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2. Akdeniz YS, Cakmak F, Ipekci A, Ikizceli I, Karatas KF, Berberoglu DB, et al. Videoscopic assisted retroperitoneal debridement in infected necrotizing pancreatitis. Phnx Med J. 2020;9(2):156-159. DOI: 10.1080/13651820701225688.

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Book section
Ipekci A, Cakmak F, Akdeniz YS. Cell death: the significance of apoptosis. In: Ikizceli I, eds. International review of cytology. Istanbul: BTM; 2019. pp. 251–306.
Single authored book
Akdeniz YS. Health economics: fundamentals of funds. Istanbul: Kara Tren Yayınevi; 2019.
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Cakmak F, Ipekci A, editors. Mental health care for elderly people. Istanbul: Fatih Yayınevi; 2019.
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Thesis
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REVIEW

Phnx Med J. July 2024, Volume 6 No 2
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Restriction due to Mental Illness among the Conditions Requiring Guardianship

Vesayeti Gerektiren Hallerden Akıl Hastalığı Sebebiyle Kısıtlama

Ceyda Çınar

Ministry of Justice, Bakırköy Courthouse Bahçelievler Annex Building, Istanbul, Türkiye

ABSTRACT

This study aims to examine guardianship, which is the legal protection provided to people who lose the power of discernment due to mental illness, in terms of mental illnesses.

In the article, mental illnesses that require guardianship within the scope of Article 405 of the Turkish Civil Code and mental illnesses that may cause restrictions within the scope of the legal regulation, and also the effects of mental illnesses determined within the scope of the legal regulation on the restrictions on individuals were examined.

It was determined that the mental illnesses examined necessitate guardianship under Article 405 of the Turkish Civil Code.

In conclusion, this study concludes that guardianship is an important legal tool to protect individuals who have lost the power of discernment due to mental illness and also the effective usage of this tool is important. Therefore, further research in this field will provide healthier results in terms of evaluating the effectiveness of existing legal regulations.

ÖZET

Bu çalışma ile, akıl hastalığı nedeniyle ayırt etme gücünü yitiren kişilere sağlanan yasal koruma olan vesayetin akıl hastalıkları açısından incelenmesi amaçlanmıştır.

Makalede, Türk Medeni Kanunu'nun 405. maddesi kapsamında vesayet gerektiren akıl hastalıkları, yasal düzenleme kapsamında kısıtlamalara neden olabilecek akıl hastalıkları ve ayrıca yasal düzenleme kapsamında belirlenen akıl hastalıklarının bireyler üzerindeki kısıtlamalara olan etkileri incelenmiştir.

İncelenen akıl hastalıklarının, Türk Medeni Kanunu'nun 405. maddesi uyarınca vesayet gerektirecek düzeyde olduğu belirlenmiştir.

Sonuç olarak, bu çalışma ile vesayetin akıl hastalığı nedeniyle ayırt etme gücünü yitiren bireyleri korumak amacıyla önemli bir yasal araç olduğu ve bu aracın etkin kullanımının önemli olduğu sonucuna varılmıştır. Bununla birlikte, bu alanda daha fazla araştırma yapılması, mevcut yasal düzenlemelerin etkinliğini değerlendirmek açısından daha sağlıklı sonuçlar elde edilmesini sağlayacaktır.

Keywords:
Mental Illnesses
Guardianship
Restriction

Anahtar Kelimeler:
Akıl Hastalıkları
Vesayet
Kısıtlama

OVERALL CONCEPT OF GUARDIANSHIP

The institution of guardianship has taken its place in our legislation by being transferred from the Swiss Civil Code to the Turkish Civil Code numbered 4721. Guardianship as named by the Family Law Book of the Turkish Civil Code, in a narrow sense, is an institution that aims to protect the interests of minors who are not under parental authority and persons who need to be restricted for reasons specified in the law. What is meant by the regulations on guardianship law in a broad sense are the regulations regarding guardianship bodies in all other laws other than the Turkish Civil Code (1).

The term "guardianship" originates from the Arabic root "wşy" and is defined in the Justice Ministry Legal Dictionary as "an institution regulated by private law that aims to protect the rights of minors or interdicted people and has the character of a public service" (2). According to Akıntürk, the term "guardianship" refers to the institution directed at protecting individuals who are not under parental authority and those who are incapable of managing themselves and their property for various reasons (3).

Although there are similar doctrinal views on the definition of guardianship, its legal nature is controversial. Some authors consider guardianship as a branch of private law, while others argue that it operates within the boundaries of both public and private law (1). The view we agree with, as the majority does, is that the institution of guardianship is a public institution. The fact that in our legislation tasks such as placing a person under guardianship, selecting and appointing a guardian, guardian being able to carry out the transactions of persons under guardianship with the permission of the guardianship and supervision authority, determining whether the guardian has fulfilled his responsibilities within the scope of supervision, whether they should be dismissed from their duties, and making

Correspondence: Ceyda Çınar, T.C. Adalet Bakanlığı Bakırköy Adliyesi Bahçelievler Ek Binası, Fevzi Çakmak, Ahmet Taner Kışlalı Cd. No: 6, 34194 Bahçelievler/İstanbul **E-mail:** ceydagungormus@hotmail.com
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decisions regarding the termination of guardianship fall within the jurisdiction of the guardianship and supervisory authorities, which are the Peace Civil Courts and the Civil Courts of First Instance, demonstrates that guardianship is indeed a public institution.

In the decisions of the Supreme Court, it is emphasized that the guardianship institution is a public institution by mentioning that placing people under guardianship is related to public order and that even if the plaintiff does not come, a decision must be made by going into the merits of the case by the principle of ex officio investigation. (Supreme Court 2nd Civil Chamber, Decision dated 03/07/2000, No: 7365-9079)

GENERAL INFORMATION ABOUT MENTAL ILLNESSES

In the Dictionary of the Turkish Language Association, mental illness is defined as the general term for diseases that manifest themselves with deficiencies or disorders in abilities such as thinking, understanding, comprehension, decision-making, taking precautions, establishing relationships with others, etc. (4) According to the American Psychological Association, mental illness is defined as "any condition characterized by cognitive and emotional disturbances, abnormal behavior, impaired functioning, or any combination of these" (5). While defining mental illness, the Association referred to the DSM book, which is the Diagnostic and Statistical Manual of Mental Disorders of the American Psychiatric Association.

Until the end of the 18th century, mentally ill people were in a system where they were stigmatized and those who exhibited abnormal behavior that the public did not expect were morally controlled by punishment. Mentally ill individuals were viewed as people who had been possessed by demons or had been struck by the devil according to the religious beliefs of the period. Since the 19th century, steps have been taken towards the development of medicine, separating from the authority of the church, efforts have been made to explain that events such as people's declarations that they are prophets and their ecstasies originate from the mind and soul (6). Since the 19th century, views on treating mentally ill patients under humane conditions have developed, and mental health departments have been opened in universities in the USA and Europe (7).

The development of psychiatry among Turks occurred after Islam with the establishment of treatment places following the rituals of Shaman belief (8). To categorization and identification of psychiatric illnesses, the Diagnostic and Statistical Manual of Mental Disorders (DSM) by the American Psychiatric Association and the International Classification of Diseases (ICD) by the World Health Organization guides are followed. In Europe and our country, psychiatric illnesses are categorized based on the International Classification of Diseases and Related Health Problems (ICD) by the World Health Organization, and classifications have been made in terms of mental illnesses in ICD-11 (9).

According to ICD-11, mental illnesses are classified as follows:

- Neurodevelopmental disorders
- Schizophrenia or other primary psychotic disorders
- Catatonia
- Mood disorders
- Disorders associated with anxiety or fear
- Obsessive-compulsive or related disorders
- Disorders specifically associated with stress
- Dissociative disorders
- Feeding or eating disorders
- Elimination disorders
- Body distress or bodily experience disorders
- Substance use or addictive disorders
- Impulse control disorders
- Disruptive or antisocial behavior disorders
- Personality disorders and related personality traits
- Paraphilic disorders
- Factitious disorders
- Neurocognitive disorders
- Mental or behavioral disorders associated with pregnancy, childbirth, or the puerperium
- Sleep-wake disorders
- Sexual dysfunctions
- Gender incongruence (10)

Although ICD 11 criteria are used as a basis in the characterization of mental illness in psychiatry, mental illnesses that affect the ability to discernment are subject to evaluation in terms of guardianship law (11).

MENTAL ILLNESS FROM THE PERSPECTIVE OF GUARDIANSHIP LAW

According to Turkish Civil Code (TCC) Article 405, any adult who, due to mental illness or mental weakness, is unable to perform their duties requires constant assistance for protection and care, or poses a danger to the safety of others, shall be restricted. Administrative authorities, notaries, and courts who learn of a situation necessitating the placement of someone under guardianship must immediately inform the competent guardianship authority. The diseases that require evaluation from the perspective of guardianship law and affect a person's decision-making ability include psychoses, mental retardation, psychoneuroses, personality disorders, and organic psychoses.

In practice, the most common reasons for guardianship are schizophrenia, dementia, mental retardation, and bipolar disorders (12). A statistical study conducted in 2017 examined the records of 810 individuals referred to a training and research hospital, and it was found that reports indicating the need for a legal representative were issued for 81.7% of them (13). The same study indicated that 31% of the referred individuals were diagnosed with dementia, 28% with a psychotic disorder, 8.1% with bipolar disorder, and 15.2% with intellectual disability. It was emphasized that reports indicating the need for guardianship were issued for 76.8% of the cases (13).

Determining whether a person has a mental illness requires expertise, and according to Turkish Civil Code Article 409 of the law, a decision on restriction due to mental illness or mental weakness can only be made based on an official health committee report. According to this law, simply classifying the illness in the DSM or ICD is not sufficient; rather, the crucial aspect is whether the psychiatric illness affects the person's decision-making ability.

The legislator places significant importance on the health report issued for mental illness or mental weakness and also in the jurisprudence of the Supreme Court, it has been stated that a comprehensive report from a fully equipped hospital with a psychiatrist should be obtained for individuals for whom guardianship is requested based on alleged mental illness. (Supreme Court 2nd Civil Chamber Decision dated 15.01.2001, No: 15160-471) Furthermore, the Supreme Court has ruled that in case of discrepancies among the reports obtained by the court, the individual subject to restriction should be re-evaluated along with the previous report to obtain a new report. (Supreme Court 2nd Civil Chamber Decision dated 12.11.2003, No: 14266-15439)

In the event of discrepancies between the health report from a fully equipped hospital and the report prepared by the Institution of Forensic Medicine's specialized department, these discrepancies will be conclusively resolved by the Institution of Forensic Medicine's General Board with the participation of expert members by Article 15 of Law No. 2659 on the Institution Forensic Medicine. However, by Decree Law No. 703 dated 02/07/2018 which is Decree-Law Concerning Amendments to Certain Laws and Decree Laws to Comply with the Amendments to the Constitution, some changes were made in the law and the Forensic Medicine Institution Law No. 2659 was renamed "Law on Some Regulations Related to the Forensic Medicine Institution". The duties and powers of Forensic Medicine Institute were rearranged with the "Presidential Decree on the Organization of Ministries, Relevant, Related Institutions and Organizations and Other Institutions and Organizations" dated 15.07.2018 and numbered 4. With this amendment regarding the Forensic Medicine Institute the repealed Article 15 was replaced by Article 16 of Decree No. 4. According to this article;

Forensic Medicine Supreme Councils;

a) Works given by forensic medicine specialized boards and specialized offices, but whose reasons are stated by the courts, judgeships, and prosecutor's offices and which are not sufficiently convincing due to their scope.

b) Works does not be decided unanimity by forensic medicine specialty boards,

c) Contradictions that arise between the reports and opinions of forensic medicine specialty boards,

d) Contradictions that arise between the reports and opinions of forensic medicine specialty boards and specialized offices,

e) Conflicts that arise between the reports and opinions given by forensic medicine specialty boards and health institutions other than the Forensic Medicine Institute as a committee, examines the issue with the participation of expert members and makes a final decision.

Within the scope of the article, any contradictions that arise between the reports provided regarding mental illness and mental weakness, which is our subject of study, and the reports given by the specialized boards or departments, will be decided by the forensic medicine higher boards.

Issuing a decision on guardianship due to mental illness or mental weakness without an official health committee report may lead to the annulment of the decision if an appeal is lodged. In the official health board report; Observations about the person, diagnosis of the disease, medical evaluations and ultimately whether there is a situation that affects the ability to distinguish due to disease should be determined (14). The committee responsible for preparing the report should avoid making legal evaluations and acting as a judge.

Although the term "mental weakness" is used in the law, mental weakness is a legal rather than a medical concept. There is no distinction made in the law regarding the illness that eliminates discerning power and mental weakness. Given that there is no practical difference in terms of applied provisions and outcomes, the content of the concepts of mental and psychological illness is important. For a person to be placed under guardianship due to mental illness, this condition must be continuous (15).

According to Article 409 of the Turkish Civil Code, a decision based on mental illness or mental weakness can only be made with an official health committee report, and the judge may hear the individual subject to restriction after taking the committee report into account. In practice, if there is a finding in the health report that it is not beneficial to hear the person due to mental illness, the judge may decide not to hear the person. Indeed, if the person's mental illness is advanced, their testimony during a trial may negatively affect their illness and hinder obtaining accurate statements. However, it would be appropriate for the court to hear from an individual placed under guardianship due to mental illness or mental weakness if there is a request for the removal of guardianship after the person has been placed under guardianship.

The last paragraph of Article 409 of the Turkish Civil Code states that when an official health committee report is required for restriction based on mental illness or mental weakness, if necessary, Article 436 of the same law may apply. By regulating that a decision can only be made after obtaining an official health committee report for individuals with mental illness or mental weakness in the fifth paragraph of Article 436, the importance of an official health committee report for restriction due to mental illness or mental weakness is once again emphasized. The article states that "to ensure the preparation of the official health committee report; it is indicated that samples such as blood or similar biological samples, hair, saliva, nails, etc., can be taken from the person's body." The Constitutional Court, with its decision dated 25/01/2023 and numbered 2020/30 main case, 2013/12 decision, declared unconstitutional the provision of Article 436/6 of the Civil Code, which allows placement in a health institution for up to 20 days based on a physician's report, due to the absence of a legal remedy that can be applied against the decision of placement in a health committee and the lack of legal safeguards that could lead to arbitrariness.

Mental illness and mental weakness alone are not sufficient for a guardianship decision to be made; the existence of one of the situations specified in the law, such as inability to perform one's duties, requiring constant assistance for one's protection and care, or endangering the safety of others, is also required.

INABILITY TO MANAGE ONE'S AFFAİRS

Article 405 of the Turkish Civil Code lists one of the conditions for being placed under guardianship due to mental illness or mental weakness as the inability to manage one's affairs. Since it is not possible for a person to completely be unable to manage their affairs, the concept in this article should be understood as inadequacy in performing tasks, as described in Article 335 of the previous Civil Code. The law has not made a regulation regarding which jobs are within the scope, and these should be understood as jobs that, if not done, may cause significant consequences in a person's life (16).

Examples of situations where tasks cannot be performed include not being able to manage one's finances, not being able to withdraw one's salary from the bank, not being able to go to the doctor, or not being able to handle social security-related procedures.

It is important to emphasize that the reason for not being able to manage one's own affairs must be due to mental illness or mental weakness, and inexperience or lack of knowledge about the tasks to be performed does not constitute grounds for guardianship.

CONTINUOUS NEED FOR ASSISTANCE FOR PROTECTION AND CARE

According to Article 405 of the Civil Code, for a person to be restricted due to mental illness or mental weakness, it is necessary for them to continuously require assistance for protection and care. For instance, a person can do his economic affairs properly, but cannot go to the hospital and receive treatment due to his epileptic seizures. Another example of this condition is that a bipolar patient who works to earn an income has suicidal thoughts due to his attacks and therefore needs personal care.

POSING A DANGER TO THE SAFETY OF OTHERS

Article 405 of the Civil Code regulates guardianship protection for the person's protection or the ability to perform their affairs, but it also adds the condition of endangering the safety of others for the protection of society as a whole.

According to Riemer, with this social condition, society is protected against people who tend to commit illegal acts (17).

The possibility of a person's illness leading to an attack on third parties may lead to guardianship. This provision should not be narrowly interpreted, as one of the most important aims of guardianship law is to ensure the protection of the individual in a two-way manner, meaning not only criminal acts but also any behavior that could endanger society should be understood.

A study found that the behaviors most expected from mentally ill individuals by others are negative emotions and problems related to personal care, and aggressive behavior is the most disturbing (18).

The situation of endangering the safety of others specified in the article should not be expected to occur due to an event, and a guardianship decision should be made due to the dangers that may arise from the side effects of the disease or the drugs used for the disease.

Mentally ill people, who are the people most addressed by the guardianship institution and who need to be protected the most, can be placed under guardianship under the conditions listed in Article 405 of the law.

CONCLUSION

Guardianship, regulated in the family law book of Turkish Civil Code No. 4721, is an institution that has the reasons specified in the law and aims to protect the interests of people who need to be protected. Considering the severity of the consequences of guardianship, a very sensitive evaluation was made by the legislator and the situations requiring guardianship were listed in a limited manner.

In our study, the concept of guardianship is explained in general, and mental illness, which is one of the conditions requiring guardianship within the scope of Article 405 of the Turkish Civil Code is examined. Additionally, it aims to reveal the criteria for detecting mental illness, the importance of official health board reports in determining this situation, and the conditions for receiving guardianship due to mental illness by the guardianship authority.

