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ORIGINAL ARTICLES

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Artificial Intelligence in Medical Education

Tıp Eğitiminde Yapay Zeka

Sezen Milli Avtan

University of Health Sciences Türkiye, Hamidiye Faculty of Medicine, Department of Medical Education, İstanbul, Türkiye

ABSTRACT

The concept of artificial intelligence (AI) encompasses systems capable of exhibiting intelligent behaviors such as perception, reasoning, learning, and communication, and performing tasks traditionally requiring human cognition. In contemporary practice, AI paradigms are increasingly employed across various domains, most notably in the automotive, finance, economics, healthcare, and education sectors. Within the context of medical education, the integration of AI-based systems, often referred to as "teacher bots," has emerged as a noteworthy innovation. These systems serve as content providers, feedback generators, and instructional modulators, enhancing the educational process. AI modules have found particular relevance in widely adopted instructional strategies such as problem-based learning (PBL) and Objective Structured Clinical Examinations (OSCEs) in undergraduate medical education. In both PBL and OSCE settings, AI technologies effectively support clinical decision-making, the generation of virtual patient cases, real-time feedback delivery, and the simulation of patient interactions. The incorporation of deep learning (DL) techniques and artificial neural networks into AI platforms has further enabled the execution of more complex and nuanced tasks. In postgraduate medical training, especially in visually intensive specialties such as radiology, dermatology, and pathology, AI has facilitated the development of machine learning models for diagnostic verification, the generation of synthetic patient imagery, and the instruction of key diagnostic features, independent of real patient data. These applications have been successfully implemented and demonstrate significant educational potential. This study aims to present selected examples of AI applications currently utilized in medical education. Furthermore, it will explore the challenges encountered, or likely to be encountered, in the implementation of AI, as well as the potential contributions AI may offer to the future of medical training.

Keywords: Artificial intelligence, medical education, undergraduate medical education

ÖZ

Yapay zeka (YZ) kavramı, algı, akıl yürütme, öğrenme veya iletişim becerileri gibi zeki davranışlar sergileyebilen ve insani görevleri yerine getirme yetisine sahip sistemleri tanımlar. Günümüzde YZ paradigmaları en çok otomotiv, finans, ekonomi, tıp ve eğitim alanlarında kullanılmaktadır. Tıp eğitiminde, "teacher bots" olarak tanımlanan; eğitim sürecine içerik sağlayıcı, geribildirim veren ve eğitimi modüle edici özellikleri olan sistemlerin yaygınlaşması önemli bir yenilik olarak kabul edilmektedir. Mezuniyet öncesi tıp eğitiminde yaygın olarak kullanılan probleme dayalı öğrenme (PBL) ve nesnel yapılandırılmış klinik sınavlar (OSCE)'da da YZ modülleri kullanıma girmiştir. PBL eğitimleri ve OSCE sınavlarında klinik karar verme, sanal vaka oluşturma, anında geribildirim ve simüle hasta desteği etkili ve verimli bir şekilde YZ tarafından sağlanmaktadır. Derin öğrenme (DL) ve yapay sinir ağlarının YZ modüllerine entegre edilmesiyle daha komplike görevlerin gerçekleştirilmesi mümkün olmuştur. Özellikle mezuniyet sonrası uzmanlık eğitiminde; radyoloji, dermatoloji ve patoloji gibi görsel figürlerin ve tanımlamaların değerli olduğu branşlarda, klinik tanıyı doğrulamaya yönelik makine öğrenmesi, yapay hasta görüntülerinin oluşturulması ve bazı spesifik tanıların olmazsa olmaz anahtar figürlerinin hasta görüntüsü olmaksızın yapay olarak eğitim alanlara öğretilmesi gibi didaktik çalışmalar yapılmış ve başarıyla uygulanmıştır. Çalışmamızda tıp eğitiminde kullanılan bazı YZ çalışmalarından örnekler sunulacaktır. Bunun yanı sıra YZ'nin uygulamasında yaşanan veya yaşanabilecek güçlükler ve ileride tıp eğitimine sağlayabileceği katkılar üzerinde durulacaktır.

Anahtar Kelimeler: Yapay zeka, tıp eğitimi, mezuniyet öncesi tıp eğitimi

Address for Correspondence: Sezen Milli Avtan, University of Health Sciences Türkiye, Hamidiye Faculty of Medicine, Department of Medical Education, İstanbul, Türkiye
E-mail: sezenavtan@gmail.com **ORCID ID:** orcid.org/0000-0003-2528-8760

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Introduction

Although artificial intelligence (AI) has gradually become integrated into our lives over the years, it is still not a concept widely understood or commonly used by many people. With the emergence of deep learning and artificial neural networks (ANNs), the significance of these technologies has steadily increased. AI refers to machines capable of exhibiting intelligent behavior such as perception, reasoning, learning, or communication, and performing human-like tasks (1). AI paradigms target various problem areas such as perception, reasoning, knowledge, planning, and communication. Today, AI applications are intensively utilized in fields such as automotive, finance, economics, medicine, and education. The use of AI in the medical field continues to grow rapidly (1). One notable advancement is that machines can achieve diagnostic success rates in radiology comparable to, or even exceeding, expert consultants (2). In addition to AI's widely publicized role in radiological diagnosis, it is also being employed as a tool for the optimal management of chronic diseases such as cancer and persistent mental health disorders (2).

In education, notable applications of AI include "teacher bots," which are teaching assistants responsible for delivering content, providing feedback, and monitoring educational progress. This growing use in education holds the potential to offer individualized support to students and identify knowledge gaps. In this way, educators can be relieved from routine tasks and offer more effective support to students, thereby enhancing the personalized and adaptive teaching process. Students also gain time to develop unique and individualized learning techniques. This aligns with a rising trend in medical education that emphasizes student autonomy in customizing their learning experience to best suit their comprehension (3,4). Medical education is a lifelong learning process spanning undergraduate, graduate, residency, and postgraduate stages, which includes "continuing medical education" (5). This process involves not only interactions with physicians but also with other healthcare professionals, including nurses and allied health personnel. Currently, there are a limited number of studies reviewing or discussing the existing applications of AI in medical education (6,7). The aim of this study is to comprehensively review the current academic literature on the use of AI in medical education. The study addresses the following questions:

- How is AI currently being used in medical education?
- What are the key challenges in implementing AI in medical education?
- How might the relationship between AI and medical education evolve in the future?

Medical Education and AI

The integration of AI and ANNs into the evaluation of medical students' curricula represents a significant advancement. One article discussed the use of AI, ANN and support vector machines (SVM) for assessing the curriculum of medical students. Chen et al. (8) described the advantage of ANN and SVM over logistic regression in the data analysis: they are more adept models for solving nonlinear problems and establishing relationships between variables.

The use of AI in evaluating medical education curricula is highly valuable, as it provides a comprehensive overview of program effectiveness and student satisfaction. Accurate evaluation is essential for assessing various educational components, ranging from entire curricula to the efficiency of small-group instruction, through diverse methodologies commonly referred to as program evaluation in medical education (8).

In curriculum development, the collection of digital data and the analysis of printed and visual materials are of great importance. While AI performs well in collecting digital data, it has not yet reached sufficient maturity in analyzing visual materials. Nonetheless, AI has found extensive use in curriculum evaluation in medical schools across Canada and the United Kingdom (9,10). AI has also been utilized in student assessments to identify knowledge gaps following examinations and to determine whether learning objectives and assessment strategies are aligned (11). Additionally, AI tools that provide feedback as a critical component for fostering lasting learning strongly support educational processes. Studies indicate that, particularly at the postgraduate level, many residents report receiving little feedback and feeling unsupported in this area, whereas AI-based tools offering instant, formative feedback have shown promising results (11,12).

However, certain observations exist regarding the nature of feedback. Effective feedback should be performance-focused and structured to support the attainment of learning objectives. While AI is capable of providing immediate and prompt feedback, its feedback pool is limited to existing data, and it lacks depth in experiential and emotional inference (13,14).

AI has also proven effective in problem-based learning (PBL) and Objective Structured Clinical Examinations (OSCE), both of which have been shown to offer more effective and efficient training compared to traditional methods (15,16). The use of AI is expanding in OSCEs and similar exams to ensure exam security, evaluate programs based on exam outcomes, and align exam results with learning objectives. AI is also playing a growing role in designing new educational programs (17,18).

System models developed using virtual reality (VR) simulation programs such as Touch, Lahystotrain, and EchoComJ, in combination with intelligent tutoring systems, have reinforced the use of AI in surgical specialties. These systems provide the benefits of both immersive virtual environments and smart instructional systems. Immersive, interactive, and safe VR settings are particularly effective in eliminating the risks associated with lengthy, strenuous, and potentially unsafe training scenarios for learners (19).

In healthcare, generative AI (GenAI) tools are increasingly being utilized in clinical settings, particularly in areas such as clinical documentation and physician-patient communication. These tools have shown promise in addressing inefficiencies in electronic health records, challenges with big data, and healthcare worker burnout (20-22).

Within the context of medical education, GenAI offers several potential advantages, including facilitating personalized learning experiences, simulating real-life scenarios and patient interactions, and enhancing communication skills training (23). However, these benefits also carry significant risks, such as concerns regarding the reliability of AI-generated content and threats to academic integrity (24,25).

Graduate medical education (GME) shares many characteristics with both underGME and other forms of health education. Research has shown that adult learners achieve better learning outcomes when motivated and autonomous, particularly when using AI-assisted learning methods focused on practical applications (26).

Historically, medical education has equated time spent in educational environments with learning success. However, in recent years, a shift toward competency-based medical education (CBME), which prioritizes the acquisition of specific competencies over time spent, has gained renewed attention (27,28). CBME forms the foundation of the Accreditation Council for GME's (ACGMEs) accreditation model. ACGME programs use "Milestones," a system designed to assess and enhance educational progress based on competency-based learning (29).

After receiving foundational training in medical sciences and basic clinical skills, residents spend little time in traditional classrooms. Most learning occurs in real clinical environments as part of a healthcare team. One of the core principles of GME, "graduated responsibility," allows learners to develop increasing levels of autonomy, ultimately achieving readiness for independent practice.

Moreover, residents are expected to become "physician-scholars." Participants in ACGME-accredited GME programs engage in academic activities such as research, scholarly writing, quality improvement initiatives, and curriculum development (30). AI modules, when aligned with defined competencies and regularly updated, provide outcome-based assessment opportunities in line with educational objectives (10-12).

In both undergraduate and postGME, AI is also used for objective assessment of students' work, including the evaluation of their portfolios and dossiers. The key benefit of this system is the ability to provide instant feedback and quickly correct errors through machine learning-based operations (31).

Numerous publications have explored the potential of GenAI in the context of residency training. For example, VR-based simulations of children with rare genetic conditions have been used in pediatric residency training instead of live patient interactions (32). Large language models (LLMs) have also been effectively used to enhance clinical decision-making skills during pediatric education (33,34). In surgical training, AI models are employed in case-based learning focused on ethical dilemmas and in the evaluation of various surgical scenarios (35,36). In studies where LLMs simulate patient conversations for specific anesthesia procedures, AI modules have demonstrated near-realistic accuracy in modeling patient reactions and behaviors (37).

One of the earliest examples of innovative AI-based teaching methods involved enhancing emergency physicians' communication skills, particularly in delivering bad news. This model simulated patient responses and dialogue during the disclosure of difficult diagnoses such as cancer (38).

Challenges in the Application of AI in Medical Education

When introducing a new model or method in medical education, the most critical factor is clearly demonstrating the benefit it provides. To evaluate this, two key aspects must be considered: how easily can the system's effectiveness be assessed? What are the difficulties and limitations in measuring the system? Studies have shown that the most reliable approach involves comparisons with traditional teaching methods. In evaluating both the model and its educational effectiveness, pre-test and post-test results should be examined, and it must be ensured that the baseline knowledge levels of comparison groups are approximately equal before any educational intervention is introduced (39). There are numerous studies showing that AI modules outperform or underperform human-based models depending on the context.

GenAI models have been found to be significantly more effective than traditional methods in various applications. They are actively used in clinical decision support, medical education, clinical documentation, research assistance, and as communication tools (40). Even though models like

ChatGPT have not been trained on specialized medical datasets, they have demonstrated near-passing or passing performance on all three stages of the United States Medical Licensing Examination (41). In some medical exams using LLMs, LLMs have achieved performance comparable to that of final-year medical students (42-45).

In one study involving AI-assisted diagnostic simulators, a statistically significant 22% improvement in diagnostic accuracy was reported compared to traditional methods. However, in another study, a web- and multimedia-based AI educational model showed an 8% improvement in student success, although this was not found to be statistically significant (46,47). The broad specialization within the field of medicine limits the applicability of any single AI model, which in turn narrows the research sample needed for reliable measurement. Other notable challenges include a shortage of experts who can design curricula compatible with machine learning and the temporal, spatial, and interpersonal difficulties in fostering collaboration between physicians and engineers. Developing AI models necessitates a multidisciplinary team comprising data scientists (to collect and process large datasets), medical professionals (to validate clinical applicability), and, ideally, biomedical engineers with dual expertise in both domains (46,47).

Some studies also emphasize the ethical challenges associated with developing and deploying AI models. These include concerns about preserving patient privacy during data collection and safeguarding user data confidentiality (46,47).

Although AI has gained considerable traction in medical diagnosis, clinical reasoning remains inherently complex. Clinical reasoning involves deep learning, deductive thinking, and substantial emotional input, which makes it unrealistic, at least for now, to expect AI to match the diagnostic capabilities of highly experienced clinicians. However, with robust implementation of machine learning and deep learning frameworks, and with active support from domain experts, AI's diagnostic capabilities can be significantly enhanced (48,49).

Several authors have discussed the potential of GenAI as a supportive tool in academic writing and research processes (50-55). This technology can be particularly helpful for non-native English speakers in improving writing skills and translating foreign language content. Many studies have highlighted the usefulness of GenAI in literature reviews and summarization tasks (56-59). However, these models have also been noted to exhibit a phenomenon known as "hallucination," where they fabricate references or present non-existent information.

This issue was clearly demonstrated in an editorial from Medical Teacher that exposed fabricated citations in a manuscript submitted for publication (60).

Such incidents and similar studies have drawn attention to unethical practices, such as presenting AI-generated content as human-authored work. They have emphasized the importance of maintaining awareness and adhering strictly to principles of academic integrity when using these tools (55-59).

Some publications have also warned of the potential negative impact of GenAI on learning. Overreliance on this technology may hinder the development of learners' critical thinking and complex problem-solving skills (56,57,59,61).

The widespread adoption of AI also poses challenges to the validity of current assessment and evaluation methods, necessitating adaptations in assessment strategies (62,63). Moreover, an excessive focus on AI-driven learning opportunities may impair human interaction and communication skills, fundamental components of medical education (51,64). Relying on AI as a primary source of knowledge could lead to the dissemination of inaccurate medical information. Therefore, the integration of AI into learning processes must be carried out in a balanced and well-regulated manner.

Future Directions

Research indicates a critical need for evidence-based studies that clearly demonstrate the superiority of AI over traditional methods. Future investigations should focus on evaluating the effectiveness of AI in medical education. To accurately assess the success of AI systems relative to conventional approaches, extensive and time-intensive research remains necessary across various medical subspecialties.

As medical curricula become increasingly digital and collaboration between data scientists and healthcare professionals intensifies, the use of AI systems is expected to expand. Consequently, data protection is emerging as an important area of inquiry. Specifically, there is a growing need for studies that explore how to enhance data security and bolster user trust in AI applications.

With the continuous advancement of technology, the potential applications of AI in medical education are expected to increase. One such development is the integration of AI with immersive technologies such as VR and augmented reality. These combinations promise to revolutionize educational experiences through simulation-based learning environments.

It is widely acknowledged that GenAI will have a broad societal impact and will be increasingly integrated into daily life. GenAI holds the potential to transform multiple sectors, including healthcare and education. Already, these systems are being used for document summarization, translation, conversation, language support, and image generation.

In the near future, they are expected to expand their capabilities to include emotion analysis and multilingual interaction.

As AI becomes more embedded in healthcare delivery processes, its integration into medical education is seen as both inevitable and transformative. This convergence has sparked intense debate regarding the potential roles, advantages, and limitations of AI in medical training.

Integrating such a transformative technology into existing educational systems requires a careful, evidence-based approach. Medical education experts must not only understand the technical capabilities and limitations of GenAI but also develop forward-looking strategies to guide its educational applications.

The articles reviewed in this study further emphasize the urgent need for research. Most current publications are speculative in nature or consist of opinion pieces. There is a significant gap in research that directly implements and evaluates this technology in student populations. To generate meaningful and applicable outcomes, future studies must be guided by carefully formulated research questions. Enhancing students' AI literacy, evaluating the impact of AI on assessment processes, identifying technical and ethical risks, and investigating the dynamics of human-AI interaction will all be essential steps.

Conclusion

Particularly when using AI-based technologies, providing students with face-to-face patient management experience is crucial. The use of AI-based applications, their role in medical education, and their advantages, disadvantages, and limitations is discussed. The active use of AI in medical education provides an innovative approach to student-centered learning. The integration of AI into education will enable the effective use of innovative technologies in future clinical practice, both in undergraduate education and in lifelong learning.

Footnotes

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REVIEW

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The Physician's Legal Liability

Hekimin Hukuki Sorumluluğu

Kadriye Kart Yaşar[1,2]

[1]*University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Infectious Diseases, İstanbul, Türkiye*

[2]*Medipol University, Institute of Social Sciences, Health Law PhD, İstanbul, Türkiye*

ABSTRACT

Throughout history, the physician's legal and ethical approach to his/her patient has been debated, as has his/her professional competence. The treatment contract between the physician and the patient imposes certain duties and obligations on the physician. The physician's professional competence, knowledge, and medical license are the grounds for the obligations of care and personal performance. In other words, the physician must both be medically successful and observe the rights of his/her patient. This study was designed to inform and raise awareness among physicians about legal responsibilities, of which they are often not consciously aware. Relationships that give rise to rights and responsibilities within the scope of patient-physician law are based on contract, tort, or public service. For this reason, the physician-patient relationship (PPR) has two important legal bases: the law of obligations and administrative law. In the study, the legal regulations in our country have been briefly compiled, and examples of legal liability in different countries, based on this legislation, have also been addressed. The relationship between the physician and the patient, based on contract and tort, is regulated by the Law of Obligations, whereas the public service relationship is regulated by the administrative law in our country. Under the power-of-attorney contract, which is the legal basis for the PPR, physicians face compensatory, criminal, and disciplinary liability for their medical acts. Therefore, physicians must act with medical, ethical, and legal responsibility towards their patients.

Keywords: Physicain liability, attorney contract, tort, physician-patient relationship, medical law

ÖZ

Tarih boyunca hekimin mesleki yeterliliğinin yanı sıra hastasına karşı hukuki ve etik yaklaşımı da tartışılmıştır. Hekim ile hasta arasındaki tedavi sözleşmesi hekime birtakım borçlar ve yükümlülükler yükler. Hekimin mesleki yeterliliği, bilgisi ve tıbbi ehliyeti, özen ve kişisel edim yükümlülüğünün temelini oluşturur. Yani hekim hem tıbbi açıdan başarılı olmak hem de hastasının haklarını gözetmek zorundadır. Bu çalışma, hekimlerin sıklıkla bilinçli olmadığı hukuki sorumluluk konusunda bilgilendirme ve farkındalık oluşturma amacıyla hazırlanmıştır. Hasta ve hekim hukuku kapsamında hak ve sorumluluk doğuran ilişkiler bir sözleşmeye, haksız fiile veya kamu hizmetine dayanır. Bu nedenle hekim-hasta ilişkisinin iki önemli hukuki dayanağı vardır: Borçlar Hukuku ve İdare Hukuku mevzuatı. Çalışmada bu mevzuat üzerinden farklı ülkelerdeki hukuki sorumluluk örneklerine de değinilerek ülkemizdeki hukuki mevzuat kısaca derlenmiştir. Ülkemizde hekim ile hasta arasındaki sözleşmeye ve haksız fiile dayalı ilişki Borçlar Kanunu ile düzenlenirken, kamu hizmeti ilişkisi İdare Hukuku tarafından düzenlenmektedir. Hekim-hasta ilişkisinin hukuki dayanağı olan vekâlet sözleşmesi uyarınca hekimler, tıbbi eylemlerinden dolayı tazminat, cezai ve disiplin sorumluluğu ile karşı karşıya kalmaktadır. Bu nedenle hekimler hastalarına karşı tıbbi, etik ve hukuki sorumluluk bilinci ile hareket etmelidir.

Anahtar Kelimeler: Hekimin sorumluluğu, vekalet sözleşmesi, haksız fiil, hasta-hekim ilişkisi, tıp hukuku

Introduction

Medicine refers to all technical and scientific studies undertaken to cure, alleviate, or prevent disease. Law, on the other hand, can be briefly defined as the order formed by the rules that regulate people's coexistence (1). Medical law, on the other hand, is a branch of health law that examines issues such as the rights and obligations of healthcare personnel, legal responsibilities, patient rights, drug law, and medical law, arising from the practice of medicine. Medical law is an interdisciplinary branch of law that involves

Address for Correspondence: Kadriye Kart Yaşar, University of Health Sciences Türkiye, Bakırköy Dr. Sadi Konuk Training and Research Hospital, Clinic of Infectious Diseases; Medipol University, Institute of Social Sciences, Health Law PhD Program, İstanbul, Türkiye

E-mail: hkkyasar@gmail.com **ORCID ID:** orcid.org/0000-0003-2963-4894

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aspects of constitutional law, criminal law, administrative law, and civil law (2). One of the fundamental legal issues in medicine is the legal responsibility of the physician in the doctor-patient relationship. This study aims to clarify the legal relationship between doctors, other healthcare professionals, and patients and to raise awareness of their legal responsibilities (including criminal, compensation, and disciplinary responsibilities).

In modern society, a physician is an individual who is granted the authority to practice medicine and perform medical interventions by the legal system. In general, medical intervention encompasses all activities of a physician aimed at healing. All activities and initiatives aimed at ameliorating a disease or disorder fall within the definition of medical intervention (3).

According to Article (Art.) 17 of the Constitution of the Republic of Türkiye (4), except for medical necessities and situations specified by law, a person's bodily integrity cannot be violated, and they cannot be subjected to scientific and medical experiments without their consent. The situation of necessity is one of the reasons that eliminate responsibility in both criminal and private law (5). it is a mechanism that prevents a person from being legally held responsible for committing an unlawful act (crime or tort) when there is no other option and in order to protect a higher value. According to Art. 63/2 of the Turkish Code of Obligations (TCO) (6), "acts committed in cases of necessity are not considered unlawful." In Art. 25 of the Turkish Penal Code (TPC) (7), it is stated that "acts committed with the necessity of escaping from a serious and certain danger that is directed towards a right belonging to oneself or another, which was not caused knowingly and for which there is no other means of protection, and provided that there is a proportion between the severity of the danger and the subject and means used, the perpetrator shall not be punished." Therefore, medical interventions applied by the physician, considering the patient's benefit and aiming to preserve the integrity of the human body, become lawful (2).

There are four conditions for a medical intervention to be lawful:

a) The person performing the medical intervention must be a physician (healthcare personnel), b) indication, c) informed consent of the patient, d) acting in accordance with the data of medical science (2,3,8).

The Legal Aspect of the Physician-Patient Relationship

The relationship between the patient and the physician or the health institution entails mutual rights and responsibilities for the parties. Relationships that give rise to rights and responsibilities within the scope of patient-physician law are based on a "contract" established explicitly or implicitly beforehand, a "tort," or a "public service" (5,9). For this reason, there are two important legal bases for the physician-patient relationship (PPR): the Law of Obligations and the Administrative Law regulations. The relationship based on contract and tort between the physician and the patient is regulated by the Law of Obligations, whereas the public service relationship is regulated by Administrative Law in our country. On the one hand, there is a skilled and qualified doctor, while on the other hand, there is a weak and vulnerable patient. Therefore, the physician must always act in accordance with professional ethical standards towards the patient. The legal relationship between the patient and either the treating physician or a private or public institution providing treatment can be examined under three headings:

Legal relationship between the patient and the independently practicing physician: When a patient seeks treatment at the office of a freely and independently practicing physician, a contractual relationship is established as soon as the physician accepts the patient and begins the examination and treatment. The contract can be implicit (tacit) or explicit, and, if explicit, it can be written. In this case, the legal relationship between the patient and the physician manifests as a "Contractual Relationship", "Unauthorized Agency", or "Tortious Relationship" (5,10,11). A contractual relationship is established between the patient and the physician through free will and consent to initiate the process of diagnosis and treatment. The contract is not required to be in writing. This relationship gives rise to rights and obligations under the TCO and becomes effective in accordance with private law rules. The prevailing opinion is that this relationship is more akin to a power-of-attorney agreement than to a work or service contract. In some medical interventions, due to the nature of the situation or the patient, a contract based on free will between the physician and the patient may not have been established. In other words, the physician can proceed with a medical intervention in the patient's best interests without the patient's consent. Situations such as a traffic accident requiring emergency intervention, a heart attack, or the necessity to expand a surgery during the operation are examples of this. In such cases of necessity, the physician's intervention with the patient creates an "acting without authority" relationship (12,13). If damage occurs before a contract is established, liability arises from the principle of good faith (culpa in contrahendo). A patient who fell and injured their foot while waiting at the door of the outpatient clinic for their appointment is an example of this situation.

According to the TCO, anyone who causes harm to another person through a wrongful and unlawful act is

obliged to compensate for that harm. In such a case, if the doctor is a self-employed practitioner, the injured party can claim compensation directly from the doctor under Art. 49 of the TCO (3,6,10).

Legal relationship between the patient and the doctor working in a private hospital: The relationship between the physician working in a private hospital and the patient is also based on contract, unauthorized act, and tort. The physician working at the private hospital and providing the treatment is not a party to the contract (according to Art. 116 of TCO, the physician acts as an auxiliary person or performer of the private hospital) (3,14).

The "Hospital Admission Agreement" is valid between the patient applying to the private hospital and the hospital (14). Under this contract, all hospital service obligations related to the patient's diagnosis, treatment, and care are covered by the private hospital. This contract can be either full or divided: in a full hospital admission contract, the hospital management is responsible for all services, while the physician serves in an auxiliary role. Under a divided hospital-admission contract, there are a treatment contract between the patient and the physician and a service contract between the hospital and the patient. Under the comprehensive hospital admission contract with a physician addendum, separate treatment contracts exist between the patient and the physician and between the patient and the private hospital. That is, the physician and the private hospital are jointly liable to the patient. When a patient wishes to file a lawsuit, they may do so against either partner (the physician or the private hospital). The legal relationship between the patient and the physician in a private hospital may also arise from "Unauthorized Representation" or "Tortious Liability", in addition to a "Contractual Relationship" (10).

Legal relationship between the patient and the physician working in the public sector: The healthcare services provided to patients in public hospitals and family health centers are of a public nature. The healthcare personnel are also public employees, and the services they provide are considered administrative actions under administrative law. The contract between the doctor's legal entity, whether working in a public hospital or as a family physician, and the patient falls under administrative law. In the event of damage, the patient can file a lawsuit against the administration to seek compensation for the damage, but cannot directly sue the physician; the hospital administration is liable for the damage under the principle of strict liability (3,10-14). In the Supreme Court's decisions, the "removable personal fault" of the physician working in a public hospital was mentioned not as the misuse of administrative authority by the public servant physician, but as the failure to act in accordance with medical science while practicing their profession. The doctor, who was sued by a patient whose arm was amputated because gangrene developed after the doctor delayed treatment of the broken arm at the state hospital, was found guilty of personal negligence. Thus, it has been emphasized that the defendant physician's action, which distinguishes personal fault from administrative duty, cannot be evaluated within the scope of Art. 129 of our Constitution, which includes the principles of state responsibility and administrative assurance (15).

The legal relationship between the patient and the physician may also arise in the form of "Unauthorized Representation" or "Tortious Liability" in the public sector.

The type of contract commonly accepted between a patient and a physician is the "mandate contract." Accordingly, the physician's duty is the act itself rather than the result of the act; it is to show the necessary care and attention to achieve the result. The contract can be written or oral, and explicit or implicit (there is no requirement regarding form). The contract must be in writing only in cases specified by law (such as hysterectomy, organ donation, or major surgery) (3,10-14).

