixed infections. In the 46-60 age group, 111 (35.7%) tested positive, with 58 (52.2%) attributed to *P. vivax*, 28 (25.2%) to *P. falciparum*, and 25 (22.5%) attributed to mixed infections. In the 61 and above age group, 37.9% tested positive, with 52.3% due to *P. vivax*, 9.5% due to *P. falciparum*, and 38.1% as mixed infections. These findings indicate a significant variation in infection frequency and species distribution across age groups. Statistical analysis confirmed that the differences were significant across all age groups (p-values ranging from 0.01 to 0.04, with overall $p<0.01$), emphasizing age as an important risk factor in malaria epidemiology.

Gender-Based Frequency of Malarial Infection Across the Administrative Units

Table 2 showed the frequency of malarial infections among male and female patients across the various administrative units in Faisalabad district, Punjab, Pakistan. Our research results revealed a significant ($p<0.001$) variation in malarial infection among males and females in Faisalabad city, with a total of 134 (41.7%) positive cases reported, and males showing a higher rate of 80 (59.7%) compared to females with 54 (40.2%). The notable differences are that *P. vivax* is responsible for infection in 48 males (60.0%) and 34 females (62.9%), while *P. falciparum* causes infection in 14 males (17.5%) and 9 females (16.6%), out of a total of 23 (17.1%) positive cases.

Data from the administrative unit Faisalabad Saddar (Table 2) shows that in males, *P. vivax* 48 (63.1%) was the leading cause of malarial infection,

followed by *P. falciparum* 17 (22.3%) and mixed infection 11 (14.4%). In females, *P. vivax* 39 (73.5%) was also the leading cause of malaria, *P. falciparum* and mixed cases showed a similar proportion of 7 (13.2%). Overall, in Faisalabad Saddar administrative unit, 58.9% male cases and 41.1% female cases were reported. Out of 129 positive cases, *P. vivax* (67.4%) was the most prevalent, followed by *P. falciparum* (18.6%), and then both *P. vivax* and *P. falciparum* (13.9%). Likewise, in Jaranwala, the males were more susceptible than females, males accounting for 62.1% of the total cases and females accounting for 37.8%.

Moreover, Table 2 shows that in Jaranwala, Table 2 the frequency of *P. vivax* (52.2%) was highest compared to *P. falciparum* (26.1%) and mixed infection (21.6%). In three other remaining administrative units of District Faisalabad, such as Samundri, Tandilianwala, and Chak Jhumra, we identified the same pattern of *Plasmodium* frequency among males and females. In Samundri, infected males comprise 62.5% of the total positive cases in comparison to females, who account for only 37.5%. Moreover, we had identified 104 total positive cases in Samundri and out of the total, (59.6%) of these *P. vivax*, (24.0%) P. falciparum, and (16.3%) mixed cases were diagnosed.

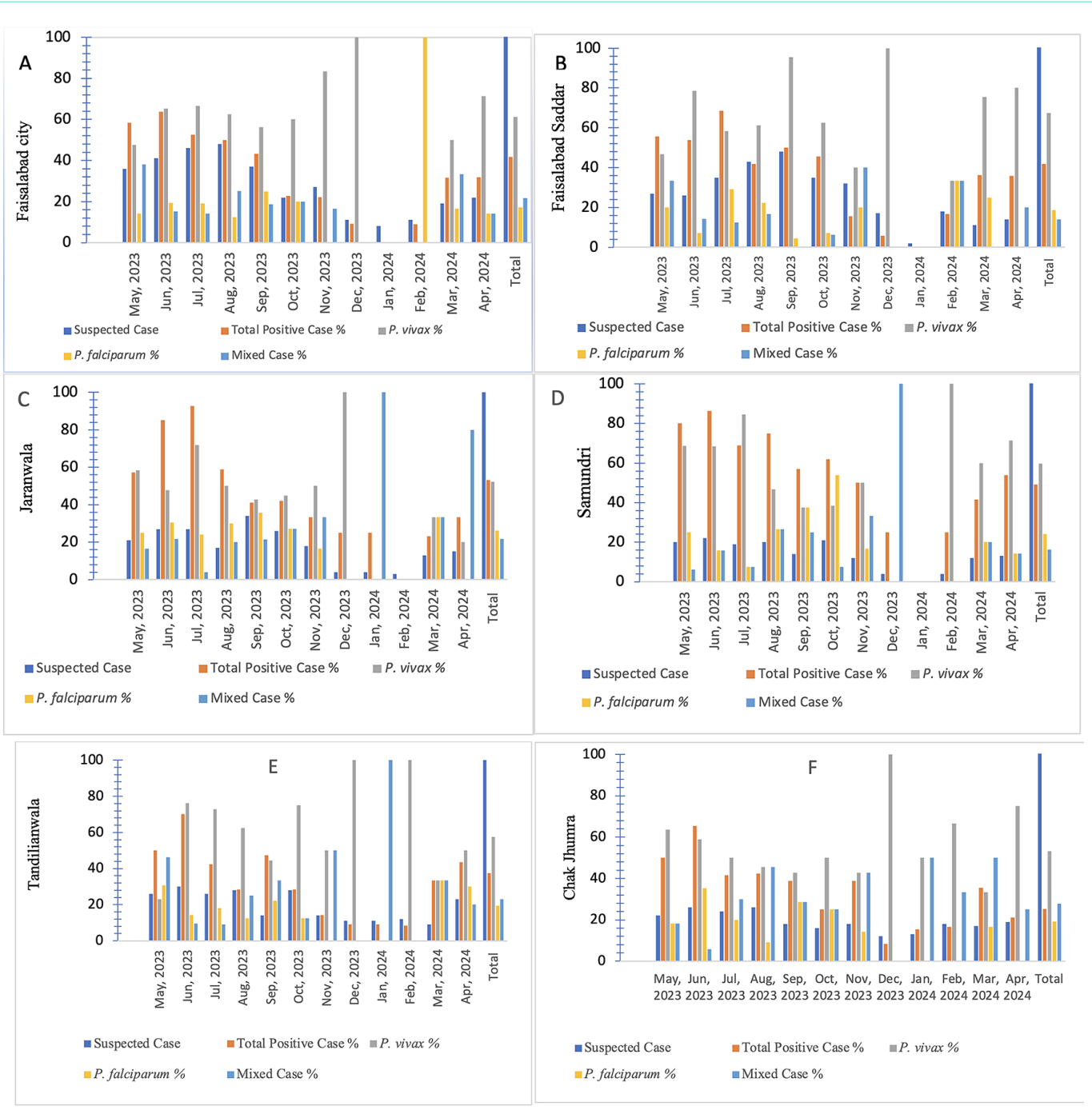


Figure 3. Monthwise frequency of malarial patients Faisalabad city (A), Faisalabad Saddar (B), Jaranwala (C), Samundri (D), Tandilianwala (E), Chak Jhumra (F).

Table 1. Age base (%) frequency of malarial infection

Age year group	Suspected case	Positive case (n, %)	*P. vivax* (n, %)	*P. falciparum* (n, %)	Mixed case (n, %)	p-value
1-15	178	111 (62.3)	80 (72.1)	13 (11.7)	18 (16.2)	0.04*
16-30	335	160 (47.7)	104 (65.0)	34 (21.2)	22 (13.7)	0.01*
31-45	470	204 (43.4)	109 (53.4)	53 (26.0)	42 (20.5)	0.01*
46-60	311	111 (35.7)	58 (52.2)	28 (25.2)	25 (22.5)	0.03*
61-above	166	63 (37.9)	33 (52.3)	6 (9.5)	24 (38.1)	0.04*
Total	1460	649 (44.4)	384 (59.1)	134 (20.6)	131 (20.1)	0.01*

*Significant

Table 2. Gender base (%) frequency of malarial infection in various administrative units