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ORIGINAL ARTICLE

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Comparison of Sperm Deformity Indexes between Patients who have and have not Experienced COVID-19

COVİD-19 Geçiren ve Geçirmeyen Hastaların Sperm Deformite İndeks Değerlerinin Karşılaştırılması

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ABSTRACT

Objective: *Ever since its identification in December 2019, the novel coronavirus SARS-CoV-2 has rapidly disseminated worldwide, giving rise to the COVID-19 (coronavirus disease-19) pandemic. The male reproductive system is susceptible to the effects of COVID-19, leading to potential alterations in semen parameters. In this study, we conducted a comparison between patients who have previously contracted COVID-19 and those who have not, specifically focusing on the sperm deformity index (SDI) as a parameter for assessing sperm morphology.*

Material and Method: *134 patients over the age of 18 who applied to Hospital Andrology Laboratory between 29 November 2022 and 29 December 2022 were included in the study. Of these, 44 were patients who have had Covid-19, and 90 were patients who have not had COVID-19. These patients were compared in terms of SDI parameter and other semen parameters (ejaculate volume, sperm concentration, total sperm count, total motility, progressive motility and percentage of normal morphology sperm). The calculation of the SDI was performed by dividing the total number of observed deformities by the total count of sperm.*

Results: *A noteworthy distinction was observed in the SDI values between the two groups, with a statistically significant difference ($p<0.001$). There were no statistically significant differences found in terms of other semen parameters between the groups ($p>0.05$).*

Conclusion: *SDI, one of the semen parameters, was found to be significantly different in both groups. Further comprehensive studies are warranted to thoroughly investigate the impact of COVID-19 on semen parameters.*

ÖZET

Amaç: Y*eni koronavirüs SARS-CoV-2, Aralık 2019'da tanımlanmasından bu yana hızla dünya çapında yayılmış ve COVID-19 (koronavirüs hastalığı-19) salgınına yol açmıştır. Erkek üreme sistemi, COVİD-19'un etkilerine karşı hassastır ve bu durum semen parametrelerinde potansiyel değişikliklere yol açabilmektedir. Bu çalışmada, özellikle sperm morfolojisini değerlendirmeye yönelik bir parametre olan sperm deformite indeksi'ne (SDI) odaklanarak, daha önce COVİD-19'a geçirmiş ve geçirmemiş hastalar arasında bir karşılaştırma yaptık.*

Gereç ve Yöntem: *Çalışmaya 29 Kasım 2022 ile 29 Aralık 2022 tarihleri arasında Adana Şehir Hastanesi Üremeye Yardımcı Tedavi Merkezi'ne başvuran 18 yaş üstü 134 hasta dahil edildi. Bunlardan 44'ü COVID-19 geçirip iyileşen, 90'ı ise COVID-19 geçirmeyen hastalardı. Bu hastalar SDI parametresi ve diğer semen parametreleri (ejakülat hacmi, sperm konsantrasyonu, toplam sperm sayısı, toplam hareketlilik, ilerleyici hareketlilik ve normal morfolojiye sahip sperm yüzdesi) açısından karşılaştırıldı. SDI hesaplanması, gözlenen toplam deformite sayısının toplam sperm sayısına bölünmesiyle yapıldı.*

Bulgular: *Her iki grup arasında SDI değerlerinde istatistiksel olarak anlamlı farkla dikkat çekici bir farklılık gözlendi ($p<0,001$). Gruplar arasında diğer semen parametreleri açısından istatistiksel olarak anlamlı farklılık saptanmadı ($p>0,05$).*

Sonuç: *Semen parametrelerinden SDI'nın her iki grupta da anlamlı olarak farklı olduğu görüldü. COVID-19'un semen parametreleri üzerindeki etkisini kapsamlı bir şekilde araştırmak için daha kapsamlı çalışmalara ihtiyaç vardır.*

Keywords:
Sperm deformity index
COVID-19
Semen parameters

Anahtar Kelimeler:
Sperm deformitesi indeksi
COVİD-19
Semen parametreleri

INTRODUCTION

In 2019, COVID-19, which emerged in the city of Wuhan, China, caused significant changes in various fields such as education, health, and economy, and it has affected the whole world. In the context of combating COVID-19, vaccine studies have been conducted worldwide, and research on the effects of the virus on human systems has also been accelerated (1). Currently, the coronavirus family, consisting of 30 members, represents the largest group of positive-sense single-stranded RNA viruses. Angiotensin-converting enzyme 2 (ACE2) and transmembrane serine protease 2 (TMPRSS2) receptors play an important role in the transmission of SARS-CoV-2. These receptors are co-expressed in the testis and male genital tract. This observation strongly suggests the high probability of the virus specifically targeting the

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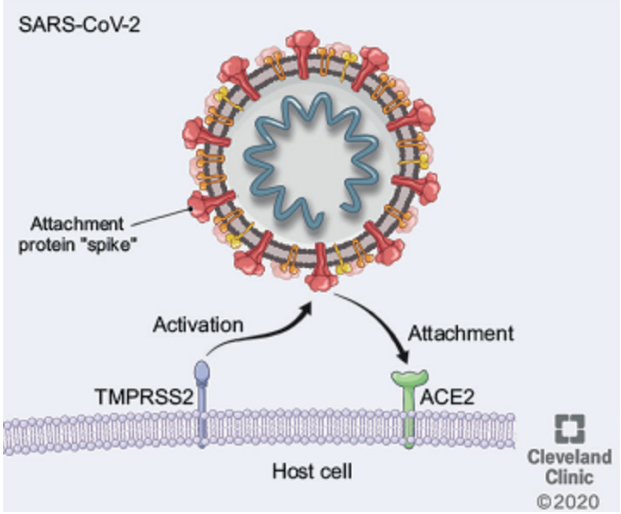

Figure 1: Cellular entry mechanism. Severe acute respiratory syndrome-coronaviruse-2 (SARS-CoV-2) infection is mediated by the binding between viral spike proteins and angiotensin I converting enzyme 2 (ACE2) cellular receptor, and the further proteolytic cleavage and activation of spike proteins by the transmembrane protease serine 2 (TMPRSS2) (5).

testis and male genital system during infection (Figure 1). Numerous studies have reported that more than 25 different viruses can enter human semen and potentially have harmful effects on spermatozoa and male fertility. Examples of such viruses include HSV (Herpes Simplex Virus) and HIV (Human Immunodeficiency Virus). The question of whether SARS-CoV-2 has similar effects in males continues to be an important research question that has not been definitively answered in preliminary studies (2-5). Semen analysis is considered a fundamental component of male fertility assessment, and guidelines established by the World Health Organization (WHO) form the basis for standardizing procedures and establishing global reference values. Routine evaluation of male fertility typically includes assessing sperm count, motility, and morphology in ejaculated semen. The incidence of morphological abnormalities in spermatozoa has been comprehensively described using indices such as the sperm deformity index (SDI), teratozoospermia index (TZI), or multiple anomaly index (MAI). These indices provide valuable measurements for evaluating the structural integrity and abnormalities of sperm cells. The SDI is calculated by dividing the total number of morphological anomalies in sperms by the total number of sperm analyzed, including both normal and abnormal sperm (6-8). The SDI represents a new approach to expressing sperm morphological parameters. Its absolute value represents the balance between the prevalence of spermatozoa with multiple structural deformities and the proportion of spermatozoa exhibiting normal morphology in a specific semen sample. Compared to both the percentage of normal sperm morphology and the multiple anomaly index, the SDI is a more reliable predictor of the outcome of in vitro oocyte fertilization. This emphasizes the importance of SDI as a valuable parameter for evaluating the fertilization potential of spermatozoa in assisted reproductive techniques. Studies have shown that SDI is associated with the fertilization rate in traditional IVF procedures (9,10). In this study, we investigated a previously underexplored topic by comparing the sperm deformity indices of patients who have and have not experienced COVID-19.

MATERIAL AND METHODS

Before starting our study, we obtained the necessary permissions from the Adana City Training and Research Hospital Ethics Committee (Meeting Number: 125, Decision Number: 2528). Our retrospective study included male patients who applied to the Adana City Training and Research Hospital Assisted Reproduction Unit for sperm analysis between November 29, 2022, and December 29, 2022. Patients under 18 years of age and those who could not provide a sperm sample through masturbation were excluded from the study. Information about whether the patients have previously had COVID-19 was obtained from the medical history form (patient files), and the patients were grouped accordingly. According to this grouping, 44 patients have previously had COVID-19, while 90 patients have not. A total of 134 patients were included in this study for analysis and review. Information on how long ago the patients have COVID-19 has obtained from the patient files. This period varied between 23±11 months. Data on ejaculate volume, sperm concentration, total sperm count, total motility, progressive motility, percentage of sperm with normal morphology, and SDI values were collected from the semen analysis report forms of the included patients. These parameters were evaluated to assess the characteristics of the semen samples. The two groups were compared based on the above-mentioned parameters according to the World Health Organization's 2021 Semen Analysis Criteria. These criteria include a minimum ejaculate volume of ≥ 1.4 ml, sperm concentration of ≥ 16 million/ml, total motility of ≥ 42%, progressive motility of ≥ 30%, and percentage of sperm with normal morphology of ≥ 4%. By applying these criteria, a comparative analysis was conducted to evaluate whether there was any difference between the two groups in terms of semen characteristics. SDI values were obtained by dividing the total number of observed deformities in a SperMac-stained slide at 1000x (100 x 10) magnification by the total number of spermatozoa. This calculation provided a quantitative measure of the proportion of deformities in the analyzed sperm population. The deformities shown in Table 1 were used as the basis for morphology assessment (7). Statistical analyses were performed using IBM SPSS Statistics 25 software package. After conducting a normality analysis of the data, various statistical techniques were used to interpret the data. The normal distribution of the data was measured using normality tests (Kolmogorov-Smirnov test, Shapiro-Wilk test). Additionally, measures of skewness and kurtosis, arithmetic mean, mode, median values, and histograms were considered. This included creating frequency tables to summarize categorical variables, calculating descriptive statistics to describe the central tendency and variability of continuous variables, and using parametric (Independent Samples t-test) and non-parametric tests (Mann-Whitney U test) depending on the nature of the variables. In our study, ejaculate volume,

Table 1: Classification of sperm morphology (7).

Location	Normal (ideal/typical) appearance	Abnormal
Head	The head should be smooth, regularly contoured and generally oval in shape. There should be a well-defined acrosomal region comprising 40–70% of the head area (96). The acrosomal region should contain no large vacuoles, and not more than two small vacuoles, which should not occupy more than one fifth of the sperm head. The post-acrosomal region should not contain any vacuoles.	• acrosome less than 40% or larger than 70% of a normal head area, or • length-to-width ratio less than 1.5 (round) or larger than 2 (elongated), or • shape: pyriform (pear shaped), amorphous, asymmetrical, or non-oval shape in the apical part, or • vacuoles constitute more than one fifth of the head area or located in the post-acrosomal area, or • double heads, or • any combinations
Midpiece	The midpiece should be slender, regular and about the same length as the sperm head. The major axis of the midpiece should be aligned with	• irregular shape, or • thin or thick, or • asymmetrical or angled insertion at head, or • sharply bent, or • any combinations
Tail	The principal piece should have a uniform calibre along its length, be thinner than the midpiece and be approximately 45 μm long (about 10 times the head length). It may be looped back on itself, provided there is no sharp angulation indicative of a broken flagellum.	• sharply angulated bends, or • smooth hairpin bends, or • coiled, or • short (broken), or • irregular width, or • multiple tails, or • any combinations
Cytoplasmic residue	Cytoplasmic droplets (less than one third of a normal sperm head size) are normal.	• residual cytoplasm is considered an anomaly only when it exceeds one third of normal sperm head size

sperm concentration, total motility, progressive motility, percentage of sperm with normal morphology, and SDI values were expressed as continuous variables. A p-value < 0.05 was considered statistically significant.

RESULTS

In our study, we found no statistically significant difference ($p > 0.05$) in terms of ejaculate volume, sperm concentration, total sperm count, total motility, progressive motility, and percentage of sperm with normal morphology between the group that have previously contracted COVID-19 and the group that have not, as indicated in Table 2. However, as shown in Table 2, we observed a significant difference in SDI values between the two groups ($p < 0.001$). This indicates that while there were no significant differences in traditional semen parameters, the SDI values reflected significant differences between the two groups.

DISCUSSION

In our study, no significant difference was found in terms of ejaculate volume between those who have and have not contracted COVID-19. However, Kurashova et al. (11) reported a significant difference in ejaculate volume between COVID-19 positive and negative groups. The difference between our study and Kurashova et al.'s could be explained by their smaller control group of 20 individuals. In a study by Rafiee et al. (12), significant differences were found in semen volume between pre-

Table 2: Analysis and statistical evaluation of sperm parameters and SDI values.

Semen Parameters	Group of individuals who have had COVID-19. (Mean-SD) (n=44)	Group that have not had COVID-19 (Mean-SD) (n=90)	p value
Volume (mL)	3.41-1.42	3.45–1.59	0.838
Concentration (Million/mL)	54.24-36.61	50.72-37.20	0.516
Total Sperm Count (Million)	179.02-134.42	165.1-137.02	0.436
Total Motility (%)	54.15-15.15	56.01-18.00	0.502
Progressive Motility(%)	44.93-16.17	46.40-20.11	0.65
Morphology (Normal)	2.36-1.95	2.22-1.35	0.694
Sperm Deformity Index	1.75-0.44	1.42-0.28	0.00

a: The data did not follow a normal distribution. When comparing the measurement values of two independent groups with non-normally distributed data, the "Mann-Whitney U" test was used. A p-value less than 0.05 was considered a significant difference when comparing the independent variables between groups.

b: The data is normally distributed. The independent samples t-test was used to compare the independent variables in the samples. A p-value less than 0.05 was considered statistically significant.

and post-disease COVID-19 positive patients. However, in their study, semen analysis was performed within 2 months after COVID-19 infection, whereas in our study, the patients have contracted COVID-19 a longer time ago. This longer duration might have allowed for the semen volume to recover. While COVID-19 might have an acute effect on semen volume reduction, the recovery process might not have a long-term impact.

In our study, no statistically significant difference was observed in sperm concentration between patients who have and have not contracted COVID-19. Li et al. (13) reported a significant decrease in sperm concentration when comparing COVID-19 positive patients with the control group. However, the number of cases in their study was not as high as in ours, and the semen samples in their study were obtained from autopsies. Guo et al. (14) investigated the impact of COVID-19 on semen parameters in men who have previously contracted and recovered from the disease. When compared with the control group, they noted a significant decrease in sperm concentration in patients who have experienced COVID-19. However, it was noteworthy that in some recovered patients, the sperm concentration in the second sample was significantly higher than in the first. This suggests that there might be temporary differences in sperm parameters among individuals who have had and recovered from COVID-19. From this, it is possible to conclude that COVID-19 might have an acute effect on reducing sperm concentration. Gharagozloo et al. (15) also mentioned the potential for recovery in sperm parameters after COVID-19 infection. The fact that the patients in our study have contracted COVID-19 a long time ago might have contributed to the lack of significant difference in sperm concentration compared to the group that did not have COVID-19. In our study, no significant difference was found in terms of total sperm count between the groups that have and have not experienced COVID-19. Guo et al. (16) reported that the total sperm count returned to normal levels within 32 days after diagnosis. Indeed, the dynamic nature of the recovery process and sperm parameters might have contributed to the lack of significant difference in total sperm count between the groups. Piroozmanesh et al. (17) found that the total sperm count was significantly lower in individuals who have experienced COVID-19 compared to those who have not. This could be attributed to the acute effect, as their study was conducted between COVID-19 positive (throat swab) and negative patients. However, our study included patients who have experienced and recovered from COVID-19. Koç et al. (18) demonstrated that COVID-19 significantly reduced both the total and progressive motility of sperm in individuals who contracted the infection. However, the limited number of patients and the study being conducted in Ankara, which may have a different population density and stress level compared to Adana, could explain the differences between their study and ours. Additionally, differences in the timing of semen analysis before and after COVID-19 infection could also affect the strength of their study. Ma et al. (19) reported in a limited study that semen parameters were normal in 8 out of 12 COVID-19 patients. Our study, especially in terms of sperm concentration, total motility, and progressive motility, is consistent with this study. In a study conducted by Temiz et al. (20), similar findings to our study were obtained regarding sperm concentration, total motility, and progressive motility in COVID-19 patients. Furthermore, Temiz et al. observed that sperm morphology was significantly lower in COVID-19 patients compared to the control group, highlighting another potential impact of COVID-19 on male fertility. The relationship with acute fever during the illness period is an interesting aspect that may require further research. However, the limited number of participants in the study and the presence of fever in the patients during their study could explain the differences between their study and ours. Our study is a retrospective study, and information about whether the patients who have recovered from COVID-19 had a fever during their illness could not be obtained. Gacci et al. (21) suggested in their study that the recovery of semen parameters in patients who have recovered from COVID-19 might be related to the severity of the disease. We could not find any studies in the literature that investigated the sperm deformity index value in COVID-19 patients, making our study unique in this regard. We found a significant difference in sperm deformity index values between patients who have and have not experienced COVID-19 ($p < 0.001$). An important finding of our study is that COVID-19 does not affect the normal morphology of sperm but increases the rate of abnormal morphology. This could be explained by the fact that COVID-19 does not cause a deterioration in normal morphology but increases the number of deformities in abnormal sperm. Aziz et al. (23) measured the amount of reactive oxygen species (ROS) in infertile patients and found that infertile patients with high ROS levels had lower SDI values. In our study, SARS-CoV-2 might have led to a significant decrease in SDI values in patients who have recovered from COVID-19 by increasing the amount of reactive oxygen species. Turner et al. (24) stated that ACE2 receptors in the testes have functions related to immunity, inflammation, and many other functions. SARS-CoV-2 might increase inflammation by binding to ACE2 receptors and increasing their numbers, potentially leading to sperm deformities.

There are some limitations to our study. The fact that information about whether patients have contracted COVID-19 was obtained from patient records relatively weakened the strength of our study. Additionally, the varying duration from COVID-19 infection to recovery among patients might have affected the semen parameters differently. This is another factor that restricted our study.

CONCLUSION

SARS-CoV-2 can affect multiple systems in the body, including the male reproductive system. To deepen our understanding of the effects of COVID-19 on semen parameters and male reproductive health, more comprehensive studies are needed.

