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Past and Present of Women's Rights and Violence Against Women

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Review Article

History

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ABSTRACT

In history, the greatest aspiration of people is that all humanity has equal rights regardless of race, language, religion or gender. Gender inequality seen in communities where patriarchal structure prevails has caused women to be deprived of their rights. The exclusion of women who have been deprived of their rights due to their gender and even exposure to violence is a global problem that continues from past to present.

Violence against women, which is as old as the history of humanity, is a phenomenon that affects all societies deeply and negatively. As a fundamental human rights and freedom problem, it continues to exist all over the World as a universal public health problem, regardless of ethnic origin, class, religion, social status, culture, economic and geographical boundaries. Domestic violence is the most common form of violence against women. In this study, the historical process of women and their rights, the place of women in society today, the historical process of violence against women, the causes and types of violence against women, femicides, the end point of violence against women, the effects of violence on public health, violence in our country will be discussed. Furthermore, institutions and organizations that women victims of violence can apply to, and suggestions against violence towards women are mentioned.

Keywords: Violence, violence against women, women rights, women in history

Kadın Hakları ve Kadına Yönelik Şiddetin Dünü ve Bugünü

ÖZ

Süreç

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Tarihte insanların en büyük arzusu, ırk, dil, din veya cinsiyet fark etmeksizin tüm insanlığın eşit haklara sahip olmasıdır. Toplumlarda ataerkillik yapısının hakim olduğu yerlerde görülen cinsiyet eşitsizliği, kadınların haklarından mahrum kalmasına neden olmuştur. Cinsiyetlerine dayalı hakları ellerinden alınan ve hatta şiddete maruz kalan kadınların dışlanması, geçmişten günümüze devam eden küresel bir sorundur.

İnsanlık tarihinde var olan kadına yönelik şiddet, tüm toplumları derinlemesine ve olumsuz bir şekilde etkileyen bir olgudur. Temel bir insan hakları ve özgürlük sorunu olarak, etnik köken, sınıf, din, sosyal statü, kültür, ekonomik ve coğrafi sınırlardan bağımsız olarak, dünya genelinde evrensel bir halk sağlığı sorunu olarak varlığını sürdürmektedir. Kadına yönelik şiddetin en yaygın biçimi, ev içi şiddettir.

Bu çalışmada, kadınların tarihsel süreci ve hakları, bugünkü toplumda kadınların yeri, kadına yönelik şiddetin tarihsel süreci, kadına yönelik şiddetin nedenleri ve türleri, kadın cinayetleri, kadına yönelik şiddetin son noktası, şiddetin halk sağlığı üzerindeki etkileri, ülkemizdeki şiddet konuları tartışılacaktır. Ayrıca, şiddete maruz kalan kadınlar için başvurabilecekleri kurumlar ve öneriler de belirtilmiştir.

Anahtar sözcükler: *Şiddet, kadına yönelik şiddet, kadın hakları, tarihte kadınlar*

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Historical Process of Women's Rights

Women's rights and the role of women in society have emerged in different ways from the first human communities to the present day. In the early ages of humanity, before human beings settled down, the family structure was matriarchal, but with the transition to settled life, it is thought that the patriarchal structure, that is, the male-dominated social structure, began to form instead of the matriarchal structure. Another view is that even matriarchal societies have a patriarchal structure and there are no situations where women are dominant[1]. There are many documents showing the existence of these women's problems, even in ancient documents. These documents reveal the inequality between men and women in the societies of that period. Most researchers agree that gender-based discrimination is a deeply rooted form of discrimination[2]. The role assigned to women throughout history has often been that of "ruler". This situation tells us that the inequality between men and women has continued to exist since antiquity, varying according to time and place[3]. One of the reasons why women started to be seen as less valuable than men is the developments in the field of production. The fact that the tools used in production were invented by men caused the material power to be in the hands of men, and the fact that the material power was in the hands of men put women in a lower position against men[4].