Species	Faisalabad city	Faisalabad Sadar			Jaranwala		Samundri		Tandilianwala		Chak Jhumra	
	Male (n, %)	Female (n, %)	Male (n, %)	Female (n, %)	Male (n, %)	Female (n, %)	Male (n, %)	Female (n, %)	Male (n, %)	Female (n, %)	Male (n, %)	Female (n, %)
P. vivax	48 (60.0)	34 (62.9)	48 (63.1)	39 (73.5)	37 (53.6)	21 (50.0)	42 (40.3)	20 (51.2)	39 (61.9)	12 (48.0)	30 (56.6)	14 (46.6)
P. falciparum	14 (17.5)	9 (16.6)	17 (22.3)	7 (13.2)	17 (24.6)	12 (28.5)	13 (12.5)	12 (30.7)	11 (17.4)	6 (24.0)	9 (16.9)	7 (23.3)
Mixed	18 (22.5)	11 (20.3)	11 (14.4)	7 (13.2)	15 (21.7)	9 (21.4)	10 (9.6)	7 (17.9)	13 (20.6)	7 (28.0)	14 (26.4)	9 (30.0)
Sub-total	80 (59.7)	54 (40.3)	76 (58.9)	53 (41.1)	69 (62.2)	42 (37.8)	65 (62.5)	39 (37.5)	63 (71.5)	25 (28.4)	53 (63.8)	30 (36.1)
Total	134 (41.7)	129 (41.8)			111 (53.1)		104 (64.6)		88 (37.5)		83 (25.2)	
Df	2	2			2		2		2		2	
F-value	55.135	119.031			22.031		26.375		10.798		15.047	
p-value	0.001**	0.001**			0.001**		0.002**		0.001**		0.001**	

**Highly significant

In Tandilianwala, Table 2 reveals a few disparities in the distribution of *Plasmodium* species between male and female cases. For instance, the *P. vivax* ratio (48.0%) was usually the max., but the infection rate for mixed cases was observed to be slightly higher (28.0%) compared to *P. falciparum* (24.0%) in females. The same pattern was observed in males, with *P. vivax* (61.9%), *P. falciparum* (17.4%), and mixed infection rate (20.6%). Overall, the infection rate among males and females was recorded as 71.5% and 28.4%, respectively. Moreover, across the municipality, Tandilianwala, *P. vivax* was predominant with a ratio of (57.4%), followed by mixed cases at 22.9%, and *P. falciparum* at (19.5%), out of a total of 88 positive cases.

In Chak Jhumra, the same pattern was observed as in the administrative unit Tandilianwala: the infection mixed cases ratio (27.7%) was recorded as high compared to that of *P. falciparum* (19.2%), and *P. vivax* infection rate (53.1%) was the highest out of the total 83 positive cases, as shown in Table 2. *P. vivax* infections were predominant, accounting for approximately 54.8% of all cases, followed by *P. falciparum* at 21.5%, and mixed infections at 23.5%. Males showed a higher frequency overall, comprising 62.5% of cases, compared to females who made up 37.5%. The present research results indicate that 406 (62.5%) males and 243 (37.4%) females out of 649 tested positive for malarial infection in the district of Faisalabad, Punjab, Pakistan. Statistical analysis showed this gender difference was significant ($p<0.03$), underscoring the relevance of gender-specific behavior and exposure patterns in malaria transmission.

Sensitivity and Specificity Analysis of Diagnostic Methods

Tables 3a and b summarize the diagnostic performance and species-specific detection across RDT, microscopy, and PCR methods. Of the 1,460 tested samples, RDT identified 384 (59.2%) *P. vivax* infections, 134 (20.6%) *P. falciparum* infections, and 131 (20.2%) mixed infections, whereas microscopy confirmed 281 (62.2%) *P. vivax* infections, 101 (22.3%) *P. falciparum* infections, and 70 (15.5%) mixed infections. PCR, used as the reference method, detected 266 (58.1%) *P. vivax*, 96 (21.1%) *P. falciparum*, and 97 (21.2%) mixed cases. The discrepancy was most notable in mixed infections, where microscopy underestimated them compared to PCR. Sensitivity and specificity values calculated using PCR as the reference standard revealed that RDT had 429 true positives, 55 false positives, 30 false negatives, and 946 true negatives, resulting in a sensitivity of 93.47% and specificity of 94.5%. In comparison, microscopy showed 435 true positives, 17 false positives, 24 false negatives, and 984 true negatives, yielding 94.78% sensitivity and 98.3% specificity. Statistical analysis confirmed significant differences among the diagnostic tools ($p<0.001$), validating that PCR consistently provided more accurate detection, particularly for mixed infections. These results demonstrate that while RDTs offer quick and useful preliminary diagnosis, confirmatory testing with microscopy and especially PCR is essential for accurate malaria detection and effective case management.

DISCUSSION

The current study, conducted from May 2023 to April 2024, provides a detailed analysis of the frequency of *Plasmodium* infection in various municipalities located in the district of Faisalabad, Pakistan. The present study showed that the frequency of malarial infection peaked in the months of June and July across the entire district of Faisalabad. For instance[27], reported a frequency of 21.3% in August, with a temperature of 34.2 °C, humidity 66.5%, and rainfall 6.64 mm, while the lowest frequency rate was recorded in January at 4.8% with a temperature

Table 3a. Sensitivity analysis of diagnostic methods (Percentages are calculated based on the number of positive cases for each method relative to the total tested population)

Species	Tested case	RDT %	Microscopy%	PCR%
P. vivax	384 (59.2%)	384 (59.2)	281 (62.2)	266 (58.1)
P. falciparum	134 (20.6%)	134 (20.6)	101 (22.3)	96 (21.1)
Mixed case	131 (20.2%)	131 (20.2)	70 (15.5)	97 (21.2)
Total	1,460	649 (44.4)	452 (30.6%)	459 (31.4)
Df		2	2	2
F-value		27.877	19.393	14.733
p-value		0.001**	0.001**	0.001**

**Highly significant.
RDT: Rapid diagnostic tests, PCR: Polymerase chain reaction.

Table 3b. Sensitivity and specificity of diagnostic methods (PCR as reference)

Method	Positive cases (n,%)	TP1*	FP2*	FN3*	TN4*	Sensitivity (%)	Specificity (%)
RDT	649 (44.4%)	429	55	30	946	93.47	94.5
Microscopy	452 (30.6%)	435	17	24	984	94.78	98.3
PCR (gold Std)	459 (31.4%)						

1* True positive; 2* False positive; 3* False negative; 4* True negative.
RDT: Rapid diagnostic tests, PCR: Polymerase chain reaction.

of 14 °C. During the summer months, the Faisalabad district region experienced heavy rainfall and temperatures ranging from 34 °C to 41 °C. That is why the high infection positivity ratios during the summer season were attributed to seasonal and climatic factors that increased mosquito densities in these Faisalabad district administrative units. Similar attributions were also recorded in the sub-Saharan Africa region.[28]

A total of 1,460 suspected malaria cases were tested across six administrative municipal units using three diagnostic methods: RDT, microscopy, and nested PCR. The highest positivity rate was observed with RDT (44.4%), followed by PCR (31.4%) and microscopy (30.6%), highlighting the tendency of RDTs to overestimate infection rates due to residual HRP2 antigen detection even after parasitemia clearance. Out of 1,460 samples, 649 (44.4%) were positive, with *P. vivax* 384 (59.1%), *P. falciparum* 134 (20.6%), and mixed 131 (20.1%) cases recorded. Our study reported a significantly higher frequency of *P. vivax* than *P. falciparum*. The present study results are in accordance with the findings of a previous study conducted in the Malakand district of Khyber Pakhtunkhwa province, which reported 59.57% *P. vivax* and 40.42% *P. falciparum* cases.[29] A previous study conducted in Khyber Pakhtunkhwa province, which also supports our findings, reported that the prevalence of *P. vivax* (92.4%) was highest compared to *P. falciparum* (4.7%) (18). Two previous studies conducted in India also exhibit the same pattern: *P. vivax* 55% and 41% were revealed higher ratio of infection showed higher ratios of infection at 55% and 41%, whereas *P. falciparum* 45% and 59% showed lower incidence showed lower incidences at 45% and 59%, respectively.[30,31] Another study conducted in District Umer kot, Sindh, Pakistan also reported that *P. vivax* had the highest incidence at 95% compared to *P. falciparum* at 4%, and 1% mixed cases.[32] The differences in our findings with respect to previous studies can be attributed to several factors, including regional ecological variations, differences in vector species composition, and diagnostic methodologies. Faisalabad's mixed urban-agricultural landscape, combined with higher population density and industrial activities, may influence vector ecology, favoring *P. falciparum* transmission and lowering the *P. vivax* incidence.

In two other previous studies, it had been demonstrated that researchers who used nPCR for the diagnosis of disease typically reported more accurate results as compared to those who depend commonly on RDTs and microscopy.[33,34] Microscopy, while shown to be a reliable method in malaria diagnosis, is extremely dependent on the technician's expertise and can miss low density infections.[35] RDTs had 95% sensitivity and 95.2% specificity for detecting PfHRP2, as reported by the World Health Organization in 2015. In our present study, we observed a higher rate of false positive cases with RDT compared to microscopy and PCR, underscoring the limitations of RDT in accurately identifying species-specific infections, particularly with the *P. falciparum*/*Pan-Plasmodium* RDT format. Prior comparative diagnostic research showed that nPCR outperforms other techniques, such as RDTs and microscopy, in producing accurate and sensitive diagnostic results, especially in cases of mixed infection.