Conflict of Interest: No conflict of interest was declared by the authors.
Ethics: This research is approved by the Adana City Training and Research Hospital Ethics Committee (Meeting Number: 125, Decision Number: 2528).
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ORIGINAL ARTICLE

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Health Literacy and Associated Factors in Medical Students

Tıp Fakültesi Öğrencilerinde Sağlık Okuryazarlığı ve İlişkili Faktörler

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ABSTRACT

Objective: *This study aims to determine the health literacy levels of medical students and to investigate the variables that may be associated with health literacy.*

Materials and Methods: *This cross-sectional study was carried out on 702 students studying in the first three years of the Necmettin Erbakan University, Faculty of Medicine. After obtaining ethical and written permission, the data of the study were collected between January and February 2023. For the research, a data collection form consisting of 53 questions was prepared by the researchers. The Turkish Health Literacy Scale-32 (TSOY-32) was used in the last part of the data collection form. SPSS 28.0 package was used for data entry and analysis. Statistical significance was accepted at p<0.05.*

Result: *Of the 702 students included in the study, 59.3% were female. The mean general index score of the participants on the TSOY-32 scale was 31.77 (26.04-36.45). According to the scores, 20.9% of the students had inadequate health literacy and 37.7% had problematic-limited health literacy. The TSOY-32 score of the first year students was significantly lower than that of the other two years. The TSOY-32 score was significantly higher than the other groups in those who reported that people with more income than their expenses most often use health care facilities for preventive services and in those who reported having heard about the concept of health literacy (p<0.05).*

Conclusion: *As a result of this research, it was found that more than half of the students had insufficient or problematic limited level of health literacy.*

ÖZET

Amaç: *Bu çalışmanın amacı tıp fakültesi öğrencilerinin sağlık okuryazarlığı düzeylerini belirlemek ve sağlık okuryazarlığı ile ilişkili olabilecek değişkenleri araştırmaktır.*

Gereç ve Yöntem: *Kesitsel tipte olan bu çalışma, Necmettin Erbakan Üniversitesi Tıp Fakültesi'nin ilk üç yılında öğrenim gören 702 öğrenci üzerinde gerçekleştirildi. Etik ve yazılı izin alındıktan sonra çalışmanın verileri Ocak-Şubat 2023 tarihleri arasında toplandı. Araştırma için araştırmacılar tarafından 53 sorudan oluşan bir veri toplama formu hazırlandı. Veri toplama formunun son bölümünde Türkiye Sağlık Okuryazarlığı Ölçeği-32 (TSOY-32) kullanıldı. Veri girişi ve analizinde SPSS 28.0 paketi kullanıldı. İstatistiksel anlamlılık p<0,05 olarak kabul edildi.*

Bulgular: *Araştırmaya dahil edilen 702 öğrencinin %59,3'ü kız idi. Katılımcıların TSOY-32 ölçeğindeki genel indeks puanı ortalaması 31,77 (26,04-36,45) olarak belirlendi. Puanlara göre öğrencilerin %20,9'unun yetersiz sağlık okuryazarlığına sahip olduğu, %37,7'sinin ise problemli-sınırlı sağlık okuryazarlığına sahip olduğu görüldü. Birinci sınıf öğrencilerinin TSOY-32 puanı diğer iki yıla göre anlamlı derecede düşüktü. Geliri giderinden fazla olan kişilerde, koruyucu hizmetler için en çok sağlık kurumlarını kullandığını belirtenlerde ve sağlık okuryazarlığı kavramını duyduğunu belirtenlerde TSOY-32 puanı diğer gruplara göre anlamlı derecede yüksekti (p<0,05).*

Sonuç: *Bu araştırma sonucunda öğrencilerin yarıdan fazlasının sağlık okuryazarlığının yetersiz veya sorunlu sınırlı düzeyde olduğu tespit edilmiştir.*

Keywords:
Health literacy
Medical faculty
Medical, student

Anahtar Kelimeler:
Sağlık okuryazarlığı
Tıp fakültesi
Tıp, öğrenci

INTRODUCTION

The World Health Organization (WHO) defines health literacy as "the level of access to, understanding of, and use of relevant sources of information to make decisions about health care, to protect, maintain, and improve health, and to improve quality of life" (1,2). According to the definition in the Dictionary of Health Promotion of the General Directorate of Primary Health Care Services of the Ministry of Health in our country, health literacy is the level of knowledge, skills and self-confidence that individuals need to change their lifestyles and conditions in order to improve their own health and public health (3). According to these definitions, health literacy is the totality of an individual's ability to access, understand, evaluate and use health-related information (4).

Health literacy is an important concept that enables people

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to make informed decisions about health-related issues. These skills are becoming increasingly important in an era where participation in health care is becoming more important, along with easy access to health information and increasing health-related resources (4,5). Health literacy is considered to be one of the most important issues in public health because of its impact on individuals' health outcomes (6).

Low levels of health literacy can have several negative consequences for individuals and societies (7). People with low health literacy may have difficulty accessing health-related information and services. As a result, some health problems, such as delayed diagnosis and treatment, may progress and become serious. They may make decisions based on incorrect and misleading health information. They may not take preventive health measures or have difficulty recognising the signs of illness. Because they do not fully understand the benefits and risks of health services, they may seek unnecessary tests and treatments, and may also be prone to unhealthy lifestyles that can increase the risk of chronic diseases such as obesity and diabetes mellitus. For these reasons, improving health literacy helps individuals make healthier decisions and use health services more effectively (8,9).

Student health literacy is a concept that aims to make the younger generation health conscious and knowledgeable. It involves developing students' ability to access, understand, evaluate and use health-related information. It provides students with basic skills in understanding and using health-related information, while helping them to adopt conscious and healthy lifestyles (10,11). Considering the importance of the concept in students, it can be assumed that health literacy is of particular importance for medical students, who are the health professionals of the future. Developing health literacy among medical students can help them become better doctors and health professionals. It also helps them to communicate more effectively with their patients and to make informed health decisions (10,11).

The aim of this study is to determine the health literacy levels of first, second and third year medical students and to examine the variables that may be associated with health literacy.

MATERIALS AND METHODS

Type of research and research permissions

Before this research, which was designed as a cross-sectional type; Written permission was obtained from the Ethics Committee of Necmettin Erbakan University, Faculty of Medicine, Non-Pharmaceutical and Medical Devices (Date: 06.01.2023, Decision Number: 2023/4119) and the Dean's Office of Necmettin Erbakan University Faculty of Medicine.

Participants

The population of the study consists of a total of 814 students in the first, second and third year of the Faculty of Medicine in the academic year 2022-2023. The sample size was not calculated for the research and the aim was to reach at least 80% (n=652) of the students. Research; Volunteered to participate in the study between 15 January and 15 February 2023 and gave verbal consent; The study was completed with a total of 702 (86%) students, 242 in the first year, 216 in the second year, 244 in the third year.

Data collection form

The data collection form prepared after the literature review in the research consists of 53 questions and three parts. In the first part, there are 13 questions about the socio-demographic characteristics of the participants. In the second part, there are 8 questions that may be related to the level of health literacy. In the third part, in order to determine the level of health literacy, the Turkish Health Literacy Scale-32 (TSOY-32), whose conceptual framework was developed by Okyay et al. The scale consists of 32 questions, the participants mark one of the answers as very easy/easy/difficult/very difficult/I have no idea according to the five-point Likert scale for the topics covered in each question. When scoring the scale, the calculated mean score is standardised to a range of 0-50 using the formula (mean-1) x (50/3). After this calculation, 0 indicates the lowest health literacy and 50 the highest health literacy. As a result of the obtained index, those with 0-25 points are classified as inadequate, those with >25-33 points as problematic-limited, those with >33-42 points as adequate, and those with >42-50 points as excellent health literacy. In the Turkish validity and reliability study of the TSOY-32 scale, it was found that the Cronbach alpha coefficient was 0.927, the factor loadings of each item were greater than 0.32, and they were grouped into a single factor (12). In this study, the calculated Cronbach alpha coefficient of the TSOY-32 scale was found to be 0.943.

Methods

After obtaining ethical approval and permission from the Dean's Office, data were collected through face-to-face interviews between student classes. All participants were informed about the study and students who agreed to participate were asked to complete the data collection forms. The data collection form was administered to the volunteer participants under observation and each form took an average of 15 minutes to complete.

Statistical analysis

Statistical analysis of the data was performed using IBM SPSS, version 28.0 (IBM Corp, Armonk, N.Y. USA). Visual (histograms and probability plots) and analytical (Kolmogrorov-Smirnov) methods were used to test the conformity of the data with the normal distribution. Numerical data were evaluated using arithmetic mean±standard deviation, median (1-3 quarters); frequency distributions and percentages were used to summarise categorical data. Categorical data with scale score; evaluated with Mann-Whitney U and Kruskal-Wallis H tests. Post-hoc Mann-Whitney U test with Bonferroni correction was performed for pairwise comparisons between groups with significant Kruskal-Wallis H test results. Correlations of non-normally distributed numerical variables were analysed using Spearman's correlation coefficient. Statistically, cases where p was less than 0.05 were considered significant.

RESULT

The mean age of the 702 students included in the study was 20.09±1.57 years. 59.3% (n=416) of the students were female. The socio-demographic characteristics of the students are shown in Table 1.

Table 1: Sociodemographic characteristics of medical students.

Features		n (%)
Gender	Female	416 (59.3)
	Male	286 (40.7)
Class	1st Class	242 (34.5)
	2. Class	216 (30.8)
	3rd Class	244 (34.8)
Family Type	Nuclear family	646 (92.0)
	Extended family	56 (8.0)
Income Status	Income less than expenses	56 (8.0)
	Income equal to expenses	401 (57.1)
	Income more than expenses	245 (34.9)
Longest residence	Village	29 (4.1)
	Country	156 (22.2)
	Provincial Centre	517 (73.6)
Mother's educational status	Middle school and below	234 (33.3)
	High school and above	468 (66.7)
Father's education	Middle school and below	122 (17.4)
	High school and above	580 (82.6)
Housing	At home with family	271 (38.6)
	Student residence	294 (41.9)
	Student house with a friend	85 (12.1)
	Living at home alone	52 (7.4)
Smoking status at any time in life	No	614 (87.5)
	Yes	88 (12.5)
Alcohol use at any time in life	No	632 (90.0)
	Yes	70 (10.0)
Presence of chronic disease	No	647 (92.2)
	Yes	55 (7.8)

When asked to rate their general state of health, 66.2% of the students rated their health as good, 31.9% as fair and 1.9% as poor. 40.9% of the participants reported that they exercised regularly (Table 2).

The mean body mass index (BMI), calculated from the height and weight of the students, was 22.41±3.50 kg/m2, and the mean number of books read per year was 6 (3-10). According to the results, 20.9% (n=147) of the students were inadequate, 37.7% (n=265) had limited problems, 27.5% (n=193) were adequate and 13.8% (n=97) were inadequate. (n=97) were found to have excellent health literacy.

Table 2: Some life characteristics of medical students.

Features		n (%)
How would you rate your overall health?	Good	465 (66.2)
	Middle	224 (31.9)
	Bad	13 (1.9)
Do you exercise regularly?	No	415 (59.1)
	Yes	287 (40.9)
Is there a doctor or health professional in your family?	No	470 (67.0)
	Yes	232 (33.0)
What is your most common reason for seeking health care?	Emergencies	474 (67.5)
	Follow-up of chronic diseases	65 (9.3)
	Preventive health services	163 (23.2)
Have you ever heard of the concept of health literacy?	No	358 (51.0)
	Yes	344 (49.0)
What resources do you usually use to access health information*?	The Internet	519 (73.9)
	Doctors and/or health professionals	397 (56.6)
	Television	42 (6.0)
	Medical books	254 (36.2)
	Newspaper, magazine	25 (3.6)

*Some respondents cited more than one source.

The comparison of TSOY-32 scores and socio-demographic characteristics of medical students is shown in Table 3. The TSOY-32 scores of female and male students were similar (p=0.415). A statistically significant difference was found between the TSOY-32 scores of students according to their class (p<0.001). It was found that this difference was due to the lower TSOY-32 scores of first year students compared to second and third year students (p<0.001; p<0.001 respectively). There was a significant difference between income status and TSOY-31 score (p<0.001). The difference was found to be due to the higher TSOY-32 scores of students who reported that their income was more than their expenses compared to those whose income was less than or equal to their expenses (p=0.002; p<0.001, respectively). There was a difference between the longest place of residence and the TSOY-32 scores (p=0.015). It was found that the difference was due to the higher scores of those who reported the province where they had lived the longest compared to those who reported the district (p=0.007). There was no difference between parental education level, place of residence, cigarette-alcohol consumption, presence of chronic diseases and TSOY-32 scores (p>0.05).

There was no difference between students' TSOY-32 scores according to their perception of their own health status as good - fair - poor (p=0.260). There was a difference between the most common reasons for visiting

Table 3: Comparison of students' TSOY-32 scores and socio-demographic characteristics.

Features		TSOY-32 Score Median (1-3 quarters)	p
Gender	Female	31.25 (26.04-35.93)	0.415*
	Male	32.29 (26.04-38.02)	
Class	1st Class	28.12 (22.39-33.33)	<0.001**
	2. Class	33.33 (29.16-39.58)	
	3rd Class	32.55 (28.12-38.02)	
Family Type	Nuclear family	31.77 (26.56-36.45)	0.097*
	Extended family	29.68 (22.52-36.84)	
Income Status	Income less than expenses	30.72 (25.13-33.33)	<0.001**
	Income equal to expenses	30.72 (25.52-35.67)	
	Income more than expenses	33.33 (28.12-38.54)	
Longest residence	Village	32.29 (26.82-42.70)	0.015**
	Country	30.20 (24.47-33.85)	
	Provincial Centre	31.77 (26.56-36.97)	
Mother's educational status	Middle school and below	32.03 (27.47-36.45)	0.603*
	High school and above	31.77 (25.52-36.45)	
Father's education	Middle school and below	31.25 (26.95-34.89)	0.347*
	High school and above	31.77 (26.04-36.45)	
Housing	At home with family	32.29 (26.56-36.97)	0.266**
	Student residence	30.72 (25.00-35.93)	
	Student house with a friend	32.29 (26.30-38.02)	
	Living at home alone	32.29 (27.60-38.02)	
Smoking status at any time in life	No	31.77 (26.56-36.45)	0.111*
	Yes	29.16 (25.00-34.24)	
Alcohol use at any time in life	No	31.77 (26.04-36.32)	0.130*
	Yes	32.81 (27.60-40.23)	
Presence of chronic disease	No	31.77 (26.04-36.45)	0.532*
	Yes	31.77 (27.60-38.54)	

*Mann-Whitney U test
**Kruskal Wallis H test

health facilities and the TSOY-32 score (p<0.001). The difference was found to be due to the fact that the median TSOY-32 score (33.33) of those who reported that they most often visited health facilities for preventive services was higher than that of those who reported that they visited for emergencies (31.25) and chronic disease follow-up (30.72) (p<0.001); p=0.010). The TSOY-32 score of those who reported having heard of the concept of health literacy was significantly higher than that of those who had not (p<0.001). The TSOY-32 scores of doctors and/or health professionals who reported receiving health information from medical books were significantly higher than those who reported not receiving information from these sources (p<0.001; p=0.019, respectively) (Table 4). No correlation was found between students' age, BMI, number of books read per year and their TSOY-32 scores (r=0.128, p=0.001; r=0.024, p=0.0519; r=0.001, p=0.990).

DISCUSSION

The aim of this study was to determine the level of health literacy among preclerkship students in the first three years of medical school, and to examine variables that may be associated with health literacy. More than half of the 702 medical students included in the study have an inadequate or problematic level of health literacy, according to their scores on the TSOY-32 scale. In a study using the TSOY-32 scale on students of the Faculty of Medicine at another university in 2020, it was found that 10.2% of students had inadequate health literacy and 30.0% had a problematic-limited level of health literacy (9). Also in our country, it was found that 27.2% of the 400 people included in the study for the development of the TSOY-32 scale in 2016 had insufficient health literacy and 42.2% had a problematic-limited level of health literacy (12). In the European Health Literacy Survey, which included Austria, Bulgaria, Germany, Greece, Ireland, the Netherlands, Poland and Spain, at least 1 in 10 (12%) had insufficient health literacy and approximately 1 in 2 (47%) had a problematic-limited level of health literacy. Of these eight countries, only 1.8% of the sample in the Netherlands had insufficient health literacy, while in Bulgaria this rate was found to be 26.9% (13). In these studies conducted in our country, similar to our study, it can be said that the

Table 4: Comparison of students' TSOY-32 scores with some life characteristics.

Features		TSOY-32 Score Median (1-3 quarters)	p
How would you rate your overall health?	Good	31.77 (26.04-36.45)	0.260**
	Middle	32.03 (26.56-36.45)	
	Bad	29.68 (17.70-33.33)	
Do you exercise regularly?	No	32.25 (26.04-35.93)	0.173*
	Yes	32.29 (26.56-38.02)	
Is there a doctor or health professional in your family?	No	31.77 (26.04-36.06)	0.470*
	Yes	31.77 (26.56-36.97)	
What is your most common reason for seeking health care?	Emergencies	31.25 (26.04-34.50)	<0.001**
	Follow-up of chronic diseases	30.72 (21.87-38.80)	
	Preventive health services	33.33 (28.12-41.14)	
Have you ever heard of the concept of health literacy?	No	30.72 (25.00-34.37)	<0.001*
	Yes	32.29 (27.60-38.02)	
Types of resources used to access health information.			
Internet	No	31.77 (27.60-38.02)	0.152*
	Yes	31.77 (26.04-35.93)	
Doctors and/or health professionals	No	30.20 (23.43-34.89)	<0.001*
	Yes	32.29 (28.12-37.50)	
Television	No	31.77 (26.04-36.45)	0.171*
	Yes	30.20 (26.04-33.33)	
Medical books	No	31.25 (25.52-35.41)	0.019*
	Yes	32.29 (27.60-38.02)	
Newspaper, magazine	No	31.77 (26.04-36.45)	0.889*
	Yes	31.77 (29.68-33.59)	

*Mann-Whitney U test
**Kruskal Wallis H test

percentage of insufficient or problematic limited health literacy is similar. However, the differences in the level of inadequate or problematic-limited health literacy in studies conducted in countries other than Turkey may be due to differences in the level of development of the countries, health policies, and socio-cultural structures of the participants included in the study. In addition, it can be assumed that the use of different scales to determine the level of health literacy.

In this study, the TSOY-32 scores of male and female students were similar. In some studies conducted with students studying in the field of health, similar to this study, it was found that there was no difference between gender and health literacy (12,14). In some community-based studies in the international and national literature, it has been found that women's health literacy scores are significantly higher than men's (15-18). The difference in some population-based studies that found a significant difference between gender and health literacy may be due to the inclusion of people with different levels of education. The fact that there was no significant difference between health literacy scores and gender in some studies that included people with the same level of education, as in our study, seems to support this idea.

Similar to the literature, in this study, as the grade level of the students increases, their health literacy scores also increase (9,19). The first professional group that comes to mind for the health education of society is generally doctors. Therefore, it is an expected finding that as the number of classes of medical students increases, their education in the field of health, their ability to access, understand and evaluate health-related information and resources increases, and with this increase, their health literacy scores increase.

In this study, the TSOY-32 scores of those whose income exceeds their expenses are significantly higher than those whose income is less than or equal to their expenses. In the literature, similar to this study, it has been found that the health literacy levels of individuals with high income levels are sufficient and excellent, while those with low income levels are found to be insufficient, problematic and limited (20-22). Health literacy has recently been seen as one of the important links between socioeconomic status and health (5,23-25). In this link; as socioeconomic status improves, it is thought that reasons such as better perception of health status, easier access to health services and health education may be effective.

In the study, there was no significant difference between the prevalence of chronic disease in students and TSOY-32. It is stated that the level of health literacy plays a key

role in the prevention and management of chronic diseases (26). It is stated that people with low health literacy experience communication problems in accessing medical information, are unable to access health services and therefore have problems in managing their illnesses. For these reasons, the incidence of chronic diseases is higher in people with low health literacy (4). In the study, it was predicted that the inability to find a difference between chronic diseases and health literacy was due to the fact that the study population consisted of young people with medical education. The lack of difference between chronic diseases and health literacy in similar studies conducted with students studying in the field of health supports our prediction (9,27).

In this study, it was found that the TSOY-32 score of those who reported that they most often visited health facilities for preventive services was higher than that of those who reported that they visited for emergencies and follow-up of chronic diseases. Studies have shown that people with low health literacy are less likely to use chronic disease management and preventive health services. For these reasons, low health literacy has been reported to be an important factor in increasing disease mortality and health service costs (13,16,28).

In the study, similar to the literature, those who said they had heard of the concept of health literacy had a higher TSOY-32 score than those who had not (29,30). The higher scores of students who had heard of health literacy may be due to the fact that they are more likely to be interested in the topic, to research it, and to obtain information about it. It is also possible that as the medical student class progresses, the likelihood of being educated about health literacy and obtaining information about the term may have an effect on this finding.