If there is any breach of contract between the doctor and the patient and the patient suffers harm due to the doctor's incorrect or inappropriate medical intervention, Art. 112 of the TCO applies. In short, the doctor becomes liable for breaching the treatment contract with the patient and is obliged to prove their innocence. It has been emphasized in the Supreme Court decisions that obtaining consent and proving this consent in writing are mandatory, as the physician acted contrary to the obligation to inform the patient. In cases where it is stated that complications developed and there are no documents, etc., in the patient file other than the physician's verbal statement regarding whether the patient was informed about all possible risks before the surgery and whether the patient gave consent knowing these risks, the higher court has deemed expert reports based on the physician's verbal statement sufficient and overturned lower court decisions that were made with insufficient examination.

The judge examines whether there is an appropriate causal link between the doctor's improper medical intervention and the patient's harm. If the harm to the patient does not result from the physician's improper medical intervention, the physician cannot be held liable (3,8). Sometimes, instead of a mandate contract, a "work contract" may be established between the parties, where the outcome of the treatment is exceptionally guaranteed (such as dental prosthetics and aesthetic surgeries). Under employment contracts, if the desired result is not achieved (for example, if the dental prosthesis is not fabricated with

the appropriate color and material or if the tattoo mark is not removed and the skin is not restored to its original state), the patient may sue the doctor (3,12). In different decisions of the Court of Cassation, there may be varied approaches to the work contract. In the case where the desired result was not achieved in an aesthetic nose surgery, but rather the nose collapsed, the face became ugly, and the doctor was sued, the court accepted the work contract; whereas in the operation aimed at removing a tumor from the body of a patient for treatment purposes, it accepted the mandate contract (15).

Under German or Austrian law, unlike in our country, it is based on the PRR service contract. From the perspective of physician liability, the obligation to inform is very important and the most common subject of malpractice lawsuits. In Switzerland, it is based on the PRR mandate contract, as in our country. In England, the basis of physician liability is negligence, which is one of the bases of tort liability. In the United States (US), as in English law, medical malpractice cases in recent years, which have become increasingly frequent, are due to negligence and technology use. In the US, regarding medical liability, PRR is based on mutual agreement; if the patient does not consent, the physician is under no obligation to provide treatment. In countries such as Belgium, Portugal, and Hungary, errors in medical practice are investigated by medical chambers, and, in addition to disciplinary penalties, sanctions such as revocation of medical licenses can be imposed when necessary. The traditional view prevailing in Italian Law was that a direct legal relationship could not be established between the doctor and the patient, and it could only be based on a tort action. This view has been gradually replaced by the understanding that obligations arise from contracts. In Finland, there is an insurance system based on strict liability for wrongful practices by healthcare personnel (no-fault system). Unlike in other countries, the doctor cannot be blamed or sued for their mistake. Damage to the patient is covered by no-fault liability insurance (15-17).

The Concept of Liability in Medical Law

Attitudes and behaviors contrary to legal rules give rise to liability. In private law, liability is defined as the obligation of a person to compensate another person for damage caused by an unlawful act (18). When one fails to do what is required or does what is prohibited, responsibility arises. In private law and, consequently, in medical law, the fundamental principle is "fault liability".

The damage caused to another person by a person's (the physician's) unlawful act and behavior (malpractice) is subject to compensation under the principle of fault-based liability. To establish the physician's fault-based liability, four conditions must be met, and if these conditions are not present, the physician cannot be held liable for fault:

- Illegality (resulting from breach of contract or tort)
- Fault
- Damage
- Causal link (between action and result) (19,20)

Illegality: The failure of a person to do something that the law commands (active behavior, such as causing injury to someone) or doing something that the law prohibits (passive behavior, such as failing to take necessary precautions).

Fault: For liability arising from breach of contract, the debtor must have neglected to perform the obligations undertaken under the contract. In this case, the fault is generally associated with a specific obligation. The debtor's intentional and willful breach of his contractual obligations is termed intent, and his failure to exercise the care and diligence expected of him to prevent the breach is termed negligence. In private law, negligence includes carelessness and imprudence. However, in contractual liability, the type and degree of fault are not important, as the debtor will be liable for all kinds of fault as a rule. In other words, breaches of contract characterized by intent or negligence give rise to liability. However, in medical practice, negligence is more common than intent (21). Fault is an essential element of fault-based liability. In the absence of fault, there is no responsibility. Negligence, on the other hand, is the failure to exercise the care and diligence required by the situation to prevent an unlawful act, even though such an act is not desired. The person lacks the intent or will to commit an unlawful act, but they lack sufficient will or ability to prevent the unlawful act. In medical law, actions performed by a physician due to negligence are referred to as "professional fault". Carelessness and inexperience are examples of slight negligence; ignorance, inability, and lack of diligence are examples of severe or gross negligence.

Severe negligence: Not knowing what everyone knows, not doing what everyone does.

Slight negligence: The failure to exercise the care that a careful and diligent person would show.

The physician's responsibility is so great that they are liable even for the slightest negligence. In the case brought by the patient, who came to the doctor with a small bleeding in the 10th week of her pregnancy, followed the doctor's medication and advice, attended the check-ups, but later had her uterus removed due to uncontrollable bleeding caused by repeated abortions after a miscarriage, the doctor was found guilty and held responsible for all the faults within his professional field. The decision emphasized that the doctor is responsible for potential complications and for managing them appropriately (22).

Damage: Reductions in a person's assets that occur against their will. In cases of unlawful acts arising from a contract, the party causing the damage (the physician) must prove that they were not at fault. In the TCO, damage is defined as death (treatment and funeral expenses, loss of support from the deceased) and bodily harm (treatment expenses, loss of earnings, loss of working capacity, or loss of economic future) (3,8,9,20). According to Turkish regulations, the physician has three types of legal responsibilities arising from the patient harm to the patient caused by faulty medical practice (23):

- Compensation liability according to the TCO
- Criminal liability according to the TPC (imprisonment or fine)
- Disciplinary liability under Administrative Law

The subject of medicine is human health, its aim is healing, its subject is the physician and its object is the patient. Therefore, the physician must always act in accordance with the rules of professional ethics towards his/her patient. The physician's primary duty is to provide health care services in accordance with ethical and legal standards. The physician is obliged to be highly competent and successful in his/her profession, to make the right decision, to exercise necessary care, and to serve without errors. When a physician violates the legal conditions for medical intervention, liability arises. The four conditions known for a medical intervention to be lawful: a) The person performing the medical intervention must be a physician (healthcare personnel), b) indication, c) informed consent of the patient, d) acting in accordance with the data of medical science. Since a physician cannot be unaware of the first three conditions, violating these conditions gives rise to "intentional liability" for the physician. However, the failure to perform a careful and diligent intervention in accordance with medical standards, which is the 4th condition, usually arises from an unintentional negligent act by the physician, and therefore, liability due to negligence is involved (8). In criminal law, intent refers to a voluntary act performed knowingly and willingly. In medical law, doctors generally do not intentionally commit crimes. In cases of negligence, on the other hand, an action is performed intentionally, but the negative outcome that may result from it is not desired and is not foreseen. In cases of conscious negligence, although the adverse outcome is foreseen and not desired, it is considered unlikely to occur. For example, a person performing a medical intervention while under the influence of alcohol may foresee that the patient will suffer adverse consequences, but they believe they can succeed and that harm will not occur. The fact that the physician cannot foresee the possibility of harm due to negligence, recklessness, or carelessness (his fault) is considered a fault. In medical interventions carried out by a team, such as those involving multiple doctors or nurses, everyone takes responsibility to the extent of their fault (23).

Table 1 summarizes the crimes listed in the TPC that are frequently committed by physicians and the subjects of malpractice cases.

In cases of injury and death resulting from a doctor's negligent medical intervention, the crimes of negligent injury and negligent manslaughter apply. According to the TPC, euthanasia, organ and tissue trafficking, experimentation on humans, and the unlawful provision of data constitute prohibited crimes that doctors may commit. Doctors are obliged to report the crimes they witness (3,23).

Finally, the disciplinary offenses for which the state-employed physician can be held responsible following a faulty medical intervention are defined by Art. 125 of the Law on Civil Servants No. 657 and are enforced by the physician's disciplinary superior (23).

- Warning
- Reprimand
- Salary deduction
- Suspension of the progress of the level
- Dismissal from civil service

Conclusion

According to Turkish Law, the contract between the patient and the physician or the accepted patient-physician relationship is a mandate contract. The physician is responsible not for the outcome but for having demonstrated the necessary care and diligence to achieve the outcome. If there is a breach of the treatment contract and the patient suffers harm due to the doctor's incorrect or inappropriate medical intervention, the doctor becomes liable to the patient for acting contrary to the treatment contract. All attitudes and behaviors that are contrary to legal rules give rise to liability in the patient-physician relationship. However, the judge seeks an appropriate causal link between the damage and the doctor's action in the given situation. In other words, it examines whether the damage to the patient resulted from the doctor's inappropriate medical intervention. If harm to the patient is not caused by an inappropriate medical intervention by the physician (in cases of complications), the physician cannot be held responsible.

The relationships between the patient and the physician that give rise to rights and obligations are based on "contract" outside of the context of agency without authority, a "tort," or a "public service". For this reason, there are two important legal bases for the PPR: the Law of Obligations and Administrative Law regulations. Because the relationship based on contract and tort between the physician and the

Table 1. The crimes and corresponding penalties listed in the Turkish Penal Code that are frequently committed by physicians and are the subject of malpractice cases

Article number in the TPC	Name of the offense in the penal code	Corresponding penalties
81	Deliberate homicide	Life imprisonment
83	Intentional homicide by negligent behavior	15-20 years of imprisonment
85	Negligent homicide	2-6 years of imprisonment
86	Intentional injury	1-3 years of imprisonment
87	Aggravated injury as a result	2-6 years or 3-9 years of imprisonment
88	Intentional injury with negligent behavior	A 1-3 year prison sentence can be reduced by 2/3
89	Negligent injury	Imprisonment from three months to one year or a judicial fine
90	Experimentation on human	1-3 years of imprisonment
91	Organ or tissue trafficking	5-9 years of imprisonment
99	Child abortion	5-10 years of imprisonment
101	Human sterilization	3-6 years of imprisonment
105	Sexual harassment	Imprisonment from three months to two years or a judicial fine
106	Deprivation of liberty of a person	Imprisonment from three months to two years
135	Recording personal data	1-3 years of imprisonment
136	Unlawfully giving or obtaining data	2-4 years of imprisonment
141	Theft	1-3 years of imprisonment
151	Damage to property	Imprisonment from four months to three years or a judicial fine
155	Abuse of trust	Imprisonment from six months to three years or a judicial fine
157	Fraud	Imprisonment from one year to five years and a judicial fine of up to five thousand days
204	Forgery of official documents	2-5 years of imprisonment
205	Distorting, destroying or concealing an official document	2-5 years of imprisonment
207	Forgery of private documents	1-3 years of imprisonment
212	Cumulation (forgery of documents + use in another crime)	The total penalty for forgery and other crimes
231	Changing the child's ancestry	1-3 years of imprisonment
235	Bid rigging	3-7 years of imprisonment
247	Embezzlement	5-12 years of imprisonment
250	Extortion	5-10 years of imprisonment
252	Bribery	4-12 years of imprisonment
257	Abuse of office	Imprisonment from six months to two years or a judicial fine
259	Trading of a public official	Up to 6 months in prison or a fine
260	Abandonment or non-performance of public duty	Imprisonment from three months to one year or a judicial fine
262	Unlawful assumption of public office	Imprisonment from three months to two years or a judicial fine
280	Failure of health workers to report the crime	Up to 1 year in prison
287	Genital examination	Imprisonment from three months to one year

TPC: Turkish Penalty Code

patient is regulated by the Law of Obligations, while the public service relationship is regulated by Administrative Law in our country.

As a result, the subject matter of medicine is human health; its aim is healing; its subject is the physician; and its object is the patient. The physician's action, i.e,. a medical intervention, is within the scope of public service. The physician-patient relationship differs slightly from other legal relationships. This is because on one side is the skilled and qualified physician, whereas on the other side is the weak and powerless patient. Therefore, the physician must always act in accordance with the rules of professional ethics towards his/her patient. It is evident that distinct legal relationships and civil and criminal consequences may arise either between the patient and the physician or between public and private health institutions. The main duty of the physician is to provide health care services in accordance with ethical and legal rules. The physician is obliged to be very good and successful in his/her profession, to make the right decision, to pay attention to the necessary care and to serve without making mistakes.

Footnotes

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The Relationship Between Complete Blood Count Parameters and Pregnancy Outcomes in Women Who Wanted to Become Pregnant

Gebelik İstemi Olan Kadınların Tam Kan Sayımı Parametreleri ile Gebelik Sonuçları Arasındaki İlişki

Deniz Taşkıran[1], Orhan Ay[2]

[1]*Giresun University Faculty of Medicine, Department of Obstetrics and Gynecology, Giresun, Türkiye*

[2]*Necmettin Erbakan University Faculty of Medicine, Department of Obstetrics and Gynecology, Konya, Türkiye*

ABSTRACT

Background: Oxidative stress due to inflammatory processes in women who want to become pregnant affects the chance of pregnancy success. In our study, we aimed to evaluate the effect of the platelet/lymphocyte ratio (PLR) and neutrophil/lymphocyte ratio (NLR), which are indicators of systemic inflammation and are assessed in the complete blood count parameters, on the pregnancy success of women who desire pregnancy.

Materials and Methods: The data of 170 patients who applied to Giresun Gynecology and Obstetrics outpatient clinic requesting pregnancy between December 2022 and December 2024 were retrospectively analyzed, and the data of 94 patients who met the inclusion and acceptance criteria were evaluated. Demographic data, ovarian reserve test data, thyroid stimulating hormone data, prolactin data, neutrophil data, lymphocyte data, platelet data, NLR, data PLR data of these patients were compared between pregnancy and non-pregnancy groups.

Results: Lymphocyte count and PLR were higher in the group with biochemical pregnancy (p=0.048 and p=0.046). PLR was significantly higher in the group with clinical pregnancy (p=0.020). There was no statistical difference in ovarian reserve tests, and other parameters between the groups, with and without biochemical and clinical pregnancy.

Conclusion: While PLR and high lymphocyte count were significant for predicting biochemical pregnancy occurrence, other parameters had no effect on pregnancy occurrence.

Keywords: Inflammation, platelet/lymphocyte ratio, pregnancy

ÖZ

Amaç: Gebelik istemi olan kadınlarda enflamatuvar süreçlere bağlı meydana gelen oksidatif stres gebelik başarı şansını etkilemektedir. Çalışmamızda gebelik istemi olan kadınların tam kan sayımı parametrelerinde değerlendirilen ve sistemik enflamasyonun göstergesi olan platelet/lenfosit oranı (PLO) ve nötrofil/lenfosit oranının (NLO) gebelik başarısı üzerinde etkisini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Giresun Kadın Hastalıkları ve Doğum polikliniğine Aralık 2022-2024 tarihleri arasında enfertilite nedeni ile başvuran 170 hastanın verileri retrospektif olarak incelendi. Dışlama ve kabul edilme kriterlerine uygun 94 hastanın verileri değerlendirildi. Bu hastaların demografik verileri, over rezerv testleri, troid stümülan hormon, prolaktin, nötrofil, lenfosit, platelet, NLO, PLO verileri değerlendirildi. Bu veriler biyokimyasal, klinik gebeliği olan ve gebelik oluşmayan hastalar olmak üzere iki grup halinde karşılaştırıldı.

Bulgular: Gruplar arasında lenfosit sayısı ve PLO biyokimyasal gebeliği olan grupta daha yüksek saptandı (p=0,048 ve p=0,046). Klinik gebeliği olan grupta PLO anlamlı şekilde yüksek saptandı (p=0,020). Over rezerv testleri ve diğer parametreler, biyokimyasal ve klinik gebeliği olan ve olmayan gruplar arasında benzer saptandı.

Sonuç: PLO ve lenfosit sayısının yüksek olması biyokimyasal gebelik oluşumu açısından anlamlı iken, diğer paramatrelerin gebelik oluşumu açısından bir etkisinin olmadığı saptandı.

Anahtar Kelimeler: Inflamasyon, platelet/lenfosit oranı, gebelik

Address for Correspondence: Deniz Taşkıran, Giresun University Faculty of Medicine, Department of Obstetrics and Gynecology, Giresun, Türkiye

E-mail: deniztaskiran93@gmail.com **ORCID ID:** orcid.org/0000-0001-7270-4566

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Introduction

Infertility is defined as the inability of couples to conceive despite one year of regular intercourse (1). Women who desire pregnancy can be evaluated, and pregnancy can be achieved with ovulation induction under appropriate conditions. Causes of infertility include poor ovarian reserve, male factor, uterine causes, and unexplained infertility where no cause is found after all these have been investigated. When couples are investigated, approximately 30% do not have an identifiable cause for infertility and this group is referred to as unexplained infertility (2).

One of the most important factors causing infertility is implantation failure. The immunological and inflammatory processes that occur during fertilization and implantation of the embryo play an important role in pregnancy. Implantation of the embryo depends on the interaction and compatibility of the trophoblast with the epithelial cells of the endometrial villi. The period between days 20-24 of the menstrual cycle, when the endometrium is favorable for implantation, is called the implantation window. This period is the time when secretory glands enlarge, and superficial protrusions called pinopods, and microvillus structures are seen (3). The density of endometrial integrins, steroid hormone levels, and cyclooxygenase 2 levels are also important for implantation. Suppression of maternal lymphocyte function and lack of fetal antigen presentation to maternal lymphocytes play a role in the development of fetomaternal immune tolerance during implantation. During pregnancy, the number of B lymphocytes does not change; the number of cluster of differentiation 4 (CD4) T lymphocytes decreases, while the number of CD8 T lymphocytes increases. In the progression of inflammatory processes, platelet count and function are also significant in addition to lymphocytes, with local effect (4). Neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) are important hematologic parameters for demonstrating systemic inflammatory status (5).

In a study where NLR and PLRs were evaluated in the diagnosis of premature ovarian insufficiency, inflammatory processes were blamed although the etiology was not clearly established. It was revealed that the NLR may be important for the diagnosis (6). In another study, it was shown that NLR, as an indicator of inflammation, was associated with the development of spontaneous abortion (7).

Neutrophil count, platelet count, NLR and PLR can be easily evaluated from a complete blood count, which is an inexpensive test to evaluate the systemic inflammatory response in women who want to have children. In our study, we retrospectively analyzed these parameters in women who wanted to have children in order to reveal the effect of these parameters on pregnancy.

Materials and Methods

Data from 170 patients who applied to our center due to infertility between 01.12.2022 and 01.12.2024 were retrospectively analyzed. The patients' age, obstetric history, treatments administered, complete blood count results, and beta (β) human chorionic gonadotropin (hCG) results were analyzed through the hospital system. Patients between the ages of 18-45 years, with no male factor and at least one year of infertility, were included in the study. Women with body mass index (BMI) >30 kg/m^2, follicle-stimulating hormone (FSH) >25 mIU/mL, known chronic diseases (hypertension, diabetes mellitus, chronic liver failure, chronic renal failure, etc.), were excluded.

In our clinic, a complete blood count is performed at the patients' first admission, to determine whether there is any abnormality without any treatment. Venous blood samples of the patients are collected in tubes containing ethylenediaminetetraacetic acid and then are studied in automatic blood analyzers. Neutrophil, lymphocyte, platelet values, NLR, and PLR were analyzed, and their effects on pregnancy were evaluated. Clinical pregnancies of the patients were recorded by assessing the β hCG value taken 14 days later. Those with a positive fetal heartbeat on ultrasonography were recorded as having a confirmed pregnancy.

Demographic information, BMI, treatment protocols, duration of infertility, menstrual patterns, basal hormone levels; FSH, luteinizing hormone (LH) estradiol (E2) and thyroid stimulating hormone (TSH), prolactin (PRL) levels taken during follow-up were recorded.

Ethics committee approval was obtained from the Giresun Training and Research Hospital Ethics Committee (approval number: 25.12.2024/04, dated: 25.12.2024) for the study.

Statistical Analysis

Statistical Package for Social Sciences for Windows (SPSS 20, Chicago, IL, USA) was used for analysis. Kolmogorov-Smirnov test was used to assess the normality of the data distribution. According to the test results, Student's t-test was used for normally distributed groups, and Mann-Whitney U test was used for non-normally distributed groups. A cut-off value will be established through receiver operating characteristic curve analysis, conducted on variables found to be statistically significant. For statistical significance, $p<0.05$ was considered significant.

Results

Patients between the ages of 18-45 years, with no male factor and at least one year of infertility were included

in the study. Women with BMI >30 kg/m^2, FSH >25 mIU/mL, and known chronic diseases (hypertension, diabetes mellitus, chronic liver failure, chronic renal failure, etc.) were excluded. Of the 170 patients screened, 45 had at least one known chronic disease, 14 had uterine anomalies, and 17 had infertility due to male factor. These patients were not included in the study. A total of 94 patients with unexplained infertility who met the inclusion criteria were included in the study.

A total of 94 patients who were receiving infertility treatment and met the inclusion criteria were included in our study. Data from 94 patients were analyzed retrospectively. There were 24 patients with positive β hCG and 8 patients with positive fetal heartbeat.

Age, BMI, FSH, LH, E2, TSH, prolactin, and antimüllerian hormone (AMH) values were similar between β hCG-positive patients (Table 1) and fetal heartbeat-positive (Table 2) and negative patients.

The biochemical pregnancy rate according to β-hCG value was 26.6%. Hematologic data of the patients showed that hemoglobin, neutrophil, platelet, and NLR did not affect biochemical pregnancy. β hCG positivity was found to be higher in patients with low lymphocyte count (p=0.048). Patients with higher PLR had a higher incidence of biochemical pregnancy positivity (p=0.046) (Table 3).

Clinical pregnancy was detected in 8.5% of the patients by fetal heartbeat positivity. Hemoglobin, neutrophil, lymphocyte, platelet, and neutrophil/lymphocyte counts had no effect on clinical pregnancy success. The clinical pregnancy rates were found to be higher in patients with a higher PLR (p=0.020) (Table 4).

A PLN ratio above 164.071 predicted hCG positivity with 50% sensitivity and 85% specificity (p=0.046), while a PLN ratio above 144.098 predicted fetal heartbeat positivity with 100% sensitivity and 68% specificity (p=0.020) (Table 5).

Discussion

This study showed that a high PLR was useful in predicting a higher biochemical and clinical chance of pregnancy success, whereas the NLR had no effect. Following fertilization, the endometrium and the embryo need to recognize and interact with each other for a healthy pregnancy. In the endometrium, macrophages, cyclo-oxygenases, and various immunologic factors play a role in preparing a favorable environment for implantation. This is achieved by development of maternal immune tolerance to the embryo (8).

Chronic inflammation is known to have a negative impact on other characteristics such as oocyte quality, folliculogenesis, hormone production, disease recovery, and fertility (9). However, the effects of these markers on the occurrence of pregnancy in women who want to become pregnant have not been adequately studied. Pre-pregnancy assessment of inflammatory processes and parameters in women who want to become pregnant can be used to predict the chances of pregnancy success.

Studies have shown that inflammatory markers and oxidative stress biomarkers in maternal blood are significantly increased in early pregnancy loss and preeclampsia (10). In contrast to a study in which NLR and PLR were found to be higher in pregnant women with miscarriage compared to normal pregnant women, our study found that the high PLR rate, measured before pregnancy, was significant in terms of clinical and biochemical pregnancy occurrence. Studies have shown that platelets play a role in immunity and/or inflammatory processes (11). NLR and PLR in peripheral blood are markers of systemic inflammatory response (12).

Table 1. Comparison of demographic characteristics and ovarian reserve test results according to β hCG value

	β hCG (n=94, %100)		p-value
	Positive (n=24, 25.6%) Mean + SD (median)	Negative (n=70, 74.4%) Mean + SD (median)	
Age (years)	30.92±5.3 (30.00)	29.30±5.0 (28.00)	0.301
BMI (kg/m^2)	25.09±3.84 (25.00)	25.11±3.24 (25.20)	0.820
FSH (mIU/L)	7.19±3.81 (6.85)	6.08±195 (6.71)	0.862
TSH (mIU/L)	1.95±0.79 (1.80)	2.05±1.34 (1.95)	0.696
LH (mIU/L)	6.38±2.91 (5.88)	7.15±3.66 (6.50)	0.640
PRL (ng/mL)	16.85±9.19 (13.35)	19.90±9.62 (19.25)	0.192
E2 (pg/mL)	38.50±12.60 (36.50)	47.73±16.11 (44.50)	0.068
AMH (ng/mL)	4.55±3.21 (3.69)	4.15±2.38 (3.70)	0.845

Mann-Whitney U test, Student t-test, p<0.05. AMH: Antimüllerian hormone, BMI: Body mass index, E2: Estrodiol, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, PRL: Prolactin, SD: Standard deviation, TSH: Thyroid stimulating hormone, β hCG: Beta human chorionic gonadotropin

Inflammatory processes occurring during miscarriage may cause changes in platelet, neutrophil, and lymphocyte counts. The difference between PLR and NLR ratios evaluated during normal pregnancy and pre-pregnancy, and PLR and NLR ratios evaluated during miscarriage, is the inflammatory processes occurring during miscarriage.

In our study, lymphocyte count was lower in women with positive pregnancy, while platelet count was similar between the groups. When inflammation occurs, the reason for a high NLR is an increase in the number of neutrophils and platelets and a decrease in the number of lymphocytes in the bloodstream (13). Although the decrease in the number of lymphocytes, which is one of the physiologic and inflammatory changes occurring in pregnancy, is similar to this study in the literature. The fact that the number of neutrophils and lymphocytes was similar in both groups is different from the results of this study. The reason for this is that immune system changes in pregnancy, occur through a different mechanism than acute inflammatory processes.

In a study conducted in patients with myocardial infarction, it was revealed that platelet aggregation increased, while platelet count decreased. The neutrophil to lymphocyte ratio also increased due to the inflammatory process that intensified during recovery (14). In our study, similar platelet counts between the groups were found to be insignificant for predicting inflammation. However, the finding that the lymphocyte count was low in hCG positive patients was consistent with the findings of this study (14) and suggested that it could be used as a marker of inflammation.