When we look at the documents found from the earliest times of humanity, it is not common for women to participate in social life, to be educated and to work, but it is possible to see examples. Narratives about prominent women physicians, architects, philosophers and women sages from Ancient Egypt, Ancient Greek Civilization or the Roman Empire have survived to the present day[5]. Although ancient Egyptian society was patriarchal, it is known that women had some special rights. They had the right to buy property and to be tried equally with men in court. However, although it is known that there were female pharaohs, it is understood from the documents that have survived to the present day that women were not brought to important places in the administration[6].

The marginalization of women increased during the Ancient Greek period. Women were left at home and excluded from society. They were seen as a commodity that could be traded. However, it was considered important for men in high positions to marry the daughters of well-known families in order to give birth to a noble man. The value of a woman's social status remained dependent on giving birth to a noble child[7]. According to the beliefs of the Sumerians, it was not the gods who created everything and owned everything, but the goddesses, that is, women. According to the surviving documents about the Sumerians, monogamy was practiced and it is understood that women and men had equal rights. In a poem written during the Sumerian period; "My mother is a light shining on the horizon, a mountain deer, a shining morning star." An example of the value given to women appears in the line[8,9].

The clay tablets written by the Assyrians who lived in the borders of today's Kayseri province show that Anatolian women were free at that time. During this period, there were city states in Anatolia. Women who took an active role in the administration of these states are described in these tablets. It is known that women were also active in trade life. [8] In the Hittites, who lived in the same region after the collapse of the Assyrian trade colonies, it is known that the powers of the Queen and the King were equal[10]. However, since there are very few documents related to the family in this period, there is not much information about the status of women in social life[11]. Nevertheless, it is known from some documents that Hittite laws did not discriminate between men and women in punishments and the same punishment was given for the same crime. In the Roman Empire, where the patriarchal structure was dominant, the justice system worked in favor of men. A serious pressure was created in social life by using concepts such as privacy and honor against women[12]. In such an environment where women were pushed out of society, Christianity, which promised equality and freedom, was born.

In Christian teachings, it is accepted that all people are equal. The place of women has been moved to a different position with the concept of family[13]. However, as seen in most religions, religious teachings have been shaped according to the habits of the community in which they are found. Christianity fused with the social mindset and became a patriarchal faith. The churches, which were the enforcers of the law, judged women more strictly than men[14].In the environment of the Middle Ages, where fiefdoms ruled, educational institutions gradually began to conform to the wishes of the church. Women's basic education became possible centuries later, provided that their families made donations to the churches[5].

The teachings of Judaism are similar to the effects of Christianity's degeneration over time on relations between men and women. Beliefs such as the idea that a woman was created from a man's rib, the belief that the human race was expelled from paradise as a result of Eve, the first woman in most religious teachings, eating the forbidden fruit, have

led to a deep prejudice against women in society. As a result of all these, women have been marginalized in society and made dependent on men[15].

Looking at the status of Turkish women in Asia in history, it is known that women played important roles and had equal rights with men. In addition to the signatures of khans, the signatures of their wives, hatuns, also appear in state documents. One of the important findings of the equality of men and women in Turks is the word "marriage". The expression "they got married" is used instead of "the man took the woman" which is frequently encountered in old documents[16].

Regarding women in the ancient Turks: "An order was not considered acceptable if it started with 'the khan says so'. It would be acceptable if it started with the words "the khan and the khan are ordering". The khan could not receive ambassadors of foreign states alone. Ambassadors could appear in front of both of them, the khan on the right and the khatun on the left. It is understood from this that the role of women in public services was as great as the khan. The right of guardianship in the family belonged not only to the father but also to both parents. There was no harem, veil or age in the ancient Turks. Women could enter any assembly."[17]. Ancient Turkish women could ride horses, shoot arrows and fight when necessary[16]. Monogamy was the law in Ancient Turks. In the light of all this information, it can be said that the Ancient Turks had a democratic and feminine mindset[18].

When we look at the historical development of women's rights; Turkish women were free and had equal rights with men in the pre-Islamic period according to the conditions of the period. Religious beliefs of the period considered women sacred[18].

The Turks entered Anatolia during the Seljuk period. The Seljuks were under the influence of Iran, where they had lived before, under the influence of the Arabs since they accepted Islam, and under the influence of the Byzantines living in the Anatolian lands they came from. During this period, Turks in Anatolia had to act according to Islamic rules while acting according to their own habits[8].