The TSOY-32 scores of students who reported receiving health information from doctors and/or health professionals and from medical books were significantly higher than those who reported not receiving information from these sources. Getting accurate information from reliable sources is very important for health. Getting accurate and reliable information from the right source can influence health-related decision making. It is expected and desired that medical students receive reliable information.

CONCLUSION

As a result of this research, conducted with 702 students studying in the first three years of the Faculty of Medicine, it was found that more than half of the students had an inadequate or problematic level of health literacy. It was found that the level of health literacy increased with class level and income level. It was found that the health literacy of those who most frequently used health facilities for preventive services was higher than that of those who used them for emergencies and chronic disease management. It was found that those who reported having heard of the concept of health literacy and those who reported receiving health information from doctors and/or health professionals and medical books had higher health literacy.

Health literacy is an important factor in increasing people's health-related knowledge, skills and positive behaviours. Medical students are in a position to play a leading role in the field of health and can play an important role in providing access to health information for society. For this reason, it is necessary to improve the health literacy of those receiving health education. By investigating the variables that may be important in the health literacy level of students, training and studies specifically for these groups should be strengthened.

LIMITATIONS

Our study had several limitations. Due to the cross-sectional design of the study, the long-term causal relationships between different factors related to health literacy could not be assessed. In addition, only students in the first three years of medical school were included in the study. The inclusion of students from different universities and faculties is an important limitation. Despite the above limitations, we believe that this study will make a significant contribution to the literature by identifying the factors associated with the level of health literacy of medical students and guiding future research in this area.

Conflict of Interest: No conflict of interest was declared by the authors.
Ethics: This study was approved by Non-Pharmaceutical and Medical Device Ethics Committee of Necmettin Erbakan University Faculty of Medicine with decision number 2023/4119 dated 06.01.2023.
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ORIGINAL ARTICLE

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Evaluation of Non-COVID-19 CT Scan Findings Detected on CT Images Performed due to Suspected COVID-19 Pneumonia: A Retrospective Analysis of 6669 Cases

COVİD-19 Pnömonisi Şüphesiyle Yapılan Bilgisayarlı Tomografi Görüntülemede Saptanan COVİD-19 Dışı Bulguların Değerlendirilmesi: 6669 Vakanın Restrospektif Analizi

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ABSTRACT

Objective: *For the past years, COVID-19 infection has continued to play a significant role in our lives as a serious threat and concern due to increase in the number of cases. During this pandemic stage, chest computed tomography (CT) has been proven to have great importance for rapid and accurate diagnosis and a pivotal role in assisting the clinical management of patients with uncertain clinical scenarios.*

The present retrospective study aimed to inform the clinicians who referred chest CT and the radiologists reporting these CTs about the frequency and variety of non-COVID-19 findings in patients who underwent chest CT examination with the suspicion of COVID-19 pneumonia.

Material and Method: *This retrospective study was approved by our Institutional Ethics Committee. The requirement for written informed consent was waived. Our study included 6669 patients who applied to the emergency room with the suspicion of COVID-19 infection between March 20th and April 20th, 2020. The inclusion criteria were patients who had suspicious symptoms of having COVID-19 infection and/or had close contact with a patient with COVID-19 infection and (ii) patients who underwent chest CT. They evaluated CT scans individually, and all non-COVID-19 findings (NCF) were recorded manually*

Results: *The study population consisted of 6669 consecutive patients (males 55.5% and females 44.5%). The overall mean age was 41.7 years [SD±15.1]. There were incidental non-COVID-19 findings in 3159 (47.4%) patients and none in 3510 (52.6%) patients*

Conclusion: *CT examinations performed in patients with suspected COVID-19 pneumonia should be examined in detail regarding clinically significant findings. It is vital to take necessary precautions in advance regarding pathologies that may be clinically significant regarding appropriate treatment and follow-up planning at the appropriate time. The clues must be stated in the radiology report so that the clinician can make appropriate management regarding these pathologies.*

ÖZET

Amaç: *Birkaç yıldır, vaka sayılarının artmasıyla birlikte ciddi bir tehdit ve endişe kaynağı olarak COVİD-19 enfeksiyonu hayatımızda önemli bir rol oynamaya devam etmektedir. Bu pandemi aşamasında toraks bilgisayarlı tomografisinin (BT) hızlı ve doğru tanı açısından büyük öneme sahip olduğu ve belirsiz klinik senaryolara sahip hastaların klinik yönetimine yardımcı olmada önemli bir role sahip olduğu kanıtlanmıştır. Bu retrospektif çalışmada, COVİD-19 pnömonisi şüphesiyle toraks BT incelemesi yapılan hastalarda, toraks BT'ye yönlendiren klinisyenlere ve bu BT'leri raporlayan radyologlara, COVİD-19 dışı bulguların sıklığı ve çeşitliliği hakkında bilgi verilmesi amaçlandı.*

Gereç ve Yöntem: *Bu retrospektif çalışma kurumsal etik kurulumuz tarafından onaylandı. Yazılı bilgilendirilmiş onam alma zorunluluğundan feragat edildi. Çalışmamıza 20 Mart- 20 Nisan 2020 tarihleri arasında acil servise COVİD-19 enfeksiyonu şüphesiyle başvuran 6669 hasta dahil edildi. Dahil edilme kriterleri, COVİD-19 enfeksiyonuna dair şüpheli semptomları olan ve/ya yakın temasta COVİD-19 enfeksiyonlu bir hastaya yakın teması olan hastalar ve toraks BT çekilen hastalardı. Toraks BT tetkikleri değerlendirildi ve COVİD-19 dışı tüm bulgular manuel olarak kaydedildi.*

Bulgular: *Çalışma popülasyonu ardışık 6669 hastadan oluşmuştur (%55.5 erkek ve %44.5 kadın). Genel ortalama yaş 41,7 yıl idi. 3159 (%47.4) hastada rastlantısal olarak COVİD-19 dışı bulgular görüldü, 3510 (%52.6) hastada ise COVİD-19 dışı bulgu yoktu.*

Sonuç: *COVİD-19 pnömonisi şüphesi olan hastalarda yapılan toraks BT incelemeleri klinik açıdan anlamlı bulgular açısından ayrıntılı olarak incelenmelidir. Klinik açıdan anlamlı olabilecek patolojilerde gerekli önlemlerin önceden alınması, uygun zamanda tedavi ve takip planlaması yapılması hayati önem taşımaktadır. Klinisyenin bu patolojilere yönelik doğru yönetimi yapabilmesi için ipuçlarının radyoloji raporunda belirtilmesi önemlidir.*

Keywords:
Incidental Finding
Computerized Tomography
X-Ray

Anahtar Kelimeler:
Rastlantısal Bulgular
Bilgisayarlı Tomografi
X-Ray

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INTRODUCTION

For about a few years, COVID-19 infection has continued to play a significant role in our lives as a serious threat and concern with the increase in the number of cases (1-3). During this pandemic stage, chest computed tomography (CT) has been proven to have great importance for rapid and accurate diagnosis and a pivotal role in assisting the clinical management of patients with uncertain clinical scenarios. Although the American College of Radiology (ACR) and other professional radiology societies have suggested against considering CT as a screening tool in the diagnosis of COVID-19, rapid and accurate diagnostic tools are urgently needed to identify, isolate, and manage the treatment of the patients as soon as possible (4). Although the specificity of the Polymerase Chain Reaction (PCR) results is high, performing imaging examination, especially chest CT, is necessary since serologic tests have some drawbacks, such as the long turnaround time and false negative test results (5). In the chest CT evaluation, the neck and upper abdominal organs, as well as the lung parenchyma and mediastinal structures, are displayed, and abnormalities of these regions can also be evaluated. As the role of CT imaging and the number of CTs for diagnosing COVID-19 pneumonia increases, more additional CT findings other than COVID-19 pneumonia are detected. In some patients, this may be beneficial in the early detection and prevention of abnormalities that are not initially clinically suspected yet urgent for diagnosis and treatment. Several recent studies have characterized CT imaging features of COVID-19 and reported the performance of radiologists in discriminating COVID-19 pneumonia from other viral etiologies. The described typical imaging patterns are bilateral, multifocal, and predominantly peripheral ground-glass opacities (GGO) associated with sub-segmental and mostly subpleural patchy consolidations, predominantly involving the lower lung lobes and posterior segments (6-9). The present retrospective study aimed to inform the clinicians who referred chest CT and the radiologists reporting these CTs about the frequency and variety of non-COVID-19 findings in patients who underwent chest CT examination with the suspicion of COVID-19 pneumonia.

MATERIAL AND METHOD

Sample and Data Collection

Our study included 6669 patients who applied to the emergency room with the suspicion of COVID-19 infection between March 20th and April 20th, 2020, and were referred to the radiology department as a result of the first clinical evaluation and underwent CT examination. The inclusion criteria were (i)patients who had suspicious symptoms of having COVID-19 infection and/or had close contact with a patient with COVID-19 infection and (ii) patients who underwent chest CT.

Ethical Consideration

This retrospective study was approved by our Institutional Ethics Committee (Date: 19.08.2020; Number: 2020-132). The requirement for written informed consent was waived.

CT Scanning Protocol

CT data were acquired using a 128-detector CT scanner (PHILIPS Ingenuity, Netherlands). The parameters of the CT scan were as follows: the patient was in the supine position and end-inspiratory acquisition, tube current–exposure time product of 200–300 mAs, tube voltage of 120 kV, and section thickness after reconstruction of 1.25 mm. CT scanning extended from the thoracic inlet to the caudally, including the upper abdomen. CT scans were obtained without contrast material administration.

Imaging Data Analysis

CT images were retrospectively evaluated by six radiologists with 5-20 years of experience in thoracic radiology who were blinded to RT-PCR test results. They evaluated CT scans individually, and all non-COVID-19 findings (NCF) were recorded manually. NCFs were classified into five groups, similar to the Computerized Tomography-Colonography Reporting and Data System (C-RADS) (10) (Table 1). Each group was classified according to its clinical significance. Groups NCF1 and NCF2 were combined as clinically insignificant findings, and groups NCF3 and NCF4 were combined as clinically significant finding groups. NCF0 was stated for limited examination due to severe artefacts or operation materials.

Table 1: Non-COVID-19 finding groups

GROUPS	DESCRIPTION	EXAMPLE
NCF0	Limited examination: compromised by artefacts or operation materials.	Artefact, sternotomy, valve replacement, intracardiac device
NCF1	Anatomic variations	Aberrant right subclavian artery, azygos fissure and lobe
NCF2	No clinically suspected finding: no workup indicated	Pulmonary fibrotic bands, simple renal cyst, simple liver cyst, renal calculus, gallstone
NCF3	Probably insignificant findings, incompletely characterized: workup may be indicated	Coronary calcification, cardiomegaly, hepatomegaly
NCF4	Probably significant findings: communicate to referring physician as per accepted practice guideline	Aortic aneurysm, aortic dissection, pulmonary mass, hydronephrosis

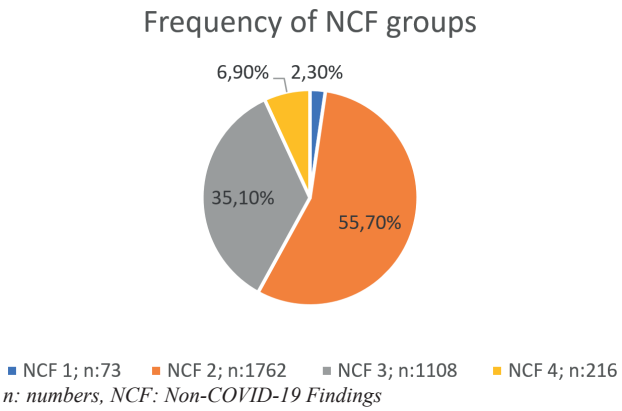
NCF: Non-COVID-19 Findings

Statistical Analysis

The statistical analysis was performed with SPSS software version 15.0. Descriptive statistical methods (mean, standard deviation, frequency, and percentage), Chi-square test, and Fisher's exact test were used for categorical variables, and Student t-test and Mann-Whitney U test were used for continuous variables in two group comparisons. Results were evaluated in a 95% confidence interval, and the statistical significance was accepted as $p < 0.05$.

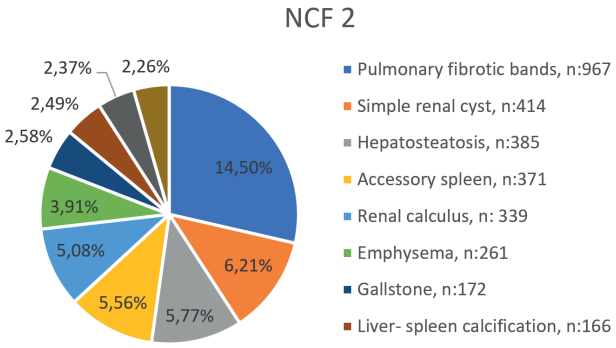
RESULTS

The study population consisted of 6669 consecutive patients (3701 males (55.5%) and 2968 females (44.5%)). The overall mean age was 41.7 years (SD 15.1); range 0-94 years, being 42.5 years (SD 15.7); range 0-94 for women and 41.1 years (SD 14.4); range 1-90 years for



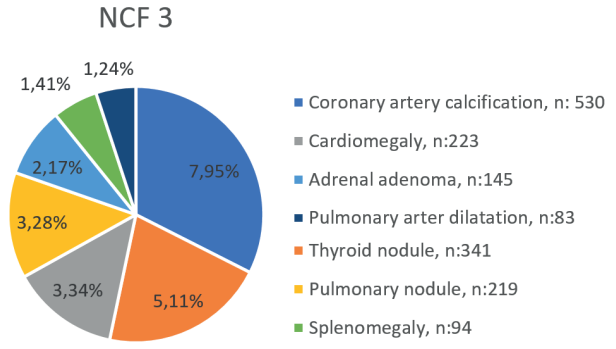
n: numbers, NCF: Non-COVID-19 Findings

Figure 1: The distribution of non-COVID findings.



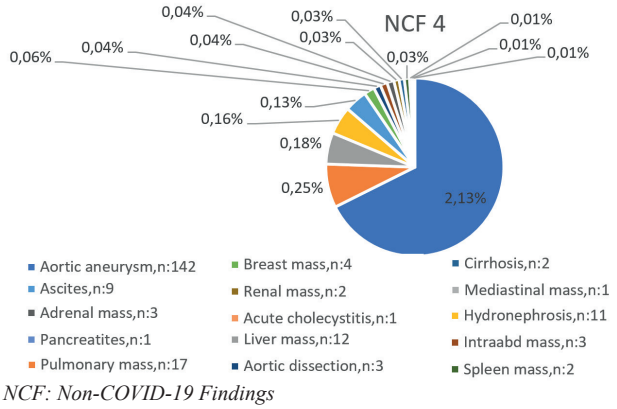
NCF: Non-COVID-19 Findings

Figure 2: Findings in the NCF2 group.



NCF: Non-COVID-19 Findings

Figure 3: Findings in the NCF3 group.



NCF: Non-COVID-19 Findings

Figure 4: Findings in the NCF4 group.

Table 2: The distribution of clinically insignificant and significant groups by gender and age

	NCF1-NCF2 n (%)	NCF3-NCF4 n (%)	p-value
Gender (n=3159)			
Female	716 (54.3)	603 (45.7)	<0.001
Male	1119 (60.8)	721 (39.2)	
	Mean (min-max)	Mean (min-max)	
Age	44 (2-93)	55 (3-94)	<0.001

NCF: Non-COVID-19 Findings

men. There were incidental non-COVID-19 findings in 3159 (47.36%) patients and none in 3510 (52.6%) patients. Figure 1 summarizes the frequency of NCF groups.

We classified NCF1 and NCF2 as the clinically insignificant groups and NCF3 and NCF4 as the clinically significant groups. The distribution of clinically insignificant and significant groups by gender and age is presented in Table 2. The mean age was 44.27±12.9 and 54.18±15.2 years in clinically insignificant and significant groups, respectively. This difference was statistically significant ($p<0.001$). The mean age was 35.73±12.6 years for patients without an incidental non-COVID-19 finding. The mean age was significantly higher in patients with an NCF ($p<0.001$). When the patient groups with and without NCFs were compared regarding gender, no significant difference was determined ($p=0.885$). Clinically insignificant NCFs were detected statistically more in both genders when compared to the clinically significant groups ($p<0.001$). Within the NCF1 group, the most common anatomic variants were azygos fissure-lobe in 62 patients (0.93%) and retroaortic left renal vein in 49 (0.7%), respectively.

Findings in the NCF2 group are summarized in Figure 2. The most common findings in this group were fibrotic bands in the lung in 967 patients (14.5%), simple renal cysts in 414 patients (6.21%), and hepatosteatosis in 385 patients (5.77%).

Findings in the NCF3 group are shown in Figure 3. The most common findings in this group were coronary artery calcification in 530 patients (7.95%), thyroid nodules in 341 patients (5.11%), and cardiomegaly in 223 patients (3.34%).

Findings in the NCF4 group are presented in Figure 4. The most common findings in this group were aortic aneurysm in 142 patients (2.13%), pulmonary mass in 17 patients (0.25%), liver mass in 12 patients (0.18%), hydronephrosis in 11 patients (0.16%), and ascites in 9 patients (0.13%).

DISSCUSSION

Several research papers have been recently published in the literature to describe characteristic CT imaging features and the temporal evaluation of imaging findings in patients with COVID-19 (6-9). Ai et al. reported the complementary role of chest CT in cases with false-negative RT-PCR test results, stating that the sensitivity of chest CT imaging was 97% in RT-PCR-confirmed cases (11). In a meta-analysis, the rate of positive chest CT imaging for pneumonia among patients suspected

of COVID-19 was determined as 89.76% (12). These findings emphasize the importance of CT imaging, especially in clinically suspected patients with negative test results.

As reported in the study of Dündar et al., CT was used as a screening method in some centers (13). Although CT is not used as a screening tool in patients with clinical suspicion of COVID-19 in our hospital, it has become a frequently used diagnostic aid due to the limited access to RT-PCR tests and the prolonged time required for the test results, especially in the early stages of the pandemic. For this reason, one of the CT units had been reserved for these patients in our clinic, as reported in the literature, within the scope of measures taken to reduce the risk of disease transmission.

CT is not a harmless diagnostic tool due to its high radiation doses, and CT has been overused in this process. As in routine, these CT examinations performed during the COVID-19 pandemic were evaluated and reported by radiologists. Since each examination performed was evaluated as a whole, every organ and anatomical structure in the imaging area was examined as well as lung findings. According to the definition of the ACR, an incidental finding, also known as an incidentaloma, can be defined as an incidentally discovered mass or lesion detected by CT, Magnetic Resonance Imaging (MRI), or other imaging methods performed for an unrelated reason (14). While these incidental findings are sometimes early diagnoses for the patients and save a life, they can occasionally lead to unnecessary further investigations.