The present research results indicate that 62.5% males and 37.4% females tested positive for malarial infection across the district Faisalabad, Punjab, Pakistan. Males were more prone to malarial infections due to their work in fields and exposure to mosquitoes. These reasons were also described in previous research papers that demonstrated that males were more susceptible than females due to their lifestyle factors and occupation.[36] Another previous study recorded the higher infection rate (54.7%) in males than (45.2%) in females, mainly infected by *P. vivax* (94.2%) and *P. falciparum* (5.6%), in district Kohat, which support our current results with little variations.[27]

Our current study determines the frequency across age groups and provides a comprehensive new analysis of malarial patients in district Faisalabad. We divided the data into five different age groups and found the max. frequencyies in the 1-15 age group, 16-30 age group, and 31-45 age group with infection rates of 62.3%, 47.7%, and 43.4%, respectively. As stated by Khan et al.,[16] our findings reveal that the children's age group had the highest infection rate when compared to others, owing to their lower immunity. The study also exhibited a 37% infection rate. A previous study conducted in Pakistan also

reported a high prevalence of malaria in the age group >14 years.[18] The study highlights a significant frequency of malaria in Faisalabad district, with *P. vivax* being the dominant species. The data indicate a higher susceptibility among males and children aged 1-15 years, particularly during the peak months of June and July. The nPCR method was found to be a highly efficient technique for diagnosing malarial infections, known for its superior sensitivity and specificity compared to other diagnostic methods. The findings underscore the importance of targeted malaria control and prevention strategies in high-risk groups and peak seasons.

Study Limitations

The limitations of this study include reliance on RDT-based positivity rates prone to false positives, restriction to government hospital data only, absence of multi-year trend analysis, lack of clinical and hematological correlation, and no assessment of mosquito vector dynamics.

CONCLUSION

This study demonstrates that while RDTs offer rapid malaria detection, they are prone to false positives due to persistent parasite antigens, particularly in low-transmission settings. PCR remains the most sensitive and specific method but is resource-intensive. Microscopy, despite being labor-intensive, still holds value when performed by trained personnel. A multi-method diagnostic approach tailored to local epidemiology may offer the most reliable results for accurate malaria diagnosis and control.

MAIN POINTS

- The frequency of malaria infection in Faisalabad district was 44.4%, with Plasmodium vivax identified as the dominant species.
- Rapid diagnostic tests showed higher positivity rates but were prone to false positives compared to microscopy and polymerase chain reaction (PCR).
- PCR demonstrated superior accuracy in detecting mixed infections and served as the most reliable diagnostic reference.
- Males and children aged 1-15 years were the most affected groups, with peak infection rates during June and July.
- Seasonal and regional variations highlight the need for confirmatory diagnostics and targeted malaria control strategies.

ETHICS

Ethics Committee Approval: The study was approved by the Ethics Review Committee of Government College University Faisalabad, Punjab, Pakistan (approval number: GCUF/ERC/460, date: 15.05.2023).

Informed Consent: Verbal informed consent was obtained from all participants prior to inclusion in the study.

Acknowledgement

The authors are appreciate the Department of Zoology, Government College University, Faisalabad, and the Integrated Genomics, Cellular Developmental and Biotechnology Laboratory (IGCDBL), University of Agriculture, Faisalabad, for providing all facilities.

Footnotes

Authorship Contributions

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

DISCLOSURES

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

Financial Disclosure: The authors declared that this study had received no financial support.

REFERENCES

1. Bhatt S, Weiss DJ, Cameron E, Bisanzio D, Mappin B, Dalrymple U, et al. The effect of malaria control on Plasmodium falciparum in Africa between 2000 and 2015. Nature. 2015; 526(7572): 207-11.
2. Report on malaria cases in Pakistan. World Health Organization. May 26, 2023. https://www.emro.who.int/images/stories/pakistan/Sitrep-26-May-Flood-Response.pdf
3. Farooq M, Yasinzai MI, Khan N, Sumbal A. Current status of malaria in district Pishin, Balochistan. Int J Mosq Res. 2020; 7(1): 33-6.
4. Naserrudin NA, Hod R, Jeffree MS, Ahmed K, Hassan MR. The emerging threat of plasmodium knowlesi malaria infection: a concept paper on the vulnerable factors in human. Int J Environ Res Public Health. 2022; 19(7): 4419.
5. Adamu J, Jigam AA. Effects of malaria infection on some hematological and biochemical parameters in the general population and pregnant malaria patients attending two district hospitals in Niger State, Nigeria. Glob J Infect Dis Clin Res. 2019; 5(1): 1-5.
6. Ayyadevara R. Effect of malaria on biochemical and hematological parameters: a hospital-based case-control study. MRIMS J Health Sci. 2022; 10(3): 41-6.
7. Sahira K, Al-Abboodi A. Comparative assessment of malaria diagnostic techniques updates. Nigerian J Parasitol. 2024; 45(1): 164-72.
8. Tasawer Z, Mannan F, Bhutta A. Prevalence of human malaria at Multan. Pak J Med Sci. 2003; 3: 123-6.
9. Siahaan L. Laboratory diagnostics of malaria. Earth Environ Sci. 2018; 125: 012090.
10. Picot S, Perpoint T, Chidiac C, Sigal A, Javouhey E, Gillet Y, et al. Diagnostic accuracy of fluorescence flow-cytometry technology using Sysmex XN-31 for imported malaria in a non-endemic setting. Parasite. 2022; 29: 31.
11. Bashir A, Arif S, Bano R, Imran T, Bashir S, Jan A. Frequency and risk factors of malaria infection in Dera Ismail Khan, Khyber Pakhtunkhwa, Pakistan. Int J Mosq. 2019; 6(5): 37-40.
12. Sumbal A, Iqbal Yasinzai M, Naseem M, Khan L, Ara T, Khan N. Frequency of Plasmodium vivax and Plasmodium falciparum malaria in school going children of Quetta (City), Balochistan. International Journal of Biosciences. 2018; 13(6): 43-50.
13. Zafar M, Mushtaq I, Masud S, Khan MZ, Khan MKA, Asmatullah. Prevalence and distribution of human malarial infection in district Multan, Punjab, Pakistan. Pure Appl Biol. 2019; 8(1): 873-81.
14. Jabeen S, Farrukh U, Hameed SA, Kanwal S, Qayyum M. An investigation on the prevalence and efficiency of immunochromatographic testing in suspected malarial patients of Rawalpindi and Islamabad, Pakistan. Turk J Med Sci. 2016; 46(5): 1329-34.
15. Rahman S, Jalil F, Khan H, Jadoon MA, Ullah I, Rehman M, et al. Prevalence of malaria in district shangla, khyber Pakhtunkhwa, Pakistan. J Entomol Zool Stud. 2017; 5: 678-82.

16. Khan MI, Qureshi H, Bae SJ, Shah A, Ahmad N, Ahmad S, et al. Dynamics of Malaria incidence in Khyber Pakhtunkhwa, Pakistan: unveiling rapid growth patterns and forecasting future trends. J Epidemiol Glob Health. 2024; 14(1): 234-42.

17. Tareen AM, Rafique M, Wadood A, Qasim M, Rahman H, Shah SH, et al. Malaria burden in human population of Quetta, Pakistan. Eur J Microbiol Immunol. 2012; 2(3): 201-4.

18. Qureshi H, Khan MI, Ambachew H, Pan HF, Ye DQ. Baseline survey for malaria prevalence in Khyber Pakhtunkhwa Province, Pakistan. East Mediterr Health J. 2020; 26(4): 453-60.

19. Hussain I, Qureshi NA, Afzal M, Shaheen N, Ali A, Ashraf A. Prevalence and distribution of human Plasmodium infection in Federally Administrative Tribal Areas of Pakistan. Acta Parasitol. 2016; 61(3): 537-43.

20. Umer MF, Zofeen S, Majeed A, Hu W, Qi X, Zhuang G. Spatiotemporal clustering analysis of malaria infection in Pakistan. Int J Environ Res Public Health. 2018; 15(6): 1202.

21. Naqvi SWA, Saeed S, Rafique A, Saeed MH, Khan N, Khan A, et al. Prevalence and distribution of malaria by sex, age groups and species in year 2019 in suspected malarial population of district DI Khan, Pakistan. Gomal Journal of Medical Sciences. 2020; 18(4): 164-73.