With the teachings of Islam, women have gained importance. They had rights over family life. According to Islamic teachings, a married woman was given valuable goods called "mahr". This practice was done so that the woman could manage herself in case her husband died or the woman was left alone, such as divorces. However, before Islam, the gifts given for the wedding were given to the woman's family and the father would marry or sell his daughter to whomever he wanted. In Islam, a woman's refusal to marry meant that the marriage was void. In pre-Islamic Arab society, women began to receive their share of inheritance, which they had not received in the past, with the teachings of Islam[19]. However, Islam, like other religions, has changed by being mixed with the values of the society in which it was formed. In Islamic belief, the differences in the creation of men and women have been determinant in social relations and this situation has caused inequality[20]. For these reasons, the social position of women changed radically after the adoption of Islam. The provisions of Islamic law and its implementation in society limited women's space in public life. Women were trapped in family and home life. Obedience and submission were expected of women in Islamic societies[21]. In order to evaluate the relations between men and women of the period, the position of women in pre-Islamic society should be taken into consideration[22].

When we look at the Ottoman Empire, we see three statuses: palace women, mansion women and public women. Palace and mansion women had to live within the framework of Islamic rules. Although some of the palace women had some works built, the majority of them were women of other nationalities. In general, palace women lived a life similar to prison life. Public women, on the other hand, were almost all productive women. They shouldered the burden of the Ottoman Empire; they sent their husbands and children to military service, worked in agriculture, raised animals, and produced food and clothing. They gave some of their earnings to the state as taxes. As a result, although the economy of the state was almost entirely in the hands of women, it is seen that girls in the Ottoman Empire were taken out of school when they were 8-9 years old and were confined to the house. Women were also restricted from going out on the streets in various ways during this period. In some regions, they were not allowed to walk or ride in cars or trams, and actions such as walking around the Grand Bazaar, sitting in a shop, or talking in a group were also forbidden to women[8].

During the War of Independence, our women worked with all their strength, produced food and clothing, and even took part in the front line for the liberation of our homeland from the enemy. Despite all these contributions, the text of the law prepared by the parliamentarians who tried to enact a law on family law in 1923 included articles such as "Since the woman is mentally and religiously weak, she must be under the protection of the man, the man can take many women and divorce them as he wishes, women's working outside disrupts social life, and science destroys women's morals." The text was not accepted in this form. However, months

before the proclamation of the Republic, Mustafa Kemal, in a speech, spoke of "freedom for women, equal educational opportunities and a social position for women no different from that of men" and said in Konya: "The fact that our women, who were under much less favorable conditions, have become equal to men, and in some cases even surpassed them, is a proof of their extraordinary abilities and equality."[23].

With the adoption of the Civil Code and the abolition of Islamic provisions (1926) and the granting of the right to vote (1930) and then to be elected (1934), Turks began to return to their past in Central Asia and the seeds of the idea of equality between men and women were sown. In the Republican era, thanks to Atatürk, women were able to step into the world of science for the first time. Before the Republic, it was impossible for women to go to university. Most of our first women scientists in the Republican years were women who had received their education abroad. After the establishment of the Republic of Turkey, with the adoption of the Law on Unified Education (1924), our education system changed and women and men were offered equal conditions in education. With the Dress Code (1925) and the Turkish Civil Code (1926), the place of women in society changed and women were granted equal rights with men[23].

With the factorization brought about by the Industrial Revolution in Europe, women started to play a more frequent role in business life. This situation played an important role in revealing the situation of women and the violence they were exposed to. Concepts such as equality, justice and peace, which began to be expressed with the French Revolution, also came to the agenda for women. (AH) With the beginning of the Age of Enlightenment, the idea of compulsory education covering the whole population began to spread. Whether or not girls should receive this compulsory education soon became a matter of debate[24]. The right to citizenship was demanded for women, and it was argued that women should also be able to receive vocational education that was only available to men. For a century, however, women were not allowed to study at universities. The reason for this situation was that women were considered physically weaker than men and that they were not suitable for such an education in terms of intellectual ability[5, 24]. By 1840, the first female students in Europe began their education at the University of Zurich. Despite all these developments, many scientists living in those years, who adopted the conventional perception of women, argued that the idea of "equality between men and women '' was unnecessary[25].