For these reasons, it is crucial to identify and report clinically significant NCFs. In the study conducted by Turkay et al. on the extracolonic findings obtained in 227 patients in the CT colonography examination, it was stated that most of the findings were clinically insignificant at the time of reporting, the importance of the pathology and recommendations should be noted clearly and in close contact with the referring clinician (15). In addition, it was reported in this study that incidental findings, especially in asymptomatic patients, were the subject of discussion, the findings were irrelevant to the clinic, and the duration of evaluation and follow-up increased patient anxiety and cost.

In our study, some incidental findings were also detected in these chest CTs taken for COVID-19 disease. A total of 3159 patients (47.36%) had NCFs. Clinically significant NCFs were detected in 1324 patients (19.85%). Similar to some studies in the literature, in our study, clinically significant findings were less common than clinically insignificant findings (16,17).

Various studies have demonstrated that COVID-19 pneumonia is more common in men. In Khan's study, men were predominantly infected (70.25%), similar to Yang's meta-analysis (18,19). In terms of NCFs, no statistically significant difference was determined according to gender in patients with clinically significant or insignificant NCFs in our study.

When the NCFs were analyzed according to age, the frequency of the findings increased statistically significantly with age. Van Vugt et al., in a European-centered study in which chest radiographs were scanned due to acute cough, revealed that incidental findings were more common in elderly patients (20). In our study, incidental findings were detected more in elderly patients, similar to Van Vugt et al.'s study.

In the literature, it has been reported that there is abundant evidence that most cases of mortality develop in COVID-19 patients with cardiovascular disease (21). Therefore, additional examinations on COVID-19 patients with cardiovascular diseases are vital for optimal management. In a study, cardiomegaly was detected on chest CT scan in 33 (26.8%) patients (21). In our study, the most common finding among the clinically significant group was coronary artery calcification, with a rate of 7.94%. The other most common clinically significant findings were thyroid nodules (5.11%), cardiomegaly (3.34%), pulmonary nodules (3.28%), adrenal adenoma (2.17 %), aortic aneurysm (2.12%), and splenomegaly (1.4%) respectively. The study by Gupta et al. reported that COVID-19 patients with any coronary artery calcification were more likely to require intubation and die than those without coronary artery calcification (22). Furthermore, increasing coronary artery calcification was associated with mortality (22). Pre-existing cardiovascular disease may increase vulnerability to COVID-19 and greatly influence pneumonia development and prognosis. It should also be noted that the secondary damage of the virus is on the cardiovascular system (22). For this reason, viral infections associated with cardiovascular disease should be paid attention to and should be mentioned in the CT report.

Incidental thyroid nodules are considered common findings in the cross-sectional imaging of the neck, constituting about 16 to 18% (23). In our study, the second most common clinically significant NCF was thyroid nodule. A thyroid nodule incidentally during CT examination is a critical finding because, although the incidence of malignancy is not high, it has been reported that early diagnosis of thyroid malignancy can have a great impact on patient outcomes (24). Most adrenal adenomas are non-functional and are detected incidentally on routine imaging performed for unrelated reasons (Figure 5a, 5b).

An adenoma is the most common adrenal tumor in patients with or without a history of extra-adrenal malignancy. The present study detected adrenal adenoma in 145 (2.17%) patients. The prevalence of adrenal adenoma is related to age and has been reported to be 7% above 70 years of age. CT does not allow distinguishing functional and non-functional adenomas from each other (25). Functioning adenomas are associated with excessive cortisol secretion and its deleterious effects, hypertension, type 2 diabetes mellitus, and an increased risk of osteoporotic fractures. On the other hand, primary adrenal cancer is associated with significantly higher mortality and morbidity and requires urgent treatment (26,27). In our study, adrenal non-adenomatous mass was detected in 3 patients. Evaluation of both adrenal adenoma and adrenal mass in terms of medical or surgical treatment are significant findings that require communication with the clinician in order.

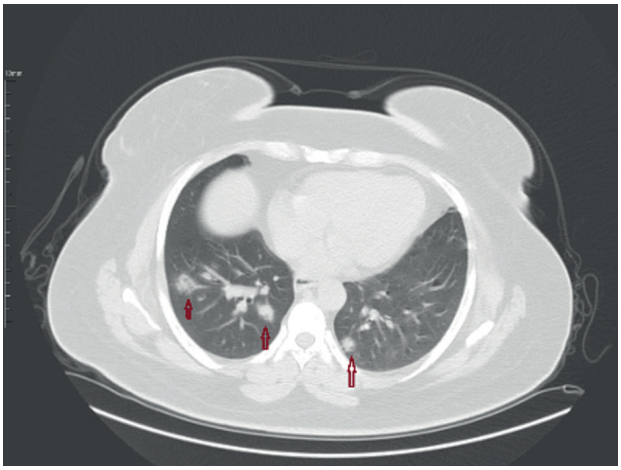


Figure 5a: 42-year- old male patient; focal consolidation in both lower lobes in the lung parenchyma window in Figure 5a (red arrows)

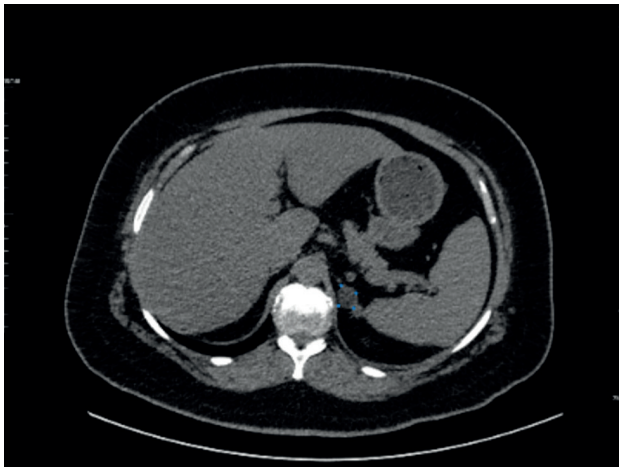


Figure 5b: A low-density, well-circumscribed lesion compatible with an adenoma in the body of the left adrenal gland in the mediastinal window in Figure 5b (blue dots).

Limitations

This study is that the detailed clinical histories were not questioned since all patients were initially investigated with the suspicion COVID-19 pneumonia. Therefore, the radiologist did not know exactly whether the pathologies were known when reporting.

CONCLUSION

CT examinations performed in patients with suspected COVID-19 pneumonia should be examined in detail regarding clinically significant findings. In addition, early detection of clinically insignificant incidental findings is also crucial. Although most of the findings detected incidentally in imaging performed for unrelated reasons are insignificant, it is vital to take necessary precautions in advance regarding pathologies that may be clinically significant regarding appropriate treatment and follow-up planning at the appropriate time. It is crucial that the clues are stated in the radiology report so that the clinician can make appropriate management regarding these pathologies.

Conflict of Interest: No conflict of interest was declared by the authors.
Ethics: This retrospective study was approved by Ethics Committee of İstanbul Haseki Training and Research Hospital, Istanbul. (Date: 19.08.2020; Number: 2020-132).
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Approval of Final Manuscript: All authors.

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ORIGINAL ARTICLE

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The Relationship Between Frank Sign and Coronary Artery Disease: A Literature Review

Frank İşareti ve Koroner Arter Hastalığı Arasındaki İlişki: Literatür Taraması

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ABSTRACT

Objective: *Coronary artery disease (CAD) is a leading cause of death and a significant public health concern. The identification of individuals at risk for CAD has been a subject of research for many years. The Frank sign is one such approach.*

Material and Methods: *This study was conducted by searching the MEDLINE database through PubMed.*

Results: *The majority of studies were conducted in China, with sample sizes ranging from 125 to 1377. Male gender was significantly predominant, and the studies focused on older age groups, with a mean age of at least 51.9 years. The results of the studies indicated that the coexistence of both conditions, namely the Frank sign and CAD, exhibited a wide range of prevalence.*

Conclusions: *The Frank sign is an independent risk factor for CAD and can be utilized in diagnostic processes, particularly in the early identification of individuals at risk. However, further studies and larger series are necessary to confirm this conclusion.*

ÖZET

Amaç: *Koroner arter hastalığı (KAH) önde gelen bir ölüm nedenidir ve önemli bir halk sağlığı sorunudur. KAH için risk altında olan bireylerin belirlenmesi uzun yıllardır araştırma konusu olmuştur. Frank işareti bu yaklaşımlardan biridir.*

Gereç ve Yöntem: *Bu çalışma PubMed aracılığıyla MEDLINE veri tabanı taranarak gerçekleştirilmiştir.*

Bulgular: *Çalışmaların çoğunluğu Çin'de gerçekleştirilmiş olup örneklem büyüklükleri 125 ila 1377 arasında değişmektedir. Erkek cinsiyet önemli ölçüde baskındır ve çalışmalar ortalama yaşı en az 51,9 olan ileri yaş gruplarına odaklanmıştır. Çalışmaların sonuçları, her iki durumun, yani Frank işareti ve KAH'ın bir arada bulunmasının geniş bir yaygınlık aralığı sergilediğini göstermiştir.*

Sonuç: *Frank işareti KAH için bağımsız bir risk faktörüdür ve tanı süreçlerinde, özellikle de risk altındaki bireylerin erken belirlenmesinde kullanılabilir. Ancak bu sonucun doğrulanması için daha fazla çalışmaya ve daha geniş serilere ihtiyaç vardır.*

Keywords:
Frank Sign
Coronary Artery Disease
Diagnosis
Emergency

Anahtar Kelimeler:
Frank İşareti
Koroner Arter Hastalığı
Tanı
Acil

INTRODUCTION

Coronary artery disease (CAD) is a leading cause of death worldwide and represents a preventable public health issue (1). Consequently, clinicians have been investigating simple and reliable risk factors in conjunction with non-invasive biomarkers for the early detection of individuals at risk of CAD, with this research ongoing (2,3). As a consequence of these studies, the Diagonal Earlobe Crease (DELC), also known as Frank sign, was first described by Sonder T. Frank in 1973, suggesting its association with vascular atherosclerosis and CAD (4).

Frank sign is a crease that extends diagonally from the tragus towards the border of the earlobe (Figure 1) (5,6). The formation of this crease in the earlobe, nourished by end arteries without collateral circulation, has been suggested to contribute to pathological conditions affecting the microvascular system, such as CAD, diabetes, and hypertension. Indeed, widespread elastin and elastic fibre loss, a pathognomonic feature of CAD reflecting

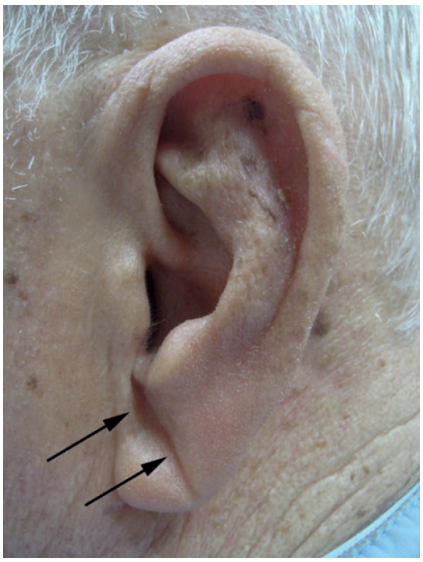

Figure 1: Frank sign in the left ear (6).

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the morphology of the coronary vasculature, has been demonstrated in biopsy samples taken from earlobe creases (3). Nevertheless, despite the existence of significant positive associations between Frank sign and CAD in some studies conducted since its initial description, others have yet to establish such a relationship. Consequently, Frank sign has been considered a contentious physical indicator for predicting CAD formation over the years (3,7).

This text aims to conduct a literature review on the Frank sign and provide recommendations to clinicians regarding its utility in clinical practice based on the findings of existing studies.

MATERIAL AND METHODS

This study was conducted by searching the MEDLINE database through PubMed using combinations of the keywords "Frank's sign", "Frank sign", "Franks sign", "earlobe crease", "ear lobe crease", "ear-lobe crease", "ear crease", "ear creases", "ear lobe creases" and "earlobes crease" on 18 December 2023. Following the initial search, 98 articles were identified in the second search, combined with "AND (Coronary Artery Disease)". The inclusion criteria were defined as being written in English, prospective in nature, including patients aged 18 and above, having undergone angiography, and having full-text accessibility. Upon reevaluation based on these criteria, it was found that only eight studies met all the requirements (Figure 2). The included studies were presented in tabular form, including the author, country of origin, year of study, number of cases, mean age, gender distribution, presence of the Frank sign, and presence of coronary artery disease according to angiography results (Table 1).

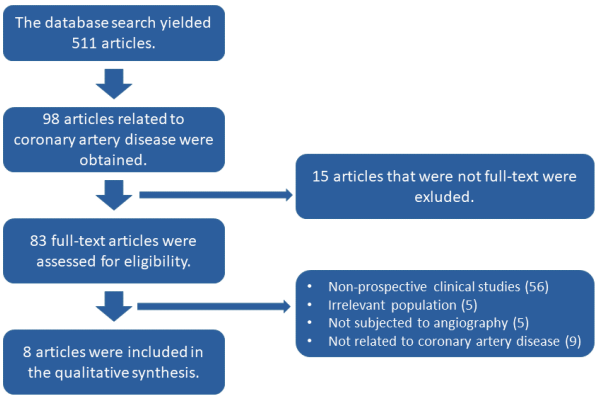

Figure 2: Flow diagram of study selection.

RESULTS

The data about the studies included in the research are presented in Table 1. The majority of studies were conducted in China, with sample sizes ranging from 125 to 1377. Male gender was significantly predominant, and the studies focused on older age groups, with a mean age of at least 51.9 years. The results of the studies indicated that the coexistence of both conditions, namely the Frank sign and CAD, exhibited a wide range of prevalence. The coexistence of both conditions being positive (Frank sign and CAD positive) was observed to vary between 35.46% and 68.42%, while the coexistence of both conditions being negative (Frank sign and CAD negative) was observed to vary between 7% and 32%. Upon examination of the relationship between the Frank sign and CAD, the majority of studies yielded a positive answer to the question of whether there is a significant relationship between the two.

DISCUSSION

The Frank sign is purported to be a straightforward physical examination finding that is harmless to the patient, easily applicable, cost-free, and purportedly associated with CAD (4). Indeed, our literature review yielded seven out of the eight studies included in our analysis mentioning the existence of this relationship, which supports this claim.

In a study conducted by Gakovic B. and colleagues related to the topic, it was claimed that the Frank sign has an acceptable level of accuracy in predicting CAD. However, in comparison with traditional cardiovascular risk factors, the Frank sign, despite providing supplementary information regarding the presence of CAD, is not a reliable indicator. Consequently, the authors recommended that diagnostic approaches should remain unchanged in patients presenting with chest pain (8). It is crucial to highlight that this recommendation was made about the evaluation of patients presenting with chest pain.

Several studies have offered differing recommendations for patients without chest pain within routine diagnostic processes. For instance, risk factors should be considered in the diagnostic methods of CAD. Accordingly, our reviewed studies also assess this aspect. In a survey by Kamal R. et al. examining the relationship between risk factors and the Frank sign, it was reported that the frequency of the Frank sign was correlated with hypertension and diabetes but not with smoking (3). Sasaki O. and colleagues investigated

Table 1: Characteristics of Included Studies.

References	Year	Country	n	Male (%)	The Average Age	Frank (+) CAD (+) (%)	Frank (+) CAD (-) (%)	Frank (-) CAD (+) (%)	Frank (-) CAD (-) (%)	Meaningful Relationship
Wang Y	2016	Chinese	558	402 (72.04)	63.63	345 (61.83)	44 (7.89)	100 (17.92)	69 (12.36)	Yes
Xing-li Wu	2014	Chinese	449	278 (61.91)	63.29 ± 11.95	188 (41.87)	92 (20.48)	62 (13.80)	107 (23.83)	Yes
Kamal R	2017	Pakistan	200	126 (63)	Unspecified	76 (38)	36 (18)	24 (12)	64 (32)	Yes
Hou X	2015	Chinese	956	546 (57.11)	53.35 ± 8.1	339 (35.46)	345 (36.09)	107 (11.19)	165 (17.26)	Yes
Sasaki O	2023	Japan	1086	826 (76.06)	66.1 ± 11.4	743 (68.42)	98 (9.02)	169 (15.56)	76 (7)	Yes
Gakovic B	2023	Serbia	1377	876 (63.62)	65 ± 10	483 (35.08)	236 (17.14)	395 (28.69)	263 (19.10)	Yes
Evrengül H	2004	Turkey	415	301 (72.53)	58.9 ± 10.3	152 (36.63)	18 (4.34)	144 (34.70)	101 (24.33)	Yes
DJ Kenny	1989	Ireland	125	112 (89.6)	51.9	56 (44.8)	9 (7.2)	45 (36)	15 (12)	No

the relationship between age and the Frank sign, suggesting that the Frank sign could serve as a valuable marker for risk stratification of patients before coronary angiography, regardless of age (7). Hou X. and colleagues emphasised the importance of combining the Frank sign and CAD risk factors, stating that the Frank sign is more reliable in individuals with multiple risk factors for CAD (4). In a study by Evrengül H. et al., it was reported that the prevalence of the Frank sign significantly increased in CAD independently of other risk factors, suggesting that the Frank sign could be an independent variable for CAD (9). Similarly, Xing-li Wu et al. also mentioned that the Frank sign could assist in the early identification of individuals at risk and in adopting active primary or secondary prevention for atherosclerosis (2). Moreover, the significant association of the Frank sign with major coronary risk factors is another important finding (9), which is consistent with the study conducted by Sasaki O. et al., where the Frank sign was independently associated with CAD, multi-vessel disease, and severe CAD (7).

Despite the aforementioned findings, it is observed that recommendations to be considered are included in the conclusion sections of the studies. For instance, DJ Kenny and colleagues stated that the Frank sign is not a marker for CAD, and both CAD and the Frank sign are associated with age. Kamal R. and colleagues proposed that further prospective studies are required to confirm this relationship. In contrast, Wang Y. and colleagues emphasized the necessity for further studies to elucidate the underlying mechanism (1, 3, 10).

LIMITATION

This study demonstrates the limitations of relying on a single search engine. However, the fact that the search engine used is one of the most widely followed sources helps to mitigate this limitation to a reasonable extent.

CONCLUSION

The Frank sign is an independent risk factor for CAD. Although it is not recommended as a criterion for evaluation in patients presenting with chest pain, it can be used in diagnostic processes, particularly in the early identification of individuals at risk. However, given the number of publications and the number of patients, further studies and larger series are required to support this conclusion.

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Ethics: The study does not require ethics committee approval. There is no such thing as any blood, saliva, violation of the rights of the patient, etc.
Funding: There is no financial support of any person or institution in this research.
Approval of final manuscript: All authors.