Although studies suggest that increased PLR and NLR ratios may provide information about inflammatory processes (15), when the numbers of lymphocytes and platelets are considered separately and these values are compared, differences occur in patients. Up to 50% of PLR cases have no clear etiology, but multifactorial conditions such as immunologic, anatomic, genetic, and hematologic disorders are known to cause PLR. It is thought that inflammatory components may cause pregnancy loss through their role

Table 2. Comparison of demographic characteristics and ovarian reserve test results according to fetal heartbeat

	Fetal heartbeat (n=94, 100%)		p-value
	Positive (n=8, 8.6%) Mean + SD (median)	Negative (n=86, 91.4%) Mean + SD (median)	
Age (years)	26.75±2.5 (26.50)	29.92±5.1 (28.50)	0.285
BMI (kg/m^2)	24.95±3.39 (25.00)	25.12±3.38 (25.20)	0.932
FSH (mIU/L)	8.27±1.91 (7.75)	6.70±2.11 (6.55)	0.114
TSH (mIU/L)	1.82±0.82 (1.75)	2.04±1.26 (1.95)	0.783
LH (mIU/L)	6.72±1.62 (6.50)	7.00±3.61 (6.45)	0.877
PRL (ng/mL)	19.27±8.45 (21.9)	19.19±9.69 (17.25)	0.960
E2 (pg/mL)	30.60±12.54 (35.50)	46.85±15.44 (44.00)	**0.046***
AMH (ng/mL)	3.73±0.89 (3.69)	4.28±2.66 (3.70)	0.945

Mann-Whitney U test, Student t-test, p<0.05*. AMH: Antimüllerian hormone, BMI: Body mass index, E2: Estrodiol, FSH: Follicle stimulating hormone, LH: Luteinizing hormone, PRL: Prolactin, SD: Standard deviation, TSH: Thyroid stimulating hormone, β hCG: Beta human chorionic gonadotropin

Table 3. Comparison of complete blood count parameters according to β hCG value

	β hCG (n=94, 100%)				p-value
	Positive (n=24, 25.6%)		Negative (n=70, 74.4%)		
	Min.-max. (median)	Mean + SD	Min.-max. (median)	Mean + SD	
Hemoglobin (gr/dL)	9.3-14.4 (12.4)	12.8±1.49	9.2-14.9 (12.4)	12.6±1.48	0.991
Neutrophil (x10^3/mL)	2.84-10.19 (6.19)	5.86±2.61	2.49-21.6 (6.22)	5.6±3.32	0.786
Lymphocyte (x10^3/mL)	0.61-3.0 (1.72)	1.81±0.67	1.06-3.62 (2.17)	2.25±0.66	**0.048***
Platelet (x10^3/mL)	143-353 (267)	273±62	145-476 (273)	251±89	0.891
Neutrophils/lymphocytes	1.62-15.9 (4.38)	3.17±3.82	0.83-6.26 (2.91)	2.82±1.18	0.208
Platelet/lymphocyte	102.00-286.24 (174.51)	158.57±64.42	50.51-413.91 (135.66)	124.86±63.64	**0.046***

Mann-Whitney U test, Student t-test, p<0.05*. Min.-max.: Minimum-maximum, SD: Standard deviation, β hCG: Beta human chorionic gonadotropin

Table 4. Comparison of complete blood count parameters according to fetal heartbeat

	Fetal heartbeat (n=94, 100%)				p-value
	Positive (n=8, 8.5%)		Negative (n=86 - 91.5%)		
	Min.-max. (median)	Mean + SD	Min.-max. (median)	Mean + SD	
Hemoglobin (gr/dL)	9.3-13.6 (11.2)	11.00±1.80	9.2-14.9 (12.5)	12.75±1.41	0.135
Neutrophil (x10^3/mL)	2.84-10.19 (6.95)	7.38±3.16	2.49-21.6 (6.1)	5.52±3.17	0.450
Lymphocyte (x10^3/mL)	1.09-2.33 (1.67)	1.63±0.64	0.61-3.62 (2.11)	2.11±0.68	0.236
Platelet (x10^3/mL)	286-353 (325)	331±32	140-476 (268)	251±85	0.122
Neutrophils/lymphocytes	2.61-5.53 (4.14)	4.22±1.28	0.83-15.9 (3.18)	2.82±2.19	0.099
Platelet/lymphocyte	150.64-256.24 (213.56)	208.69±65.43	50.51-413.91 (138.88)	126.13±62.59	**0.020***

Mann-Whitney U test, Student t-test, p<0.05*. Min.-max.: Minimum-maximum, SD: Standard deviation

Table 5. Evaluation of value cut off

		AUC	p-value	Cut off	Sensitivity	Specificity
PLR	**hCG**	0.692	**0.046***	≥164.071	0.50	0.85
	Fetal heartbeat	0.854	**0.020***	≥144.098	1.00	0.68

AUC: Area under curve, hCG: Human chorionic gonadotropin, PLR: Platelet/lymphocyte ratio

in implantation (16). In a study, a relationship was found between complete blood count parameters and pregnancy loss in patients with threatened miscarriage (17). In addition, the NLR, which is presented as a marker of inflammation, is similar between patient groups; this similarity may mislead the clinician to use it to predict clinical pregnancy success.

The fact that there was no difference in age, BMI, FSH, LH, TSH, prolactin, and AMH between the pregnant and non-pregnant groups suggests that there is no difference in ovarian reserve between them and that these parameters have no effect on pregnancy.

The small number of patients evaluated in our study is one of our limitations. Increasing the number of patients may increase the power of the study.

Conclusion

After excluding other factors, the evaluation of complete blood count parameters, which is a simple and inexpensive test, may be useful in predicting the chances of pregnancy success in women trying to conceive.

Ethics

Ethics Committee Approval: Ethics committee approval was obtained from the Giresun Training and Research Hospital Ethics Committee (approval number: 25.12.2024/04, dated: 25.12.2024) for the study.

Informed Consent: Consent was obtained from the patients.

Footnotes

Authorship Contributions

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

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Comparison of Intraperitoneal and Extraperitoneal Approaches in Laparoscopic Incisional Hernia Surgery

Laparoskopik İnsizyonel Herni Cerrahisinde İntraperitoneal ve Ekstraperitoneal Yaklaşımların Karşılaştırılması

Hüseyin Kılavuz[1,2], Sibel Yaman[2], Murat Demir[2], Feyyaz Güngör[2], İdris Kurtuluş[1,2]

[1]*University of Health Sciences Türkiye, Hamidiye Faculty of Medicine, Department of General Surgery, İstanbul, Türkiye*

[2]*University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of General Surgery, İstanbul, Türkiye*

ABSTRACT

Background: Incisional hernias (IHs) are one of the most important problems that can be seen after abdominal surgeries. In recent years, the application of minimally invasive techniques in the repair of these hernias has increased. Laparoscopic IH surgeries (LIHSs) can be performed with an intraperitoneal or extraperitoneal approach. In this study, we aimed at compare the approaches to LIHSs performed from these two different planes.

Materials and Methods: In our single-center and retrospective designed study, LIHSs performed by a hernia-specific general surgery team between January 2022 and December 2023 were scanned. They were evaluated in two groups as intraperitoneal and extraperitoneal. Demographic data, hernia findings, duration of surgery, postoperative pain score, duration of hospital stay, complications, and follow-up results were analyzed.

Results: A total of 79 laparoscopically operated IH cases were included in the study. Of these patients, 49 were operated on intraperitoneally and 30 were operated on extraperitoneally. No significant difference was observed between the groups in terms of age, gender, body mass index, anesthesia score, and smoking. The duration of surgery was significantly shorter in the intraperitoneal group ($p<0.001$). The pain score on the first postoperative day was lower in the extraperitoneal group ($p=0.001$). No significant difference was found between the groups in terms of seroma and recurrence in the follow-up.

Conclusion: In LIHS, both intraperitoneal and extraperitoneal techniques can be safely applied due to low complications and acceptable recurrence rates.

Keywords: Extraperitoneal, incisional hernia, intraperitoneal onlay mesh, laparoscopic hernia surgery

ÖZ

Amaç: İnsizyonel herniler (İH), abdominal cerrahilerden sonra görülebilen en önemli sorunlardan biridir. Son yıllarda bu hernilerin onarımında minimal invaziv tekniklerin uygulanması artmıştır. Laparoskopik İH cerrahileri (LİHC) intraperitoneal veya ekstraperitoneal yaklaşımla gerçekleştirilebilir. Bu çalışmada, bu iki farklı plandan gerçekleştirilen LİHC yaklaşımları karşılaştırmayı amaçladık.

Gereç ve Yöntemler: Tek merkezli ve retrospektif olarak tasarlanmış çalışmamızda, Ocak 2022 ile Aralık 2023 arasında herniye özgü genel cerrahi ekibi tarafından gerçekleştirilen LİHC tarandı. İntraperitoneal ve ekstraperitoneal olmak üzere iki grupta değerlendirildi. Demografik veriler, herni bulguları, ameliyat süresi, postoperatif ağrı skoru, hastanede kalış süresi, komplikasyonlar ve takip sonuçları analiz edildi.

Bulgular: Çalışmaya laparoskopik olarak opere edilen toplam 79 insizyonel herni olgusu dahil edildi. Bu hastalardan 49'u intraperitoneal, 30'u ise ekstraperitoneal olarak opere edildi. Gruplar arasında yaş, cinsiyet, vücut kitle indeksi, anestezi skoru ve sigara kullanımı açısından anlamlı fark gözlenmedi. Ameliyat süresi intraperitoneal grupta anlamlı olarak daha kısaydı ($p<0,001$). Ameliyat sonrası birinci gün ağrı skoru ekstraperitoneal grupta daha düşüktü ($p=0,001$). Gruplar arasında takipte seroma ve nüks açısından anlamlı fark bulunmadı.

Sonuç: LİHC hem intraperitoneal hem de ekstraperitoneal teknikler düşük komplikasyon ve kabul edilebilir nüks oranları nedeniyle güvenle uygulanabilir.

Anahtar Kelimeler: Ekstraperitoneal, insizyonel herni, intraperitoneal onlay mesh, laparoskopik herni cerrahisi

Address for Correspondence: Hüseyin Kılavuz, University of Health Sciences Türkiye, Hamidiye Faculty of Medicine, Department of General Surgery; University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of General Surgery, İstanbul, Türkiye

E-mail: drhuseyinkilavuz@gmail.com **ORCID ID:** orcid.org/0000-0001-8860-0630

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Introduction

Incisional hernias (IHs) are a common complication that can be seen especially after open abdominal surgeries, and have an incidence of 2-20% (1). IHs can be asymptomatic or can lead to serious complications such as incarceration and strangulation, and they can especially cause pain and problems that impair the quality of life of patients (2). Surgical repairs constitute the basis of hernia treatment. The importance of hernia surgery is increasing due to an increasing number of major surgical operations performed with laparotomy and the prevalence of risk factors such as obesity and an elderly population (3).

Until the recent past, IHs were treated with open mesh repair methods. In recent years, laparoscopic hernia surgeries have become increasingly preferred due to advantages such as fewer wound complications and shorter hospital stay, as well as the ability to detect additional hernias with a wide field of view during surgery (4). In laparoscopic IH surgery (LIHS), the first intraperitoneal onlay mesh (IPOM), which is based on the principle of intraperitoneal mesh placement, and later the IPOM Plus technique, which is modified by closing the hernia defect, was applied (5). With the concern that the intraperitoneal approach carries some complication risks, the enhanced-view totally extraperitoneal (e-TEP) technique was developed for LIHS, based on the totally extraperitoneal (TEP) technique in inguinal hernia surgery (6). After these techniques became increasingly widespread, LIHS expanded its scope. In particular, the definition of various technical modifications and the introduction of different mesh types led to the lack of a general standard approach for LIHS (7).

In this study, we aimed to compare our surgical results using the intraperitoneal (IPOM Plus) and extraperitoneal (e-TEP) techniques, which are the most commonly applied techniques in LIHS and are studied in different anatomical planes.

Materials and Methods

Case Selection and Data Collection

After the establishment of a hernia-specific surgery unit within the general surgery clinic of our hospital, data from LIHS performed by the hernia team between January 2022 and December 2023 were retrospectively scanned for inclusion in the study. The classifications of the European Hernia Society (EHS) were used for both midline and non-midline IHs (8). Age, gender, body mass index (BMI, kg/m^2), presence of comorbidity, smoking, American Society of Anesthesiology (ASA) score, location of hernia (according to EHS), hernia diameter (4 cm = W1, 4-10 cm = W2), surgical technique (intraperitoneal/extraperitoneal), surgical duration, Visual Analog Scale (VAS) score on the first postoperative day (pain grading as "0" points for no pain and "10" points for the most severe pain), hospital stay (days), complications (seroma, hematoma) within the first three months of postoperative surgery, unexpected re-admissions within the first 30 days of postoperative surgery, and recurrence status within at least one year of follow-up were retrospectively recorded and analyzed. Cases that started with laparoscopic surgery and were converted to open surgery, and patients who did not continue their postoperative follow-up were not included in the study.

Surgical Techniques

The decision on which technique to apply to the patients was made according to patient factors and surgeon preference. Very large hernias (diameter 10 cm and above) and complex volume hernias (presence of loss of domain) were not included in this study because different protocols were conducted.

Intraperitoneal Technique

Trocar sites were determined so that the monitor was placed opposite the surgeon, and the sites formed a triangular position relative to the hernia area (Figure 1). The abdomen was explored under 12 mmHg pressure using a 10 mm camera trocar, with the help of a Veress needle and an optical trocar. At least two 5 mm working trocars were inserted into the abdomen. If the hernia content was not reducible, it was reduced and adhesiolysis was performed (Figure 2). Even if the hernia defect was small, the defect was first closed with barbed suture. The measurement was then made, and the appropriate-sized composite mesh was laid from the abdomen to the hernia area and fixed with an absorbable tacker (IPOM Plus).

Extraperitoneal Technique

The monitor was positioned opposite the surgeon to be worked with effectively. Depending on the location of the hernia, an incision was made close to the costal arch in the right or left upper quadrant of the abdomen, through which the anterior rectus sheath and rectus muscle were accessed using an optical trocar (Figure 3). After entering the retromuscular area and opening it with optical dissection, at least two more 5 mm trocars were inserted into the site. After completing the hernia sac dissection through passing from the linea alba plane to the contralateral retrorectus plane, the posterior and anterior defects were closed with a barbed suture. After measuring the mesh area, the prolene

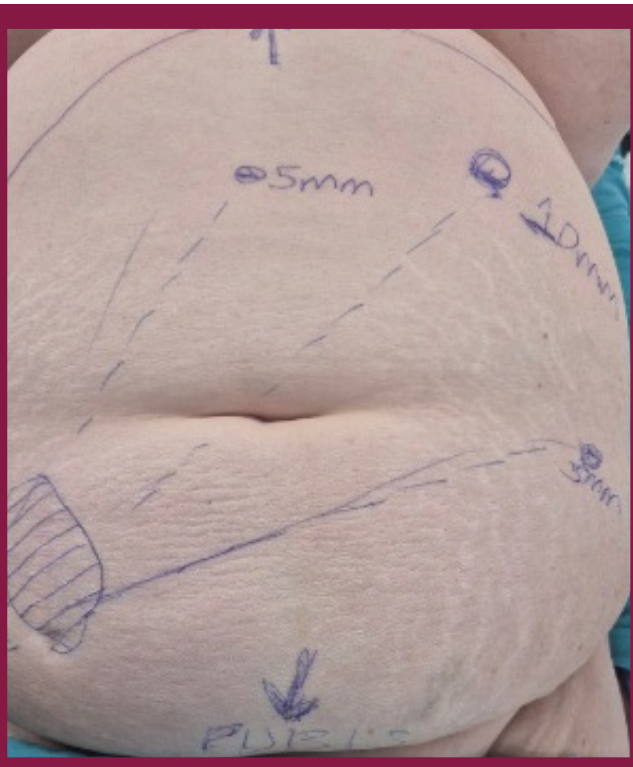

Figure 1. Port placement positions according to hernia location for intraperitoneal approach

mesh was prepared and laid in the retromuscular area, and the surgery was terminated with desufflation and trocar removal (e-TEP Rives-Stoppa, Figure 4). In large defects, a transversus abdominis release modification was added to allow tension-free closure of the hernia area.

Postoperative Follow-up Protocol

A respiratory exercise ball was used for postoperative respiratory physiotherapy. Postoperative outpatient clinic follow-ups are routinely performed in our hernia-specific unit in the first week, first month, third month, sixth month, and first year. In case of hematoma, seroma, or recurrence findings in physical examination, radiological examinations are used. Follow-up examination information is recorded in the hospital information management system.

Statistical Analysis

The statistical analyses of this study were performed using the IBM SPSS Statistics program for Windows, Version 29.0.2.0 (IBM Corp., Armonk, NY, USA). The conformity of continuous variables with a normal distribution was assessed with Kolmogorov-Smirnov and Shapiro-Wilk tests. In comparisons between groups, the Pearson chi-square test or the Fisher's exact test was used for categorical variables

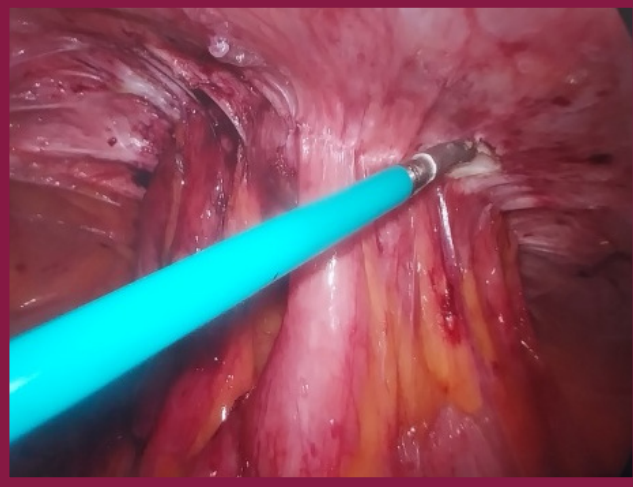

Figure 2. Visualization of hernia contents from the intraperitoneal area and initiation of adhesiolysis process

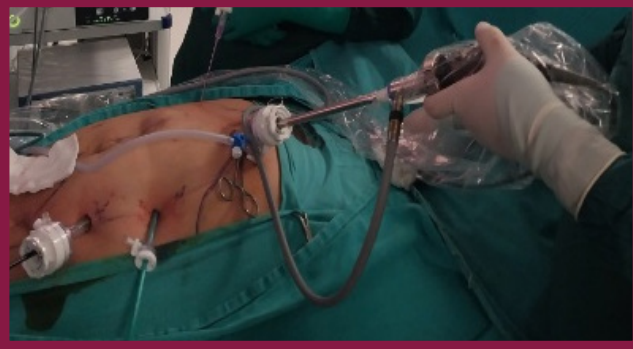

Figure 3. Placement of ports for extraperitoneal technique

Figure 4. Placement of polypropylene mesh in the extraperitoneal space

Table 1. Demographic data and preoperative clinical characteristics of groups

n		IPOM Plus		e-TEP		Total		p-value
		%	n	%	n	%		
Gender	Female	29	59.2	19	63.3	48	60.8	0.714
	Male	20	40.8	11	36.7	31	39.2	
Age	Mean ± SD	52.84±11.34		49.87±11.44		51.71±11.40		0.266[b]
BMI (kg/m²)	Mean ± SD	30.75±4.13		30.90±3.88		30.81±4.02		0.872[b]
ASA score	ASA 1	8	16.3	5	16.7	13	16.5	0.137[a]
	ASA 2	27	55.1	22	73.3	49	62	
	ASA 3	14	28.6	3	10	17	21.5	
Comorbidity	No	26	53.1	24	80	50	63.3	**0.016[a]**
	Yes	23	46.9	6	20	29	36.7	
Smoking	No	26	53.1	15	50	41	51.9	**0.792[a]**
	Yes	23	46.9	15	50	38	48.1	

[a]Pearson chi-square test, [b]Independent samples t-test
ASA: American society of anesthesia, BMI: Body mass index, IPOM: Intraperitoneal onlay mesh, e-TEP: Enhanced-view totally extraperitoneal, SD: Standard deviation

under appropriate conditions. An independent samples t-test was applied when continuous variables showed a normal distribution, or a Mann-Whitney U test was applied when they did not show a normal distribution. Categorical data were reported as frequency and percentage [% (n)], normally distributed continuous data as mean ± standard deviation, and non-normally distributed continuous data as median [interquartile range (IQR)]. In all tests, p<0.05 was considered statistically significant.

Ethical Approval

This single-center and retrospective study followed the "Strengthening the Reporting of Observational Studies in Epidemiology" guidelines. The study protocol was developed in accordance with the ethical principles of the current Declaration of Helsinki. Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee (approval number: 2023-624, dated: 13.12.2023). All patients were informed about the surgical procedures before surgery and signed an informed consent form.

Results

A total of 79 patients who underwent LIHS during the study period and met the study criteria were included. Of these patients, 49 were operated on intraperitoneally with the IPOM Plus technique (62%) and 30 were operated on extraperitoneally with the e-TEP technique (38%). Gender and age distribution was similar between the groups, and no statistical difference was found (p=0.714/p=0.266). No significant difference was found between the groups in terms of mean body mass index and ASA scores (p=0.872/p=0.137).

A total of 29 patients (36.7%) had at least one additional disease. The rate of additional diseases was significantly lower in the e-TEP group (p=0.016). No significant difference was found between the groups in terms of smoking (p=0.792); a total of 38 patients (48.1%) were smokers, and 41 patients (51.9%) were non-smokers (Table 1).

The most common location in the midline (M-midline) distribution was the umbilical region (M3). It was detected in 54 patients (68.4%). Lateral (L) localizations were observed in 14 patients (Table 2).

When evaluated for W-width, the defect width was measured at less than 4 cm (W1) in 8 patients (10.1%). The defect width of all e-TEP patients was between 4 and 10 cm (W2) (p=0.021).

The operation time was found to be significantly longer, with a median of 155 minutes (IQR: 120-188.7) in the e-TEP group and 95 minutes (IQR: 75-142.5) in the IPOM Plus group (p<0.001). Postoperative first day pain scores were higher in the IPOM Plus group, with a median of 4 (IQR: 3-6) compared to the e-TEP group, with a median of 3 (IQR: 3-4) (p=0.001) (Table 2).

The number of patients who developed complications was 11 (13.9%) in total, with 6 patients (12.2%) in the IPOM Plus group and 5 patients (16.7%) in the e-TEP group (p=0.582). Seroma development was observed in 9 patients (11.4%). Five of these patients were in the IPOM Plus group and four in the e-TEP group (p=0.671). The number of patients with hematoma was 4 (5.1%); 2 cases were detected in both groups (p=0.611). The number of

Table 2. Comparison of perioperative and postoperative outcomes of groups

		IPOM Plus		e-TEP		Total		p-value
		n	%	n	%	n	%	
Hernia locations (according to EHS)	M2: Epigastric	10	20.4	1	3.3	11	13.9	NA
	M3: Umbilical	33	67.3	21	70	54	68.4	
	M4: Infraumbilical	2	4.1	2	6.7	4	5.1	
	M5: Suprapubic	0	0.0	3	10	3	3.8	
	L1: Subcostal	2	4.1	1	3.3	3	3.8	
	L2: Flank	1	2.0	0	0.0	1	1.3	
	L3: Iliac	1	2.0	1	3.3	2	2.5	
	L4: Lumbar	0	0.0	1	3.3	1	1.3	
Width (cm)	W1:<4	8	16.3	0	0.0	8	10.1	**0.021**[a]
	W2:4-10	41	83.7	30	100	71	89.9	
Surgery time (minutes)	Median (IQR)	95	75-142.5	155	120-188.7	115	85-160	**<0.001**[b]
VAS score (po day 1)	Median (IQR)	4	3-6	3	3-4	4	3-5	**0.001**[b]
Length of stay (days)	Median (IQR)	3	2-3.5	3	2-3	3	2-3	0.944[b]
Complication	No	43	87.8	25	83.3	68	86.1	0.582[a]
	Yes	6	12.2	5	16.7	11	13.9	
Seroma	No	44	89.8	26	86.7	70	88.6	0.671[a]
	Yes	5	10.2	4	13.3	9	11.4	
Hematoma	No	47	95	28	93.3	75	94.9	0.611[a]
	Yes	2	4.1	2	6.7	4	5.1	
Unexpected readmission (first 30 days)	No	46	93.9	27	90	73	92.4	0.528[a]
	Yes	3	6.1	3	10	6	7.6	
Recurrence (at least 1 year)	No	46	93.9	29	96.7	75	94.9	0.583[a]
	Yes	3	6.1	1	3.3	4	5.1	

[a]Fisher's exact test, [b]Mann-Whitney U test
NA: Not applicable, EHS: European Hernia Society, e-TEP: Enhanced-view totally extraperitoneal, IQR: Interquartile range, IPOM: Intraperitoneal onlay mesh, Po: Postoperative, VAS: Visual Analog Scale

patients who were re-admitted to the hospital within the first 30 days after surgery was 3 (6.1%) in the IPOM Plus group and 3 (10.0%) in the e-TEP group, totaling 6 (7.6%) (p=0.528). The reasons for these applications were subileus and abdominal pain in the IPOM Plus group and nonspecific abdominal pain in the e-TEP group. All patients were followed up as outpatients with symptomatic treatment. During the follow-up period, a total of 4 patients (5.1%) developed recurrence. Three of them were in the IPOM Plus group and one in the e-TEP group (p=0.583) (Table 2). No intraoperative complications developed in any patient. No hernia-related mortality was observed during the hospitalization and follow-up periods.

Discussion

Yet, there is no consensus in the literature on which technique is superior in LIHS (9). In this study, the results of IPOM Plus and e-TEP methods were compared in the context of LIHS in our hernia-specific general surgery unit. Although the e-TEP procedure seemed to be advantageous in terms of postoperative pain, longer operative times were a disadvantage.

Intraperitoneal approaches have a faster learning curve due to the wide field of view, but they are not preferred by some surgeons due to various associated risks. Since the procedures are operated in a narrower area, the learning curve of the e-TEP technique requires significant experience. Therefore, intraoperative times are longer in the

e-TEP technique (10). Sholapur et al. (11) reported that in their prospective study comparing IPOM Plus and e-TEP in ventral hernias, the hospital stay (5.9±2.19 days) and the postoperative first day VAS score (3.2±1.11) were higher in the IPOM Plus group, while the surgery time (192.3±16.20 minutes) was higher in the e-TEP group.

The intraoperative success of intraperitoneal and extraperitoneal approaches is affected by demographic and personal factors to a minor extent. In a study comparing intraperitoneal and extraperitoneal techniques, no statistically significant difference was found between the groups in terms of age, gender, BMI, ASA score, and active smoking (12). In our study, no difference was found between the groups in terms of gender, age, ASA score, BMI, and smoking. The main determinant of patient comfort in the early period after hernia surgeries is the severity of pain. In the intraperitoneal technique, the use of absorbable or nonabsorbable tacker during the fixation of the mesh to the parietal peritoneum significantly shortens the operation time and is the main cause of postoperative pain (13). On the other hand, in the extraperitoneal technique, because the mesh placed in the retromuscular area does not need to be fixed most of the time, it eliminates an additional cause of pain. Although it is considered advantageous in terms of less postoperative pain, the longer operation time in the e-TEP technique has been identified as a disadvantage in many studies. In the same studies, VAS scores were found to be high due to significant postoperative pain in the intraperitoneal technique, and this was shown to be the cause of prolonged hospital stays (10-12).

Another undesirable situation after hernia surgery is unexpected re-admissions. Especially in the intraperitoneal technique, the direct contact of the mesh with the abdominal organs was associated with paralytic ileus attacks in the postoperative period (14). In our study, unexpected admissions occurred in the first month after both procedures. While non-specific abdominal pain was observed in the e-TEP group, subileus attacks were the main reason for admission in the intraperitoneal technique group. Wieland et al. (15) presented general and subgroup analyses regarding postoperative complications in their study comparing both techniques. The general postoperative complication rate was found to be higher in the IPOM group (e-TEP: 4.17%, IPOM: 25%, p=0.009). However, complications were more severe in the e-TEP group, and those that could be managed with symptomatic treatment were more prominent, in the IPOM group (15). There are also studies in the literature that provide different results, and a meta-analysis including 433 patients reported that there was no significant difference in the incidence of seroma, hematoma, intraoperative complications, and postoperative ileus between the e-TEP and IPOM groups (16). Similarly, the overall complication rate in our study was 13.9%. All of these were mild complications that could be treated symptomatically, and there was no significant difference between the groups.

Seromas, which are frequently observed after hernia surgery, are usually asymptomatic. Since most seromas regress spontaneously, it is recommended to wait unless they cause serious symptoms, and to avoid performing aspiration if possible due to the risk of infection (3,14). The overall seroma rate in our study was 11.4% and all seromas regressed completely within three months without the need for additional intervention.

In the literature, the recurrence rate after LIHS is reported to be between 1% and 7% (17-19). However, since publications reporting low recurrence rates include data from a six-month postoperative follow-up period, this period may not be sufficient to detect recurrences. Therefore, we planned the shortest follow-up period to be 12 months in our study.

Study Limitations

This study has some limitations. The most important of these are the retrospective study design, single-center study nature, and the small number of patients included in the study. The limitations resulting from the small sample size and single-center design prevent the generalization of the study results. In addition, since laparoscopic procedures require technological infrastructure, these procedures may not be applicable in every hospital. Despite all these limitations, it should not be forgotten that the surgical team in the study was a general surgery team working specifically on hernias. This specialization may have prevented some additional problems caused by inexperience.

Conclusion

Since there are no major complications in LIHS, both techniques can be applied safely. The shorter operation time in the IPOM technique and less postoperative pain in the eTEP technique can be seen as advantages. Patient factors and surgeon experience come to the fore in the selection of the procedure based on current information.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Clinical Research Ethics Committee (approval number: 2023-624, dated: 13.12.2023).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.K., S.Y., M.D., F.G., İ.K., Concept: H.K., İ.K., Design: H.K., S.Y., M.D., Data Collection or Processing: H.K., S.Y., F.G., İ.K., Analysis or Interpretation: H.K., F.G., Literature Search: H.K., S.Y., M.D., F.G., Writing: H.K., M.D., F.G.

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

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ORIGINAL ARTICLE

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Scientific Trends in Infectious Diseases and Clinical Microbiology: A Bibliometric Analysis of Five Turkish National Journals (2005-2023)

Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Alanında Bilimsel Yönelimler: Türkiye'den Beş Ulusal Derginin Bibliyometrik Analizi (2005-2023)

Semiha Çelik Ekinci[1], Işıl Deniz Alıravcı[2]

[1]*University of Health Sciences Türkiye, Fatih Sultan Mehmet Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Türkiye*

[2]*Çanakkale 18 Mart University Faculty of Medicine, Department of Diseases and Clinical Microbiology, Çanakkale, Türkiye*

ABSTRACT

Background: Bibliometric analysis is a quantitative method used to evaluate scientific research, authors, journals, and institutions compared to their peers. This study aimed to analyze five Turkish journals publishing in the field of "Infectious Diseases" and "Clinical Microbiology" and to examine the thematic evolution over time.