22. Pradhan S, Hore S, Maji SK, Manna S, Maity A, Kundu PK, et al. Study of epidemiological behavior of malaria and its control in the Purulia district of West Bengal, India (2016-2020). Sci Rep. 2022; 12(1): 630.

23. Rizwan A. Socio-economic problems of people living in peri-urban areas of Faisalabad and its effects on their health: a case study in district Faisalabad, University of Agriculture, Faisalabad. Pakistan, 2015.

24. Guidelines for the treatment of malaria, 3rd edition. Geneva: World Health Organization; 2015. http://apps.who.int/medicinedocs/documents/s21839en/s21839en.pdf

25. Zakeri S, Kakar Q, Ghasemi F, Raeisi A, Butt W, Safi N, et al. Detection of mixed Plasmodium falciparum & P. vivax infections by nested-PCR in Pakistan, Iran & Afghanistan. Indian J Med Res. 2010; 132(1): 31-5.

26. Rougemont M, Van Saanen M, Sahli R, Hinrikson HP, Bille J, Jaton K. Detection of four Plasmodium species in blood from humans by 18S rRNA gene subunit-based and species-specific real-time PCR assays. J Clin Microbiol. 2004; 42(12): 5636-43.

27. Khan MI, Qureshi H, Bae SJ, Khattak AA, Anwar MS, Ahmad S, et al. Malaria prevalence in Pakistan: a systematic review and meta-analysis (2006-2021). Heliyon. 2023; 9(4): e15373.

28. Paton RS, Kamau A, Akech S, Agweyu A, Ogero M, Mwandawiro C, et al. Malaria infection and severe disease risks in Africa. Science. 2021; 373(6557): 926-31.

29. Imran M, Ahmad I, Kalim M. Identification of Plasmodium vivax and Plasmodium falciparum in the northern areas (district Malakand) of Khyber Pakhtunkhwa, Pakistan. PSM Microbiology. 2017; 2(3): 59-62.

30. Surve KM, Kulkarni AS, Rathod SG, Bindu RS. Study of hematological parameters in malaria. Int J Res Med Sci. 2017; 5(6): 2552-57.

31. Yadav RK, Kumar S. To study hematological profile in malaria patients. Int J Adv Med. 2017; 4(3): 707-12.

32. Hussain M, Fatah A, Akhtar W, Javeed F, Kashif M, Ahmed W. Malarial infection in population of district Umerkot, Sindh & its effects on hematological parameters. Pak J Pathol. 2021; 32(1): 15-8.

33. Kim JY, Ji SY, Goo YK, Na BK, Pyo HJ, Lee HN, et al. Comparison of rapid diagnostic tests for the detection of Plasmodium vivax malaria in South Korea. PLoS One. 2013; 8(5): e64353.

34. Cook J, Xu W, Msellem M, Vonk M, Bergström B, Gosling R, et al. Mass screening and treatment on the basis of results of a Plasmodium falciparum-specific rapid diagnostic test did not reduce malaria incidence in Zanzibar. Int J Infect Dis. 2015; 211(9): 1476-83.

35. Murray CK, Gasser RA Jr, Magill AJ, Miller RS. Update on rapid diagnostic testing for malaria. Clin Microbiol Rev. 2008; 21(1): 97-110.

36. Okiring J, Epstein A, Namuganga JF, Kamya EV, Nabende I, Nassali M, et al. Gender difference in the incidence of malaria diagnosed at public health facilities in Uganda. Malar J. 2022; 21(1): 22.

CASE REPORT

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2024-164
Cyprus J Med Sci 2025;10(5):343-346

A Unique Case of Acute Promyelocytic Leukemia with Disseminated Intravascular Coagulation and Spontaneous Tumor Lysis Syndrome

Amin A. Alamin[1], Amna F. Bashir[1], Imad A. Mohamed[2]

[1]Department of Pathology, Taif University Faculty of Medicine, Taif, KSA
[2]Department of Microbiology, Taif University Faculty of Medicine, Taif, KSA

Abstract

Acute promyelocytic leukemia (APL) is a rare and specific subtype of acute myeloid leukemia involving characteristic genetic translocations and the accumulation of abnormal promyelocytes. Severe coagulopathy is common and can result in disseminated intravascular coagulation (DIC), a major early cause of death. Furthermore, tumor lysis syndrome is a life-threatening complication of hematologic malignancies that typically develops after treatment initiation. Spontaneous tumor lysis syndrome (STLS) occurring prior to the initiation of treatment is an exceedingly rare event in cases of APL. We present a rare case of a 25-year-old male who developed STLS along with DIC before any treatment. Metabolic imbalances consistent with STLS, including hyperkalemia and hyperuricemia, were identified as laboratory findings, along with evidence of DIC. The patient was treated with all-trans retinoic acid and arsenic trioxide along with supportive measures against metabolic imbalances and coagulopathy. However, the patient's condition quickly deteriorated despite prompt therapeutic intervention, and the patient died of multiorgan failure within one week of admission. The outcome of this case emphasizes the importance of early recognition and aggressive management of complications, such as (example 1) and (example 2), in APL, with a high mortality risk when both complications are present. More research is needed to better understand the pathophysiology and treatment strategy for STL Sin APL.

Keywords: Disseminated intravascular coagulation, spontaneous tumor lysis syndrome, acute promyelocytic leukemia, coagulopathy, multiorgan failure

INTRODUCTION

Acute promyelocytic leukemia (APL), or M3 in the French-American-British system, is a special subtype of acute myeloid leukemia characterized by the t(15;17) translocation, creating the *PML-RARA* fusion gene.[1] Coagulopathy is a common finding in APL patients and most frequently takes the form of disseminated intravascular coagulation (DIC), which is present in more than 80% of newly diagnosed patients and is a major cause of early death before treatment.[2]

The pathophysiology of DIC in APL involves the release of procoagulant factors, such as tissue factors and cancer procoagulants, from leukemic promyelocytes. This initiates the coagulation cascade, leading to excessive fibrin formation, the consumption of clotting factors, and a clinical phenotype characterized by both thrombosis and hemorrhage.[3] Rapid diagnosis and initiation of all-trans retinoic acid (ATRA) therapy are important. ATRA not only induces remission but also controls coagulopathy.[4]

Another life-threatening complication of chemotherapy is spontaneous tumor lysis syndrome (STLS), which usually develops in patients with hematologic malignancies. Massive tumor cell breakdown is characterized by the release of intracellular components, including

To cite this article: Alamin AA, Bashir FA, Mohamed IA. Unique case of acute promyelocytic leukemia with disseminated intravascular coagulation and spontaneous tumor lysis syndrome. Cyprus J Med Sci. 2025;10(5):343-346

ORCID IDs of the authors: A.A.A. 0000-0002-4405-5826; A.F.B. 0000-0002-7624-5034; I.A.M. 0000-0003-1636-7205.

Corresponding author: Amin A. Alamin
E-mail: amakki@tu.edu.sa
ORCID ID: orcid.org/0000-0002-4405-5826

Received: 09.01.2025
Accepted: 19.02.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

potassium, phosphate, and uric acid.[5] This causes metabolic imbalances such as hyperkalemia, hyperphosphatemia, hyperuricemia, and even potential renal failure. STLS is a rare entity in which tumor lysis occurs without therapeutic intervention, indicating a high tumor burden. APL patients are extremely rare among those with STLS, which is a real diagnostic and therapeutic challenge.[6] Cases of DIC and STLS coexisting in APL patients are rare, and both conditions demand timely but contrasting therapeutic procedures. Treatment for DIC consists of supportive measures, such as platelet transfusions and cryoprecipitation, plus ATRA, to induce promyelocyte maturation. In contrast, STLS management is characterized by aggressive hydration, urate-lowering therapies, and close monitoring of electrolyte imbalances.[7] In this report, we present a rare case of a newly diagnosed APL patient who developed DIC and STLS, at the same time, which complicates the management of these life-threatening conditions. We present the case of a patient who most likely has APL complicated by both DIC and STLS. Early diagnosis and multidisciplinary treatment are highly important to avoid fatal outcomes, particularly in the setting of more aggressive leukemic phenotypes.

CASE REPORT

An otherwise healthy 25-year-old male presented with fatigue, weakness, and easy bruising for one week. He was pale, with petechial and ecchymotic rashes on physical examination. Pancytopenia was detected via laboratory findings, including a white blood cell count of 1,500/µL (80% promyelocytes), a hemoglobin level of 7 g/dL, and a 20,000/µL platelet count. Coagulation studies revealed coagulopathy, demonstrated by an elevated prothrombin time (18 s), activated partial thromboplastin time (60 s), and D-dimer level (2.0 µg/mL). Electrolyte abnormalities consistent with STLS were also noted: hyperkalemia (6.5 mmol/L), hyperphosphatemia (6.0 mg/dL), and hyperuricemia (10.0 mg/dL) (Table 1).