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ORIGINAL ARTICLE

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Impact of Subclinical Hypothyroidism on Pregnancy and Newborn

Subklinik Hipotiroidinin Gebelik ve Yenidoğan Üzerine Etkisi

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ABSTRACT

Objective: *The normal free T4 level together with a high TSH level is called subclinical hypothyroidism. In this study, we investigated cases of subclinical hypothyroidism diagnosed in the first trimester for possible adverse effects. The study aims to show the pregnancy outcomes and neonatal effects.*

Material and Methods: *The study we planned was conducted retrospectively as a record study based on diagnoses. Three hospitals; one city and two state hospitals, were included in our study. Pregnant women treated at these centers between 2019 and 2021 were included the screening of newborns was similarly performed by our pediatric colleagues, based on the diagnosis in the form of scanning the files.*

Results: *It became statistically significant when prematurity (p: 0.005), fetal weight, and week of birth were evaluated. The T4 values of the pregnant women who taken part in the study were normal, and their TSH values were ≥ 2.5-4 mIU/L. The evaluation showed that preterm birth was statistically higher and fetal weight and week of birth were significantly lower.*

Conclusions: *In the study of pregnant women diagnosed with subclinical hypothyroidism, it was found that the preterm delivery rate was higher than in the control group, and the delivery week was also lower than in the control group.*

ÖZET

Amaç: Y*üksek TSH düzeyi ile birlikte normal serbest T4 düzeyine subklinik hipotiroidizm denir. Bu çalışmada olası yan etkiler açısından ilk trimesterde teşhis edilen subklinik hipotiroidi vakalarını araştırdık. Çalışma, gebelik sonuçlarını ve yenidoğan etkilerini göstermeyi amaçlamaktadır.*

Gereç ve Yöntem: *Planladığımız çalışma tanılara dayalı olarak retrospektif olarak kayıt çalışması şeklinde yürütülmüştür. Üç hastane; bir şehir ve iki devlet hastanesi çalışmamıza dahil edildi. 2019-2021 yılları arasında bu merkezlerde tedavi gören gebeler dahil edilmiş, yenidoğan taramaları benzer şekilde pediatrik meslektaşlarımız tarafından dosyaların taranması şeklinde tanıya dayalı olarak yapılmıştır.*

Bulgular: *Prematürite (p: 0,005), fetal ağırlık ve doğum haftası değerlendirildiğinde istatistiksel olarak anlamlı hale geldi. Çalışmaya katılan gebelerin T4 değerleri normal, TSH değerleri ≥ 2.5-4 mIU/L idi. Değerlendirme, erken doğumun istatistiksel olarak daha yüksek olduğunu ve fetal ağırlığın ve doğum haftasının önemli ölçüde daha düşük olduğunu gösterdi.*

Sonuç: *Subklinik hipotiroidi tanısı alan gebelerde yapılan çalışmada erken doğum oranının kontrol grubuna göre daha yüksek olduğu ve doğum haftasının da kontrol grubuna göre daha düşük olduğu bulundu.*

Keywords:
Pregnancy
Subclinical hypothyroidism
Newborn

Anahtar Kelimeler:
Gebelik
Subklinik hipotiroidi
Yenidoğan

INTRODUCTION

Thyroid disorders are one of the most common problems in pregnancy, with the incidence increasing up to four percent during pregnancy (1). During pregnancy, thyroid functions may decrease and lead to hypothyroidism or may increase and lead to hyperthyroidism (2). Apart from this, it can also occur in the form of subclinical hypothyroidism, which is our research topic. The condition in which TSH is above 10 mIU/L and free T4 is lower than expected is called hypothyroidism (3). In contrast to this situation, high TSH values in subclinical hypothyroidism are accompanied by typical free T4 values (4). Iodine deficiency affects the size of the thyroid gland. In regions where iodine deficiency is not seen, the size of the gland is smaller than in the areas with iodine deficiency (2-4). The iodine passed from the mother to the baby plays a significant role. It is known to be mainly responsible for fetal growth and fetal neural development in the early stages of pregnancy (5). The main reason this is so important is that the developing fetus does not have the maturity to produce its free T4 (3, 4). The only source of free T4 is the mother. It is essential in the initial stages of pregnancy for proper neural development and the well-being of the child (6). This importance continues unabated in the later stages of pregnancy and plays a vital role in the smooth completion of neuronal migration (7). The thyroid

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gland, which must cope with the physiological changes of the mother during pregnancy, also gains importance by working for the fetus that is not yet born (8). From the second month of pregnancy, the level of thyroxine-binding globin reaches about twice the average level due to the high amount of estrogen. It should be remembered that an elevated level of HCG during pregnancy has an effect like that of thyroid hormone. In the first trimester of pregnancy, there is a transient increase in free T4 levels and a decrease in TSH levels (9). While free T4 levels decrease in the next period, TSH increases toward normal levels with this decrease (10). These variable values change as pregnancy progresses. The American Thyroid Association (ATA), which aims to set up a standard for these variable values, has agreed on the values that can be used as reference values for each trimester (11). According to the results of this consensus, values of 0.1-2.5 mIU/L in the first trimester can be used as normal limits; 0.2-3.0 mIU/L in the second trimester; and 0.3-3.5 mIU/L in the third trimester (12). Although many studies on this topic have had controversial results, the National Academy of Clinical Biochemistry (NACB) recommends the range between the 2.5 and 97.5 percentile within normal limits (13). ATA updated its recommendations in the literature and suggested the use of a value of 4.0 mIU/L as an upper limit in cases where there is no TSH value that we can rely on before pregnancy (12). There are many studies linking thyroid problems in the mother to pregnancy complications. Normally, existing hypothyroidism should be treated and there is consensus on this (12). In contrast, however, there is no consensus on our subject, subclinical hypothyroidism. Our motivation to conduct this study stems from the fact that we think we can contribute to the literature. Our study aimed to evaluate the presence of an association with possible complications by comparing pregnant women with subclinical hypothyroidism, whom we examined in the first trimester, with a control group.

MATERIAL AND METHODS

The study we planned was conducted retrospectively as a file study based on diagnoses. Three hospitals, one urban and two state hospitals were included in our study. Pregnant women treated at these centers between 2019 and 2021 were included. Newborn screening was similarly performed by our pediatric colleagues, based on diagnosis retrospectively. If the patient remembered the last menstruation, the gestational age was decided from this date; if this information was not available, it was decided by ultrasound at the twentieth week (14). In the medical history of all patients, information such as the number of births, the number of pregnancies, and the number of live births was added to the sources we used for statistics. Written informed consent was obtained from all patients. Information such as chronic diseases, family history, substance abuse, smoking, and alcohol consumption was recorded in the data we used. Based on these medical histories, mothers with thyroid disease before pregnancy were not included in our study. To obtain more efficient results, blood tests were performed in the fasting state (15). In these examinations, TSH and free T4 levels were checked. Our control group consisted of pregnant women with normal TSH and T4 levels. Another group consisted of pregnant women with normal free T4 and TSH values of ≥ 2.5-4 mIU/L; pregnant women with TSH values ≥ 4-10 mIU/L formed another group (16). 669 pregnant women took part in our study. The birth modes of these pregnant women, weights, and demographic characteristics of the babies were recorded. In addition, weight characteristics such as LGA, SGA, and neonatal complications were also recorded by our pediatric colleagues. In the maternal part of the data, our colleagues from obstetrics recorded many variables from adequate amniotic fluid to premature rupture of membranes. The principles of the Declaration of Helsinki were followed in this study. This study was approved by the University of Afyon, Medical Faculty Clinical/Human Research Ethics Committee with the date 10.12.2021 and decision number 119. Input errors were checked and corrected before analysis. The Mann-Whitney u test and chi-square tests were used for comparisons. The 26th version of the spss software was used for analysis. Calculations with p values less than 0.05 were considered statistically significant.

RESULTS

Our pregnant women were divided into 3 groups based on their free T4 and TSH values. The first group was the control group consisting of healthy pregnant women, the second and third groups were formed according to their TSH values (Table 1). While our patients in the second group had TSH ≥ 2.5-4 mIU/L, the patients in our third

Table 1: Obstretric results

	Control Group (n/%)	Group 2 (n/%)	Group 3 (n/%)	p(G2)*	p(G3)*
PRETERM	63/ 9.48%	23/18.16 %	3/12.14%	0.005	0.868
NICU	21/3.98%	2/3.99%	1/1.02%	0.962	0.366
PROM	40/7.2%	7/7.32%	1/7.11%	0.946	0.921
PPROM	5/1.96%	1/0.63%	1/0.92%	0.321	0.473
LBW	36/5.8%	9/7.87%	1/1.47%	0.342	0.165
SGA	24/4.96%	6/5.47%	2/4.22%	0.421	0.403
LGA	67/9.78%	11/8.27%	8/13.71%	0.096	0.503

chi-square tests, NICU: Neonatal Intensive Care Unit, PROM: Premature Rupture of Membranes, PPROM: Preterm Premature Rupture of Membranes, LBW: Low Birth Weight, SGA: Small for Gestational Age, LGA: Large for gestational age*
Control group: Free T4 normal,TSH normal,
Group 2: Free T4 normal,TSH ≥ 2.5-4 mIU/L,
Group 3:Free T4 normal, TSH ≥ 4-10 mIU/L

and final group were selected from patients with TSH ≥ 4-10 mIU/L. When the first and second groups were compared, there was no difference between the frequency of cesarean sections and the demographic data. When the first group, which is also the control group, and the third group were compared, no difference was found in the same variables. However, when we included birth weights in the comparison between group 2 and the control group, it was found that the mean values for fetal weight were statistically significantly lower in our group. Significant results were seen when comparing the control group and the second patient group in terms of the frequency of preterm births (p = 0.005).

DISCUSSION

If we must define it, subclinical hypothyroidism is a condition in which normal free T4 levels are accompanied by elevated TSH levels (11, 12). Definitions of the association between hypothyroidism and poor pregnancy outcomes exist in the literature, but absolute conclusions about subclinical hypothyroidism have not been drawn (17). We felt it right to divide our pregnant women with subclinical hypothyroidism into two groups based on their TSH levels, as this may lead to clearer and more detailed results. As a result of our evaluation, we found that the rate of preterm birth was higher in pregnant women who belonged to the group with TSH levels between 2.5-4 mIU/L. At the same time, it was found that the fetal birth weight was significantly low, and the week of birth was statistically low. Several studies have commented on the benefit of thyroid testing before pregnancy (18). However, there are studies believe that it should be done and those that say the opposite (17, 18). Some of the studies advocate that it should be before pregnancy, while others claim that it should only be in pregnant women who are considered in a high-risk group (17, 18). However, most studies point to the first trimester as the most recommended time for screening in high-risk pregnancies (19). In our study, we performed thyroid function tests in the first trimester at an average of nine weeks. When utilizing a threshold of above 2.5 mIU/L in our research, the occurrence of subclinical hypothyroidism was recorded at 21%. However, when the TSH level was raised to 4 mIU/L, the incidence dropped to 6%. If we ask ourselves why we have higher rates compared to other studies, we can count that our centers included in the studies are second and third-tier hospitals, where the number of patient applications is high. One of the reasons why it is not easy to clearly define the right TSH ranges could be that the values are influenced by the ethnicity of the patient and the geographic region in which she lives (20). In a study from India, the authors used the 5th to 95th percentile as the normal reference range (21). In a similar study, they extended the normal reference range from 5 to 95%.The normal range for TSH in early pregnancy is 5.0-6.0 mIU/L. However, different studies reach different conclusions. In India, the authors accept a TSH value of 3.0 mIU/L for subclinical hypothyroidism instead of 4.0 mIU/L as in the revised guidelines from ATA 2017 (22). In a similar study, the risks of prom, low birth weight, and pregnancy-related hypertension were higher in patients with subclinical hypothyroidism (23). There was no significant difference in the incidence of pregnancy loss or complications such as gestational diabetes, and placenta previa (24). Neurodevelopmental, cognitive, and intellectual outcomes were worse in children of pregnant women with subclinical hypothyroidism compared with the control group (25). On the other hand, no significant difference was found in subclinical hypothyroidism and preterm birth in different studies (26). In our study, the level of preterm birth rate was found to be statistically significant. (p: 0.05). In the group with TSH values of 4-10 mIU/L, the risk of preterm birth was not statistically significant. In another study, the risk of severe preeclampsia was found to be increased in pregnant women diagnosed with subclinical hypothyroidism (27). However, in our study, there was no statistically significant increase in the incidence of preeclampsia or detachment. Bein M et al. In their study, no significant difference was found in the subclinical hypothyroidism group when babies with SGA were compared with the control group (7). Although the rate of babies with SGA was higher in our study than in the control group, it was not statistically significant.Chen J et al. state that there is no association between subclinical hypothyroidism and adverse neonatal outcomes (23). According to another study, although there is an association between gestational diabetes and hypothyroidism, there is no similar association between subclinical hypothyroidism and hypothyroidism (28). In our study, there was no increase in gestational diabetes when comparing the 2nd and 3rd groups with the control group. Fetal loss is seen only in untreated cases of hypothyroidism (28). Because the TSH values of the followed-up patients with subclinical hypothyroidism did not reach high values as in hypothyroidism, no increase in mortality was seen. In contrast to our results, Maraka S et al reported in their study that mortality was also high in patients with subclinical hypothyroidism (4).

CONCLUSION

As a result of statistical analysis performed on pregnant women diagnosed with subclinical hypothyroidism and TSH levels between 2.5-4 mIU/L, it was found that the rate of preterm birth was high, while the rate of fetal weight and preterm birth was low. Only checking the thyroid functions of pregnant women, whom we have classified as substantial risk, will lead to an increase in the number of overlooked patients and complications. Studies in larger groups may help to find consensus on studies that stand for different opinions.

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ORIGINAL ARTICLE

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Toxoplasmosis: Seroprevalence in Women of Reproductive Age and Approach in Pregnancy

Toksoplazmoz: Doğurganlık Çağındaki Kadınlarda Seroprevalans ve Gebelikteki Yaklaşım

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ABSTRACT

Objective: *Toxoplasmosis is a parasitosis that is mostly asymptomatic. It can lead to severe clinical conditions in immunosuppressed patients and fetal infections. Since it is possible to prevent congenital toxoplasmosis with appropriate follow-up and treatment, our study aimed to determine the susceptible population and seroprevalence of our region and to evaluate the course of infections in this group.*

Material and Method: *Patients who applied to our tertiary hospital in the last five years and to whose Anti Toxoplasma IgM and IgG tests were performed were included in our study. Toxoplasmosis seroprevalence, the course of primary infection in pregnant women, the treatments applied, and also acute toxoplasmosis infections in non-pregnant patients were examined.*

Results: *The seropositivity rate was found to be 30.7% (n=1703) in 5545 women included in the study, and the seropositivity rate was 31% (n=1399) in 4503 pregnant women. Sixteen pregnant women with primary infection were followed up in our hospital; one underwent medical abortion at the request of the family, and only four used the recommended treatment. Congenital toxoplasmosis was not detected in any newborn. Of the patients included, 26 (0.4%) were examined to investigate the etiology of fever, 37 (0.6%) for lymphadenopathy (LAP), and 29 (0.5%) for elevated liver enzymes. Among the patients with LAP, four (10.8%) were diagnosed with acute toxoplasmosis.*

Conclusion: *As a result, it is important to determine the seroprevalence of toxoplasmosis, to detect possible primary infections, especially in pregnant women, and ensure close monitoring of these patients.*

ÖZET

Amaç: *Toksoplazmoz çoğunlukla asemptomatik seyreden paraziter enfeksiyon hastalığıdır. Bağışık yanıtı baskılanmış konaklarda ve fetal enfeksiyonlarda ağır klinik tablolara yol açabilmektedir. Özellikle konjenital toksoplazmozun uygun takip ve tedavi şekliyle engellenebilmesinin mümkün olması nedeniyle çalışmamızda bölgemizin duyarlı popülasyonunun ve seroprevelansının belirlenmesi ve bu grupta enfeksiyonların seyrinin değerlendirilmesi amaçlanmıştır.*

Gereç ve Yöntem: *Çalışmamıza son beş yılda üçüncü basamak hastanemize başvuran ve Anti Toxoplasma IgM ve IgG testi çalışılan hastalar dahil edildi. toxoplasmosis seroprevelansı, gebelerdeki primer enfeksiyonun seyri ve uygulanan tedaviler, ayrıca gebe olmayan hastalardaki akut toksoplazmoz enfeksiyonları incelendi.*

Bulgular: *Çalışmaya dahil edilen 5545 kadında seropozitiflik oranı %30.7 (n=1703), 4503 gebede ise seropozitiflik oranı %31 (n=1399) olarak tespit edilmiştir. Primer enfeksiyonu olan 16 gebeden birine ailenin isteğiyle tıbbi abortus uygulanmış, gebelerin yalnızca dördü gebelik sonuna kadar önerilen tedaviyi kullanmış, izlem sırasında hiçbir yenidoğanda konjenital toksoplazmoz tespit edilmemiştir. Çalışmaya dahil edilen hastaların 26'sı (%0.4) ateş, 37'si (%0.6) lenfadenopati (LAP) ve 29'u (%0.5) karaciğer fonksiyon testlerindeki yüksekliğinin sebebinin araştırılması için tetkik edilmiş, LAP ile izlenen hastalardan 4'üne (%10.8) akut toksoplazmoz tanısı* ***koyulmuştur.***

Sonuç: *Toksoplazmoz seroprevelansının belirlenerek özellikle gebelerdeki olası primer enfeksiyonların tespiti ve bu grup hastaların izlem ve tedavilerinin aksamaması uğruna klinisyenlerin hastaları doğru yönlendirmesi konjenital toksoplazmozun engellenmesi adına oldukça önemlidir.*

Keywords:
Congenital Toxoplasmosis
Serology
Fever
Lymphadenopathy

Anahtar Kelimeler:
Konjenital Toksoplazmoz
Seroloji
Ateş
Lenfadenopati

INTRODUCTION

Toxoplasmosis; is a zoonosis caused by *Toxoplasma gondii* (*T. gondii*). The final host of this obligate intracellular parasite, which causes infection in humans and many animals, is felines. Toxoplasma infection can develop through the consumption of raw or undercooked meat and shellfish, contaminated raw vegetables or water, or direct contact with contaminated products or oocysts found in cat feces. It can also be transmitted vertically from mother to baby or through organ transplantation. Clear data on the seroprevalence of the infection are not available. It is estimated that 30% of the world's population is infected with toxoplasma, the prevalence of latent toxoplasmosis in pregnant women worldwide is 33.8%, and the congenital

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infection rate is less than 0.1% (1,2). Centers for Disease Control and Prevention (CDC) stated toxoplasmosis is one of the five neglected parasitic diseases of the United States and it is estimated that approximately 40 million people are infected (3).