Materials and Methods: Data from five journals published between January 1, 2005, and January 27, 2024, were obtained from the Web of Science database and analyzed.

Results: The dataset included 2,418 original articles authored by 5,825 individuals, with 73 sole authors. International co-authorship accounted for 1.73%. Among the articles, 1,137 were open access, 1,331 were indexed in the Emerging Sources Citation Index, and 1,087 were indexed in the Science Citation Index Expanded. A total of 1,872 articles were published in Turkish and 543 in English. Journal-1 and Journal-2 contributed the most, with 1,087 and 625 articles, respectively. After excluding 5,527 self-citations, the articles received 7,087 citations, averaging 2.93 per article. Journal-2 was the first journal indexed in Web of Science (h-index: 11, g-index: 16, m-index: 0.55). Institution-3 was the top contributor with 134 documents and a total link strength of 14,303. The most prolific author was affiliated with Institution-1. Thematic analysis from 2007 to 2021 showed early focus on "serodiagnosis," "gram-negative bacteria," "field gel electrophoresis," and "culture." From 2016 onwards, the focus of attention shifted to "infection," "epidemiology," and "susceptibility." Recently, clinical management and disease-related terms such as "diagnosis," "risk," "mortality," and "severity" became prominent. The keyword "infection" appeared 210 times, and "antibiotics and antimicrobials" were the most common thematic categories with 687 occurrences.

Conclusion: While microbiology-centered topics were more prominent in the early 2000s, the findings suggest a growing shift toward clinically oriented subjects in recent years.

Keywords: Bibliometrics, infectious diseases, publications, Türkiye

ÖZ

Amaç: Bibliyometrik analiz, bilimsel araştırmaların, yazarların, dergilerin ve kurumların akranlarıyla karşılaştırmalı olarak değerlendirilebildiği matematiksel ve istatistiksel bir yöntemdir. Bu çalışmada, Türkiye'de "Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji" alanında yayın yapan beş derginin bibliyometrik analizini sunarak, bu alandaki konuların yıllar içindeki dağılımını incelemeyi amaçladık.

Gereç ve Yöntemler: Beş dergiye ait 01.01.2005-27.01.2024 tarihleri arasındaki veriler "Web of Science" veri tabanından incelenmiştir.

Bulgular: Veri setinde beş kaynaktan 2.418 orijinal makale saptanmıştır. Bu makalelerde, 73'ü tek yazarlı olmak üzere toplam 5.825

Address for Correspondence: Semiha Çelik Ekinci, University of Health Sciences Türkiye, Fatih Sultan Mehmet Training and Research Hospital, Clinic of Infectious Diseases and Clinical Microbiology, İstanbul, Türkiye

E-mail: dr_semiha@hotmail.com **ORCID ID:** orcid.org/0000-0002-6264-1685

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ÖZ

yazar yer almakta ve uluslararası ortak yazarlık oranı %1,73'tür. Makalelerin 1.137'si açık erişim kategorisindedir. Bin üç yüz otuz biri Emerging Sources Citation Index, 1.087'si Science Citation Index Expanded kapsamında yayımlanmıştır. Makalelerin 1.872'si Türkçe, 543'ü İngilizce dilindedir. En çok katkıyı sağlayan dergiler sırasıyla Dergi-1 (1.087 makale) ve Dergi-2'dir (625 makale). Dergilerin kendi kendilerine yapılan 5.527 atıf hariç tutulduğunda, toplam 7.087 atıf alınmış ve makale başına ortalama 2,93 atıf düşmektedir. Web of Science'de ilk indekslenen dergi Dergi-2 olup bu derginin h-indeksi 11, g-indeksi 16 ve m-indeksi 0,55'tir. En çok katkı sağlayan kurum, 134 belge ve 14.303 toplam bağlantı gücü ile Kurum-3'tür. En çok yayın yapan yazar, Kurum-1'e bağlı olarak kaydedilmiştir. 2007-2021 dönemine ait konu başlıklarının dağılımı incelendiğinde, ilk yıllarda "serodiagnoz", "gram negatif bakteriler", "alan jel elektroforezi" ve "kültür" gibi konuların öne çıktığı; 2016 itibarıyla ise "enfeksiyon", "epidemiyoloji" ve "duyarlılık" gibi temalara doğru bir kayma olduğu görülmüştür. Son yıllarda ise "tanı", "risk", 'yönetim', "mortalite" ve "şiddet" gibi klinik yönetim ve hastalık odaklı başlıklara belirgin bir yönelim gözlemlenmiştir. Anahtar kelimeler arasında en sık geçen terim 210 kez ile "enfeksiyon" olurken, en yaygın konu başlığı 687 kez ile "antibiyotikler ve antimikrobiyaller" olmuştur.

Sonuç: 2000'li yılların başlarında mikrobiyoloji ağırlıklı konuların öne çıktığı görülürken, ilerleyen yıllarda klinik odaklı başlıklara eğilimin arttığı sonucuna varılmıştır.

Anahtar Kelimeler: Bibliyometri, enfeksiyon hastalıkları, yayınlar, Türkiye

Introduction

Bibliometric analysis is a statistical and mathematical method used to investigate and evaluate extensive bodies of scientific literature. As a relatively recent technique, it offers insights into the developmental dynamics of a given field while identifying emerging trends. By mapping the research activities of institutions, authors, or publishing organizations on a global scale, this method enables the positioning of the evaluated work within the broader scientific landscape and helps assess its contribution to knowledge advancement (1-3). In essence, bibliometric analysis provides a comprehensive overview of the current status of scientific studies within the international research context.

In recent years, significant progress has been observed in the fields of infectious diseases and clinical microbiology in Türkiye. This study compares five Turkish microbiology journals specializing in infectious diseases and clinical microbiology. The primary objective is to evaluate their contributions to the fields of Infectious Diseases and Clinical Microbiology, particularly regarding author distribution and citation impact. Furthermore, this study aims to deliver an overarching perspective for researchers, academics, and readers, while identifying key national research trends over time, as reflected in the Web of Science database.

A review of the existing literature indicates a lack of studies specifically addressing bibliometric trends in this field. Existing publications primarily focus on journal comparisons or topic-specific analyses. This study represents original research intended to address this gap. Accordingly, a bibliometric analysis was conducted on journals publishing in the field of Infectious Diseases and Clinical Microbiology in Türkiye, with a focus on the evolution and distribution of subject areas over time.

Materials and Methods

Search Method

Bibliometrics is an interdisciplinary field that applies statistical and mathematical methods to quantitatively analyze information sources. It enables a comprehensive and objective evaluation of a body of literature, covering aspects such as contributions, collaborations, publication patterns, and the knowledge base.

In this study, standard bibliometric indicators were used to assess publication trends in selected journals. All core Türkiye-based journals exclusively focused on infectious diseases and clinical microbiology were included. Selection criteria were based on continuous publication history, official affiliation with national professional societies, and recognized contributions to the field.

Journal-1 is a nationally recognized publication specializing in clinical and microbiological research. Journal-2 serves as the official organ of a specialty society in the field and is internationally indexed, contributing to growing global visibility. Journal-3 represents a professional association in Türkiye and functions as a central platform for scientific exchange among its members. Journal-4 has a regional focus on infectious diseases, microbes, and antimicrobials. Journal-5 is the longest-standing continuously published journal in this field in Türkiye and is considered a foundational source for microbiology research.

The purpose of selecting these five journals was to identify the most representative and influential national scientific contributions in the field of infectious diseases and clinical microbiology. This selection provides a methodologically coherent and comprehensive overview of the national research landscape.

Data for the study were retrieved from the Web of Science database (https://www.webofscience.com/), which is updated daily. Data transfer was performed on January 27, 2024.

The study focused on five Turkish journals indexed in the Emerging Sources Citation Index (ESCI) and Science Citation Index Expanded (SCI-E) under the subject categories "Infectious Diseases" and "Clinical Microbiology." Journal names were used as the basis for pooled analysis in the Web of Science search engine. Only articles were selected as the document type, and the analysis was conducted solely based on journal titles.

Data Extraction

All retrieved records were saved in plain text format and exported as full records with cited references under the file name "download.txt"

Statistical Analysis

To facilitate data visualization, Microsoft Excel, VOSviewer (version 1.6.18), and Biblioshiny, were utilized in conjunction with the built-in features of the Web of Science database (4,5).

The study presents a comprehensive bibliometric analysis, including annual publication and citation counts, keyword mapping, detailed examination of institutions and authors with the highest output, and topic-based citation analysis. These analyses were conducted to assess the publication profiles, collaboration networks, and academic influence of the five selected journals. The bibliometric approach enabled the evaluation of national contributions in the field of infectious diseases and clinical microbiology.

The analysis focused exclusively on five core journals published in Türkiye, each dedicated to infectious diseases and/or clinical microbiology. Selection criteria included a defined subject focus within the field, indexing in Web of Science (ESCI or SCI-E), consistent publication records, and official affiliation with professional societies.

Other Türkiye-based journals with broader or general medical scopes that occasionally publish content related to infectious diseases or microbiology were deliberately excluded. The aim was to analyze specialized journals representing the core of national scientific activity, rather than providing a general survey across a wide range of publications.

Bibliometric Indices

Several bibliometric indices were applied to assess journal impact. The h-index, g-index, and m-index were used to evaluate research productivity and influence, particularly at the author and journal levels.

The h-index, proposed by physicist Hirsch (6) in 2005, measures both the productivity and impact of a researcher's publications. A scholar has an h-index of h if h of their papers have each been cited at least h times.

The g-index, introduced by Egghe (7), builds on the h-index by considering citation distribution. It is defined as the largest number g such that the top g publications received together at least g squared citations.

The m-index adjusts the h-index based on career length. It is calculated by dividing the h-index by the number of years since the author's first publication, offering a normalized measure of research impact (8).

Another metric used is the Average Total Citations per Article, calculated by dividing the total number of citations by the number of articles. A higher average reflects a stronger citation impact.

Publication Characteristics and Open Access Categories

The journals were also examined in terms of publication characteristics, including counts in categories such as "Open Access," ESCI, and SCI-E.

The Web of Science database includes articles available without copyright or licensing restrictions, categorized as Open Access. In some cases, research is accessible via alternative platforms other than the publisher's site. These are referred to as Green Open Access articles. Accepted but unpublished manuscripts fall under Accepted Green Open Access, whereas published versions are labeled Published Green Open Access.

Under the Gold Open Access model, authors cover publication costs through article processing charges, thus allowing readers free access and authors to retain copyright. The Hybrid Open Access model allows authors to make individual articles openly accessible by paying a fee. Bronze Open Access or Free to Read categories refer to content that is accessible at no cost via publisher websites, though often without a clear reuse license (9,10).

Results

General Information

The dataset spans the period from 2005 to 2023 and includes 2,418 documents sourced from five journals. It demonstrates an annual growth rate of 10% and an average document age of 8.02 years. A total of 5,825 authors contributed to the dataset, with an average of 5.25 co-authors per article. International co-authorship accounted for 1.73% of all collaborations.

A review of publication characteristics revealed that 1,137 articles were classified as open access: 951 under the "Gold" category, 73 as "Gold-Hybrid", 112 as "Free to Read", 3

as "Green Published", and 48 as "Green Submitted". Notably, journals may provide multiple open access options.

Among the indexed articles, 1,331 were published in ESCI and 1,087 in SCI-E. In terms of language, the majority of articles were published in Turkish (1,872), followed by English (543). French, Italian, and Spanish were the least common, each represented by a single article.

Journal Metrics, Article and Citation Counts by Year

Among the five journals analyzed, Journal-1 had the highest output, contributing 1,087 articles. Journal-2 followed with 625 articles, Journal-3 with 363 articles, Journal-4 with 243 articles, and Journal-5 with 100 articles. Collectively, the articles received 7,087 citations, of which 5,527 were self-citations. The average number of citations per article was 2.93 (Table 1).

Table 1 presents key journal metrics. Journal-1 recorded the highest values with an h-index of 23, a g-index of 28, an m-index of 1.278, and 5,641 citations across 1,087 articles.

Figure 1 shows a fluctuating trend in annual publication output between 2005 and 2023. A general upward trend is observed, peaking in 2022, followed by a slight decline in 2023.

Figure 2 presents the annual distribution of articles across journals. Journal-1 demonstrates a consistent increase in publication volume, reaching 1,087 articles by 2023, followed by Journal-2 (625 articles), and Journal-3 (363 articles).

Figure 3 depicts the mean total citations and mean citations per article between 2005 and 2023. While mean citations initially increase, a notable decline is observed from 2015 onwards, reflecting a downward trend in citation frequency in recent years.

Contributing Countries, Most Profilic Institutions, and Authors

As shown in Table 2, Türkiye is the leading contributor with 6,275 articles. Other contributing countries include

Table 1. Journal metrics and number of articles

Journal	h-index	g-index	m-index	Total citations	Number of articles	First indexing year in Web of Science
Journal-1	23	28	1.278	5641	1087	2007
Journal-2	11	16	0.55	1163	625	2005
Journal-3	5	6	0.625	87	363	2017
Journal-4	4	5	0.308	134	243	2012
Journal-5	3	4	0.6	42	100	2020

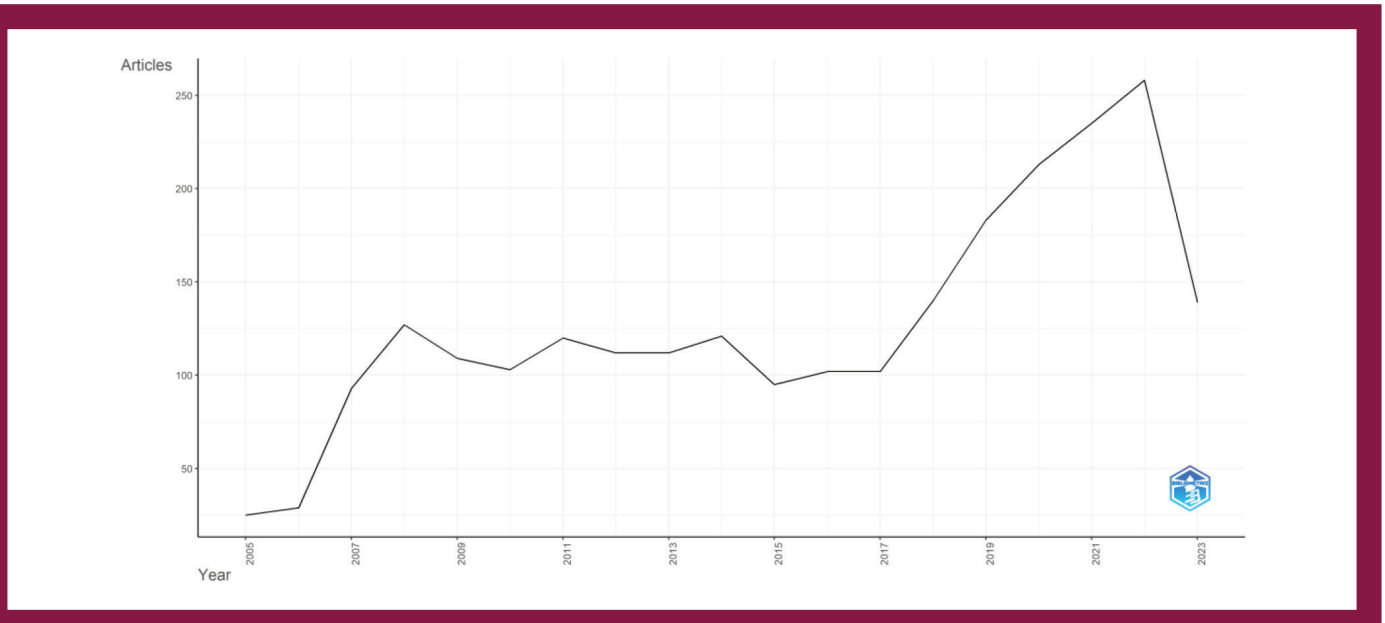

Figure 1. Annual scientific production

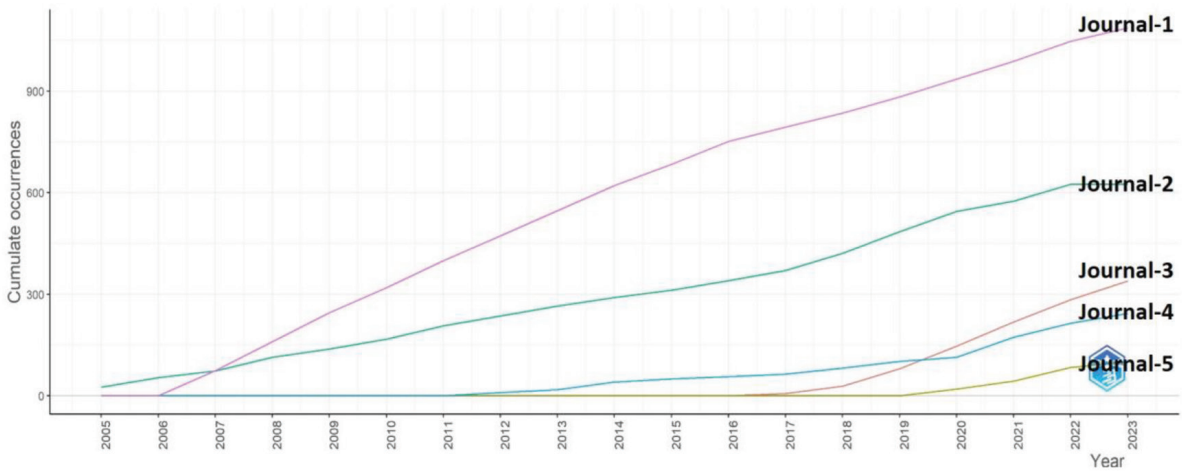

Figure 2. Sources' production over time

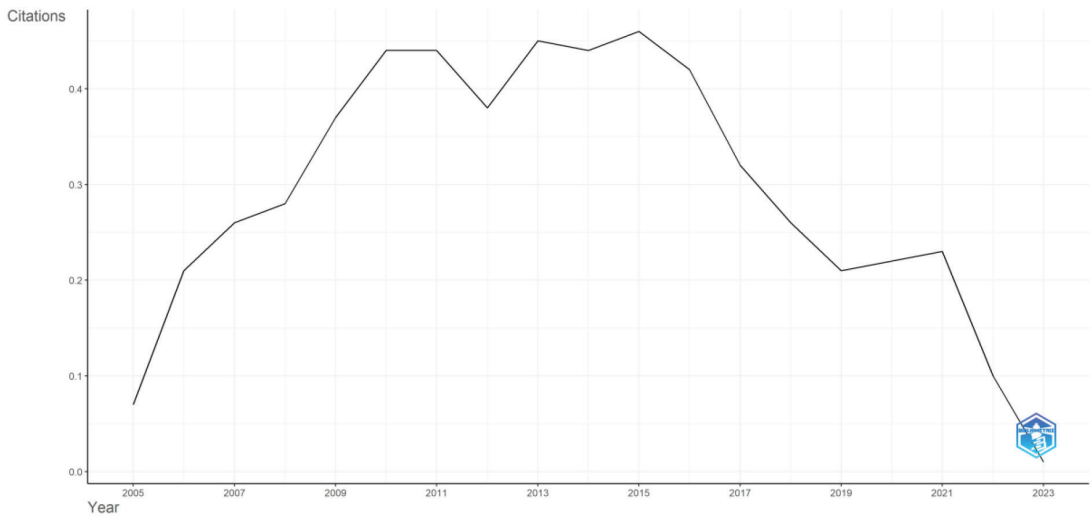

Figure 3. Average citations per year

Iran (77), the Turkish Republic of Northern Cyprus (31), India (15), Switzerland (14), and the United States (11).

Figure 4 illustrates the temporal evolution of article output by the top ten institutions, based on first author affiliation. Institution-1, Institution-2, and Institution-3 show consistently high research output. In 2023, Institution-1 led with 283 articles, followed by Institution-2 (223 articles) and Institution-3 (196 articles).

The author affiliated with Institution-1 had the highest publication count. Authors with the second-highest number of publications are depicted in Figure 5. Figure 6 presents a three-field plot that illustrates the relationship between authors, institutions, and topics, with a maximum occurrence of 10 for each field.

Keyword Analysis and Trend Topics

Figures 7a and 7b, generated using VOSviewer, depict the thematic structure and temporal evolution of keyword significance. Figure 7a shows a network visualization where bubble size represents keyword frequency, and connecting lines indicate thematic relationships. Figure 7b provides an overlay visualization for the period 2000-2023, highlighting the relative importance of topics over time. Notably, post-2020 data show that the novel Coronavirus Disease 2019 (COVID-19) became the most prominent theme.

As presented in Table 3, "infection" was the most frequently occurring keyword (210 occurrences), followed by "diagnosis" (177 occurrences).

Table 4 provides citation data by subject area. The most frequently cited subject headings include "Antibiotics and Antimicrobials," "General Virology," and "Medical Mycology."

Figure 7c presents a comprehensive timeline of keyword trends, indicating the frequency, year of first appearance,

Table 2. The countries of origin of the authors of the articles

Country	Number of articles
Türkiye	6,275
Iran	77
Turkish Republic of Northern Cyprus	31
India	15
Switzerland	14
USA	11
Morocco	8
Germany	7
Jordan	5
Nigeria	5
Israel	4
Japan	4
Malaysia	4
Cuba	3
Netherlands	3
UK	3
Argentina	2
Czech Republic	2
France	2
Iraq	2
Italy	2
Portugal	2
Azerbaijan	1
Belgium	1
China	1
For all authors	

Table 3. Frequency of terms in the journals between 2005 and 2024 - Word Cloud

Keyword	Frequency
Infection	210
Diagnosis	177
Epidemiology	170
Prevalence	149
Infections	143
Türkiye	97
Risk-factors	95
Management	92
Resistance	83
Susceptibility	70
Identification	68
Children	65
Strains	63
Risk	61
Outbreak	60
Polymerase chain reaction	58
Therapy	56
Disease	55
Surveillance	53
Virus	46
Bacteremia	41
Impact	40
Antibodies	39
Enterobacteriaceae	37
Seroprevalence	37
Mortality	36
Assay	35
Genes	35
Antimicrobial resistance	34
Emergence	34
DNA	33
Escherichia coli	33
Antibiotic-resistance	32
Adults	30
Transmission	30
United-States	28
Region	27
Efficacy	26
Patient	26
Polymerase-chain-reaction	26
Association	25
Outcomes	24
Prevention	24
Bacteria	23
Colonization	23
Pathogens	23
Specimens	22
Blood-stream infections	21
Combination	21
Guidelines	21

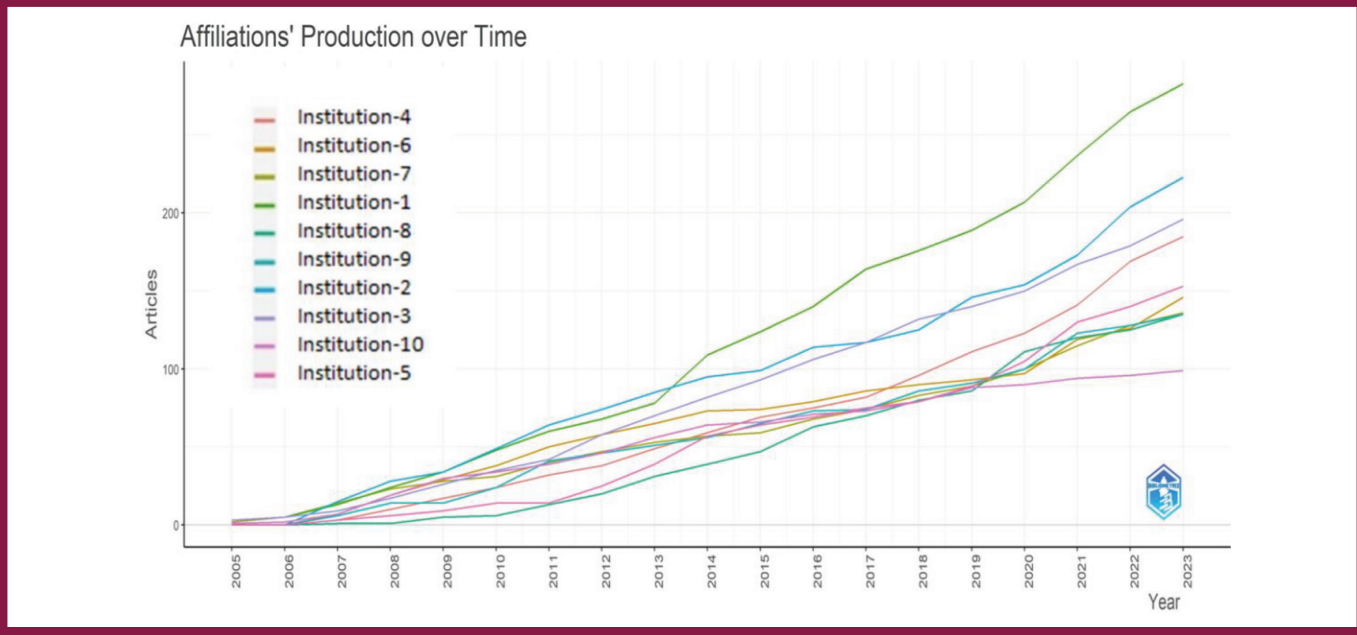

Figure 4. The number of articles over time for the top 10 institutions with the highest number of publications

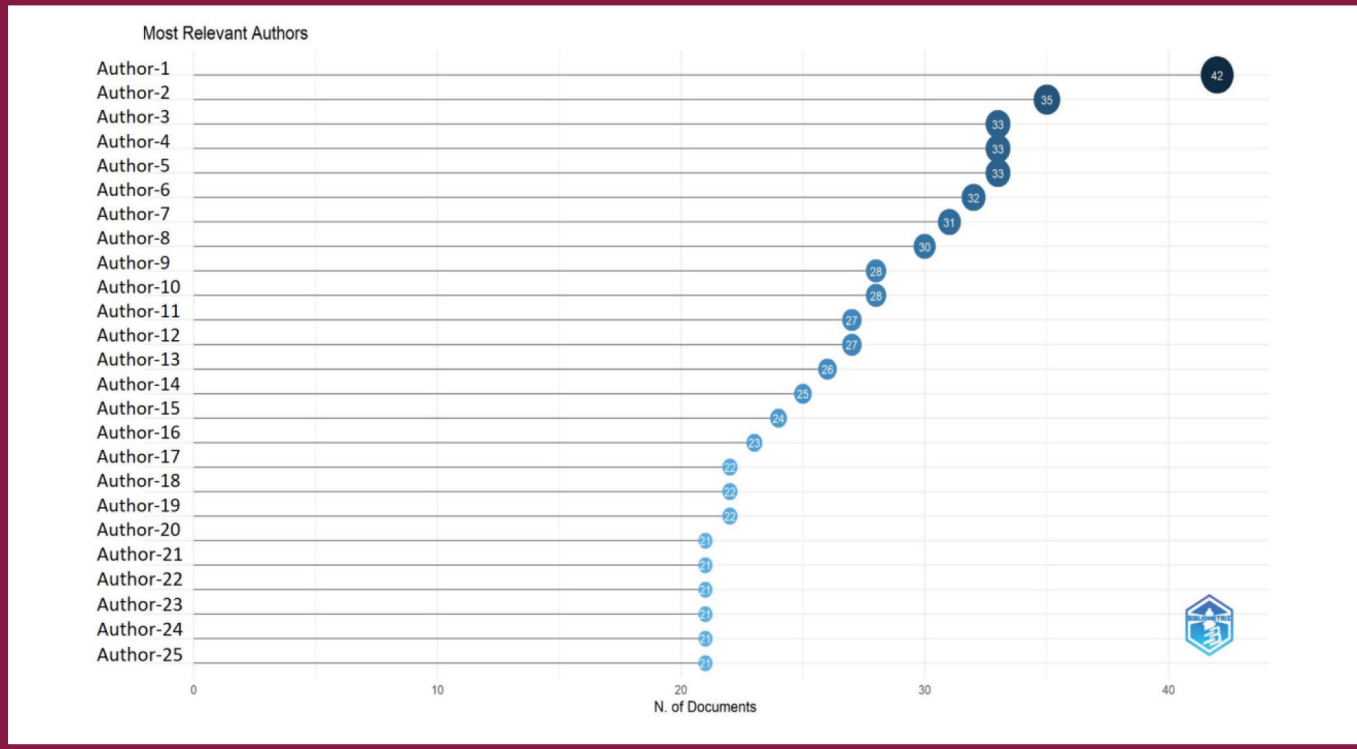

Figure 5. Most profilic authors

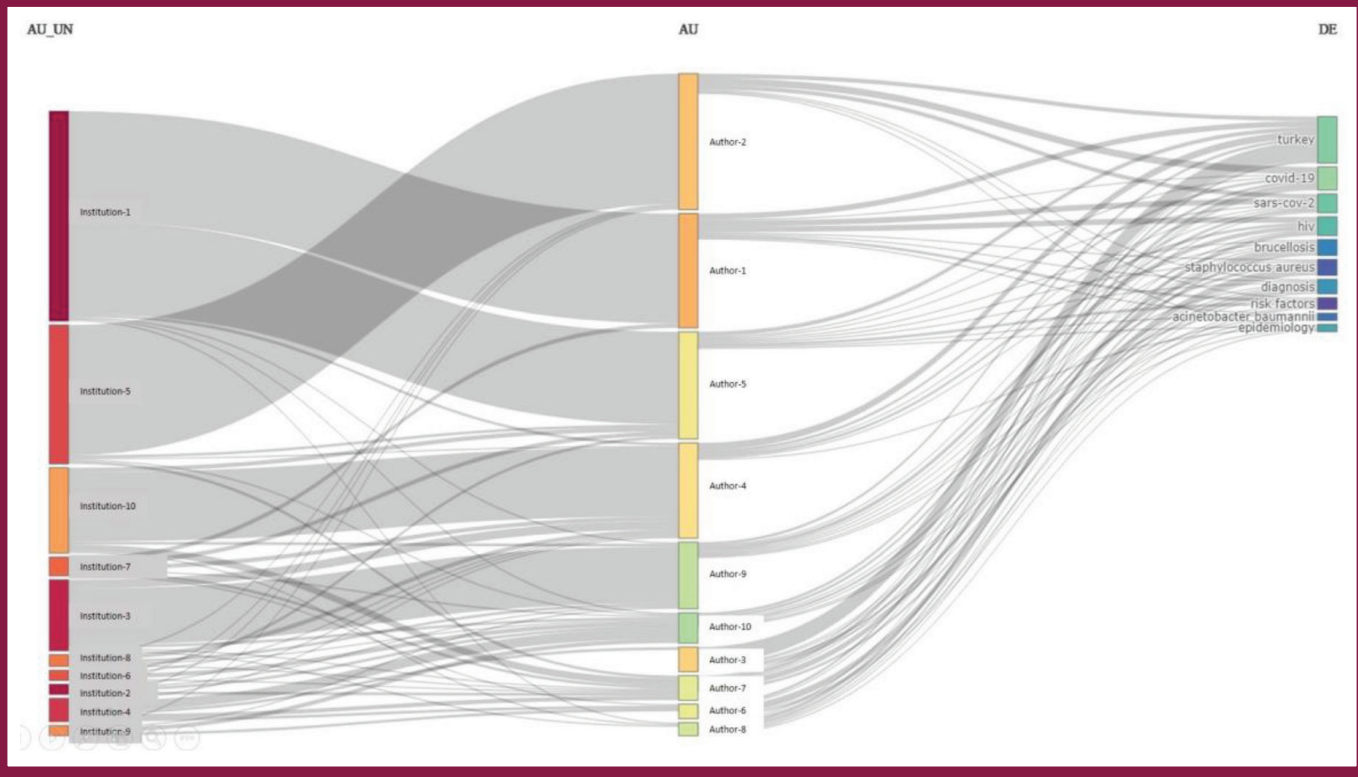

Figure 6. Three-field plot

peak occurrence, and most recent observation. Among these, "epidemiology," "diagnosis," and "infection" were the most frequently used keywords in 2020.