A peripheral blood smear and bone marrow aspirate confirmed the diagnosis of APL with numerous abnormal promyelocytes containing Auer rods (Figure 1).

The diagnosis of APL was confirmed through flow cytometry and chromosomal analysis (Figure 2). Standard induction therapy for APL for this patient included ATRA (45 mg/m²/day orally) and arsenic trioxide (ATO) (0.15 mg/kg/day intravenously). Supportive care consists of red blood cell transfusions, platelet transfusions, intravenous fluids, and medications to resolve electrolyte imbalances. Hyperuricemia was treated, and renal complications were prevented with rasburicase. Interventions were performed while the patient was in critical condition due to coagulopathy from DIC and STLS complications. The patient was admitted to the hospital and received the outlined therapy. Despite the interventions, one week after admission, the patient developed acute kidney injury (AKI) and multiorgan dysfunction, leading to death. Written informed consent was obtained from the patient for the publication of clinical details and images. Identifying information has been anonymized where possible, and any potentially identifying images or details are included with explicit consent.

DISCUSSION

In untreated patients, DIC often complicates APL and is the most common cause of early mortality. In APL, DIC arises from leukemic promyelocytes releasing procoagulants such as tissue factor, triggering excessive fibrin formation, clotting factor consumption, and a dual phenotype of thrombosis and hemorrhage.[3] Although DIC is a well-known APL complication, STLS is very uncommon. However, STLSs are frequently observed in rapidly proliferating malignancies e.g., burkitt lymphoma, but are uncommon in untreated APLs.[6] In this case, the patient presented with metabolic derangements characteristic of TLS, such as hyperkalemia, hyperphosphatemia, and hyperuricemia, at the time of diagnosis. The rapid breakdown of tumor cells in patients with STLS causes metabolic disturbances and AKI.[5]

This case provides a rare instance of STLS in APL, emphasizing several unique insights. While STLS is typically associated with malignancies such as burkitt lymphoma[8], its occurrence in APL is uncommon because of slower tumor turnover. These findings suggest that certain aggressive APL phenotypes may predispose patients to STLS, emphasizing the importance of identifying high-risk subtypes. The metabolic derangements, such as hyperkalemia, hyperphosphatemia, and hyperuricemia observed before treatment initiation, could serve as early warning signs of STLS in APL patients. This case demonstrates the difficulty of managing both conditions simultaneously. The challenge of balancing aggressive hydration and electrolyte management for patients with STLS, with control of coagulopathy in DIC, requires careful attention. The simultaneous presence of DIC and STLS poses clinical complications that create a need to intervene, with urgent treatment directed at each condition. Managing overlapping DIC and STLS poses unique challenges because of their opposing pathophysiology and treatment goals. DIC requires anticoagulation and clotting factor replacement to address bleeding and thrombosis, whereas STLS requires aggressive hydration, rasburicase, and electrolyte correction to prevent renal failure and arrhythmias. The therapeutic balance is delicate, as interventions for one condition may worsen the other-e.g., fluid resuscitation for STLS can exacerbate bleeding in thrombocytopenic DIC patients. Overlapping laboratory abnormalities (e.g., hypocalcemia, elevated lactate dehydrogenase) further complicate monitoring, necessitating frequent reassessment of coagulation profiles, electrolytes, and renal function. The absence of consensus guidelines for this overlap underscores the need for individualized, multidisciplinary management to mitigate risks and optimize outcomes.[9,10] Other important supportive care methods include transfusions of platelets and clotting factors. Prompt initiation of ATRA and ATO, as per current guidelines, significantly reduces early mortality.[11] However, aggressive

Table 1. Laboratory parameters of the patient

Parameter	Patient value	Reference range[7]
White blood cell count	15,000/µL	4,500-11,000/µL
Promyelocytes	80%	0%
Hemoglobin	7 g/dL	13.5-17.5 g/dL (males)
Platelet count	20,000/µL	150,000-450,000/µL
Prothrombin time	18 seconds	11-13 seconds
Activated partial thromboplastin time	60 seconds	25-40 seconds
D-dimer	2.0 µg/mL	<0.5 µg/mL
Electrolyte abnormalities:		
Potassium	6.5 mmol/L	3.5-5.0 mmol/L
Phosphorus	6.0 mg/dL	2.3-4.7 mg/dL
Uric acid	10.0 mg/dL	4.0-8.5 mg/dL (males)

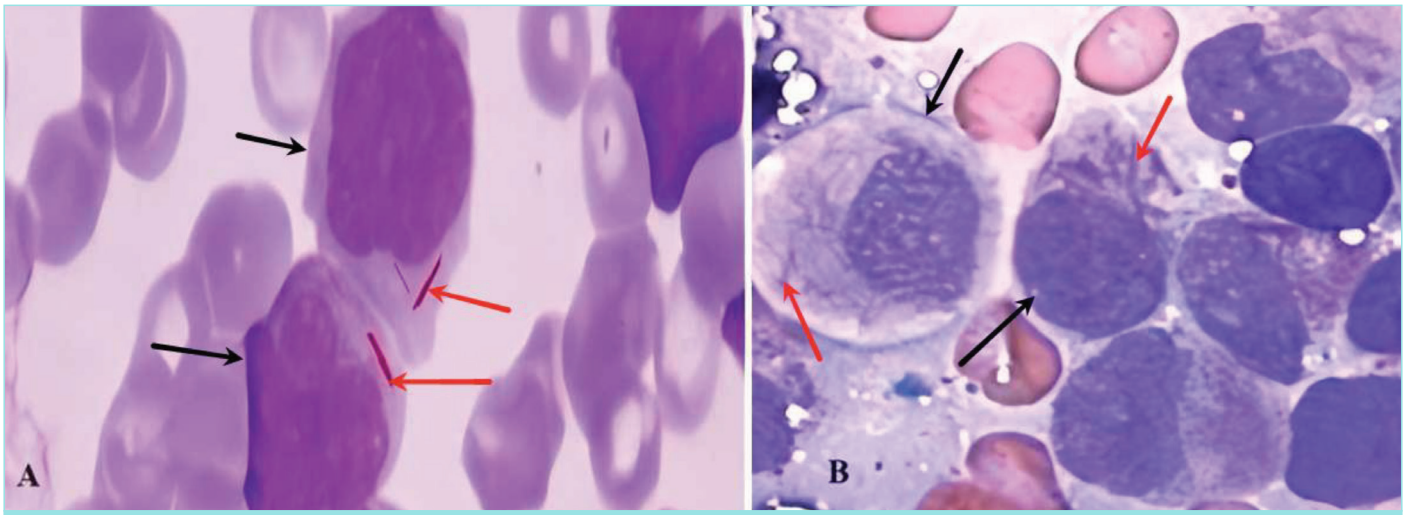


Figure 1. Peripheral blood smear and bone marrow aspiration.

Peripheral blood smear and bone marrow aspiration: (A) blood film showing blasts with auer rods (red arrow). (B) bone marrow aspirate showing a high number of abnormal promyelocytes (black arrow) with auer rods (black arrow) (original magnification 1000x).