While 80-90% of patients are asymptomatic or have mild symptoms, flu-like symptoms, lymphadenitis, myalgia, headache, and sore throat may occur in mild cases (4). Cervical lymph nodes are often affected, and the disease usually limits itself within months. It can cause serious clinical conditions, especially in immunosuppressed patients, or congenital infections that develop after the primary infections of seronegative pregnant women. Central nervous system, lung, eye involvement, or disseminated toxoplasmosis may be seen in immunosuppressed patients. In severe cases of congenital toxoplasmosis, hydrocephalus, intracranial calcifications, retinochoroiditis and fetal death may occur (5). Serological tests, molecular methods, histological examinations, and isolation of the microorganism can be used in the diagnosis of toxoplasma infection. It is possible to minimize fetal effects by following diagnostic-treatment algorithms developed especially to detect mothers with primary infection and to prevent vertical transmission (6-8).

This study aims to determine the seropositivity rate of women of reproductive age in our province, to examine the course of pregnant women who are thought to have primary infection and acute toxoplasmosis infections in the study population, and to raise the awareness of clinicians by identifying our situation and deficiencies in this process.

MATERIALS AND METHODS

Our study is a retrospective observational study. In this study, female patients of reproductive age between the ages of 18 and 45 who applied to Recep Tayyip Erdoğan University, Training and Research Hospital in the five-year period between 01.01.2018 and 31.12.2022 and underwent Anti-*T. gondii* IgM or Anti-*T. gondii* IgG testing were included. Patients for whom only IgM testing was performed were excluded. The results of serological tests, the infection status of pregnant women, and treatments applied to patients thought to have primary infection, the course of these patients and pregnancy outcomes were evaluated. In addition, the reason for requesting tests from patients and the evaluation for toxoplasmosis in non-pregnant women were also examined. Examination results and follow-up and treatment information of the patients were accessed from the hospital information system. Patients for whom only IgM testing was performed were excluded from the study because it was insufficient to evaluate the presence of infection and did not contribute to the seroprevalence study. The results of serological tests, especially the infection status of pregnant women, advanced tests and treatments applied to patients thought to have primary infection, the course of these patients, and pregnancy outcomes were evaluated. Examination results, follow-up and treatment information of the patients were accessed from the hospital information system.

Pregnancy follow-up: Anti *T. gondii* IgM and IgG tests are performed on pregnant women followed in our hospital at their first admission, and patients with IgM positivity or intermediate values are referred to our clinic. Avidity test is applied to patients with positive anti *T. gondii* tests, and patients with negative tests are monitored for IgG seroconversion. Patients who are thought to have a primary infection are informed about follow-up, antimicrobial treatment, and termination of the pregnancy, and when necessary, appropriate medical treatment is initiated to prevent congenital infection and patients are monitored together with the gynecology and obstetrics departments.

Serological Analysis: Quantitative measurement of Anti Toxoplasma gondii IgM and IgG antibodies and avidity measurement of IgG antibodies were performed with ARCHITECT® *T. gondii* IgM, IgG, and Avidity kits working with the chemiluminescence microparticle immunoassay (CMIA) method.

Statistical Analysis: The IBM Statistical Package for the Social Sciences (SPSS) version 26.0 (Armonk, NY: IBM Corp) program was used to evaluate the data of the study. The suitability of the variables to normal distribution was examined using analytical methods (Kolmogorov Smirnov/Shapiro Wilk tests). Descriptive analyses were given using mean ± standard deviation for data that conformed to normal distribution, and median (lowest value-highest value) for data that did not comply with normal distribution. The data of the patients were calculated as a ratio.

Ethics Committee Approval: Approval for the study was received from Recep Tayyip Erdoğan University ethics committee with decision number 2023/156 dated 15.06.23.

RESULTS

We identified 6590 patients who underwent Anti-*T. gondii* IgM or IgG tests during the defined period. Of these, 1045 patients were excluded from the study because IgG testing was not performed, 5545 patients were included, and 4503 of them were pregnant. The median age of the patients was 32 (range 18-45) years. Serological tests were most commonly performed due to pregnancy (n=4503, 81.2%), and in 26 (0.4%) patients to investigate the etiology of fever, 37 (0.6%) patients to investigate the etiology of lymphadenopathy and in 29 (0.5%) patients to examine abnormal liver function tests. The remaining patients were scanned before pregnancy or for other reasons. The seronegativity rate (both Anti-*T. gondii* IgG and IgM negativity) was determined as 66.3% (n=3681), IgG positivity rate was 30.7% (n=1703), isolated IgG positivity rate was 28.7% (n=1590), and IgM positivity rate was 1.6% (n=90) (Table 1).

Anti *T. gondii* IgG and IgM results of pregnant women were examined, 3007 (66.7%) of them were seronegative, 1399 (31%) had IgG positivity, and 1327 (29.4%) had isolated IgG positivity (Table 1). Four of the eight patients with IgG (-), and IgM (+) test results were considered false positive because IgG seroconversion didn't happen during the 4-6 week follow-up. Twenty-three of 57 patients who were IgG and IgM positive were not referred to the infectious diseases outpatient clinic and no further examination was requested. The IgG avidity of 11 patients who underwent further evaluation was found to be 'low' and early infection was considered in these patients (Figure 1). One of the patients with low avidity underwent

Table 1: Results of anti-*T. gondii* IgM and IgG tests.

All patients		**Anti-*T. gondii* IgM**				
		Negative	Positive	Borderline	None	Total
Anti-*T. gondii* IgG	Negative	3683	12	4	45	3744
	Positive	1590	77	18	18	1703
	Borderline	96	1	0	1	98
	Total	5369	90	22	64	5545
Pregnant women		**Anti-*T. gondii* IgM**				
		Negative	Positive	Borderline	None	Total
Anti-*T. gondii* IgG	Negative	3007	8	3	4	3022
	Positive	1327	57	13	2	1399
	Borderline	82				82
	Total	4416	65	16	6	4503

T. gondii: Toxoplasma gondii

medical abortion voluntarily, three patients were started on spiramycin treatment, and the treatment continued until the end of pregnancy, one did not receive any treatment voluntarily, three did not complete the treatment, and three continued to be followed up in another center. The IgG avidity test of 23 patients resulted as 'high'. Twenty patients with high avidity were considered to have latent infection as their gestational age was less than 18 weeks and one of them also had IgG positivity in previous pregnancies. One of our patients, whose "high avidity" test result was detected in the examinations performed on the 24th week, used spiramycin for six weeks. At the 30th week, intrauterine growth retardation secondary to preeclampsia was detected and premature labor occurred. The newborn was evaluated for postpartum congenital toxoplasmosis, and no involvement was detected as a result of eye and central nervous system evaluations. (Figure. 1, Table 2). In the follow-ups to date, no findings in favor of congenital toxoplasmosis have been detected in the babies of any of the pregnant women with possible primary infection who were followed up in our hospital and gave birth.

Non-pregnant patients were also evaluated. Anti-Toxoplasma IgM and IgG were detected positive in six of the 37 patients examined for LAP, and with further evaluation, four patients (10.8%) were diagnosed with acute toxoplasmosis. Two of these patients were followed up without treatment because they had a mild course, and their clinical findings resolved spontaneously, while two of them were treated with antimicrobial treatment (trimethoprim sulfamethoxazole and spiramycin) and responded to the treatment. None of the 29 patients were examined due to abnormal liver function tests and the 26 patients were examined to investigate the etiology of high fever diagnosed with acute toxoplasmosis.

DISCUSSION

While toxoplasmosis generally causes asymptomatic or self-limiting clinical conditions in immunocompetent individuals, it may present with serious conditions in

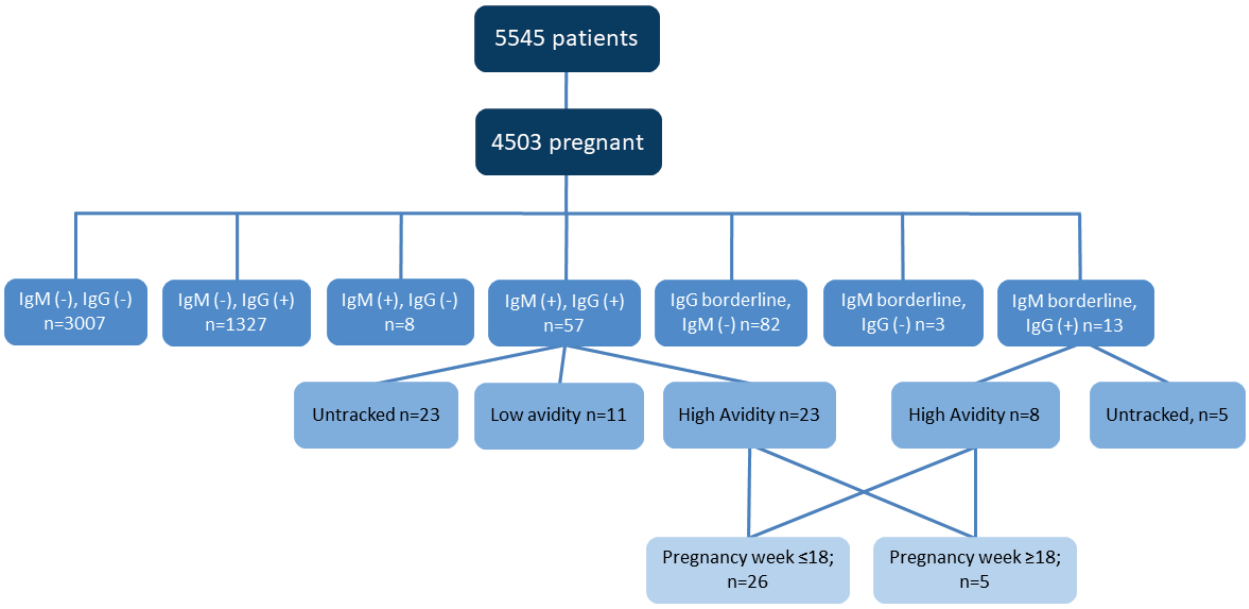

Figure 1: Anti-*T. gondii* IgM, IgG and IgG Avidity test results in pregnant women.

Table 2: Evaluation, follow-up and results of possible primary *T. gondii* infection in pregnant women.

Anti *T. gondii* IgM (+), IgG (-) (n=8)		4 false positives 4 untracked
Anti *T. gondii* IgM (+), IgG (+) (n=57)		
IgG Avidity	Not evaluated (n=23)	
	Low (n=11)	1 is terminated at the request of the mother 1 did not receive treatment voluntarily 3 completed the treatment until the end of pregnancy 3 did not finish treatment 3 untracked
	High (n=23)	20 pregnant women with a gestational age of ≤ 18 weeks had an infection before pregnancy 3 pregnant women with gestational age ≥ 18 weeks 1 infection before pregnancy 1 premature birth due to IUGR after 6 weeks of spiramycin use 1 untracked
Anti *T. gondii* IgM (borderline), IgG (+) (n=13)		
IgG Avidity	Untracked (n=5)	
	High (n=8)	6 pregnant women with a gestational age of ≤ 18 weeks had an infection before pregnancy. 2 pregnant women with gestational age ≥ 18 weeks 1 untracked 1 was followed without treatment

T. gondii: Toxoplasma gondii

cases of acute infection or reactivation of latent infection or congenital infections in immunosuppressants. For this reason, it is very important to closely monitor risk groups in terms of toxoplasma infections and to take effective interventions when necessary.

The seroprevalence of toxoplasmosis, a zoonotic disease, varies according to the climatic conditions of the regions and the nutritional and hygiene habits of the communities. In a review evaluating *T. gondii* seroprevalence in blood donors, anti-*T. gondii* IgG positivity rate was found to be 7.8% in Asia, 32.8% in America, 40.7% in Africa, 34% in Antarctica, and 38.1% in Europe (9). In a study conducted by Karakullukçu et al., which included 1066 people over the age of 20 living in Trabzon/Turkey, the anti-*T. gondii* IgG positivity rate was found to be 58.8% (10). In a study by Sert et al., among 84,587 pregnant women in Ankara/Turkey, the anti-*T. gondii* IgG positivity rate was found to be 22.3%, whereas in another multicenter study by Kul et al. the seropositivity rate was found to be 21% (11,12). In a study by Demiray, Emine Kübra Dindar et al. investigating the Toxoplasmosis seroprevalence in pregnant women from Turkey by pool analyses method; the anti- Toxo IgG rate was found to be 36.76% in Turkey and 31.8% in Black Sea Region (13). In our study, toxoplasma seroprevalence among women of childbearing age in our city was determined to be 30.7% which was similar to the last-mentioned study. It is thought that both regional differences and the inclusion of only women in a certain age range may be effective in the difference in seroprevalence rates.

Toxoplasma serological tests are mostly performed on pregnant women to detect acute infection and prevent possible congenital infections and to detect latent infection and determine the risk of reactivation in people with suppressed immune systems who are susceptible to the disease. Tests can also be performed to investigate the etiology of LAP, elevated liver enzymes, and high fever. As expected, since the group included in our study was women of reproductive age, the rate of patients examined due to pregnancy was quite high (n = 4503, 81.2%), however, we could not find any study that evaluated the reasons for requesting Anti-*T. gondii* tests and the rates of requesting tests according to etiology.

Congenital toxoplasmosis can develop as a result of primary infection experienced by the mother during pregnancy, reactivation in a highly immunosuppressed mother, or re-infection with a virulent strain. With early detection of acute infection and rapid treatment, the risk of transmission to the fetus can be significantly reduced (14). When maternal infection occurs in the early gestational weeks, the probability of transmission is lower, and the risk of sequelae is higher. These rates reverse as the gestational week progresses. In a study evaluating 603 confirmed maternal toxoplasmosis cases, the vertical transmission rate was found to be 29%, and the risk of transmission, which was 6% in the 13th week, reached 72% in the 36th week (1). While toxoplasmosis screening during the antenatal period is not recommended in some countries because it is not cost-effective, in some countries it is recommended to include it in routine pregnancy follow-up and monitor seronegative pregnant women at regular intervals (15-17). In our country, it is recommended that the decision to screen for toxoplasma infection in the antenatal period be made according to regional prevalence (5). In the first 18 weeks (4 months) IgG positive and IgM negative test results suggest an infection acquired before pregnancy. Patients with isolated IgM positivity are monitored for 2-6 weeks for IgG seroconversion, and if seroconversion does not occur, this situation is considered to be false positive. In patients with positive results for both tests, IgG avidity and gestational age are evaluated, and antibiotic treatment is recommended to prevent congenital transmission in pregnant women who are thought to have acute infection. If the fetus gets infected during follow-up, it is appropriate to use drugs for the treatment of fetal infection (5,18). As a result of the evaluations, only four of the pregnant women who were considered to have primary toxoplasma infection and were followed up in our hospital completed

prophylactic antibiotic treatment as recommended, and no congenital toxoplasma infection was detected in the babies of any of the pregnant women. However, it was observed that some of the pregnant women requiring further evaluation based on the examination results were not referred to our clinic, some of the pregnant women for whom prophylaxis was recommended after further evaluation did not use the treatment voluntarily, and usually, difficulties were encountered regarding both the clinical approaches of the physicians and the treatment compliance of the patients.

In immunocompetent patients, acute toxoplasmosis can usually present with an asymptomatic or self-limiting clinic. LAP with bilateral cervical pain is one of the most common clinical findings, cervical LAP can be seen in 20-30% of cases (4, 5). Anti-Toxoplasma IgM was found to be positive in 6.7% of 138 patients in a study examining the etiology of LAP by Güreser et al. (19). Similarly, in our study, acute toxoplasmosis was detected in 6.25% of the patients examined to investigate the etiology of LAP. In addition to lymphadenopathy in acute toxoplasmosis, serious conditions such as pneumonia, encephalitis, myo-pericarditis, and hepatitis may also be observed in some patients. Although it is a rare complication, it is recommended that toxoplasmosis be evaluated in the differential diagnosis of acute hepatitis. Serological evaluation and histopathological examination of the liver can guide the diagnosis (20). In addition, there are studies showing a relationship between Anti-*T. gondii* IgG positivity and chronic liver disease (21,22). Toxoplasmosis was not detected in any of the patients included in our study and examined due to disorders in liver function tests. The most common cause of fever of unknown origin (FUO) is infections. While toxoplasmosis is a rare infection in classical FUO, it can cause high fever more frequently, especially in HIV-infected individuals (20,23,24). Toxoplasmosis should also be kept in mind as one of the causes of fever in patients presenting with lymphadenopathy or hepatosplenomegaly and in contact with cats or consumption of potentially contaminated food. Acute toxoplasmosis was not detected in any of the febrile patients evaluated in our study.

The most important limitation of our study is that it is retrospective. In addition, since most of the pregnant women with possible primary infection were not referred to the infectious diseases department and some of them were followed up in different centers, no information could be obtained about the pregnancy outcome of this group of patients. It is also an important deficiency that the recommended follow-up algorithms could not be followed in some patients, due to clinician or patient-related reasons. However, a large number of patients were included in our study, important information about local seroprevalence was obtained, the course of acute infections in women of childbearing age could be monitored and, unlike other studies, infections in non-pregnant patients were also evaluated.

CONCLUSION

To know the local incidence of toxoplasma infections, which can cause serious diseases, especially in pregnant women and immunosuppressed patients, to create follow up algorithms for risk groups, and to start antimicrobial drugs when necessary, is important in terms of preventing morbidity and mortality. Although, as far as we know, we did not have a baby diagnosed with congenital toxoplasmosis during the study period, there were many pregnant women whom we could not follow up. Working together between obstetricians and infectious disease specialists to identify and follow-up pregnant women with primary infection will ensure more accurate approach to these patients. In addition, informing seronegative pregnant women about possible transmission routes is very important in order to prevent new primary infections and congenital infections.

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LETTER TO EDITOR

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Exploring the Potential Effect of Negative Air Ions for Rehabilitation in Cerebral Palsy and Polycystic Ovary Syndrome

Serebral Palsi ve Polikistik Over Sendromunda Rehabilitasyon için Negatif Hava İyonlarının Potansiyel Etkisinin Araştırılması

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Dear Editor,

The population of Pakistan is steadily growing, leading to a corresponding rise in both communicable and non-communicable diseases. Though it seems counterintuitive, negative air ions (NAIs) are beneficial, and positive air ions are detrimental to health. Diseases may occur when there is an imbalance of positive and negative ions in the body, halting normal human functioning.

NAIs have been known for over a century (1). They are oxygen molecules with negatively charged electrons within their structure. One cannot sense NAIs as they are tasteless, odorless, and invisible. Two sources of NAIs include natural and man-made sources. NAIs are abundant in the natural environment and are more likely present in cosmic rays, clean air, green mountains, thunderstorms, forests, sea, rainfall, sunlight, and waterfalls. Man-made sources include energy stones, antibacterial showers, anion napkins, negative ion generators, special bracelets, and sanitary pads.

Research findings suggest that NAIs have the potential to ameliorate allergies, anxiety, attention, abnormal behavior, cognition, depression, energy levels, fatigue, mood, ovarian cancer, performance, respiratory function, sleep quality, spasticity, and numerous other bodily functions by fostering alkalinity within the body (2-6). A notable limitation of existing research is the predominant reliance on animal samples rather than human subjects, thereby impeding a robust assessment of the potential beneficial role of NAIs in humans.