Today, even in developed countries, women are still not equal to men in social life and human rights. In developed countries, gender discrimination and the obstacles placed in front of women at every stage of their working life, from admission to employment to promotion, are the most common forms of this inequality. In addition to the problems in developed countries, problems in basic life situations such as being subjected to violence and being deprived of education are more common in developing countries.

Violence Against Women

For centuries, violence against women, as a violation of human rights and a form of discrimination, continues to exist all over the world, regardless of ethnicity, class, religion, social status, cultural, economic and geographical boundaries.

According to the patriarchal mentality, even if a woman is a victim of violence, she is the one who harbors the cause of the crime. Considering that every woman victim of violence may have provoked the perpetrator, her "criminal" behavior is questioned.

Violence is defined by the UN as all individual or collective acts that cause physical or mental harm to people by applying force and pressure[26].

Violence against women is defined by the World Health Organization as any behavior that results or is likely to result in physical, sexual, psychological, economic harm to women, including the prevention of freedom through coercion, whether in public or private life[27].

Violence against Women in the Historical Process

Archaeological studies trace the origin of women's experiences of physical violence back to 3000 years ago in ancient times. While 9-20% of the bones of male mummies found in these studies were fractured, this rate was 30-50% in female mummies. During the Roman Empire, it is known that men could beat their wives and had the right to kill them for reasons such as adultery and drunkenness. In England, the law allowed men to beat their wives until 1887. In ancient Indian traditions, it is known that women whose husbands died were burned together with their husbands. In pre-Islamic Arab geography, girls were often buried alive because they were seen as a disgrace to society.

When the dates show March 8, 1857, the incident in which 129 women workers died as a result of the police intervention against striking workers in a textile factory in New York, the workers were locked in the factory, and then the workers could not

escape in the fire that broke out, is one of the biggest examples of violence against women in our recent history. March 8 was first celebrated as Women's Day in Denmark in 1910, and is now commemorated annually as International Women's Day following a decision taken by the United Nations (UN) General Council in 1977.

On November 25, 1960, three sisters, Patria Mercedes, Minerva Argentina and Maria Terasa (the Mirabel sisters), were taken out of their car, raped and murdered as they went to visit their husbands in prison. With the resolution adopted by the UN General Assembly in 1999, November 25th of each year is celebrated as the "International Day for the Elimination of Violence against Women and International Solidarity".

Causes of Violence against Women

Sexist approach that does not believe in equality (gender inequality), family conflicts and disharmony, low income level, personality disorders, exposure to violence in childhood, substance abuse (alcohol, drugs, etc.), traditional assumptions (reflection of patriarchal structure), low level of education, honor and ritual excuses are the most common causes of violence against women. The most fundamental cause of violence against women is gender discrimination and asymmetrical power relations stemming from the patriarchal social structure. In the UN action plan on combating violence against women (2016-2020), the concept of gender is defined as the socially constructed roles, behaviors, masculinities and attitudes that a given society deems appropriate for women and men. We are one of the countries with the highest gender inequality and the deepest "gender gap". In this study conducted by the World Economic Forum in 2021, we ranked 133rd out of 156 countries. In the same study, we are the 1st country in the world in the rate of dismissal of women during the Covid-19 pandemic[28].

The Most Common Types of Violence against Women

Physical violence, psychological violence, sexual violence, economic violence, stalking, forced or child marriage, trafficking in women and forced prostitution, genital mutilation of women are the most common forms of violence against women. According to the World Health Organization, one in every three women is subjected to physical or sexual violence by an intimate partner. Two out of every five women (43%) are known to have experienced psychological violence by their current or former partner/life partner. Worldwide, 38% of femicides are committed by the victim's partner or intimate partner. Twice as many women die in domestic violence as in wars and global conflicts. Women aged 15-44 are more likely to die from rape and domestic violence than from cancer, traffic accidents or infectious diseases[27].