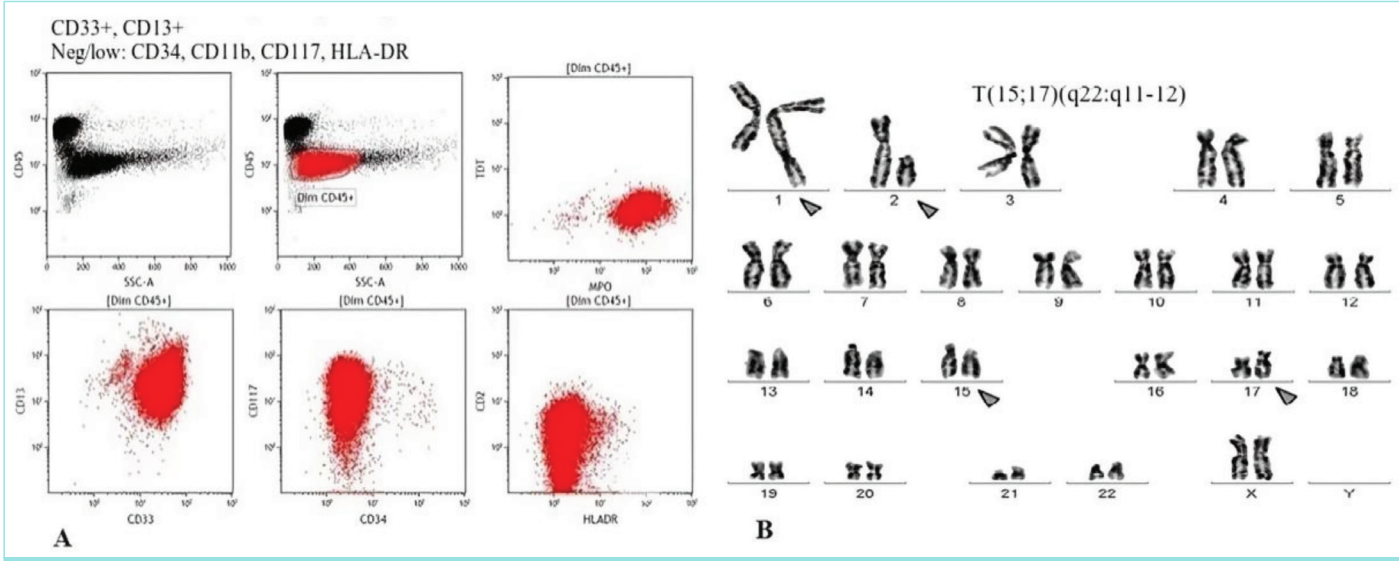


Figure 2. Flow cytometry analysis and chromosomal study.

Flow cytometry analysis and chromosomal study: (A) flow cytometry analysis demonstrating the immunophenotypic profile of abnormal promyelocytes, which is consistent with APL. (B) the chromosomal study revealed the characteristic translocation t (15;17) (q24;q21) associated with APL. APL: Acute promyelocytic leukemia.

hydration, electrolyte correction, and urate lowering measures, which are required for the management of TLS, using urinary drugs such as rasburicase, have the potential to precipitate and worsen AKI.[6] However, the patient's condition did not improve but rather worsened, leading to the development of multiorgan failure and illustrating how severe the condition of overlapping DIC and STLS was. This case highlights the need for early recognition of DIC and STLS in APL patients followed by aggressive management. The initiation of ATRA and ATO should be carried out rapidly to avoid DIC, and metabolic derangements related to STLS must be corrected promptly. When both complications are present, the mortality risk remains high and represents an indication for vigilant monitoring and rapid therapeutic adjustments. Cases of STLS in APL patients are extremely rare, with few reported in the literature.[7,12] In this case, additional knowledge about STLS in APL patients is provided, and further research is needed to improve the management strategy of patients with both complications. We report here an uncommon case of concomitant life-threatening events of DIC and STLS in an APL patient with newly diagnosed APL. Although the existence of DIC as a complication in APLs is well known, spontaneous TLS prior to starting therapy is incredibly rare. These severe complications can be recognized and treated early with ATRA, ATO, and supportive care. Consequently, the risk decreases. Proper management of these conditions is possible, but the high mortality naturally associated with the overlap underscores the need for operator

surveillance and prompt initiation of treatment. Further studies are needed to clarify the pathophysiology of STLS in patients with APL and to change the treatment strategy for this high-risk patient group.

CONCLUSION

This case highlights the fatal cytotoxicity of the simultaneous flows of DIC and STLS in untreated APL. Even when diagnosed and treated with ATRA, ATO and intense supportive care, the patient still inevitably progressed to multiorgan failure. The occurrence of refractory coagulopathy in connection with hyperkalemia, hyperuricemia, and hyperphosphatemia at the same time points to the need of increased clinical awareness, early biochemical screening, and interdisciplinary management at the point of presentation. Seeing that such presence of contradictory complications is much more of a therapeutic gauntlet, it is necessary to conduct more studies regarding the mechanism of this setup and how evidence-based tailored treatment guidelines could be created to deal with this issue.

MAIN POINTS

- Acute promyelocytic leukemia (APL) commonly presents with disseminated intravascular coagulation (DIC), which significantly contributes to early mortality, and the rare occurrence of spontaneous tumor lysis syndrome (STLS) in untreated APL patients is a diagnostic challenge.
- A 25-year-old male with newly diagnosed APL developed both DIC and STLS before treatment and presented with metabolic abnormalities, including hyperkalemia, hyperphosphatemia, and hyperuricemia, along with coagulopathy.
- Despite the administration of all-trans retinoic acid and arsenic trioxide, combined with supportive care for electrolyte imbalances and coagulopathy, the patient's condition rapidly deteriorated, leading to multiorgan failure and death within one week.
- The coexistence of DIC and STLS in APL patients necessitates urgent and contrasting treatment strategies for both conditions, emphasizing the importance of early recognition and aggressive management.
- This case underscores the need for further research into the pathophysiology and management of STLS in APL patients to improve treatment outcomes and survival in high-risk patients.

ETHICS

Informed Consent: Written informed consent was obtained from the patient for the publication of clinical details and images.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.A.A., Concept: A.A.A., A.F.B., I.A.M., Design: A.A.A., A.F.B., Data Collection and/or Processing: A.A.A., I.A.M., Analysis and/or Interpretation: A.A.A., A.F.B., Literature Search: A.A.A., I.A.M., Writing: AA.A.A., A.F.B., I.A.M.

DISCLOSURES

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

Financial Disclosure: The authors declared that this study had received no financial support.

REFERENCES

1. Coombs CC, Tavakkoli M, Tallman MS. Acute promyelocytic leukemia: where did we start, where are we now, and the future. Blood Cancer J. 2015; 5(4): e304.
2. Avvisati G. Coagulopathy in APL: a step forward? Blood. 2012; 120(1): 4-6.
3. Breen KA, Grimwade D, Hunt BJ. The pathogenesis and management of the coagulopathy of acute promyelocytic leukaemia. Br J Haematol. 2012; 156(1): 24-36.
4. Castaigne S, Chomienne C, Daniel MT, Ballerini P, Berger R, Fenaux P, et al. All-trans retinoic acid as a differentiation therapy for acute promyelocytic leukemia. I. Clinical results. Blood. 1990; 76(9): 1704-9.
5. Howard SC, Jones DP, Pui CH. The tumor lysis syndrome. N Engl J Med. 2011; 364(19): 1844-54.
6. Cairo MS, Bishop M. Tumour lysis syndrome: new therapeutic strategies and classification. Br J Haematol. 2004; 127(1): 3-11.
7. Montesinos P, Lorenzo I, Martín G, Sanz J, Pérez-Sirvent ML, Martínez D, et al. Tumor lysis syndrome in patients with acute myeloid leukemia: identification of risk factors and development of a predictive model. Haematologica. 2008; 93(1): 67-74.
8. Pan S, Shen Q, Zhou J, Li T. Spontaneous tumor lysis syndrome (STLS) during biopsy for burkitt lymphoma: a case report. BMC Pediatr. 2024; 24(1): 209.
9. Tallman MS, Altman JK. How I treat acute promyelocytic leukemia. Blood. 2009; 114(25): 5126-35.
10. Levi M, Scully M. How I treat disseminated intravascular coagulation. Blood. 2018; 131(8): 845-54.
11. Sanz MA, Fenaux P, Tallman MS, Estey EH, Löwenberg B, Naoe T, et al. Management of acute promyelocytic leukemia: updated recommendations from an expert panel of the European LeukemiaNet. Blood. 2019; 133(15): 1630-43.
12. Cairo MS, Thompson S, Stern L, Sherman S. Incidence of treatment-related, laboratory, and clinical tumor lysis syndrome. Blood. 2012; 120(21): 238.

CASE REPORT

CYPRUS
JOURNAL OF MEDICAL SCIENCES

DOI: 10.4274/cjms.2025.2025-33
Cyprus J Med Sci 2025;10(5):347-350

Medial Antebrachial Cutaneous Nerve Injury During Routine Venous Blood Collection: Could A Low Body Mass Index be A Risk Factor?