Cerebral palsy (CP) is a neurological condition characterized by impairments in balance, coordination, movement, muscle tone, and motor skills, whereas polycystic ovary syndrome (PCOs) involves endocrine dysregulation leading to menstrual irregularities and metabolic dysfunction. Both CP and PCOs involve serotonin, crucial for neurodevelopment and endocrine modulation. Studies indicate that superoxide ions contribute to the effects of NAIs (7,8), which can reduce serotonin levels by oxidizing it into tryptamine-4,5-dione. Reduced serotonin levels resulting from NAIs are linked to specific biological effects and may offer potential improvement for individuals inflicted with CP and PCOs. However, despite evidence from studies (2-8), medical professionals are still wary regarding the use of NAIs.

After reviewing existing literature, we conducted a first-phase clinical trial to assess the effects of NAIs on individuals with CP and PCOs, aiming to determine if NAI intervention could improve these conditions. Permission for the trial was obtained from the Institutional Bio-Ethics Committee of the University of Karachi (IBC-2017) as well as from the participating individuals. The participants were allocated randomly to the control and intervention groups. In multiple experimental trials, researchers have utilized concentrations of NAIs ranging from 1,600 to 1,500,000 NAIs/cm³, with durations spanning from less than one hour to weekly intervals (9). In our investigation, an intervention group was subjected to a concentration of 10,000 NAIs/cm³ for a duration of 45 minutes over six weeks, facilitated by a negative ionizer device. The sessions were held in a controlled room environment to ensure consistent levels of NAIs, with monitoring conducted using an air ion counter. The investigation encompassed the evaluation of blood parameters and cognitive functions both preceding and after the intervention, aimed at monitoring its effects. Blood parameters were assessed through biochemical, hematological, and hormonal analyses, while cognitive functions were assessed using Lumosity software. Findings would be of considerable interest to cognitive scientists, neuroscientists, and gynecologists as they may help them in rehabilitating patients with these disorders.

We suggest that it is important to raise awareness of the beneficial and deleterious effects of NAIs on human health and scientists shall extend research endeavors in this domain to procure more precise evidence.

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IMAGE PRESENTATION

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A Case of Esophageal Walnut Ingestion

Özofagusta Ceviz Yutulması Vakası

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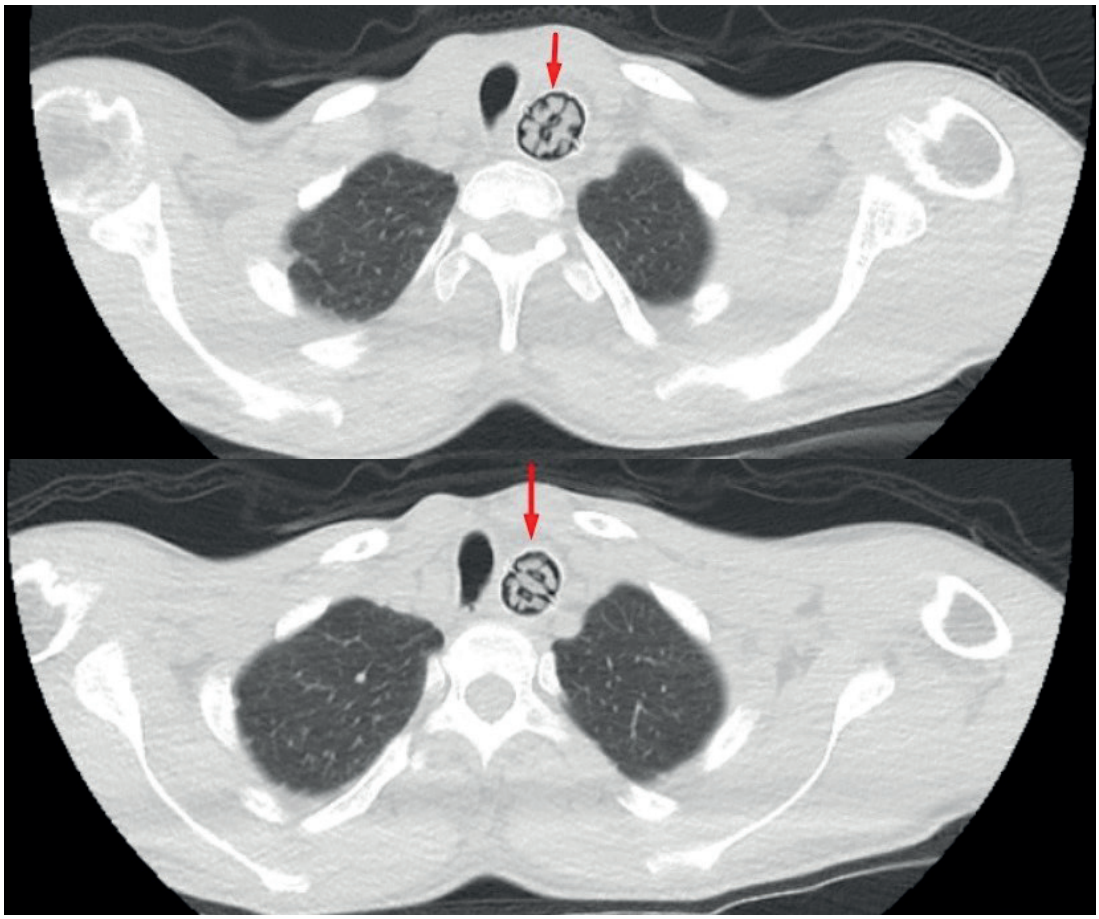

Figure 1: The cervical computed tomography of the patient (Red arrows show the foreign body within the esophagus at the level of the first thoracic vertebra)

A 32-year-old mentally retarded male patient presented to the emergency department with respiratory distress following the ingestion of a foreign body. The parents reported that they did not witness the type of foreign body ingested. The patient was conscious but non-cooperative, and disoriented, with vital signs within normal limits.

A cervical computed tomography revealed a foreign body in the esophagus at the level of the first thoracic vertebra (Figure 1). An esophagoscopy was performed, revealing a whole walnut shell within the esophageal lumen. Despite the repeated use of a mesh snare and tripod during the procedure, the foreign body could not be extracted. The procedure was continued using a rigid bronchoscope. The esophageal foreign body was successfully removed using a rigid bronchoscope, and no complications were observed after the procedure.

The esophagus, a vital component of the digestive system situated between the stomach and the mouth, is susceptible to encounters with foreign bodies, presenting various health challenges. The inadvertent ingestion of small objects often results in foreign bodies entering the esophagus, a condition that may require immediate

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intervention (1).

The entry of foreign bodies into the esophagus typically occurs due to the accidental swallowing of small objects, a phenomenon commonly observed in children. In adults, instances may be associated with ingesting food or other materials. Foreign bodies in the esophagus can result in obstruction, irritation, or even perforation, highlighting the significance of prompt and appropriate management (1,2).

The approach to foreign bodies depends on the patient's symptoms and the nature of the foreign object. Endoscopy emerges as a particularly effective method for detecting and extracting foreign bodies within the esophagus. Employing endoscopic intervention allows for a visual examination of the esophageal interior, facilitating the safe removal of foreign bodies (2).

In such cases, swift and effective intervention is crucial in preventing potential complications. Procedures related to esophageal foreign bodies should be conducted by healthcare professionals with expertise in the field to ensure the identification of the safest and most effective treatment options for the patient.

In conclusion, timely and skillful intervention by experienced healthcare professionals is essential for managing esophageal foreign bodies effectively and minimizing the risk of complications. Swift identification and appropriate treatment options, such as endoscopic intervention, are crucial for ensuring the optimal outcome and safety of the patient.

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Approval of final manuscript: All authors

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CASE REPORT

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Spontaneous Triceps Hematoma and Radial Nerve Impairment due to Warfarin Use

Warfarine Kullanımına Bağlı Spontan Triseps Hematomu ve Radial Sinir Arazı

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ABSTRACT

Intramuscular hemorrhages and hematomas are a complication of anticoagulation in patients using warfarin as an anticoagulant. Hematomas may be due to trauma or may develop spontaneously. Neuropathies due to direct compression of hematomas or hemorrhage around the nerve may rarely occur. We aimed to present a case of spontaneous hematoma in the triceps muscle and associated radial nerve deficit in a patient taking warfarin for valvular disease. The hematoma was evacuated after prothrombin complex concentrate and vitamin K. The patient's nerve deficit improved in the follow-up. Early evacuation of the haematoma may be important for favorable outcomes.

ÖZET

Antikoagülan olarak warfarin kullanan hastalarda kas içi kanamalar ve hematomlar antikoagülasyonun bir komplikasyonu olarak karşımıza çıkmaktadır. Hematomlar travmaya bağlı olabileceği gibi spontan da gelişebilir. Hematomların direk basısı nedeniyle veya sinir çevresine olan kanamalara bağlı olarak nöropatiler nadiren karşımıza çıkabilmektedir. Kapak hastalığı nedeniyle warfarin kullanan hastada spontan triseps kası içerisinde hematom ve buna bağlı gelişen radial sinir arazı gelişen olgumuzu sunmayı amaçladık. Protrombin kompleks ektresi ve K vitamini sonrası hemotom boşaltılmış ve takibinde hastanın sinir kusuru düzelmiştir. Hematomun erken boşaltılması yüz güldürücü sonuçlar açısından önemli olabilir.

Keywords:
Warfarin
Triceps hematoma
Radial nerve deficit

Anahtar Kelimeler:
Warfarine
Triseps hematomu
Radial sinir arazı

INTRODUCTION

Anticoagulant drugs are used to prevent thromboembolic events. Warfarin, a vitamin K antagonist, has an important place among anticoagulant drugs. However, regular international normalization ratio (INR) monitoring is needed to ensure effective dosing and to prevent unwanted complications. The annual incidence of bleeding in warfarin users is around 2-8 (1). Although bleeding complications can be grouped as major and minor, this definition is not standardized. Intracranial hemorrhage is the most serious bleeding complication with a mortality rate of 60% (2). Although intramuscular hematomas may be seen as a complication of anticoagulation, the incidence of neuropathy is not known exactly (3).

Although hemorrhage-induced neuropathy is a rare condition, its prominent clinical findings may be a warning in terms of diagnosis (3). Symptoms and signs include pain in the distribution area of the involved nerve, sensory deficit and motor involvement. Although neuropathy after hematoma has been reported in the literature, reports of radial neuropathy are rare (1,4). Here, we aimed to discuss a patient with a hematoma in the triceps muscle after warfarin use and associated radial nerve impairment.

CASE REPORT

A 70-year-old woman presented to the emergency department with bruising on the right elbow and upper arm. She had no history of trauma. She had a history of mitral valve replacement and heart failure. The patient was taking diltiazem, digoxin, furosemide and warfarin. On physical examination, the patient was conscious, oriented and coherent. Blood pressure arterial: 104/55 mmHg, pulse: 101 beats/minute, temperature 36 ^{0}C, oxygen saturation 98%. There were ecchymosis on the right elbow lateral and medial and above the elbow (Figure 1). Radial and ulnar pulses were obtained. Radial, ulnar and median nerve examinations were normal. Although the patient had no history of trauma, X-ray imaging of the right elbow and right humerus was performed because of the ecchymosis. No fracture was observed on X-ray. INR level was 11.43 and platelet count was 291 *10^3/ µL. Other laboratory tests were normal. The patient was administered 5 mg vitamin K intravenously (IV) with an INR >10, to prevent compartment syndrome from bleeding in the arm and for rapid onset of action. One day later, the patient was externed with a recommendation for outpatient follow-up. The next day, the patient presented to the emergency

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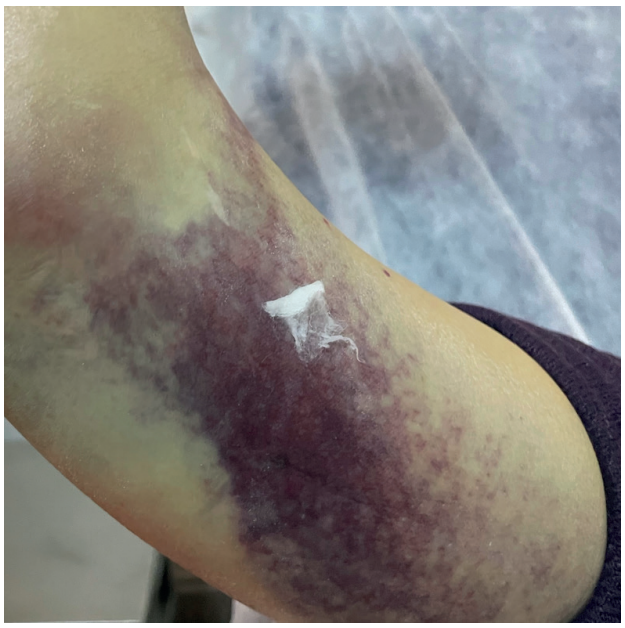

Figure 1: Ecchymosis on the patient's arm

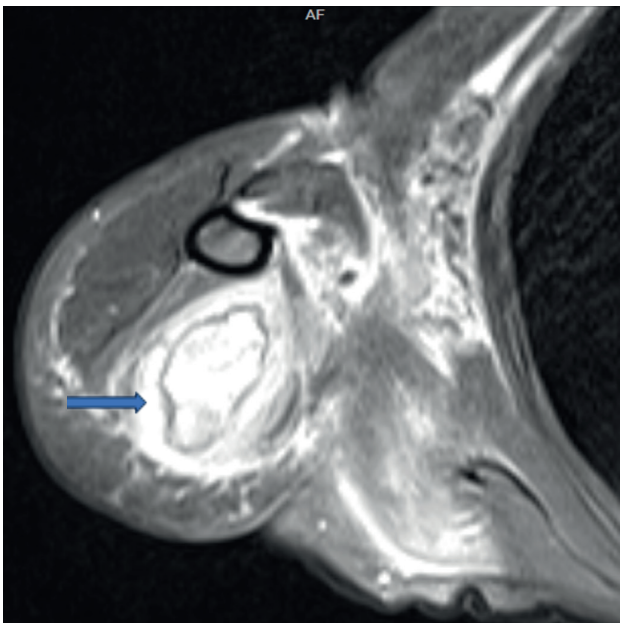

Figure 2: MR image of the hematoma

department again with the complaint of inability to extend the right hand. Physical examination revealed no right hand dorsiflexion movement. There was loss of sensation in the 1st finger of the right hand and loss of sensation except pain sensation in the other fingers. Complete blood count and INR tests were performed. INR level was 6.52, platelet count was 270 *10^3/ µL. Other tests were normal. Superficial ultrasonography (USG) was performed on the right arm. In the USG report, there was an intramuscularly located organized hematoma area extending from the proximal 1/3 of the dorsal aspect of the right arm to the elbow level and reaching a depth of 4 cm. Hematoma evacuation was planned because the patient's symptoms were new. After administration of prothrombin complex concentrate (PCC) and 5 mg vitamin K IV 65 cc hematoma was drained by interventional radiology. The patient was evaluated with the orthopedic clinic and hospitalized in the orthopedic clinic for follow-up and treatment. One day later, right elbow magnetic resonance imaging (MRI) was performed. Hematoma size was measured as 126*40 mm (Figure 2). The patient was discharged on the fifth day with normal neurological examination and no increase in hematoma size.

DISCUSSION

In addition to anticoagulants such as heparins and vitamin K antagonists, there is a new generation of anticoagulants that directly target the enzymatic activity of thrombin and factor Xa. Anticoagulants are used in conditions such as myocardial infarction, venous thromboembolism and atrial fibrillation. An estimated 1% of the European population uses warfarin, a vitamin K antagonist (2). The most serious side effect of these drugs is bleeding. The risk of major bleeding varies between 1% and 7.4% (2). Intracranial hemorrhage, gastrointestinal bleeding, compartment syndrome due to intramuscular hemorrhage are serious bleeding complications. There are studies in the literature showing that these complications occur more frequently in the elderly without trauma (5). Our patient also had a spontaneously developing intramuscular hematoma. On initial examination, neurovascular examination was normal and there was no clinical evidence of compartment syndrome. However, the following day the patient developed radial nerve impairment due to hematoma.

Warfarin is monitored by INR level. Bleeding can be observed in 40% of patients with normal INR levels (1). Although the risk of bleeding increases as the level increases, cases of compressive neuropathy in the therapeutic range have been reported in the literature (1,3). The first INR measured in our patient was 11.43. She had intramuscular non-traumatic hematoma due to high INR level.

Anticoagulation-related hematoma may occur in various muscle groups and cases of neuropathy related to it are available in the literature (6, 7). In the literature, it is observed that this complication is more frequent in heparin treatment (45%) compared to warfarin treatment (18%) and involves the lower extremity nerves more frequently with a rate of 87% (7). Although the pathophysiology has not been fully elucidated, neuropathy is observed probably due to bleeding into the nerve or nerve compression of the hematoma. Cases of spontaneous hematoma-related neuropathy in patients using warfarin have been reported in the literature (4). These cases include femoral nerve, sciatic nerve, median and ulnar nerve compression (1,3,5). In our case, radial nerve impairment due to hematoma developing in the triceps was present.

In cases of INR elevation or bleeding due to Warfarin overdose, the treatment that can be applied is discontinuation of the drug and oral or IV administration of vitamin K. The first of the two important factors here is the indication and the need for ongoing anticoagulation, and the second is the rate of INR reversal required by bleeding. Other treatment options include fresh frozen plasma and PCC. Treatment options may vary depending on the INR level of the patient and the type of bleeding. Rapid INR decrease is important in major bleeding states (2). In our patient, vitamin K was used in the first treatment in order to prevent any findings other than intramuscular

hematoma and to prevent this hemorrhage from causing compartment syndrome.

Conservative treatments were used in 85% of hematoma-related neuropathies (8). Evacuation of the hematoma is another treatment option to reduce compression. In a study, it was emphasized that surgical treatment may be a good option (9). In hematomas drained within 48 hours, it is observed that neurologic loss is completely recovered, but after 48 hours, the success rate decreases to 50% and the neurologic deficit becomes difficult to reverse (8). Therefore, conservative approach becomes more prominent as time passes after hematoma formation, but delay in treatment may result in permanent damage (3). Since there are few cases in the literature, it is controversial whether a conservative approach or early drainage is more appropriate. However, drainage of the hematoma may reverse ischemia by decreasing the pressure effect. There are publications in the literature recommending surgical drainage (4). In our case, the hematoma was drained after administration of PCC and vitamin K with rapid onset of action in order to reduce the compression. Early recovery of the nerve defect suggested that this treatment approach may be beneficial. It has been reported that even small drainage may be beneficial (9).

CONCLUSION

Although neuropathies due to intramuscular hematoma have been reported, there is no clear treatment procedure. Therefore, we believe that hematoma evacuation should be considered as a treatment for neuropathies, which is a rare complication, and early treatment may be beneficial.

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