Institutional Research Collaborations and Citation Metrics

Table 5 provides an overview of inter-institutional research collaborations, including article counts, citation numbers, and collaboration strength. Among 1,361 institutions involved in collaborative efforts, 133 had published at least five articles.

Institution-3, Institution-1, and Institution-2 were the most prolific contributors, with 134, 132, and 130 publications, respectively. These institutions also recorded the highest total link strength: 14,303, 7,739, and 9,325, respectively. The table presents a detailed view of collaboration patterns among universities and research centers in Türkiye. The "Total Link Strength" column reflects the intensity of collaborative relationships between institutions.

Discussion

Figure 2 demonstrates the annual distribution of articles across the analyzed journals, with the majority of publications originating from Journal-1.

Several prior bibliometric studies have explored keyword distributions in the field of infectious diseases. For instance, Amusa et al. (11) conducted a bibliometric analysis on the epidemiology of infectious diseases, identifying 3,054 articles. The most productive sources in their study were the Journal of Medical Internet Research and PLOS One, each with an h-index of 18. In comparison, the most productive sources in the present analysis were Journal-1 (h-index=23) and Journal-2 (h-index=11). Additionally, a Web of Science-based analysis on "Big Data" within the field of "Infectious Diseases" revealed that Harvard Medical School was the top contributing institution, accounting for 7.9% of publications (137 articles). In Türkiye, Institution-1 emerged as the leading contributor with 283 articles (11).

The current study identified the most frequently cited national journals in the fields of clinical microbiology and infectious diseases. Journal-1, indexed since 2007, had received 5,641 citations, followed by Journal-2 (indexed since 2005) with 1,163 citations, and Journal-3 (indexed since 2017) with 363 citations. A comparative analysis by Yilmaz Hanci (12) of the 100 most cited articles in the Web of Science database (1975-2023) reported Clinical Infectious Diseases as the most cited journal globally, with 21,289 citations from a dataset of 552,828 publications.

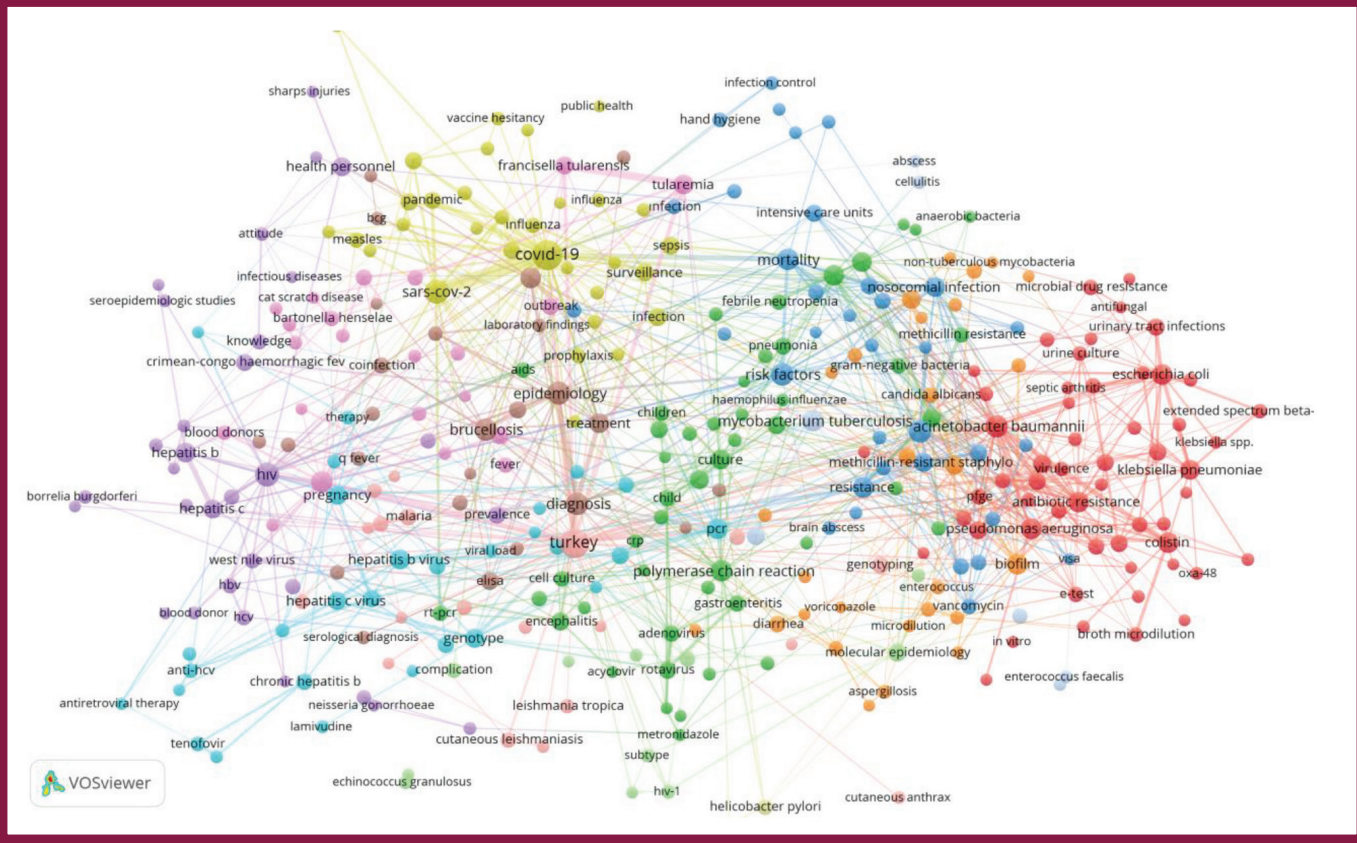

Figure 7a. Network vizualisation

The citation data in the current study reveals a high proportion of self-citations. A study by Diekhoff et al. (13) demonstrated that as the proportion of English-language articles increases in multilingual journals, self-citation rates decrease and impact factors improve. Authors are also more likely to cite their own work when writing in their native language, potentially explaining the high self-citation rates in Turkish-language publications. Similarly, Moskaleva and Akoev (14) reported that non-English publications indexed in Scopus and Web of Science are generally associated with lower visibility and citation counts compared to English-language articles, largely due to language barriers.

Self-citation is often used as a strategy to increase visibility and journal impact factor, particularly in national-language journals. This trend has also been associated with the limited citation pool available in such contexts (15,16).

As of 2022, Clinical Infectious Diseases had an h-index of 372, with 995 articles published in that year alone. Over the past three years, it recorded 4,107 citations and a total citation count of 29,673, with a two-year citation rate of 7.79 per article. In comparison, Journal-1 had an h-index of 24, 175 publications in 2023, 167 citations in the last three years, and a two-year citation rate of 0.96. Journal-2 followed, recording an h-index of 10, 44 publications in 2023, 55 citations in the past three years, and a two-year citation rate of 0.38 (17).

An examination of historical records showed that Journal-2 has been indexed since 2005 with 625 articles, and Journal-1 has been indexed since 2007. Journal-3 began indexing in 2017 with seven articles; Journal-4 in 2012 with nine articles; and Journal-5 in 2018 with 82 articles. Missing data from earlier years do not necessarily indicate a lack of publication activity, as such gaps may result from indexing errors or delays (Table 1). Citation counts across all journals peaked around 2015, followed by a significant decline, reflecting variations in article impact and citation models. These trends are consistent with the broader global pattern, where the volume of publications in infectious diseases and clinical microbiology increased rapidly until 2019-2020, after which a noticeable decline occurred (11,18,19).

Table 2 illustrates the countries of origin of the authors who contribute to the journals in question. These data demonstrate that the journals accept international articles and have a global reach and a collaborative network.

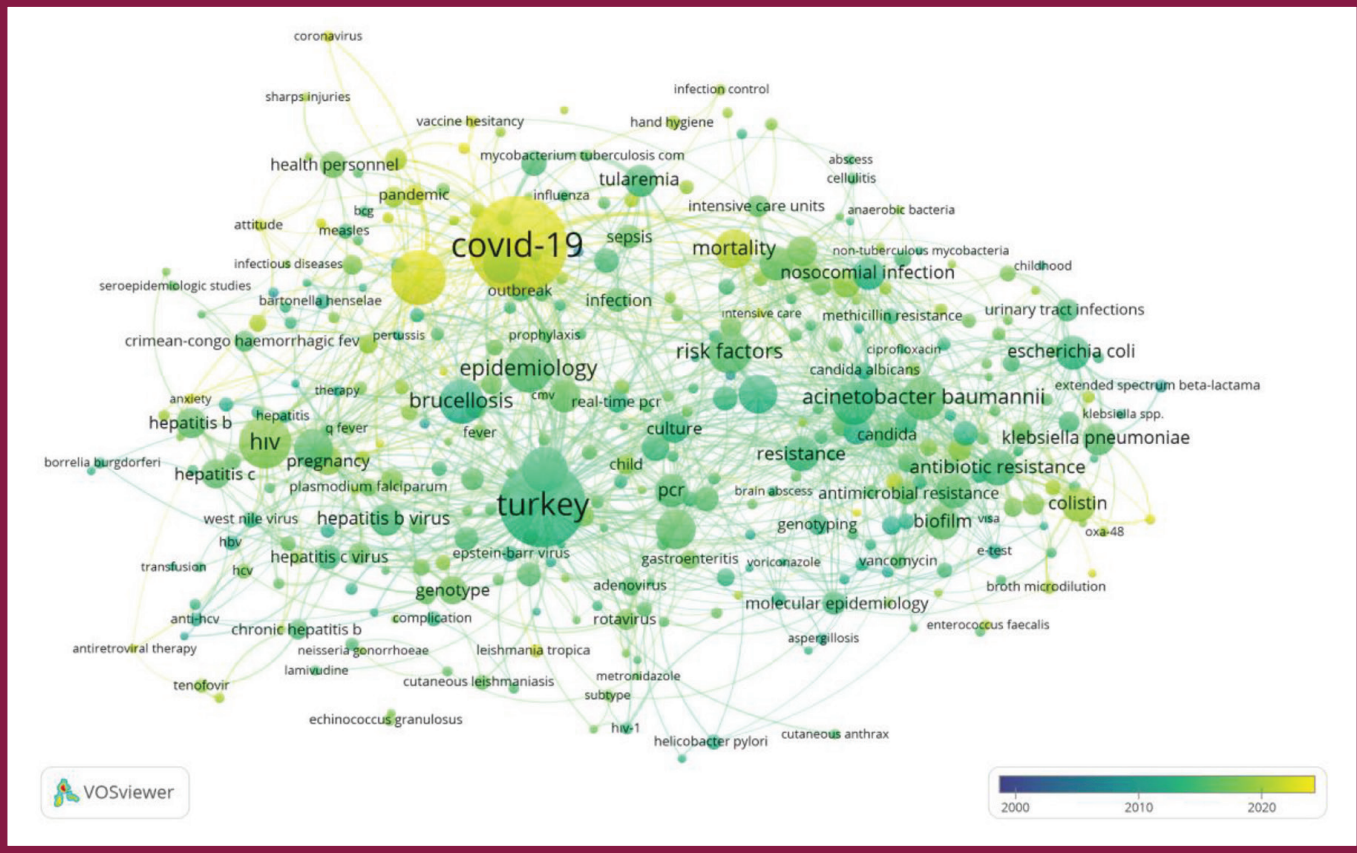

Figure 7b. Overlay vizualisation between 2000-2023

Table 2 shows the countries of origin of authors contributing to the analyzed journals. The inclusion of international articles suggests some degree of global engagement and collaboration. However, the overall level of international collaboration remains limited. This finding aligns with prior research indicating that scientific output in countries with constrained research funding tends to be nationally concentrated (20,21). Barriers such as language, limited access to international research networks, and insufficient funding mechanisms for joint projects likely contribute to this trend (22,23).

Moreover, although incentive programs such as those implemented by the Scientific and Technological Research Council of Türkiye (TÜBİTAK) and the Council of Higher Education (YÖK) in Türkiye aim to stimulate research productivity, they often fail to encourage international collaborations and may inadvertently disincentivize co-authorship with foreign researchers (24).

A key strength of this study lies in its comprehensive coverage of five nationally published journals over a defined timeframe. The integration of quantitative bibliometric methods—such as citation and co-authorship analysis—with interpretive comparisons allows for a multifaceted understanding of national trends in infectious diseases and clinical microbiology (2,25). Comparison with international benchmarks further contextualizes national publication dynamics.

However, several limitations should be acknowledged. First, the analysis is confined to journals indexed in Web of Science, which may exclude relevant literature published in other databases (26,27). Second, language and indexing biases may influence both visibility and citation patterns of Turkish-language publications (28). Third, while citation and co-authorship data provide valuable insights, they do not fully capture the scientific quality or societal impact of the research.

Future research could broaden the scope by incorporating additional national and international journals, including alternative metrics (altmetrics), and conducting comparative analyses with neighboring or economically similar countries (29,30). Qualitative methods, such as interviews with journal editors and researchers, may also yield deeper insights into publication practices, collaboration patterns, and perceived challenges (31).

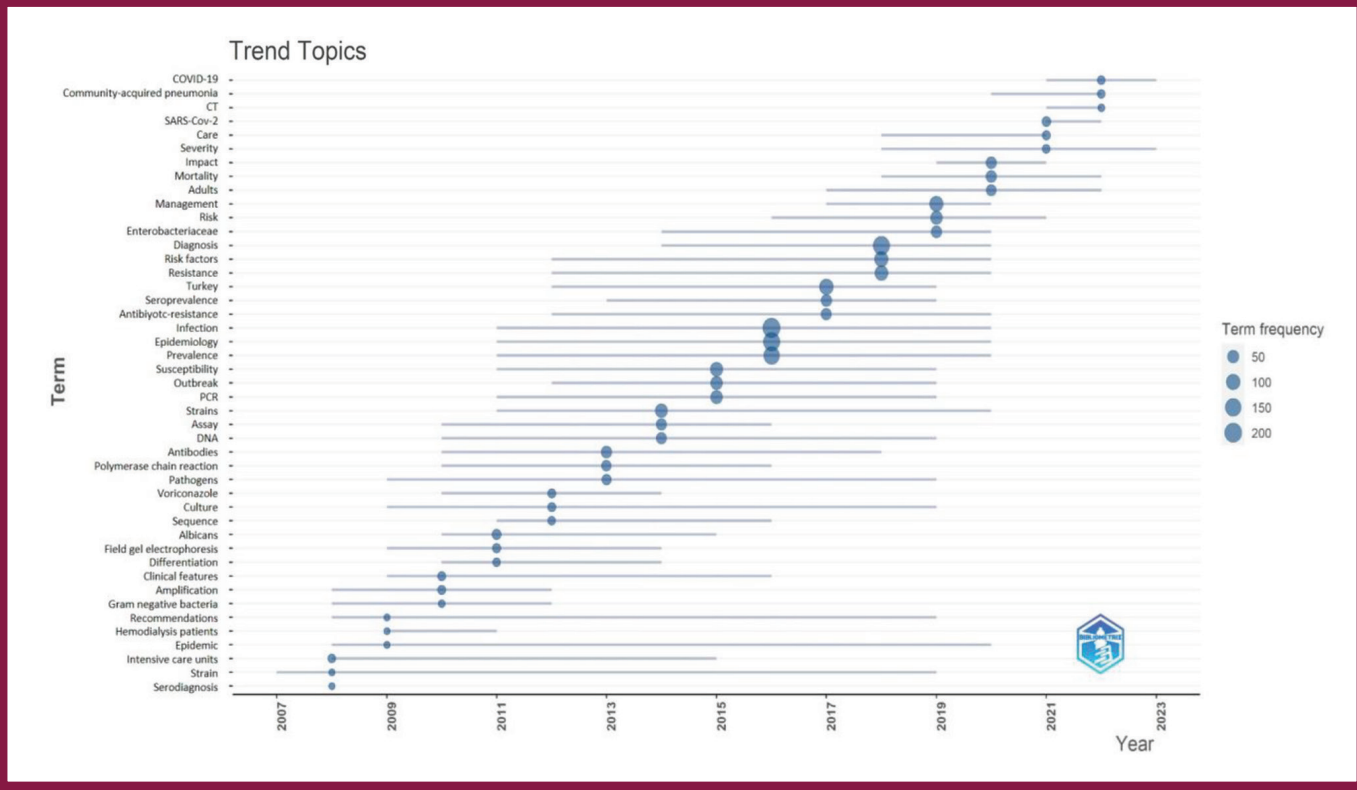

Figure 7c. Trend topics

Temporal trends in publication activity, as illustrated in Figure 4, reveal fluctuating levels of output across institutions, with some universities showing limited or no activity in certain years.

Keywords such as prevalence, epidemiology, and infections emphasize the importance of understanding the dynamics of disease emergence and spread. Terms such as management, risk factors, and resistance reflect a multidisciplinary approach that integrates clinical, epidemiological, and public health perspectives. The thematic diversity of keywords—e.g., children, antibiotic resistance, transmission—underscores the complex nature of research in this field (Table 3).

Between 2005 and 2023, the frequency of keywords such as infection, diagnosis, epidemiology, prevalence, risk factors, and resistance showed a steady increase, indicating heightened research interest in public health and infectious diseases. Infection remained the most frequently used term in 2023 (210 occurrences), followed by diagnosis and epidemiology (Table 4).

Trend topics visualized in Figure 7c reveal that terms such as epidemiology, diagnosis, and infection have consistently dominated discussions. The frequent appearance of the term Türkiye between 2012 and 2019 suggests a persistent national focus. Terms such as risk factors, management, and resistance peaked in 2020, while susceptibility was most frequent between 2011 and 2015. Terms like risk and strains showed consistent usage, with risk peaking in 2021. The terms 'PCR' and 'outbreak' reached their highest frequency of use in 2019.

The emergence of computed tomography as a keyword in 2021, and its increased frequency alongside COVID-19 and community-acquired pneumonia in 2022, point to the significant influence of the COVID-19 pandemic on research themes in infectious diseases and clinical microbiology.

Study Limitations

The study is subject to several limitations, including its reliance on data drawn exclusively from the Web of Science database, the imposition of language restrictions to English and Turkish, and the potential for bias resulting from the narrow scope of the citation analysis confined to this database. This may restrict the range of perspectives not fully reflect the entirety of the microbiological research landscape in Türkiye. Furthermore, the temporal scope of the study and the exclusion of articles published outside this

Table 4. Frequency of citation topics in the journals between 2005-2024

	n
Antibiotics & Antimicrobials	687
Virology - General	256
Medical Mycology	200
Hepatitis	198
Bacteriology	156
Zoonotic Diseases	125
Tuberculosis & Leprosy	122
HIV	107
Virology - Tropical Diseases	89
Virology - Identification & Sequencing	60
Diarrheal Diseases	54
Parasitology - Malaria, Toxoplasmosis & Coccidiosis	52
Parasitology - General	39
Sexually Transmitted Infections	34
Bacterial Toxins & Diseases	32
Parasitology - Trypanosoma & Leishmania	31
Lymphomas	24
Inflammatory Bowel Diseases & Infections	22
Oncology	22
Vascular, Cardiac & Thoracic Surgery	22
Bioengineering	15
Immunology	12
Gastrointestinal & Esophageal Diseases	11
Assisted Ventilation	11
Rheumatology	10
Vasculitis & Autoimmune Disorders	10
Allergy	9
Entomology	7
Statistical Methods	4
Dermatology- Skin Allergies	4
Ophthalmology	4
Liver Disease	3
Migraine and Headaches	3
Phytochemicals	3
Prostate Cancer	2
Strokes	2

period may not provide a comprehensive view of ongoing academic activities. The selected bibliometric indicators may not encompass all pertinent aspects, and alternative methodologies may contribute to a more comprehensive analysis.

Table 5. Research collaborations and publication citation numbers of institutions of top profilic institutions

Institutions	Number of documents	Number of citations	Total link strength
Institution-1	132	490	7739
Institution-2	130	567	9325
Institution-3	134	517	14303
Institution-4	117	396	9617
Institution-5	88	415	10382
Institution-6	77	306	7517
Institution-7	76	238	5900
Institution-8	67	258	4388
Institution-9	67	294	11200
Institution-10	65	263	3582
Institution-11	63	273	5359
Institution-12	54	222	3464
Institution-13	53	256	4596
Institution-14	51	126	3470
Institution-15	48	195	6772

The study has another limitation because it relies solely on Web of Science as a data source. This may limit the scope of the data set. It is possible that the exclusion of databases such as Scopus or PubMed may limit the generalisability of the findings.

It should be noted that our study analysed the data available in the Web of Science database from 2005. As some journals were first published after the study start date, the classification of the journals that contributed most to the study in terms of the number of articles could cause misunderstandings and errors in the reader's interpretation of this information.

The selected journals were from among infectious disease and/or microbiology specialty society journals available in Türkiye. Other journals were not considered for evaluation. The limited inclusion of only five journals restricts the generalizability and representativeness of the findings and may not fully reflect the scientific publishing landscape in Türkiye in this field.

Conclusion

This study provides a comprehensive comparative analysis of five national journals in the field of infectious diseases and clinical microbiology, focusing on their scientific contributions, authorship patterns, and citation impact. While microbiology-oriented topics such as serological diagnosis, bacterial strains, and outbreaks were more prominent in the early 2000s, there has been

a noticeable shift towards clinical topics in recent years. These include diagnosis and treatment methods, antibiotic resistance, disease management, and mortality. This thematic evolution reflects a growing clinical orientation in the field, in line with changing healthcare priorities. The selected journals have played a critical role in shaping the national research landscape by offering rich content and diverse perspectives, thereby enhancing our understanding of key subjects such as antibiotics, virology, and infectious diseases.

Ethics

Ethics Committee Approval: This study was carried out using an open-access database. Moreover, since it is a literature review that does not include any human or animal subjects, ethics committee approval was not required.

Informed Consent: Not required.

Footnotes

Authorship Contributions

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

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ORIGINAL ARTICLE

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Associations of Acute Phase Reactants with Disease Activity and Radiological Involvement in Pulmonary Tuberculosis

Akciğer Tüberkülozunda Akut Faz Reaktanlarının Hastalık Yaygınlığı ile İlişkisi

Esra Usta Bülbül[1], Murat Yalçınsoy[2], Pakize Sucu[3], Abdurrahman Yılmaz[4], Eylem Tunçay[4], Sinem Güngör[1], Esen Akkaya[1]

[1]*University of Health Sciences Türkiye, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Clinic of Pulmonary Disease, İstanbul, Türkiye*

[2]*İnönü University Faculty of Medicine, Department of Pulmonary Disease, Malatya, Türkiye*

[3]*Arnavutköy State Hospital, Clinic of Pulmonary Disease, İstanbul, Türkiye*

[4]*University of Health Sciences Türkiye, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, Clinic of Pulmonary Disease, İstanbul, Türkiye*

ABSTRACT

Background: Smear microscopy is widely used in diagnosing tuberculosis (TB), but its sensitivity may be limited in cases with low bacillary load or extrapulmonary involvement. This has led to growing interest in laboratory biomarkers that reflect disease activity. The immune response to *Mycobacterium tuberculosis* stimulates the release of inflammatory cytokines, triggering an acute-phase reaction. This study aimed to evaluate the associations of acute-phase reactants-including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and mean platelet volume (MPV)-with bacillary load, radiological involvement, and hospital stay in pulmonary TB patients.

Materials and Methods: This retrospective study included 137 patients diagnosed with pulmonary TB. They were grouped as smear-positive or smear-negative, and culture-positive. Data on demographics, laboratory results (CRP, ESR, MPV), chest radiography, bacillary load, culture results, and length of hospital stay were analyzed. Radiological involvement was categorized as minimal, moderate, or extensive

Results: The cohort was 69% male with a median age of 42 years. Smear positivity was found in 71% and culture positivity in 74% of cases. Radiological assessments showed minimal (47%), moderate (41%), and extensive (12%) involvement. CRP levels were significantly higher in smear-positive patients ($p<0.001$) and increased with more extensive radiological involvement ($p=0.02$). These patients also had longer hospital stays ($p=0.001$). No significant associations were found between MPV or ESR and bacillary load or radiological extent ($p>0.05$).

Conclusion: CRP is a sensitive marker of inflammatory activity in pulmonary TB, correlating with both bacillary burden and radiological spread. It may be useful for evaluating disease severity and treatment response. MPV and ESR, however, appear to have limited clinical relevance in this context.