Halit Fidancı[1], Seda Mençekoğlu Baştin[2], Halil Can Alaydın[1], Çağatay Küçükbingöz[3]

[1]Division of Clinical Neurophysiology, Clinic of Neurology, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye
[2]Clinic of Neurology, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye
[3]Clinic of Algology, University of Health Sciences Türkiye, Adana City Training and Research Hospital, Adana, Türkiye

Abstract

The medial antebrachial cutaneous nerve (MACN) is rarely affected on its own. MACN injury may occur as a result of trauma or compression. We present a 23-year-old female patient with neuropathy of the anterior branch of the MACN, associated with venous blood collection from the left antecubital fossa. This case aims to contribute to the understanding of MACN injury by presenting clinical findings, neurophysiological results, and possible risk factors, including low body mass index (BMI). The patient had severe pain in the medial forearm during the blood collection procedure. The patient's BMI was 17.6 kg/m^2. Patients' score on the Leeds Assessment of Neuropathic Symptoms and Signs scale was 19. In the sensory nerve conduction study, the left MACN amplitude was found to be lower than that of the right. The findings in this case indicate that neuropathic pain may represent a major component of the clinical picture in MACN injury. This case also raises the possibility that a low BMI could increase vulnerability to such neuropathies. Accordingly, procedures involving venipuncture or intravenous access may require greater caution in individuals with low BMI.

Keywords: Body mass index, medial antebrachial cutaneous nerve, peripheral neuropathy, venous blood collection

INTRODUCTION

The medial antebrachial cutaneous nerve (MACN), originating from the medial cord of the brachial plexus, provides sensory innervation to the medial aspect of the forearm. Isolated involvement of the MACN typically results in sensory deficits in the medial forearm without associated motor weakness.[1,2] MACN involvement is possible in brachial plexopathies in which the lower trunk is affected or in diseases such as thoracic outlet syndrome.[1,2] Isolated MACN involvement is rare.[3-6] It has been reported that MACN injury may develop as a result of MACN neuroma or compression of the MACN by a disorder such as a lipoma or from invasive interventions on the elbow region.[3,5-7]

Nerve injury following venipuncture is uncommon, with an estimated incidence of approximately 1 in 65,000, while neuropathic pain occurs in about 1 in 30,000 cases.[8,9] A study by Tsukuda et al.[8] reported 16 nerve injuries following just over one million venipunctures, eight of which involved the MACN, suggesting an estimated incidence of approximately one MACN injury per 135,000 venipunctures. Nonetheless, the potential for neuropathic pain underscores the need to recognize such injuries.[9] Moreover, the fact that MACN injury does not occur in every patient suggests that certain individuals may be more susceptible. Therefore, the rarity of this condition, the associated risk of neuropathic pain, and the uncertainty regarding patient susceptibility highlight the importance of identifying and reporting these cases. We present a

To cite this article: Fidancı H, Mençekoğlu Baştin S, Alaydın HC, Küçükbingöz Ç. Medial antebrachial cutaneous nerve injury during routine venous blood collection: could a low body mass index be a risk factor? Cyprus J Med Sci. 2025;10(5):347-350

ORCID IDs of the authors: H.F. 0000-0001-6573-9090; S.M.B. 0009-0007-8218-2694; H.C.A. 0000-0002-5503-0413; Ç.K. 0000-0002-2527-3510.

Corresponding author: Halit Fidancı
E-mail: dr.halitfidanci@gmail.com
ORCID ID: orcid.org/0000-0001-6573-9090

Received: 07.04.2025
Accepted: 20.08.2025
Epub: 29.09.2025
Publication Date: 09.10.2025

patient who developed MACN injury after venous blood collection from the antecubital fossa. This case is presented to draw attention to a rare complication involving isolated MACN injury after venous blood collection from the antecubital fossa and to emphasize the potential role of individual risk factors, such as a low body mass index (BMI).

CASE REPORT

A 23-year-old female nurse had severe pain and a tingling sensation on the medial left forearm, immediately following a venous blood collection from the antecubital fossa for a routine blood biochemical examination. The patient stated that there was a slight swelling in the region where the injection was made, and then, this swelling decreased within weeks. Four months later, she was referred to our clinical neurophysiology laboratory. The patient initially considered the symptoms to be temporary and did not pursue medical attention. However, as the pain, paresthesia, and sensory disturbances persisted and began to affect her daily functioning, she was referred for further evaluation. During the four-month interval, no specific medical treatment was administered, and no neurological evaluation was performed. She did not receive analgesics or undergo physical therapy. The referral to our laboratory was her first neurophysiological assessment related to these complaints. The patient did not have a chronic disease. The patient's height, weight, and BMI were 158 cm, 44 kg, and 17.6 kg/m^2, respectively. The patient had pain, allodynia, tingling, hypoesthesia, and decreased pain-temperature sensation on the region innervated by the anterior branch of the MACN (Figure 1A). Muscle strength examination was normal. The Turkish version of the Leeds Assessment of Neuropathic Symptoms and Signs scale (LANSS) was applied to the patient.[10] The scores of the pain questionnaire and sensory testing of LANSS were eleven and eight, respectively. The patient reported a mean Visual Analog Scale (VAS) score of 6 for pain during the four-month period between symptom onset and her presentation to the clinical neurophysiology laboratory. The patient was not followed longitudinally after the neurophysiological evaluation. Neuropathic pain assessment using the LANSS and VAS scales was performed only once at the time of presentation.

Previously recommended methods and normal values were used for median and ulnar nerve conduction studies.[11] The nerve conduction study of MACN was performed antidromically as previously suggested.[12,13] The lower reference limits for MACN compound nerve action potential (CNAP) amplitude and nerve conduction velocity were 10 µV and 41.7 m/s, respectively.[12] Sensory nerve conduction study findings of median, ulnar, lateral antebrachial cutaneous, and superficial radial nerves were normal. The left MACN CNAP amplitude was lower than the right side's amplitude. The nerve conduction study of bilateral MACNs is shown in Figure 1B. Median and ulnar motor nerve conduction study findings and F-waves of these nerves were normal. The needle electromyography findings of the left abductor pollicis brevis, the first dorsal interosseous, the abductor digiti quinti, the extensor indicis proprius, the biceps brachii, the triceps, and the deltoid muscles were normal. There was no abnormality in the direct X-ray and magnetic resonance imaging (MRI) of the elbow and forearm. Written informed consent was received from the patient.

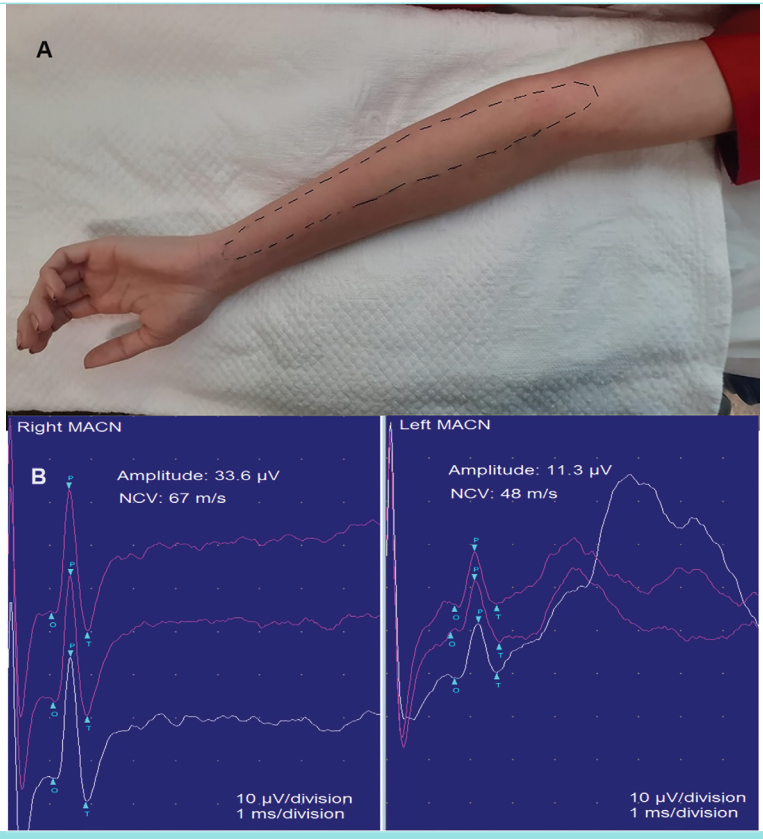


Figure 1. (A) Area of sensory abnormality in the patient's extremity. (B) The nerve conduction study of the medial antebrachial cutaneous nerve.
MACN: Medial antebrachial cutaneous nerve, NCV: Nerve conduction velocity.

DISCUSSION

Isolated injury to MACN is an uncommon condition. In this report, we present a rare case of MACN injury that occurred following venous blood sampling, with particular attention to the presence of neuropathic pain and the patient's BMI, both of which may have played a role in the development and persistence of symptoms.