Femicides

In general terms, it is the killing of women or girls, regardless of who commits it, because they are women. It is evaluated separately from male homicides due to its purpose, i.e. gender discrimination.

In 2019, in the Global Homicide Report published by the United Nations Office on Drugs and Crime, which investigates the rates of women being killed because they are women, it was reported that approximately 87000 women were victims of homicide in 2017 all over the world. Approximately 3/5 of these women were murdered by their lover, spouse or family member. Asian countries lead the list of countries where femicides are most common, followed by African and American countries. [29] In Turkey, 303 women were murdered in 2015, 328 women in 2016, 409 women in 2017, 440 women in 2018, 474 women in 2019, 413 women in 2020, 419 women in 2021, 403 women in 2022, 284 women in 2023 so far (19/09/2023)[30].

The Effects of Violence Against Women on Human Health

Violence deprives women of their right to health, which is their most fundamental right. Women victims of violence face physical and psychological consequences. Violence can lead to negative health behaviors such as smoking, alcohol and substance abuse, decreased physical activity, overeating and obesity. Negative effects on mental health such as low self-perception, post-traumatic stress disorder, depression, anxiety, phobias, panic attacks and social exclusion can be observed. Unwanted pregnancies, sexually transmitted diseases, gynecological diseases such as pelvic inflammatory disease, pregnancy complications, unsafe abortion may occur, which may negatively affect women's reproductive health. It has been reported that women who experience violence during pregnancy are negatively affected in terms of reproductive health, and newborns and fetuses are also affected by this situation[31]. Violence can result in homicide or suicide and have fatal consequences.

Where Can Women Victims of Violence Apply?

89% of women who are subjected to violence do not apply to any institution. 8% apply to law enforcement agencies, 5% to family courts, 4% to health institutions, 3% to prosecutor's offices, 1% to bar associations.

In our country, women who have been subjected to violence can apply to administrative law enforcement bodies (governorships, district governorships), judicial law enforcement bodies (Police Centers under the General Directorate of Security, Gendarmerie Police Stations under the General Command of Gendarmerie), public prosecutor's offices, family court judgeships, health institutions, the Ministry of Family and Social Services and its affiliated units, local governments, bar associations and non-governmental organizations[32].

Preventing Violence against Women

The "Universal Declaration of Human Rights" drafted by the UN after World War II. Although the "Universal Declaration of Human Rights" prepared by the UN after World War II is a comprehensive international convention, it is not legally binding. Published in 1979 to combat all forms of discrimination against women, the "CEDAW" convention is legally important. It has been accepted by 165 countries, including Turkey[33]. CEDAW was prepared based on the basic principles and principles in the Universal Declaration of Human Rights, and it has put the fundamental rights and freedoms for all human beings on a legal basis for women.

One of the internationally recognized and binding conventions on violence against women is the Istanbul Convention. It was adopted on April 7, 2011. With this convention, physical violence against women, domestic violence, sexual violence including rape, psychological violence, stalking, forced marriages, forced abortion, forced sterilization and sexual harassment are defined as violence against women. The Istanbul Convention aims to prevent violence against women, protect victims, punish perpetrators of violence, and develop holistic state policies on the issue[34]. It was repealed in our country with the Presidential Decree published in the Official Gazette No. 31429 on March 20, 2021[35].

The most important piece of legislation on violence against women in Turkey is the "Law No. 6284 on the Protection of the Family and Prevention of Violence against Women", which was drafted in light of the provisions of the Istanbul Convention and entered into force in 2012. Another important piece of legislation, the "Regulation on the opening and operation of women's guesthouses" entered into force in January 2013. The "Regulation on Violence Prevention and Monitoring Centers (ŞÖNİM)" on Violence Prevention and Monitoring Centers to which women victims of violence can apply entered into force in 2016. There are ŞÖNİM in 73 provinces and 144 guest houses in 81 provinces[36].