Keywords: C-reactive protein, erythrocyte sedimentation rate, pulmonary tuberculosis, mean platelet volume, inflammation

ÖZ

Amaç: Tüberküloz (TB) tanısında kullanılan yayma mikroskopisi, basil yoğunluğunun düşük olduğu veya ekstrapulmoner tutulumun bulunduğu olgularda yetersiz kalabilmektedir. Bu nedenle hastalık aktivitesini değerlendirmeye yönelik laboratuvar belirteçlerine olan ilgi artmıştır. Bu çalışmada, akciğer TB'li hastalarda akut faz reaktanlarından C-reaktif protein (CRP), eritrosit sedimantasyon hızı (ESH) ve ortalama trombosit hacmi (MPV) düzeylerinin; basil yoğunluğu, radyolojik tutulum ve hastanede yatış süresi ile olan ilişkileri araştırılmıştır.

Gereç ve Yöntemler: Retrospektif olarak tasarlanan bu çalışmaya, akciğer TB'si tanısı almış 137 hasta dahil edilmiştir. Olgular yayma pozitif (ARB pozitif) ve yayma negatif-kültür pozitif olmak üzere iki gruba ayrılmıştır. CRP, ESH, MPV düzeyleri, radyolojik tutulum (minimal, orta, ileri), basil yoğunluğu ve hastanede yatış süreleri değerlendirilmiştir.

Address for Correspondence: Esra Usta Bülbül, University of Health Sciences Türkiye, Süreyyapaşa Chest Diseases and Thoracic Surgery Training and Research Hospital, Clinic of Pulmonary Disease, İstanbul, Türkiye

E-mail: esraustabulbul@hotmail.com **ORCID ID:** orcid.org/0000-0002-4356-715X

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ÖZ

Bulgular: Katılımcıların %69'u erkek, yaş ortancası 42 (25-56) yıldır. Yayma pozitiflik oranı %71, kültür pozitiflik oranı %74 olarak bulunmuştur. Radyolojik olarak %47 minimal, %41 orta, %12 ileri düzey tutulum mevcuttur. Yayma pozitif hastalarda CRP düzeyleri anlamlı şekilde daha yüksektir (p<0,001) ve bu hastalarda hastanede yatış süresi de daha uzundur (p=0,001). Radyolojik tutulum arttıkça CRP düzeylerinde de anlamlı artış saptanmıştır (p=0,02). MPV ve ESH düzeyleri ile basil yoğunluğu veya radyolojik tutulum arasında anlamlı ilişki gözlenmemiştir.

Sonuç: CRP düzeyi, TB hastalarında hastalık yaygınlığını ve enflamatuvar aktiviteyi yansıtan duyarlı bir biyobelirteç olarak öne çıkmaktadır. Buna karşılık MPV ve ESH'nin sınırlı prediktif değeri olduğu görülmüştür.

Anahtar Kelimeler: C-reaktif protein, eritrosit sedimantasyon hızı, akciğer tüberkülozu, ortalama trombosit hacmi, enflamasyon

Introduction

Tuberculosis (TB), caused by *Mycobacterium tuberculosis*, remains a significant global public health concern, particularly in developing countries. Early diagnosis and effective monitoring are crucial for controlling the disease and improving patient outcomes. Acute phase reactants (APRs) such as C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and mean platelet volume (MPV), a hematological parameter, have been investigated as potential biomarkers for the diagnosis and prognosis of TB (1-3).

CRP is an acute phase protein whose levels increase in response to various inflammatory conditions. Previous studies have demonstrated significantly elevated CRP levels in patients with active pulmonary TB compared to healthy individuals. Furthermore, CRP levels have been shown to correlate with disease severity and radiological involvement, suggesting that CRP may serve as a valuable marker for evaluating TB activity and monitoring treatment response (1,4). Similarly, elevated ESR levels have been observed in patients with active pulmonary TB, with significant correlation to radiological extent. Therefore, ESR may also be considered an indicator of disease severity and a useful parameter for assessing treatment efficacy (1).

MPV reflects the average size of platelets and is considered a marker of platelet activation and production rate. Although inflammatory states may influence MPV levels, findings on its association with TB are inconsistent. Some studies have reported decreased MPV levels in active TB, suggesting a reduction during systemic inflammation, while others have found no significant difference between TB patients and healthy controls (5). These discrepancies may be attributed to differences in study populations, disease severity, and methodological variations.

Evaluating APRs such as CRP, ESR, and MPV in TB patients has important clinical implications. Increases in CRP and ESR may support early detection of active TB, especially in cases with non-specific or absent clinical symptoms. Moreover, monitoring these biomarkers during treatment can provide insight into disease progression and therapeutic response. A decrease in CRP and ESR levels may indicate effective treatment and disease regression, whereas persistently elevated levels may suggest treatment failure or the presence of complications (5,6).

In this study, we aimed to investigate the relationship between the APRs CRP, ESR, and MPV and radiological involvement, bacillary load, and length of hospital stay in patients with pulmonary TB.

Materials and Methods

This retrospective cohort study included 137 patients diagnosed with pulmonary TB who received inpatient treatment in the TB ward. Patients were classified into two groups: smear-positive (Group 1) and smear-negative but culture-positive (Group 2). Patients with chronic obstructive pulmonary disease, asthma, bronchiectasis, human immunodeficiency virus (HIV) infection, or other inflammatory conditions (e.g., connective tissue diseases, inflammatory bowel diseases, acute or chronic infections, endocrinological, hematological, hepatic, or renal disorders, peripheral vascular disease, hypertension, or diabetes mellitus) were excluded, as these conditions could potentially influence MPV. In addition, patients who had returned from treatment failure; had interrupted and later resumed treatment, were referred from other centers; had chronic forms of the disease; had received anti-TB treatment for more than one week; or had missing data for complete blood count, CRP, ESR, sputum and culture results, or chest radiography, were also excluded from the study.

Data were obtained by reviewing electronic medical records and patient files. Patients were included if they were either smear-positive for acid-fast bacilli (AFB) or smear-negative but culture-positive, and had received anti-TB treatment. Demographic data (age and sex), laboratory parameters (complete blood count, ESR), chest X-ray findings, bacteriological test results, and duration of hospitalization were recorded. All laboratory parameters, including complete blood count, CRP, ESR, and MPV, were measured at baseline, prior to the initiation of anti-TB

therapy, to ensure that the recorded values reflected the patients' pretreatment status without the influence of anti-TB medications. Smear-positive patients were compared with those diagnosed based on culture positivity, despite a negative smear.

Chest Radiograph Assessment

Chest X-rays were classified as minimal, moderate, or advanced involvement based on radiological scoring (7).

- Minimal lesions included non-cavitated, mildly to moderately dense lesions, limited to one lung or both lungs but not exceeding one lung volume, and not extending beyond the second chondrosternal junction and the level of the fourth or fifth thoracic vertebra.
- Moderate lesions could be unilateral or bilateral, involving an entire lung with mild-to-moderate density or bilateral involvement of similar volume. If cavitation had been present, its diameter did not exceed 4 cm.
- Advanced lesions indicated more extensive and confluent involvement beyond the criteria for moderate lesions.

Additionally, radiological findings such as infiltration, consolidation, cavitation, nodules, lymphadenopathy, and pleural effusion were recorded.

Bacteriological Examination

Sputum samples were examined using the Ziehl-Neelsen staining method for direct smear microscopy and reported as AFB positive or negative. Smear results were semi-quantitatively graded based on bacillary count:

- Negative: No bacilli in 300 fields
- +: 1-9 bacilli in 100 fields
- ++: 1-9 bacilli in 10 fields
- +++: 1-9 bacilli in 1 field
- ++++: ⩾10 bacilli in 1 field (8)

Sputum samples were also cultured and reported as either positive or negative.

CRP levels were measured nephelometrically using CardioPhase hsCRP (Siemens Healthcare Diagnostics Inc., Newark, DE, USA) on a Siemens BN II analyzer. The reference range was 0-5 mg/L, and the threshold for bacterial infections was 40 mg/L. Complete blood counts were analyzed using a Beckman Coulter analyzer (Tokyo, Japan), and ESR was measured using the Alifax analyzer (Italy).

The study was approved by the University of Health Sciences Türkiye, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, Scientific Research Ethics Committee (approval number: 2024/397, dated: 26.12.2024), in accordance with the principles of the Declaration of Helsinki. As this was a retrospective study, informed consent was not obtained; however, patient confidentiality was strictly maintained.

Statistical Analysis

Statistical analyses were performed using SPSS version 24. The distribution of variables was assessed using analytical methods (Kolmogorov-Smirnov and Shapiro-Wilk tests). Non-normally distributed variables were expressed as medians and interquartile ranges (IQRs). Since the duration of hospitalization and biochemical parameters did not follow a normal distribution, they were compared between groups using the Kruskal-Wallis test, and pairwise comparisons were conducted with the Mann-Whitney U test, applying Bonferroni correction. Spearman correlation coefficients were used to assess relationships between pairs of variables where at least one variable was non-normally distributed or ordinal. A p-value of less than 0.05 was considered statistically significant.

Results

A total of 137 patients diagnosed with TB were included in the study. Among them, 69% were male, and the median age was 42 years. The proportion of patients with a history of smoking was 54%. The median length of hospital stay was 23 days (IQR: 8-30).

AFB smear positivity was observed in 71% of patients, and culture positivity was observed in 74%. Based on chest radiograph scoring, 47% of the patients had minimal, 41% moderate, and 12% advanced pulmonary involvement. The most common radiographic findings were infiltration (44%), cavitation (24%), and pleural effusion (21%). Demographic and clinical characteristics of the study population are summarized in Table 1.

Age, sex distribution, and smoking status were similar between smear-positive and culture-positive groups ($p>0.05$ for all comparisons; $p=0.81$ for smoking). The median length of hospital stay was significantly longer in the smear-positive group (21 days, IQR: 12-33) compared to the culture-positive group (10 days, IQR: 5-19) ($p=0.001$).

Leukocyte count, platelet count, MPV, and ESR levels were also similar between the two groups ($p=0.25$, $p=0.91$, $p=0.34$, and $p=0.06$, respectively). In contrast, CRP levels were significantly higher in smear-positive patients [median: 50 mg/L (IQR: 24-89)] than in culture-positive patients [median: 16 mg/L (IQR: 5-52)] ($p<0.001$) (Table 2).

Acute Phase Reactants According to Radiological Involvement

CRP levels were significantly higher in patients with moderate and advanced radiological involvement

Table 1. Demographic and clinical characteristics of the cases (n=137)

Case group, n (%) AFB positive Culture positive	 97 (71) 40 (29)
Sex, male, n (%)	94 (69)
Age, years, median (25-75)	42 (25-56)
Smoking status, n (%) Non-smoker Smoker	 63 (46) 74 (54)
Length of stay, days, median (25-75)	23 (8-30)
Chest X-ray score, n (%) Minimal Moderate Advanced	 64 (47) 56 (41) 17 (12)
Chest X-ray lesion, n (%) Infiltration Consolidation Cavity Nodule Lymphadenopathy Pleural effusion	 60 (44) 6 (4) 33 (24) 5 (4) 4 (3) 29 (21)
AFB, n (%) Negative + ++ +++ ++++	 73 (53) 38 (28) 12 (9) 8 (6) 6 (4)
Culture, n (%) Negative Positive	 36 (26) 101 (74)
Resistance, n (%) None H E S H + S H + R + S H + Z + S	 126 (92) 3 (2.2) 1 (0.7) 2 (1.5) 2 (1.5) 2 (1.5) 1 (0.7)

AFB: Acid-fast bacilli, H: Isoniazid, E: Ethambutol, S: Streptomycin, R: Rifampicin, Z: Pyrazinamide

Table 2. Comparison of clinical and laboratory parameters in accordance to AFB and culture positivity

	AFB positive, n=97	Culture positive, n=40	p-value
Sex, male, n (%)	**67 (71)**	**27 (29)**	**0.85**
Age, years, median (25-75)	40 (24-61)	36 (26-54)	0.82
Smoking status, n (%) Non-smoker Smoker	 44 (70) 53 (72)	 19 (30) 21 (28)	0.81
Length of stay, age, median (25-75)	21 (12-33)	10 (5-19)	**0.001**
Chest X-ray score, n (%) Minimal Moderate Advanced	 44 (69) 40 (71) 13 (76)	 20 (31) 16 (29) 4 (24)	0.81
Chest X-ray lesion, n (%) Infiltration Consolidation Cavity Nodule Lymphadenopathy Pleural effusion	 38 (63) 5 (83) 27 (82) 2 (40) 2 (50) 23 (79)	 22 (37) 1 (17) 6 (18) 3 (60) 2 (50) 6 (21)	0.14
Leukocyte, median (25-75)	8.420 (7.000-11.000)	7.680 (6.500-9.900)	0.25
Platelet, median (25-75)	306 (240-384)	287 (240-385)	0.91
MPV, mean ± SD	8.1±0.9	8.2±0.9	0.34
ESR, median (25-75)	80 (50-105)	50 (30-110)	0.06
CRP, median (25-75)	50 (24-89)	16 (5-52)	**<0.001**

AFB: Acid-fast bacilli, MPV: Mean platelet volume, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, SD: Standard deviation

compared to those with minimal findings (p=0.02 for both comparisons). MPV and ESR levels were similar across all radiological groups (p>0.05) (Table 3).

Discussion

TB is a disease that requires both clinical and laboratory-supported evaluations throughout the diagnostic and therapeutic process. In recent years, the role of APRs in assessing the presence and extent of active disease has been increasingly explored. In our study, higher CRP levels were observed in patients with positive smears and greater radiological involvement, reflecting increased inflammatory activity. Likewise, CRP levels showed a stepwise increase in accordance with the progression of radiological severity from minimal to advanced disease.

The observed parallel between increased radiological extent and elevated CRP levels supports the potential role of CRP as an indirect marker of disease activity. Kagujje et al. (4) similarly reported that CRP demonstrated high sensitivity in TB diagnosis and had 100% negative predictive value for ruling out active TB among HIV-positive individuals with CD4 counts ⩾350.

Regarding MPV levels, no significant differences were observed across groups in terms of radiological extent or bacillary burden. This is consistent with previous reports suggesting that MPV has limited value as a negative APR in TB. For example, Gunluoglu et al. (6) concluded that MPV is not a reliable marker of inflammation in active pulmonary TB and does not reflect disease severity. Similarly, Yildiz et al. (9) emphasized the limited utility of MPV as a marker of inflammatory activity in *Mycobacterium tuberculosis*

Table 3. Relationship between chest X-ray severity and CRP, MPV, ESR

	Minimal, n=64	Moderate, n=56	Advanced, n=17	Minimal-moderate, p	Minimal-advanced, p	Moderate-advanced, p
CRP, mg/L, median (25-75)	14 (7-52)	48 (22-79)	54 (35-82)	0.02	0.02	0.43
MPV, fl, median (25-75)	7.95 (7.6-8.7)	7.8 (7.6-7.9)	7.9 (7.6-7.9)	0.32	0.38	0.50
ESR, mm/s, median (25-75)	80 (30-120)	75 (50-110)	90 (40-125)	0.88	0.90	0.90

Comparisons were performed using the Kruskal-Wallis test and Bonferroni-adjusted Mann-Whitney U tests for pairwise comparisons. CRP: C-reactive protein, ESR: Erythrocyte sedimentation rate, MPV: Mean platelet volume

infection. These findings collectively suggest that MPV may not be suitable as a standalone marker for diagnosis or assessment of disease activity in chronic infections such as TB. Gunluoglu et al. (6) reported that although MPV levels were lower in TB patients than in healthy controls, the difference was limited, and MPV did not correlate with disease extent. Additionally, no significant correlations were observed between MPV and inflammatory markers such as CRP or ESR in their study. These findings are in line with our results, indicating that MPV does not serve as a determinant of TB activity.

Although ESR levels were higher in smear-positive patients (80 mm/h vs. 50 mm/h), the difference did not reach statistical significance (p=0.06). This may be attributed to the non-specific nature of ESR and its susceptibility to various confounding factors. Nevertheless, the trend toward increased ESR in patients with advanced lesions suggests that it may still have clinical relevance during follow-up.

No significant relationship was found between hospitalization duration and APRs. This supports the notion that length of hospital stay is influenced not only by clinical severity but also by various factors such as socioeconomic status, access to healthcare, and comorbidities. In addition, our analysis focused on hospitalization length rather than the total duration of anti-TB therapy. The study was not designed to assess treatment completion time beyond discharge. Further studies specifically addressing this issue are warranted to clarify whether elevated baseline CRP levels are associated with prolonged treatment courses in pulmonary TB.

A significant increase in CRP levels was observed with increasing radiological involvement. While CRP levels were notably lower in patients with minimal disease, they were significantly higher in those with moderate or advanced disease. This finding further supports the role of CRP as a surrogate indicator of inflammatory activity and, by extension, disease burden. Radiological involvement in our study was classified according to the system proposed by Falk et al. (7), which divides pulmonary TB into minimal, moderate, and advanced disease. This classification has long been used in clinical practice and research, providing consistency and comparability with earlier studies. However, more contemporary scoring systems have been proposed in recent years, which allow a more quantitative and detailed assessment of pulmonary involvement (7,8). While we used the Falk classification to maintain methodological consistency, future studies may benefit from incorporating these newer approaches to further refine radiological evaluation in TB.

In contrast, MPV and ESR levels did not differ significantly across radiological subgroups. This aligns with previous findings highlighting the limited ability of MPV to reflect inflammatory status in TB (10,11). The lack of association between ESR and radiological extent may be explained by its non-specific nature and its susceptibility to systemic and chronic influences. Although several studies have reported elevated ESR values in TB patients; one study found high ESR levels in 98% of TB cases (12)-its non-specific profile limits its utility as a sole indicator of disease extent.

Overall, our findings suggest that among the evaluated APRs, CRP stands out as the most informative and reliable biomarker in pulmonary TB. Its association with both bacillary burden and radiological extent highlights its potential role not only in reflecting inflammatory activity but also in evaluating disease progression and treatment response. In contrast, MPV and ESR appeared to have limited value in this setting, showing no clear relationship with disease severity or extent. Therefore, CRP may be considered a useful tool for monitoring inflammatory status and guiding clinical follow-up in patients with pulmonary TB.

Conclusion

In conclusion, CRP was the only APR that consistently reflected disease severity in pulmonary TB, showing clear associations with both bacillary burden and radiological extent. MPV and ESR did not demonstrate meaningful

clinical value. Overall, CRP appears to be the most useful biomarker for assessing inflammation and supporting clinical follow-up in pulmonary TB.

Ethics

Ethics Committee Approval: The study was approved by the University of Health Sciences Türkiye, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, Scientific Research Ethics Committee (approval number: 2024/397, dated: 26.12.2024), in accordance with the principles of the Declaration of Helsinki.

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

Concept: E.U.B., M.Y., E.A., Design: E.U.B., M.Y., E.T., E.A., Data Collection or Processing: E.U.B., P.S., S.G., Analysis or Interpretation: E.U.B., M.Y., Literature Search: E.U.B., P.S., A.Y., S.G., Writing: E.U.B., M.Y., E.T., S.G., E.A.

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The Value of Systemic Inflammation Indices in Predicting Survival in Critical Flame Burn Patients: A Single-Center Retrospective Analysis

Sistemik İnflamasyon İndekslerinin Kritik Alev Yanığı Hastalarında Sağkalımı Öngörmedeki Değeri: Tek Merkezli Retrospektif Bir Analiz

Feyyaz Güngör[1], Hüseyin Kılavuz[1], Oğuzhan Aytepe[1], Mehmet Kuluş[1], Ceren Gökduman[2], Mustafa Turan[1]

[1]*University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of General Surgery, İstanbul, Türkiye*

[2]*University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of Anesthesia and Intensive Care, İstanbul, Türkiye*

ABSTRACT

Background: Burns are an important health problem that causes serious morbidity and mortality all over the world. Mortality in patients with critical burns is related to factors such as age, inhalation injury, and total burn surface area (TBSA). In recent years, it has been suggested that systemic inflammation indices may also be related to prognosis. In this study, we aimed to evaluate the potential prognostic value of systemic inflammation indices in predicting in-hospital mortality in patients with critical flame burns.

Materials and Methods: This retrospective study included 53 patients who were followed up in the burn intensive care unit at our center due to flame burns between January 1, 2024, and January 1, 2025. Patients' demographic data, burn etiology, inhalation injury, TBSA, revised Baux score, intubation status, operative debridement details, and systemic inflammation indices on the first, third, and fifth days of admission were analyzed. Patients were compared either as survivors or non-survivors. The Mann-Whitney U test was used for continuous variables, and the Pearson chi-square test was used for categorical variables.

Results: Mortality developed in 6 patients (11.3%). In the non-survivor group, inhalation injury (p=0.038), TBSA (p<0.001), and Baux score (p<0.001) were significantly higher. There were no differences between groups in the indices on the first day. However, on the third day, the lymphocyte/monocyte ratio (LMR) was lower and the systemic inflammation response index (SIRI) was higher in those who did not survive (p=0.018; p=0.002). Similar results were obtained on the fifth day (both p<0.001).

Conclusion: In our study, high LMR and low SIRI values on the third and fifth day were found to be associated with better survival. Prospective and multicenter studies with larger sample sizes are needed to confirm these results.

Keywords: Flame burn, survival, systemic inflammation, PLR, LMR, NLR, SII, SIRI

ÖZ

Amaç: Yanıklar, tüm dünyada ciddi morbidite ve mortaliteye yol açan önemli bir sağlık sorunudur. Kritik yanığı olan hastalarda mortalite; yaş, inhalasyon hasarı ve toplam yanık yüzey alanı (TYYA) gibi faktörlerle ilişkilidir. Son yıllarda, sistemik enflamasyon indekslerinin de prognozla ilişkili olabileceği öne sürülmüştür. Bu çalışmada, kritik alev yanığı olan hastalarda sistemik enflamasyon indekslerinin hastane içi mortaliteyi öngörmedeki potansiyel prognostik değerini değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Bu retrospektif çalışmaya, 1 Ocak 2024-1 Ocak 2025 tarihleri arasında merkezimizde alev yanığı nedeniyle yanık yoğun bakımda izlenen 53 hasta dahil edildi. Hastaların demografik verileri, yanık etyolojisi, inhalasyon hasarı, TYYA, revize Baux skoru, entübasyon durumu, operasyonel debridman ayrıntıları ve başvurunun birinci, üçüncü ve beşinci günlerindeki sistemik enflamasyon indeksleri analiz edildi. Hastalar sağ kalanlar ve sağ kalamayanlar olarak karşılaştırıldı. Sürekli değişkenler için Mann-Whitney U, kategorik değişkenler için Pearson ki-kare testi kullanıldı.

Address for Correspondence: Feyyaz Güngör, University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital, Clinic of General Surgery, İstanbul, Türkiye
E-mail: feyyaz.gngr@gmail.com **ORCID ID:** orcid.org/0000-0002-4066-6072

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ÖZ

Bulgular: Hastaların 6'sında (%11,3) mortalite gelişti. Sağ kalmayan grupta inhalasyon hasarı (p=0,038), TYYA (p<0,001) ve Baux skoru (p<0,001) anlamlı olarak daha yüksekti. İlk gün indekslerde gruplar arasında fark yoktu. Ancak üçüncü günde sağ kalmayanlarda lenfosit/monosit oranı (LMO) daha düşük, sistemik enflamasyon yanıt indeksi (SİYİ) daha yüksek bulundu (p=0,018; p=0,002). Beşinci günde de benzer sonuçlar elde edildi (her ikisi p<0,001).

Sonuç: Çalışmamızda, üçüncü ve beşinci günlerde yüksek LMO ve düşük SİYİ değerlerinin daha iyi sağkalım ile ilişkili olduğu tespit edilmiştir. Sonuçların doğrulanabilmesi için daha geniş örneklemlerle, prospektif ve çok merkezli çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Alev yanığı, sağkalım, sistemik enflamasyon, TLO, LMO, NLO, Sİİ, SİYİ

Introduction

Burns are a global health problem that affects approximately 11 million people each year and causes significant morbidity and mortality (1-3). The World Health Organization reports that burns are a leading cause of death, especially in low- and middle-income countries (4). Although mortality rates from flame burns vary by country income level, the rate reported in the United States is 5.52% (5). Mortality in critically burned patients can reach rates as high as 20% to 50%, depending on factors such as burn depth, patient age, and inhalation injury (6,7).

Accurately identifying risk factors associated with mortality is crucial for optimizing clinical management and enhancing patient outcomes. Traditional prognostic parameters, such as total body surface area affected (TBSA), age, and inhalation injury, have been extensively investigated for many years and remain among the primary determinants in clinical decision-making processes (8,9). However, considering the complex pathophysiologic processes and poor prognosis in burn patients, it is important to evaluate new biomarkers reflecting the systemic inflammatory response, not limited to traditional parameters (10,11). In recent years, the literature has focused on inflammation-based systemic indices that provide simple, rapid, and objective measurements with high practical applicability in this field (10,11). The potential value of these biomarkers in predicting survival in burn patients holds promise for making clinical management more personalized and effective.

This study aims to analyze the prognostic value of systemic inflammation indices in predicting survival in patients, followed up in the burn intensive care unit (BICU) due to critical flame burns, based on current literature.

Materials and Methods

This retrospective study included patients with flame burns who were admitted to the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital BICU between January 1, 2024, and January 1, 2025.

Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Scientific Research Ethics Committee No. 2 (approval number: 2025-60, dated: 28.02.2025). The study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki.

Inclusion criteria for the study:

- Patients being followed in the BICU due to flame burns
- Patients whose data were fully accessible from the hospital database or clinical records

Exclusion criteria for the study:

- Patients hospitalized to the BICU other than flame burns
- Patients with major trauma in addition to their burns
- Patients with combined burns

Two hundred thirty-one patients were followed in the BICU during the study period, and 53 patients who met the specified criteria were included in the study. Demographic characteristics, fire classes, inhalation injury, TBSA, burn depth, revised Baux score, timing of admission to the hospital, blood parameters on the 1st, 3rd, and 5th days of admission, systemic inflammation indices, intubation status, intubation duration, details of operative debridement performed, and survival of the patients included in the study were analyzed. Patients were divided into two groups according to in-hospital survival status, and analyses were performed between these two groups.

Systemic inflammation indices were calculated as follows:

Platelet/lymphocyte ratio (PLR): Platelet count (109/L)/ lymphocyte count (109/L)

Lymphocyte/monocyte ratio (LMR): Lymphocyte count (109/L)/monocyte count (109/L)

Neutrophil/lymphocyte ratio (NLR): Neutrophil count (109/L)/lymphocyte count (109/L)

Systemic immune-inflammatory index (SII): Neutrophil count (109/L) x platelet count (109/L)/lymphocyte count (109/L)

Systemic immune reflex index (SIRI): Neutrophil count (109/L) x monocyte count (109/L)/lymphocyte count (109/L)

TBSA was calculated by a burn-experienced surgical team using a combination of the "rule of nine" and Lund and Browder's chart (12). Burn depth was evaluated clinically. The revised Baux score was calculated for each patient using the following formula:

Revised Baux score = age (years) + TBSA (%) + 17 (if suffering from inhalation injury)

Inhalation injury was defined by the specialist physician based on clinical evaluation and bronchoscopic findings. Fire types are categorized into three groups: liquid-sourced, gas-sourced, and others.

Patient Management

After the initial evaluation, all patients underwent wound cleansing, and dressings were changed daily. In the initial assessment, a paraffin wound dressing containing 0.5% chlorhexidine and an appropriate antibiotic cream were used as wound dressings.

Tetanus prophylaxis was administered to all patients, and pain control was achieved with appropriate analgesic treatment. Patients were dynamically evaluated for compartment syndrome and operative debridement, and treatment algorithms were individualized on an individual basis. The decision regarding intubation of patients was based on American Burn Association criteria (13). All patients received low molecular weight heparin, antiulcer prophylaxis, and enteral nutritional support when clinically necessary. Intravenous fluid resuscitation was planned based on the Parkland formula, and treatment was continued to maintain urine output of 0.5-1 mL/kg/h.

Blood, wound, urine, and sputum cultures were obtained from all patients admitted to the BICU. Antibiotic treatment was administered based on the patients' clinical condition and culture results.

In patients requiring operative intervention, procedures such as tangential and facial excision, skin grafting, escharotomy, fasciotomy, and amputation were performed in accordance with the patient's clinical condition. In the permanent closure of burn defects, autologous partial-thickness skin grafts were performed, based on patient-specific decisions. In cases of deep or extensive tissue loss, biosynthetic skin coverings were used to support closure and neoderm formation.