MACN neuropathy may be caused by a neuroma or a lipoma.[3,6] In addition, MACN injury has been reported due to interventional procedures, or surgery involving the elbow region or antecubital fossa.[4,5,7] Horowitz[5] reported MACN injury in 5 of 11 patients with a peripheral nerve injury, which may be associated with routine venipuncture. In addition to arteries and veins, the MACN is also associated with the cubital fossa,[7] which means that the MACN may be damaged during invasive procedures in this region. In the present case, MACN injury developed during blood collection from the antecubital fossa. The immediate onset of pain and paresthesia may mean that the nerve is directly affected.[7] This condition, is well known in sciatic nerve injury due to intramuscular injection.[14] If the nerve is directly affected, the complaints begin immediately or within seconds. If fibrosis affects the nerve or a toxic substance affects the nerve through diffusion, the complaints may begin within hours/days.[7,14] Therefore, in the present case, it can be considered that the nerve is directly affected. In addition, previously reported cases indicate that neuropathic pain is a significant factor in MACN injury.[3-5,7] Similarly, the patient's LANSS score was above 12 and she had allodynia.

It may be important that the BMI of the patient was below 18.5 kg/m^2. It is known that low BMI may be a risk factor for sciatic nerve injury due to intramuscular injection.[14,15] This may be because thin people have less muscle mass protecting the sciatic nerve.[14,15] Similarly, it is thought that peroneal neuropathy at the head of the fibula associated with weight loss may be due to decreased peroneal nerve protective tissue.[16,17] In the present case, reduced protective tissue in the medial elbow region may have increased MACN vulnerability and contributed to nerve injury. In individuals with low BMI, the lack of subcutaneous fat may leave superficial nerves more exposed to external trauma. Similar mechanisms have been described in sciatic and peroneal neuropathies associated with low BMI.[14-17] Even routine procedures like venipuncture may pose a higher risk in such patients. In addition to BMI, factors such as the type of syringe used for blood collection, the angle of needle insertion, and the depth of penetration into the antecubital fossa may also play a critical role.[14] However, even with attention to these, anatomical variations can predispose to MACN injury.[7]

The nerve conduction study of the posterior branch of MACN was not performed. This can be considered a limitation of the report. Involvement of the posterior branch of the MACN may help localize the lesion, as simultaneous involvement of both anterior and posterior branches suggests a lesion proximal to the elbow region. In this case, the presence of sensory symptoms limited to the area innervated by the anterior branch, with no sensory changes in the region supplied by the posterior branch, supports the conclusion that the injury was caused by the venipuncture procedure. The absence of ultrasonography (USG) as an imaging method in this case may also be considered a limitation for diagnosing MACN injury. USG can offer certain advantages over MRI in visualizing peripheral nerves.[18] However, the small caliber of the MACN and its close proximity to surrounding soft tissue structures may reduce its diagnostic utility in such cases.[18] Although USG was not employed in this case, it is important to note that X-ray and MRI effectively ruled out other potential etiologies, such as fractures, hematoma, and edema. X-ray was preferred initially to rule out structural causes such as bone lesions or fractures, as it was more readily available in the clinical setting. Despite these limitations, this case offers two notable contributions to the literature. First, it highlights the occurrence of neuropathic pain following isolated MACN injury, rarely been emphasized. Second, it raises the possibility that low BMI may serve as an anatomical risk factor for such injuries. Future studies examining the association between MACN injury and BMI may help identify patient-related risk factors for nerve injury following venipuncture. Additionally, research focusing on neuropathic pain in cases of MACN injury may help clarify the underlying mechanisms.

CONCLUSION

The delayed referral and absence of early neurological assessment in this case, reflect the possibility that such injuries may initially be underrecognized. Increased clinical vigilance is essential, especially when patients report immediate pain and paresthesia during venipuncture. In conclusion, this case highlights the need for greater caution during venipuncture in the antecubital fossa, particularly in patients with low BMI, as they may be more susceptible to MACN injury. Additionally, neuropathic pain can be a presenting symptom in such cases.

MAIN POINTS

- Medial antebrachial cutaneous nerve (MACN) injury can occur following routine venous blood collection, particularly in the antecubital fossa.
- Patients with low body mass index may be at increased risk for MACN injury due to reduced soft tissue protection.
- Neuropathic pain, including allodynia and sensory deficits, can be a prominent and persistent symptom of isolated MACN neuropathy.

ETHICS

Informed Consent: Written informed consent was received from the patient.

Footnotes

Authors Contributions

Surgical and Medical Practices: H.F., S.M.B., H.C.A., Ç.K., Concept: H.F., S.M.B., H.C.A., Ç.K., Design: H.F., S.M.B., Data Collection and/or Processing: H.F., S.M.B., H.C.A., Ç.K., Analysis and/or Interpretation: H.F., S.M.B., H.C.A., Ç.K., Literature Search: H.F., S.M.B., H.C.A., Ç.K., Writing: H.F., S.M.B., H.C.A., Ç.K.

DISCLOSURES

Conflict of interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Li H, Zhu W, Wu S, Wei Z, Yang S. Anatomical analysis of antebrachial cutaneous nerve distribution pattern and its clinical implications for sensory reconstruction. PLoS One. 2019; 14(9): 0222335.

2. Rubin DI. Brachial and lumbosacral plexopathies: a review. Clin Neurolphysiol Pract. 2020; 5: 173-93.

3. Yıldız N, Ardic F. A rare cause of forearm pain: anterior branch of the medial antebrachial cutaneous nerve injury: a case report. J Brachial Plex Peripher Nerve Inj. 2008; 3: 10.

4. Ashegan M, Khatibi A, Holisaz MT. Paresthesia and forearm pain after phlebotomy due to medial antebrachial cutaneous nerve injury. J Brachial Plex Peripher Nerve Inj. 2011; 6: 5.

5. Horowitz SH. Peripheral nerve injury and causalgia secondary to routine venipuncture. Neurology. 1994; 44(5): 962-4.

6. Seror P. Forearm pain secondary to compression of the medial antebrachial cutaneous nerve at the elbow. Arch Phys Med Rehabil. 1993; 74(5): 540-2.

7. Kim HJ, Park SK, Park SH. Upper limb nerve injuries caused by intramuscular injection or routine venipuncture. Anesth Pain Med. 2017; 12(2): 103-10.

8. Tsukuda Y, Funakoshi T, Nasuhara Y, Nagano Y, Shimizu C, Iwasaki N. Venipuncture nerve injuries in the upper extremity from more than 1 million procedures. J Patient Saf. 2019; 15(4): 299-301.

9. Kato J, Araki H, Kimura M, Takahashi K, Ueda K, Iida R, et al. Incidence and prognosis of persistent pain induced by venipuncture for blood sampling: an observational study over a 5-year period. Pain Med. 2012; 13(12): 1627-30.

10. Yucel A, Senocak M, Kocasoy OE, Cimen A, Ertaş M. Results of the leeds assessment of neuropathic symptoms and signs pain scale in Turkey: a validation study. J Pain. 2004; 5(8): 427-32.

11. Fidancı H, Öztürk İ, Köylüoğlu AC, Yildiz M, Buturak S, Arlier Z. The needle electromyography findings in the neurophysiological classification of ulnar neuropathy at the elbow. Turk J Med Sci. 2020; 50(4): 804-10.

12. Pribyl R, You SB, Jantra P. Sensory nerve conduction velocity of the medial antebrachial cutaneous nerve. Electromyogr Clin Neurophysiol. 1979: 19(1-2): 41-6.

13. Prahlow ND, Buschbacher RM. An antidromic study of the medial antebrachial cutaneous nerve, with a comparison of the differences between medial and lateral antebrachial cutaneous nerve latencies. J Long Term Eff Med Implants. 2006; 16(5): 369-76.

14. Kim HJ, Park SH. Sciatic nerve injection injury. J Int Med Res. 2014; 42(4): 887-97.

15. Fidancı H, Öztürk İ, Köylüoğlu AC, Yildiz M, Arlıer Z. Bilateral nerve conduction studies must be considered in the diagnosis of sciatic nerve injury due to intramuscular injection. Neurol Sci Neurophysiol. 2020; 37(2): 94-9.

16. Sprofkin BE. Peroneal paralysis; a hazard of weight reduction. AMA Arch Intern Med. 1958; 102(1): 82-7.

17. Marwah V. Compression of the lateral popliteal (common peroneal) nerve. Lancet. 1964; 2(7374): 1367-9.

18. Chang KV, Mezian K, Nanka O, Wu WT, Lou YM, Wang JC, et al. Ultrasound Imaging for the cutaneous nerves of the extremities and relevant entrapment syndromes: from anatomy to clinical implications. J Clin Med. 2018; 7(11): 457.