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 25.0 (IBM Corp., Armonk, NY, USA). The distribution properties of the continuous variables were evaluated using the Kolmogorov-Smirnov test, and it was determined that none of the continuous data showed a normal distribution. Therefore, the Mann-Whitney U test was used for comparisons between groups, and the Pearson chi-square (χ^2) test was used for comparisons of categorical variables. Continuous variables were presented as median (interquartile range); categorical variables as number (n) and percentage (%). A p-value of <0.05 was considered statistically significant.

Results

A total of 53 patients were included in the study, and in-hospital mortality occurred in 6 of these patients (11.3%). The median age of the study population was 35 years (range, 21-46 years), and 81.1% (n=43) of the patients were male. When the fire type was examined, the most common type was caused by flammable liquids, accounting for 49.1% (n=26) of the cases. Forty-five patients (84.9%) were admitted to the hospital within the first 3 hours. In the non-survival group, only one patient (16.7%) was admitted after more than 3 hours. While inhalation burns were present in 18.9% (n=10) of the patients, deep partial-thickness burns were detected in 50.9% (n=27). The median TBSA was 40% (37.5-47), and the revised Baux score was 80 (64-105) (Table 1).

When survival status was compared, inhalation injury was observed at a significantly higher rate in the non-survival group (50% vs. 14.9%; p=0.038). Similarly, the TBSA was significantly larger in the non-survival group [73 (57.5-82.5) vs. 40 (35-40.5); p<0.001]. The revised Baux score was also significantly higher in the non-survival group [122.5 (111-160.25) vs. 76 (64-96); p<0.001].

While the intubation rate was 100% in the non-survival group, it was determined to be 14.9% in the survivors (p<0.001). When the length of stay was evaluated, the median intubation length of stay in the entire study population was determined to be 4 (2-14) days. While this period was 3 (2-4) days in the survival group, it was 14 (7-20) days in the non-survival group. The median BICU stay for all patients was 15 (6-35) days, although the duration was longer in the non-survival group; the difference was not statistically significant [22.5 (6.5-37.75) vs. 14 (6-35); p=0.736].

Although the rate of deep partial thickness burns was higher in the non-survival group (83.3% vs. 46.8%), the difference was not statistically significant (p=0.092). The median number of operative debridements was 3.5 (2-8) in the survivors and 6 (3-10) in the non-survival group, and the difference was not significant (p=0.251). When operative interventions were evaluated, tangential and/or fascial excision was performed in 49 patients (92.5%), escharotomy in 30 patients (56.6%), fasciotomy in four patients (7.5%), and split-thickness skin grafting in 12 patients (22.6%).

When systemic inflammation indices were examined, PLR was calculated as 110.85 (51.66-212.74), LMR as 4.71

Table 1. Comparison of clinical characteristics and systemic inflammation indices between survivors and non-survivors

	All patients (n=53)	Survivors (n=47)	Non-survivors (n=6)	p-value
Age (years)	35 (21-46)	33 (20-46)	45 (33.5-72.5)	0.084#
Male sex$^{\beta}$	43 (81.1)	39 (83)	4 (66.7)	0.336*
Fires classes$^{\beta}$ Liquids Gasses Others	 26 (49.1) 10 (18.9) 17 (32.1)	 23 (48.9) 10 (21.3) 14 (29.8)	 3 (50) - 3 (50)	 0.376*
Inhalation injury$^{\beta}$ (yes)	10 (18.9)	7 (14.9)	3 (50)	0.038*
Intubation$^{\beta}$ (yes)	13 (24.52)	7 (14.89)	6 (100)	<0.00*
TBSA^{W}	40 (37.5-47)	40 (35-40.5)	73 (57.5-82.5)	<0.001#
Burn depth$^{\beta}$ (deep partial-thickness)	27 (50.9)	22 (46.8)	5 (83.3)	0.092*
Baux score^{W}	80 (64-105)	76 (64-96)	122.5 (111-160.25)	<0.001#
Number of operative debridements^{W}	6 (3-10)	6 (3-10)	3.5 (2-8)	0.251#
BICU days^{W}	15 (6-35)	14 (6-35)	22.5 (6.5-37.75)	0.736#
1st day of hospital admission				
PLR^{W}	116.14 (84.16-203.24)	116.14 (89.67-207.9)	110.85 (51.66-212.74)	0.632#
LMR^{W}	2.62 (1.21-5.42)	2.44 (1.19-4.28)	4.71 (1.47-7.15)	0.314#
NLR^{W}	4.73 (2.2-8.82)	5.17 (2.18-9.26)	2.72 (1.97-8.06)	0.555#
SII^{W}	1224.54 (539.95-2905.49)	1224.54 (514.17-2525.64)	2421.46 (539.25-4461.65)	0.612#
SIRI^{W}	3.18 (1.44-11.12)	3.33 (1.49-11.1)	2.4 (1.36-20.83)	0.816#
3rd day of hospital admission				
PLR^{W}	114.09 (80.13-169.8)	115.03 (81.2-169.23)	106.48 (36.22-212.87)	0.774#
LMR^{W}	1.86 (1.2-2.47)	1.9 (1.32-2.52)	0.67 (0.31-2.69)	0.018#
NLR^{W}	4.64 (3.56-7.39)	4.64 (3.58-7.01)	5.93 (2.92-14.9)	0.574#
SII^{W}	893.66 (609.1-1368.8)	800.14 (591.13-1311.42)	2062.73 (654.96-4562.44)	0.128#
SIRI^{W}	4.37 (2.87-9.07)	4.34 (2.63-8.15)	31.61 (10.44-65.73)	0.002#
5th day of hospital admission				
PLR^{W}	171.89 (98.35-236.88)	183.67 (103.71-237.57)	114.57 (69.94-200)	0.218#
LMR^{W}	1.61 (1.1-2.69)	1.63 (1.18-3.2)	0.35 (0.11-0.52)	<0.001#
NLR^{W}	5.27 (3.41-7.45)	5.24 (3.36-7.31)	6.51 (4.17-15.28)	0.197#
SII^{W}	1535.65 (748.62-2275.77)	1433.51 (737.43-2272.35)	2079.33 (1192.47-2694.58)	0.301#
SIRI^{W}	4.95 (2.72-9.7)	4.2 (2.54-7.27)	48.4 (34.63-120.72)	<0.001#

$^{\beta}$: Numbers (%), ^{W}: Median (IQR), *: Chi-square, #: Mann-Whitney U test. BICU: Burn intensive care unit, LMR: Lymphocyte-to-monocyte ratio, NLR: Neutrophil-to-lymphocyte ratio, PLR: Platelet-to-lymphocyte ratio, Baux score: Revised Baux score, SII: Systemic immune-inflammation index, SIRI: Systemic inflammation response index, TBSA: Total body surface area

(1.47-7.15), NLR as 2.72 (1.97-8.06), SII as 2421.46 (539.25-4461.65), and SIRI as 2.40 (1.36-20.83) on the first day of hospital admission in the non-survival group. However, no statistically significant relationship was found between any of these parameters and survival, with all p-values being above 0.05 (e.g., p=0.632, p=0.314, p=0.555, p=0.612, p=0.816). On the third day, LMR was significantly lower in the non-survival group [0.67 (0.31-2.69) vs. 1.9 (1.32-2.52); p=0.018], and SIRI was significantly higher [31.61 (10.44-65.73) vs. 4.34 (2.63-8.15); p=0.002]. Similarly, on the fifth day, LMR was significantly lower in the non-survival group [0.35 (0.11-0.52) vs. 1.63 (1.18-3.2); p<0.001] and SIRI was significantly higher [48.4 (34.63-120.72) vs. 4.2 (2.54-7.27); p<0.001].

Discussion

In this study, we aimed to evaluate the potential prognostic value of systemic inflammation indices in predicting in-hospital survival in critical flame burns. The most commonly used parameters to predict mortality in burns are age, TBSA, and inhalation injury. The Baux score,

which combines these variables, and the revised Baux score, which also includes inhalation injury, are among the most widely accepted prognostic scores in the literature (8-10,14). In our study, although there was no statistically significant difference between the groups in terms of age, statistically significant differences were observed in terms of inhalation injury, TBSA, and revised Baux score.

Our study found that survival was significantly lower in patients requiring intubation. This finding may be related to the greater severity of burns in patients requiring intubation, or it may be due to the reduced tolerance of these patients to critical stress conditions resulting from their lower physiological reserves. Therefore, intubation can be considered a marker reflecting not only the need for respiratory support but also a more severe clinical picture and a high-risk patient group. However, it should not be forgotten that in critical burns, unnecessary intubation increases the risk of complications related to intubation, and intubation performed late, due to ignoring early intubation criteria specified in the current literature, can negatively affect survival (13).

In critical burns, a severe systemic inflammatory response may develop, which can lead to organ failure and death (15). Burn wounds contain many cell types, including neutrophils, lymphocytes, platelets, monocytes, macrophages, and fibroblasts (16). This cellular response plays a crucial role in determining the clinical manifestations of systemic inflammation. Parameters such as neutrophils, lymphocytes, platelets, and monocytes can be obtained easily and at low cost through routine blood tests, which can help physicians predict the clinical course at an early stage. However, it has been reported that these parameters alone have limited value in determining the prognosis of critical burns, as they can be influenced by numerous systemic factors (10). In contrast, there is increasing evidence that systemic inflammation indices, which are obtained by calculating the proportions of these parameters, reflect the immune response more holistically and have prognostic value in inflammatory diseases (10,11). Our study is the first in the literature to evaluate systemic inflammation indices specifically in critical flame burns, with a focus on etiology.

PLR is defined as the ratio of platelets to lymphocytes and is considered an indicator of the balance between proinflammatory and anti-inflammatory processes (17). High PLR values have been associated with worse outcomes in critically ill patients (18,19). In our study, no statistically significant difference was found in PLR values between the groups in patients with critical flame burns. In a meta-analysis by Wang et al. (11), including 11 studies, a significant association was found between high PLR values and short-term mortality in severely burned patientss. However, since all studies included in the meta-analysis had an observational design, this relationship cannot be interpreted at the level of causality. Additionally, all burn etiologies were evaluated collectively in the analysis, and etiology-specific subgroup analyses were not conducted.

LMR reflects the immune balance between lymphocytes and monocytes. Monocytes are responsible for the release of various proinflammatory cytokines, such as interleukin (IL)-1, IL-6, IL-10, and tumor necrosis factor-alpha, which are associated with poor prognosis, especially in critically ill patients (20). Therefore, a high LMR level may indicate better functioning of the immune system, and this has been associated with better prognosis in various diseases such as malignancy (21). However, studies examining the prognostic value of LMR in burn patients are not available in the literature, and our study is the first in this respect. In our study, in patients with critical flame burns, no statistically significant difference was found between the groups in the LMR value on the first day of hospital admission, but a significant difference was found between the LMR values on the third and fifth days. Although there is no direct study on burn patients, the better prognosis the group with high LMR levels is similar to the findings in other clinical studies on LMR.

It is reported in the literature that NLR reflects systemic inflammation more sensitively than evaluating neutrophil and lymphocyte levels alone, and is therefore considered a stronger biomarker (22). There are conflicting findings regarding NLR in the literature. Studies have shown that the change in NLR (ΔNLR) on the first and seventh days after injury is a significant biomarker for evaluating prognosis and disease severity in severe burn cases (23,24). While studies report that NLR is not a reliable prognostic risk factor in large-surface burns (10). In our study, no statistically significant difference was found between the groups in terms of NLR levels according to survival status in patients who developed critical burns from flame burns.

SIRI is calculated based on monocyte and neutrophil-to-lymphocyte ratios and has been identified as a highly sensitive biomarker of inflammation in various clinical conditions such as cancer, cardiovascular diseases, and infection (25,26). SII, derived from platelet counts and neutrophil-lymphocyte ratio, provides a more comprehensive reflection of the immune-inflammatory status when evaluated together with SIRI. Neutrophils, lymphocytes, and platelets are considered essential components of the inflammatory response in many clinical settings (27). Evaluating these parameters as ratios or composite indices enhances their predictive value and enables a more comprehensive evaluation of systemic inflammation (26). The number of studies evaluating the value of SII and SIRI in predicting survival in burn patients

is quite limited. Li et al. (10) examined SII and SIRI in extensive burns. On the third day, the SII value was found to be statistically significantly higher in the survival group, while no significant difference was found between the groups in terms of SIRI. In our study, while no significant difference in SII values was found between the groups, a statistically significant difference in SIRI value levels was observed on the third and fifth days. Our study is the first in the literature to associate low SIRI values with a better prognosis in critical flame burns.

This study has some limitations. The research was designed retrospectively, which does not allow for the direct establishment of cause-and-effect relationships. Additionally, the study's single-center design and limited patient population restrict the generalizability of the findings.

Conclusion

In conclusion, this study is one of the first in the literature to evaluate the predictive value of systemic inflammation indices for survival in critical flame burn patients. Our findings confirmed the prognostic value of inhalation injury, TBSA, and revised Baux score, while the values of systemic inflammation indices LMR and SIRI on the third and fifth days were significantly associated with survival. High LMR and low SIRI values have been found to be associated with better survival. However, the results obtained need to be supported by larger samples prospective and multicenter studies. Further research may contribute to personalized burn treatment by revealing in which clinical subgroups these biomarkers may become more significant.

Ethics

Ethics Committee Approval: Ethical approval for the study was obtained from the University of Health Sciences Türkiye, Başakşehir Çam and Sakura City Hospital Scientific Research Ethics Committee No. 2 (approval number: 2025-60, dated: 28.02.2025).

Informed Consent: Retrospective study.

Footnotes

Authorship Contributions

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

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

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Prospective Evaluation of Antinuclear Antibody Positivity in Children: Clinical Course and Diagnostic Outcomes

Çocuklarda Antinükleer Antikor Pozitifliğinin Prospektif Değerlendirmesi: Klinik Gidiş ve Tanısal Bulgular

Gülşah Kavrul Kayaalp, Ayşenur Doğru Kılınç, Selen Duygu Arık, Nuray Aktay Ayaz

İstanbul University, İstanbul Faculty of Medicine, Department of Pediatrics, Division of Pediatric Rheumatology, İstanbul, Türkiye

ABSTRACT

Background: Antinuclear antibody (ANA) testing is widely used in children with non-specific symptoms, yet its clinical relevance remains uncertain due to high positivity rates in healthy individuals. This study aimed to prospectively assess the clinical course and diagnostic outcomes of children referred for ANA positivity, to better inform follow-up strategies.

Materials and Methods: Forty-eight ANA-positive pediatric patients without a prior rheumatologic diagnosis and referred to the pediatric rheumatology clinic were prospectively followed for at least two years using a standardized protocol.

Results: Of the 48 patients included in the study, 35 (72.9%) were female. The most common referring department was general pediatrics (n=23, 47.9%), followed by pediatric hematology (n=13, 27.1%). The most frequent reason for ANA testing was joint pain (n=14, 29.2%), followed by thrombocytopenia (n=6, 12.5%) and urticaria (n=6, 12.5%). During follow-up, two patients were diagnosed with systemic lupus erythematosus and one with juvenile idiopathic arthritis. ANA titers became negative over time in 39.6% of the patients. Among those who did not receive a diagnosis, the median follow-up duration was 34 months (interquartile range: 26.5-50).

Conclusion: ANA positivity in children is often transient and clinically insignificant, and management should prioritize clinical context and symptom-guided monitoring rather than routine extensive evaluation.

Keywords: Antinuclear antibody, connective tissue diseases, lupus, pediatric rheumatology

ÖZ

Amaç: Antinükleer antikor (ANA) testi, özgül olmayan semptomları olan çocuklarda yaygın olarak kullanılmaktadır. Ancak sağlıklı bireylerde de yüksek pozitiflik oranları görülmesi nedeniyle klinik önemi belirsizliğini korumaktadır. Bu çalışmanın amacı, ANA pozitifliği nedeniyle çocuk romatoloji polikliniğine yönlendirilen hastaların klinik gidişatını ve tanı sonuçlarını prospektif olarak değerlendirmek ve takip stratejilerine daha iyi yön verebilmektir.

Gereç ve Yöntemler: Daha önce romatolojik hastalık tanısı olmayan ve ANA pozitifliği nedeniyle çocuk romatoloji polikliniğine yönlendirilmiş 48 pediatrik hasta, standart bir protokol ile en az iki yıl boyunca prospektif olarak takip edilmiştir.

Bulgular: Çalışmaya dahil edilen 48 hastanın 35'i (%72,9) kızdı. Hastaların en sık yönlendirildiği bölüm çocuk sağlığı ve hastalıkları idi (n=23, %47,9), bunu çocuk hematolojisi izledi (n=13, %27,1). ANA testi istenme nedenleri arasında en sık eklem ağrısı (n=14, %29,2), ardından trombositopeni (n=6, %12,5) ve ürtiker (n=6, %12,5) yer aldı. Takip süresince iki hastaya sistemik lupus eritematozus ve bir hastaya jüvenil idiyopatik artrit tanısı konuldu. Hastaların %39,6'sında ANA titresi zamanla negatifleşti. Tanı almayan hastalarda takip süresinin medyanı 34 ay (çeyrekler arası açıklık: 26,5-50) idi.

Sonuç: Çocuklarda ANA pozitifliği çoğu zaman geçici ve klinik olarak önemsizdir. Bu nedenle yönetimde klinik bağlam ve semptomlara dayalı izlem ön planda tutulmalı, rutin olarak kapsamlı değerlendirmelerden kaçınılmalıdır.

Anahtar Kelimeler: Antinükleer antikor, bağ dokusu hastalıkları, lupus, pediatrik romatoloji

Address for Correspondence: Nuray Aktay Ayaz, İstanbul University, İstanbul Faculty of Medicine, Department of Pediatrics, Division of Pediatric Rheumatology, İstanbul, Türkiye

E-mail: nurayaktay@gmail.com **ORCID ID:** orcid.org/0000-0003-3594-7387

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Introduction

Antinuclear antibody (ANA) are autoantibodies directed against various nuclear antigens and are widely used as diagnostic biomarkers in connective tissue diseases, particularly systemic lupus erythematosus (SLE). The ANA test was first described in the 1940s through the identification of the lupus erythematosus cell phenomenon, in which sera from SLE patients induced nuclear changes in healthy bone marrow cells (1). Today, the gold standard for ANA detection is the indirect immunofluorescence assay (IIFA) using HEp-2 cells (2). However, clinical implementation of the test has revealed that ANA positivity is not specific to autoimmune diseases and can also be found in healthy individuals or in non-rheumatologic conditions (3,4).

Population-based studies have reported ANA positivity rates up to 30% in healthy individuals (5-7). These rates increase with age, are more common in females, and are usually observed at low titers (1:40, 1:80). In the pediatric population, ANA positivity has been reported in 10-15% of children (8,9). This variability contributes to uncertainty regarding the clinical relevance of incidental ANA positivity, particularly in children, and makes interpretation in the absence of systemic findings challenging.

In daily clinical practice, ANA testing is frequently requested in children presenting with non-specific complaints. Positive results often lead to referrals to pediatric rheumatology clinics, even in the absence of other abnormal findings. There is still no consensus on the optimal follow-up strategy for ANA-positive children, and reliable predictive markers for future disease development remain unclear. Most of the available evidence comes from retrospective studies, which limits the ability to draw firm conclusions about the natural course and clinical relevance of ANA positivity in children.

This study aimed to prospectively follow children referred for ANA positivity over a two-year period, to evaluate the clinical course, changes in ANA status, and the proportion of patients who developed a diagnosis of connective tissue disease. The goal was to generate evidence that might guide the clinical management of this frequently encountered patient group.

Materials and Methods

This study included 48 pediatric patients aged 0-18 years who were referred to the Pediatric Rheumatology Outpatient Clinic of İstanbul University Faculty of Medicine due to ANA positivity. Initial ANA testing for all patients was performed at multiple external laboratories prior to referral to our center. Most laboratories used IIF on HEp-2 cell substrates, while a minority employed enzyme-linked immunosorbent assays (ELISA), resulting in minor variations in assay platforms and manufacturers across centers. Because these tests were conducted externally, detailed information regarding sample handling and storage conditions was not consistently available. All referred patients with a positive ANA titer of ⩾1:40 were included. Patients who had a previously established diagnosis of any rheumatologic disease were excluded from the study. All patients were followed at 6-month intervals in the pediatric rheumatology clinic.

From the initial visit and throughout the follow-up period, patients were evaluated for signs and symptoms suggestive of systemic connective tissue diseases. Additional laboratory tests were performed as clinically indicated. Each patient was assessed using a standardized evaluation form, and clinical findings and laboratory data were systematically recorded. Only patients with a minimum follow-up duration of two years were included in the final analysis.

The study recorded the initial clinical complaints that prompted ANA testing, the referring department, clinical findings at presentation, ANA titers and staining patterns, results of other autoantibody tests, and laboratory parameters. Changes in ANA titers over time, newly emerging clinical findings, and final diagnoses—if established—were documented during follow-up.

Informed consent was obtained from all participants prior to inclusion in the study. The study was approved by the Ethics Committee of İstanbul Faculty of Medicine (approval number: 223382, dated: 27.10.2020), and was conducted in accordance with the ethical principles of the Declaration of Helsinki.

Statistical Analysis

All data were compiled using Microsoft Excel (Microsoft Corporation, Redmond, WA) and analyzed with SPSS version 17.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were used to summarize the data. Categorical variables were presented as frequencies and percentages (n, %). Continuous variables were reported as mean ± standard deviation for normally distributed data, and as median with interquartile range (IQR) for non-normally distributed data. Normality of distribution was assessed using visual inspection (histograms and Q-Q plots) and the Shapiro-Wilk test.

Results

Of the 48 patients included in the study, 35 (72.9%) were female. The mean age at initial presentation was 10.22±3.08 years for the entire cohort. Among patients who did not receive a diagnosis, the median follow-up duration was 34 months (IQR: 26.5-50).

ANA testing was most commonly performed due to joint pain (n=14, 29.17%), followed by thrombocytopenia (n=6, 12.5%) and urticaria (n=6, 12.5%). Patients were most frequently referred by general pediatrics clinics (n=23, 47.92%), followed by pediatric hematology clinics (n=13, 27.08%) (Table 1).

At presentation, the most common positive clinical findings were arthralgia (19 patients, 39.58%), recurrent aphthous stomatitis (11 patients, 22.92%), and non-specific rash (10 patients, 20.83%). The most frequently reported ANA titer in the cohort was 1:640 (12 patients, 25.0%), although ANA patterns showed considerable variability. Detailed data regarding clinical findings, ANA titers, and patterns are presented in Table 2.

During follow-up, ANA became negative in 19 patients (39.58%). Baseline positivity of other autoantibodies was evaluated, and detected as follows: anti-dsDNA in 4 patients, anti-Sm in 1 patient, antiphospholipid antibodies in 2 patients, and anti-SSA and anti-SSB each in 1 patient (Table 2). Among these patients, the positivity for anti-Sm and anti-SSA/SSB antibodies spontaneously regressed. Of the 4 patients positive for anti-dsDNA, one was diagnosed with SLE, one with juvenile idiopathic arthritis (JIA), and spontaneous regression was observed in the other two. Both patients, positive for antiphospholipid antibodies, were diagnosed with SLE.

Table 1. Demographic characteristics, family history, referral sources, and initial reasons for ANA testing in the study cohort

Demographic characteristics	
Female, n (%)	35 (72.9)
Age at presentation (years), mean ± SD	10.22±3.08
Duration of follow-up (months), median (IQR: 25-75)	34 (26.5-50)
Referring clinic	**Frequency (n, %)**
General pediatrics	23 (47.92)
Pediatric hematology	13 (27.08)
Pediatric allergy and immunology	4 (8.33)
Dermatology	3 (6.25)
Pediatric nephrology	2 (4.17)
Pediatric infectious diseases	1 (2.08)
Pediatric gastroenterology	1 (2.08)
Pediatric neurology	1 (2.08)
Reason for initial ANA testing	**Frequency (n, %)**
Joint pain	14 (29.17)
Thrombocytopenia	6 (12.5)
Urticaria	6 (12.5)
Recurrent oral aphthae	3 (6.25)
Neutropenia	2 (4.17)
Abdominal pain	2 (4.17)
Malar rash	2 (4.17)
Other reasons*	
Positive history of rheumatic diseases in first degree relatives	**Frequency (n, %)**
Total	14 (29.17)
RA	6 (12.5)
SLE	3 (6.25)
FMF	2 (4.17)
Sarcoidosis	2 (4.17)
Vasculitis	1 (2.08)

*Other reasons include dry eyes, pancytopenia, proteinuria, screening due to family history, hypertension, recurrent diarrhea, menometrorrhagia, ecchymosis, hair loss, thrombocytosis, and evaluation for multiple sclerosis (each 1 case, 2.08%). ANA: Antinuclear antibody, SD: Standard deviation, IQR: Interquartile range, RA: Rheumatoid arthritis, SLE: Systemic lupus erythematosus, FMF: Familial Mediterranean fever

Table 2. Summary of positive clinical findings, ANA titers and patterns at baseline, ANA negativization during follow-up, and presence of other autoantibodies

Positive clinical findings at presentation	**Frequency (n, %)**
Arthralgia	19 (39.58)
Rash (non-specific)	10 (20.83)
Recurrent aphthous stomatitis	11 (22.92)
Thrombocytopenia	5 (10.42)
Leukopenia	2 (4.17)
Photosensitivity	2 (4.17)
Alopecia	1 (2.08)
Malar rash	1 (2.08)
Raynaud's phenomenon	1 (2.08)
Dry eyes	1 (2.08)
Elevated erythrocyte sedimentation rate	1 (2.08)
ANA titer at baseline	
1:40	5 (10.42)
1:80	4 (8.33)
1:160	10 (20.83)
1:320	9 (18.75)
1:640	12 (25.0)
1:1280 and above	7 (14.58)
Titer not known*	1 (2.08)
ANA pattern at baseline	
Homogenous	10 (20.83)
Speckled	11 (22.92)
Dense fine specked (DFS-70)	4 (8.33)
Nucleolar	2 (4.17)
Granular	1 (2.08)
Other (nuclear membrane, dots)	2 (4.17)
Pattern not known*	18 (37.5)
ANA became negative during follow-up	19 (39.58)
Presence of other autoantibodies at baseline	
Anti-dsDNA	4 (8.33)
Anti-Sm	1 (2.08)
Antiphospholipid antibodies	2 (4.17)
Anti-SSA/anti-SSB	1 (2.08)

*Missing values are due to incomplete clinical documentation at baseline. ANA: Anti-nuclear antibodies, Anti-dsDNA: Anti-double-stranded DNA, Anti-Sm: Anti-Smith antibodies, Anti-SSA: Anti-Sjögren's syndrome-related antigen A, Anti-SSB: Anti-Sjögren's syndrome-related antigen B

Among the followed patients, 3 (6.25%) were diagnosed with a rheumatologic disease during the follow-up period, of these, 2 were diagnosed with SLE and 1 with JIA.

Patient 1: An 8-year-old female patient initially presented with arthralgia and was found to have a positive ANA at a titer of 1:1280 (pattern unknown). Baseline evaluation revealed elevated erythrocyte sedimentation rate, and positive anti-dsDNA antibodies, while other autoantibodies were negative. During follow-up, the patient developed arthritis by the third month and anti-dsDNA antibodies subsequently became negative. No additional autoantibody positivity or clinical features consistent with SLE emerged. The patient

has been followed for 66 months with a persistent diagnosis of rheumatoid factor (RF)-negative polyarticular JIA and no clinical or serological evidence of SLE.

Patient 2: A 16-year-old girl was evaluated for livedo reticularis on the lower extremities and demonstrated a homogeneous ANA pattern at a 1:320 titer. Baseline clinical features included arthralgia, livedo reticularis, and Raynaud's phenomenon. Laboratory findings showed positivity for anti-dsDNA and antiphospholipid antibodies, alongside decreased complement C4 levels. Based on these findings, a diagnosis of SLE was established.

Patient 3: A 10-year-old girl, previously followed in pediatric hematology for chronic immune thrombocytopenic purpura, was referred after detection of ANA positivity at a titer of 1:40 (pattern unknown). Baseline laboratory results revealed thrombocytopenia, ANA positivity, and anticardiolipin antibody positivity, without other clinical or laboratory abnormalities. At three-month follow-up, new symptoms of fatigue prompted repeat testing, which showed a marked increase in ANA titer to 1:1000 with centromere and diffuse fine speckled patterns, positivity for anti-centromere and anti-Sm antibodies, decreased C4 levels, and positivity for ribosomal P antibodies. The patient was diagnosed with SLE.

Discussion

In this prospective study, we followed children referred to a pediatric rheumatology clinic due to positive ANA tests, aiming to explore the clinical significance and evolution of ANA positivity over time. Our findings indicate that the most common reason for ANA testing was non-specific symptoms, particularly joint pain, and the majority of referrals came from general pediatrics clinics. Notably, ANA positivity reverted to negative in a significant proportion (39.58%) of the patients during follow-up, and only three patients developed a diagnosis of a rheumatologic disease (two with SLE and one with JIA).

The clinical significance of isolated ANA positivity in children has long been debated with existing studies—mostly retrospective—reporting variable diagnostic outcomes. Aygun et al. (10) retrospectively analyzed 409 ANA-positive children and found that joint pain was the most common presenting symptom, with 15% later diagnosed with systemic autoimmune disease. Similarly, Wang et al. (11) described joint pain, rash, and recurrent fever as leading complaints among ANA-positive adults. These findings align with our cohort, where joint manifestations were also the most frequent reason for referral. However, the rate of confirmed rheumatologic disease in our study was notably lower.

In contrast, Perilloux et al. (12) reported a much higher diagnostic rate, with 55% of children receiving a rheumatologic diagnosis—most commonly JIA and SLE. Likewise, McGhee et al. (13) evaluated 110 children referred for ANA positivity and identified 10 cases of SLE, one of mixed connective tissue disease, and 18 of juvenile rheumatoid arthritis. Nearly half of the remaining children had non-specific musculoskeletal pain. Importantly, their study showed that ANA titer did not distinguish JIA from benign musculoskeletal conditions, but very high titers (≥1:1080) were strongly predictive of SLE, with a reported positive predictive value of 1.0 for such titers (13).

In our cohort, most patients who received a diagnosis did so within the early months of follow-up. Among the two children diagnosed with SLE, one fulfilled classification criteria at baseline with multiple clinical and serological features, while the other initially presented with ANA positivity and lupus-suggestive symptoms, eventually meeting full criteria during follow-up. This illustrates the evolving nature of autoimmune diseases, where diagnostic features may develop gradually over time. Conversely, the patient with arthralgia and ANA positivity was ultimately diagnosed with RF-negative polyarticular JIA—highlighting that ANA positivity alone is insufficient for diagnosing SLE, and must be interpreted in clinical context.

These discrepancies across studies likely stem from differences in referral patterns, patient selection, ANA titers, laboratory methods (e.g., IIFA vs. ELISA), and follow-up duration. Moreover, the retrospective nature of many studies introduces potential selection bias, as patients with concerning features are more likely to be followed, while others with mild or non-specific symptoms may not undergo further evaluation. This limits the generalizability of retrospective findings and may either inflate or underestimate the true predictive value of ANA positivity in pediatric populations.

Our findings—where ANA reverted in nearly 40% of patients and only 6.25% received a definitive rheumatologic diagnosis—reinforce that ANA positivity in children is often transient and of limited clinical relevance. Similarly, a large study in adult patients found that the overall positive predictive value of ANA for systemic autoimmune diseases was only 8.8%, increasing with higher titers (11.6% at 1:160 and 26.9% at 1:640) (14).

Similarly, Myckatyn and Russell (15) observed that after a mean follow-up of 5.4 years, only 3 of 53 ANA-positive adults developed connective tissue disease (CTD), despite the majority remaining persistently ANA-positive. Another long-term follow-up study by Wijeyesinghe and Russell (16) reported that although 78% of patients remained ANA-

positive after 11.5 years, only 5 out of 62 (8.06%) developed CTD. These findings support the notion that ANA testing, although sensitive, lacks specificity and should not be used in isolation to screen for autoimmune disease.

Study Limitations

This study has several limitations. First, although all patients were referred for ANA positivity, the initial ANA testing was performed in various external laboratories prior to referral. Therefore, ANA testing is not standardized across the cohort. Variations in test sensitivity, cutoff thresholds, and pattern reporting may have influenced which patients were referred and how results were interpreted. It is possible that a result considered positive in one laboratory might have been negative in another, potentially affecting which patients were referred and, consequently, the overall composition of the study population. This non-uniformity of ANA testing represents a limitation that impacts both the interpretation of individual results and the generalizability of our conclusions. Nevertheless, our prospective data reinforce that incidental ANA positivity in children, particularly in the absence of high titers or specific clinical signs, does not necessitate immediate extensive evaluation or referral, supporting a symptom-guided and cautious clinical approach. Second, the relatively small number of patients who developed definitive rheumatologic diagnoses limits the statistical power to identify predictive factors for disease progression. Despite these limitations, the study's prospective design and structured follow-up protocol provide valuable insight into the clinical trajectory of ANA-positive children in real-world settings.

Conclusion

In conclusion, these findings reinforce the notion that incidental ANA positivity in children, especially in the absence of specific clinical signs or high titers, should not prompt immediate extensive evaluation or referral. However, in the presence of accompanying symptoms, strong family history, or high-titer ANA, close clinical monitoring remains warranted. Our study provides valuable prospective evidence on the natural course of ANA positivity in children, supporting a cautious and symptom-guided approach to management.

Ethics

Ethics Committee Approval: The study was approved by the Ethics Committee of İstanbul Faculty of Medicine (approval number: 223382, dated: 27.10.2020), and was conducted in accordance with the ethical principles of the Declaration of Helsinki.

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

Footnotes

Authorship Contributions

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

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A Paradox in Clinical Practice: Smoking Among Pulmonologists

Klinik Pratikte Bir Paradoks: Göğüs Hastalıkları Uzmanlarında Sigara Kullanımı

Büşra Durak[1], Ayşe Erdoğan Kaya[2]

[1]*Hitit University Faculty of Medicine, Department of Chest Diseases, Çorum, Türkiye*

[2]*Hitit University Faculty of Medicine, Department of Psychiatry, Çorum, Türkiye*

ABSTRACT

Background: Tobacco use remains one of the leading preventable causes of death worldwide. Although healthcare professionals are expected to act as role models in tobacco control, previous studies have reported conflicting findings regarding smoking prevalence among physicians.

Materials and Methods: This descriptive cross-sectional study was conducted between July 2024 and May 2025 among volunteer pulmonologists actively working in Türkiye. Data were collected through an online survey including sociodemographic characteristics, smoking status, and the Fagerström Test for Nicotine Dependence (FTND).

Results: Among the 156 participating physicians, 24 (15.4%) were current smokers, 18 (11.5%) were former smokers, and 114 (73.1%) were non-smokers. The mean FTND score among current smokers was 2.8±2.8, with 62.5% classified as having low nicotine dependence. Multivariate analysis showed that having family members who smoke [odds ratio (OR)=3.737; 95% confidence interval (CI)=1.334-10.469; p=0.012) and being unmarried (OR=3.120; 95% CI=1.194-8.156; p=0.020) were significantly associated with smoking behavior. No significant association was found with age, sex, or years of medical practice.

Conclusion: The prevalence of smoking among pulmonologists in Türkiye is lower than that in the general population and among other physician groups. This may be attributed to their higher level of professional awareness regarding tobacco-related health risks. However, the influence of family smoking behavior and marital status suggests that tobacco cessation interventions for healthcare professionals should address both individual and environmental factors.

Keywords: Pulmonologist, smoking prevalence, nicotine dependence, Fagerström Test

ÖZ

Amaç: Tütün kullanımı, dünya genelinde önlenebilir ölümlerin önde gelen nedenlerinden biri olmaya devam etmektedir. Sağlık profesyonellerinin tütün kontrolünde rol model olmaları beklenmesine rağmen, önceki çalışmalar hekimler arasındaki sigara içme prevalansı konusunda çelişkili bulgular bildirmiştir.

Gereç ve Yöntemler: Bu tanımlayıcı kesitsel çalışma, Temmuz 2024 ile Mayıs 2025 tarihleri arasında Türkiye'de aktif olarak çalışan gönüllü göğüs hastalıkları uzmanları arasında yürütülmüştür. Veriler; sosyodemografik özellikler, sigara içme durumu ve Fagerström Nikotin Bağımlılık Testi (FNBT) içeren çevrimiçi bir anket aracılığıyla toplanmıştır.

Bulgular: Çalışmaya katılan 156 hekimin 24'ü (%15,4) aktif içici, 18'i (%11,5) eski içici, 114'ü (%73,1) ise hiç içmemişti. Aktif içicilerde ortalama FNBT puanı 2,8±2,8 idi ve %62,5'i düşük nikotin bağımlılığı düzeyine sahipti. Çok değişkenli analizde, ailesinde sigara içen birey bulunması [olasılık oranı (OR)=3,737; güven aralığı (GA)=1,334-10,469; p=0,012] ve bekar olmak (OR=3,120; GA=1,194-8,156; p=0,020) sigara içme davranışıyla anlamlı şekilde ilişkiliydi. Yaş, cinsiyet ve mesleki deneyim süresi ile anlamlı bir ilişki saptanmadı.

Sonuç: Türkiye'deki göğüs hastalıkları uzmanları arasında sigara içme sıklığı, genel nüfusa ve diğer hekim gruplarına göre daha düşüktür. Bu durum, tütün kaynaklı sağlık risklerine dair mesleki farkındalıklarının daha yüksek olmasına bağlanabilir. Ancak ailede sigara içme davranışı ve medeni durum gibi etkenlerin rolü, sağlık çalışanlarına yönelik sigara bırakma müdahalelerinde hem bireysel hem çevresel faktörlerin dikkate alınması gerektiğini göstermektedir.

Anahtar Kelimeler: Göğüs hastalıkları uzmanı, sigara prevalansı, nikotin bağımlılığı, Fagerström Testi

Address for Correspondence: Büşra Durak, Hitit University Faculty of Medicine, Department of Chest Diseases, Çorum, Türkiye

E-mail: drbusradurak@gmail.com **ORCID ID:** orcid.org/0000-0002-2638-1513

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Introduction

Tobacco use remains one of the leading preventable causes of death worldwide. In 2022, approximately 25.3% of the global adult population was tobacco users, down from 34.4% in 2000 (1). In Türkiye, as of 2022, the prevalence of smoking among adults aged 15 and older was reported as 30.7%, with 41.9% in men and 19.6% in women. It is estimated that nearly 20 million adults use tobacco products, with annual per capita cigarette consumption reaching 67.3 packs. These figures indicate that tobacco use continues to pose a major public health issue in Türkiye (2). In this context, healthcare professionals are expected not only to provide counseling and treatment for tobacco cessation but also to serve as role models for society. However, studies investigating the prevalence of smoking among healthcare workers and even among physicians have yielded results that contradict this expectation (3,4).

The literature indicates considerable variation in smoking rates among physicians from different specialties. In some specialties, the prevalence of smoking approaches or even exceeds that of the general population (5,6). Higher rates have been observed among general practitioners and family physicians, while specialties more closely associated with tobacco-related diseases, such as pulmonology and cardiology, typically report lower smoking rates (4). Nonetheless, current and comprehensive data specific to smoking prevalence and nicotine dependence among pulmonologists in Türkiye are limited. Some studies in the literature suffer from limitations in sample size, scope, or methodological consistency. Moreover, there remains a need for updated data to assess behavioral changes among physicians following recent national tobacco control policies.

Gaining deeper insight into the effectiveness of tobacco control policies and the role of healthcare workers in this process can contribute both to the development of interventions promoting behavioral change within the health system and to the restructuring of cessation programs specifically targeted at healthcare professionals.

This study aims to evaluate the prevalence of smoking, the level of nicotine dependence, and the sociodemographic factors associated with smoking behavior among pulmonologists working across Türkiye.

Materials and Methods

Study Design and Duration

This descriptive and cross-sectional study was conducted to determine the prevalence of smoking and the level of nicotine dependence among pulmonologists, as well as to evaluate the sociodemographic factors associated with these behaviors. The study was carried out between July 25, 2024, and May 25, 2025, with volunteer pulmonologists actively working across Türkiye.

Inclusion and Exclusion Criteria

Physicians were included in the study if they were actively working as pulmonologists in Türkiye and had voluntarily completed the questionnaire in full. Exclusion criteria included physicians from non-pulmonology specialties, incomplete questionnaire responses, physicians without an active professional status (e.g., retired individuals), and physicians who reported a current diagnosis of psychiatric or neurological disorders.

Data Collection Method

Participants were contacted via an online questionnaire distributed through the Google Forms platform. The form consisted of three main sections. The first section gathered demographic information, including age, sex, marital status, years of professional experience, level of healthcare institution, presence of comorbidities, and whether there were smokers in the participant's family. The second section inquired about smoking status, and participants were categorized as never smokers, former smokers, or current smokers. The third section involved the administration of the Fagerström Test for Nicotine Dependence (FTND), which had been adapted and validated for use in Turkish. The Turkish version was validated by Uysal et al. (7), with a reported Cronbach's alpha coefficient of 0.56 (8). FTND scores range from 0 to 10; a score of 0-4 indicates low dependence, 5 indicates moderate dependence, and 6-10 indicates high dependence.

Sample Characteristics

Data from a total of 156 participants who completed the questionnaire in full were included in the analysis. For current smokers, additional information was collected, including age at smoking initiation, daily cigarette consumption, and FTND score.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics version 22.0. After calculating descriptive statistics, group differences were analyzed using the chi-square test, independent samples t-test, and Mann-Whitney U test where appropriate. Multivariate logistic regression analysis was conducted to identify independent variables associated with smoking behavior. A p-value of <0.05 was considered statistically significant for all analyses.

Ethics Approval and Informed Consent

Ethical approval for this study was obtained from the Clinical Research Ethics Committee of Hitit University (approval number: 2024-50, dated: 10.07.2024). The study was conducted in accordance with the principles of the Declaration of Helsinki. All participants were informed about the purpose and scope of the study and provided written informed consent prior to completing the questionnaire. Participation was entirely voluntary and anonymous.

Results

A total of 156 pulmonologists participated in the study. The mean age of the participants was 37.5±9.8 years, and 48.7% (n=76) were female. Regarding marital status, 67.9% (n=106) of the physicians were married. Based on the institutions where they worked, 81.4% (n=127) were employed in tertiary healthcare centers. It was reported that 47.4% (n=74) of the participants had at least one family member who smoked. The mean duration of professional experience was 13.1±9.8 years. Additionally, 19.9% (n=31) of the physicians reported having at least one comorbid condition.

When assessed for smoking status, 73.1% of the participants identified as non-smokers, 11.5% as ex-smokers, and 15.4% as current smokers. Among the 24 current smokers, the mean age at smoking initiation was 21.9±4.9 years, mean daily cigarette consumption was 10.7±7 cigarettes, and the mean FNDT score was 2.8±2.8. In terms of nicotine dependence levels, 62.5% were found to have low dependence, 16.7% moderate dependence, and 20.8% high dependence (Table 1).

Table 1. General characteristics of the participants (n=156)

Variable	n (%), mean ± SD
Age (years)	37.5±9.8
Gender (female)	76 (48.7%)
Marital status	
Married	106 (67.9%)
Single	50 (32.1%)
Institution type	
Tertiary care center	127 (81.4%)
Secondary care center	23 (14.7%)
Primary care center	6 (3.9%)
Years in professional practice	13.1±9.8
Family member who smokes	74 (47.4%)
Comorbidity present	31 (19.9%)
Smoking status	
Non-smoker	114 (73.1%)
Ex-smoker	18 (11.5%)
Current smoker	24 (15.4%)

SD: Standard deviation

Participants were categorized into three groups based on their smoking status: non-smokers (n=114; 73.1%), ex-smokers (n=18; 11.5%), and current smokers (n=24; 15.4%). The mean age was 35±16 years in the non-smoker group, 33±19 years in the ex-smoker group, and 33±7 years in the smoker group (p=0.505). The proportion of female participants was 50.9%, 44.4%, and 41.7%, with no significant difference in gender distribution among the groups (p=0.663). The average duration of medical practice was also similar across groups (p=0.481). Although there was no statistically significant difference in the presence of comorbidities among the groups (p=0.089), the ex-smoker group had a relatively higher rate (38.9%) compared to the other groups. In contrast, statistically significant differences were observed regarding marital status and having a family member who smokes. The proportion of married individuals was higher in the non-smoker and ex-smoker groups, while it was lower in the smoker group (45.8%) (p=0.041). Similarly, having a family member who smokes was significantly more common in the smoker group (75%) compared to the non-smoker group (38.6%) (p=0.001) (Table 2).

According to the multivariate logistic regression analysis evaluating factors associated with smoking status, physicians with family members who smoke were significantly more likely to be smokers themselves [odds ratio (OR)=3.737; 95% confidence interval (CI)=1.334-10.469; p=0.012). Similarly, the likelihood of smoking was approximately three times higher among single physicians compared to their married counterparts (OR=3.120; 95% CI=1.194-8.156; p=0.020). Gender (p=0.283), age (p=0.894), and years in medical practice (p=0.990) were not significantly associated with smoking behavior (Tables 3 and 4).

This figure illustrates the OR and 95% CI for factors associated with smoking behavior among pulmonologists. Each black dot represents the OR of a given variable, while the horizontal lines denote the 95% CI. The dashed vertical line at OR=1 represents the point of no association. The presence of a family member who smokes and being single were both significantly associated with increased odds of smoking (p<0.05) (Figure 1).

Table 2. Characteristics of current smokers (n=24, 15.4%)

Variables	n (%), mean ± SD
Age at initiation of smoking (years)	21.9±4.9
Daily cigarette consumption (number)	10.7±7
FTND score (0-10)	2.8±2.8
Level of nicotine dependence	
Low (0-4)	15 (62.5)
Moderate (5)	4 (16.7)
High (6-10)	5 (20.8)

FTND: Fagerström Test for Nicotine Dependence, SD: Standard deviation

Table 3. Participant characteristics by smoking status

Variables	Non-smoker, n=114 (73.1)	Ex-smoker, n=18 (11.5)	Smoker, n=24 (15.4)	p-value
Age (years)**	35±16	33±19	33±7	0.505
Gender* Female, n (%)	58 (50.9)	8 (44.4)	10 (41.7)	0.663
Marital status* Married, n (%)	82 (71.9)	13 (72.2)	11 (45.8)	**0.041**
Duration of medical practice (years)**	10±18	9±19	9±8	0.481
Family members who smoke Yes, n (%)*	44 (38.6)	12 (66.7)	18 (75)	**0.001**
Comorbidity present * Yes, n (%)	19 (16.7)	7 (38.9)	5 (20.8)	0.089

*chi-square test, **Mann-Whitney U test

Table 4. Logistic regression analysis of factors associated with smoking behavior

Variable	B	SE	Wald	p-value	Exp. (B)	95% CI (lower-upper)
Gender Male=1	-0.533	0.497	1.151	0.283	0.587	0.222-1.554
Years in medical practice	0.002	0.177	0.000	0.990	1.002	0.709-1.417
Family members who smoke Yes=1	1.318	0.526	6.293	0.012*	3.737	1.334-10.469
Age (years)	-0.023	0.175	0.018	0.894	0.977	0.694-1.376
Marital status Married=1	1.138	0.490	5.387	0.020*	3.120	1.194-8.156
Constant	-3.186	4.402	0.524	0.469	0.041	–

Nagelkerke R Square: 0.172. B: Regression coefficient, CI: Confidence interval, Exp.: Odds ratio, SE: Standard error

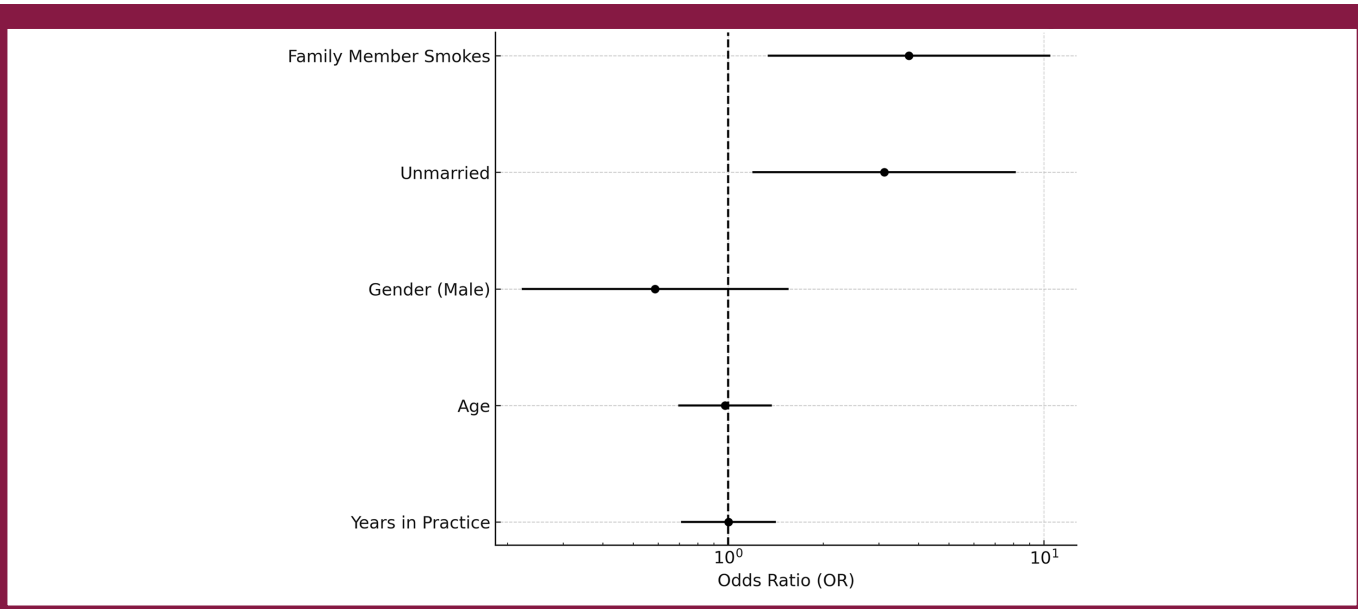

Figure 1. Odds ratios of factors associated with smoking behavior

Discussion

In this study, among 156 pulmonologists who voluntarily participated in the nationwide survey, the prevalence of smoking was found to be 15.4%, and the majority of current smokers were identified as having low levels of nicotine dependence. Multivariate analysis revealed that smoking behavior was significantly associated with having a family member who smokes and marital status. Specifically, physicians with family members who smoked had approximately 3.7 times higher odds of smoking, while single physicians were about three times more likely to smoke compared to their married counterparts. In contrast, no statistically significant association was observed between smoking behavior and demographic variables such as age, gender, or years of professional experience.

When compared with the literature, the 15.4% smoking rate identified in our study is notably lower than the rates reported in other physician groups in Türkiye. For instance, the smoking rate among family physicians has been reported as 30.9% (6), and it can rise up to 42.15% in other specialties (5). In a study conducted in a secondary healthcare facility in İstanbul, the overall smoking prevalence among healthcare workers was found to be 37.2%, whereas the rate among physicians was reported as 9.8% (9). In a study conducted among medical school students, the smoking rate was found to be 26.1% (10). Similarly, in a study conducted by Üzer (10) in 2018, the smoking rate among physicians was found to be 23.8%, which was lower than that of other hospital staff. In another study involving pulmonologists in Türkiye, the current smoking rate was reported as 9.9%, while 21.1% of participants were ex-smokers (11). When compared with international data, a study conducted by Kotz et al. (12) in the Netherlands reported a smoking rate of 3.5% among pulmonologists. These findings suggest that pulmonologists tend to have lower smoking rates than the general physician population, which may be associated with increased professional awareness. According to the systematic review and meta-analysis published by Besson et al. (4) in 2021, the global prevalence of smoking among physicians is approximately 21%. This rate varies by medical specialty: 24% among family physicians, 18% among surgeons, 17% among psychiatrists, 11% among anesthesiologists, 9% among radiologists, and 8% among pediatricians. These rates are notably lower in developed countries. For example, the prevalence has been reported as 6.9% in Australia and 8.3% in the United States, whereas much higher rates have been observed in developing countries such as China (45.2%), Pakistan (42.1%), and Egypt (59.5%) (4). Compared to European countries, the relatively high smoking prevalence among pulmonologists in Türkiye highlights the need to strengthen the effectiveness of national tobacco control policies. The high rate of smoking among physicians in developing countries may be associated with factors such as stress, social influences, and insufficient awareness of their role model status. Therefore, smoking cessation programs targeting healthcare professionals should go beyond simply providing information and instead focus on behavioral and social support interventions.

In Üzer's study, the mean FTND score among healthcare workers was reported as 4, and it was noted that the majority of participants had a low level of nicotine dependence (10). In another study conducted by Zorlu on physicians, 32% of participants were found to have very low or low levels of nicotine dependence (5). In a separate study involving 1233 family physicians in Türkiye, the mean FTND score was reported as 3.76±2.48 (13). Similarly, in a survey conducted among 2,939 smoking physicians in Estonia, the mean FTND score was found to be 2.8±2.1, which is largely consistent with the average score in our study (14). When evaluated in light of these similar findings in the literature, the identification of low nicotine dependence among most of the smoking physicians in our study suggests that smoking may be more closely associated with behavioral habits and social influences than with physiological addiction. This implies that personalized counseling approaches and targeted awareness programs may be effective in increasing the success of smoking cessation among physicians.

The association between having a family member who smokes and being unmarried, with an increased likelihood of smoking behavior, can be interpreted within the framework of social learning theory. According to this theory, individuals develop behaviors by modeling those observed in their social environment; thus, family members who smoke may play a significant role in the adoption of this habit. In terms of marital status, the presence of stronger social support systems among married individuals may serve as a facilitating factor in the smoking cessation process. Similar findings have been reported in the literature. In a study conducted among healthcare workers in Türkiye, a statistically significant relationship was found between the presence of smoking family members and the individual's smoking status, while no such association was observed with marital status (15). Likewise, in Eroğlu's study, 87% of physicians who smoked had at least one family member who also smoked, although no significant relationship with marital status was identified (8). On the other hand, in a 2018 meta-analysis by Wang et al. (16), it was reported that family members' smoking significantly increased the risk of e-cigarette use among adolescents; each additional smoking family member increased the risk by approximately 47% (OR=1.47), and the risk rose to OR=1.87, if a sibling

smoked. In another study conducted by Ramsey et al. (17) involving 11,889 individuals, smoking prevalence was found to be significantly higher among single or never-married individuals. Our study is significant in that it highlights the critical role of social support, even among highly educated groups such as physicians. While spousal or child support may help reduce stress in married physicians, smoking may become a self-directed coping strategy among those who are single.

Although previous studies have indicated that male gender and older age may be associated with smoking behavior (3,4), no significant relationship was found with these variables in our study. In the literature, it has been reported that increased socioeconomic status among women, particularly higher education and income levels, may sometimes encourage smoking (18). The absence of such a difference in our findings may be attributed to the fact that the study sample consisted exclusively of pulmonologists, a group likely to possess higher socioeconomic characteristics.

One of the strengths of our study is that it reached pulmonologists working in various healthcare institutions across Türkiye, resulting in a professionally homogeneous sample. In addition, nicotine dependence was assessed using the FTND, which has been validated for reliability, and factors influencing smoking behavior were analyzed through multivariate statistical methods.

Study Limitations

The study has some limitations. Data were collected through self-reporting, which may have introduced social desirability bias and affected the accuracy of responses. Moreover, the cross-sectional design of the study limits the ability to infer causality between smoking behavior and associated factors.

Conclusion

In our study, the smoking rate and level of nicotine dependence among pulmonologists in Türkiye were found to be lower than the general population and other physician groups, reflecting a high level of professional awareness. Additionally, a significant association was observed between smoking behavior and having family members who smoke, as well as being single, which highlights the influence of the social environment on tobacco use. Despite limitations such as the cross-sectional design and self-reported data, this study provides important insights into the smoking profile of pulmonologists. Future research with larger and longitudinal samples may enhance the effectiveness of smoking cessation interventions. Furthermore, in-service training and awareness campaigns could help strengthen the role model responsibility of healthcare professionals. In conclusion, although the low smoking rate is a positive finding, supporting physicians who smoke and mitigating social influences remain crucial for improving both individual and public health.

Ethics

Ethics Committee Approval: Ethical approval for this study was obtained from the Clinical Research Ethics Committee of Hitit University (approval number: 2024-50, dated: 10.07.2024).

Informed Consent: All participants were informed about the purpose and scope of the study and provided written informed consent prior to completing the questionnaire. Participation was entirely voluntary and anonymous.

Footnotes

Authorship Contributions

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

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

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