Conclusion and Recommendations

Enacting laws to eliminate gender discrimination, making arrangements to ensure equal opportunities in education, increasing women's employment in business life, providing women with the same economic freedom as men, strengthening and supporting women's social and economic status, ensuring women's equal representation in politics and decision-making mechanisms and their effective participation in these areas, ensuring that the media conveys the negativity of violence in an appropriate language and raising awareness in society. It is important for us to prevent violence against women and gender discrimination, to make programs based on gender equality on state radio and television, to include courses on women's human rights and gender equality in the curriculum, to make preventive and deterrent regulations on early and forced marriages (child brides, religious marriages, polygamy and honor killings), to change the socio-cultural structure dominated by patriarchal structure, to develop decisive state policies to prevent gender inequality and to improve women's rights.

Compliance with Ethical Standards

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Pars Planitis Epidemiology, Diagnosis, Follow-Up and Prognosis

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ABSTRACT

Pars planitis (PP) is an idiopathic intermediate uveitis accompanied by snowbanks and snowballs that often affects the pediatric and adolescent age groups. PP accounts for 5-26.7% of pediatric uveitis in different series. Histopathological and clinical findings indicate autoimmune etiology. It shows bilateral and asymmetrical involvement. While patients often complain of blurred vision and floaters, sometimes PP can be asymptomatic. Complications develop as a result of chronic involvement. Diagnosis is made by clinical examination and imaging methods. Treatment aims to suppress inflammation in the acute period and to reduce the frequency, severity and complications of exacerbations in the long term. The ultimate goal is to prevent ocular morbidity by providing complete remission. Conventional treatments include corticosteroids and immunomodulatory (IMT) agents such as methotrexate (MTX), azathioprine (AZA), cyclosporine A (CSA), mycophenolate mofetil (MFM). In recent years, new treatment options including biological agents such as anti-TNF-α therapy have become widespread and are used effectively in treatment. The most important point regarding the necessity of surgical treatment is that surgical success depends on the complete suppression of ocular inflammation with medical treatment. Therefore, it must be ensured that full inflammation control is achieved before surgery.

Keywords: Pars planitis, pediatric uveitis, biological agent

Pars Planitis Epidemiyolojisi, Tanısı, Takibi ve Prognozu

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ÖZ

Pars planit (PP) sıklıkla pediatrik ve adölesan yaş grubunu etkileyen snowbank ve snowball'ların eşlik ettiği idiyopatik intermediate üveittir. PP farklı serilerde pediatrik üveitlerin %5-26,7'sini oluşturmaktadır. Histopatolojik ve klinik bulgular otoimmün etiyolojiye işaret eder. Bilateral, asimetrik tutulum gösterir. Hastalar sıklıkla bulanık görme ve uçuşma şikayetiyle başvurur. Bazen de asemptomatik seyreder. Kronik tutulum sonucu komplikasyon gelişimine rastlanabilir. Tanı klinik muayene ve görüntüleme yöntemleriyle konur. Tedavinin amacı akut dönemde enflamasyonu baskılamak, uzun dönemde ise atakların sıklığını, şiddetini ve komplikasyonları azaltmaktır. Nihai amaç, tam bir remisyon sağlanarak oküler morbiditenin önlenmesidir. Geleneksel tedaviler arasında steroitler ve metotreksat (MTX), azatioprin (AZA), siklosporin A (CSA), mikofenolat mofetil (MFM) gibi immunomodülatuar (İMT) ajanlar bulunmaktadır. Son yıllarda; anti-TNF-α tedavisi gibi biyolojik ajanları kapsayan yeni tedavi seçenekleri yaygınlaşmış olup tedavide etkin şekilde kullanılmaktadır. Cerrahi tedavi gerektiğinde ise dikkat edilmesi gereken en önemli nokta; cerrahi başarının oküler enflamasyonun medikal tedavi ile tamamen baskılanmasına bağlı olduğudur. Bu nedenle cerrahi öncesi tam enflamasyon kontrolü sağlandığından emin olunmalıdır.

Anahtar sözcükler: **P**ars planitis, pediatric üveit, biolojik ajan

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Introduction

Intermediate uveitis is primarily an inflammation of the anterior vitreous, ciliary body and peripheral retina. It can be idiopathic or associated with infectious or systemic diseases. Pars planitis (PP) is described as idiopathic intermediate uveitis accompanied by snowbanks and snowballs, which predominantly affects the pediatric and adolescent age group[1]. In children, intermediate uveitis often presents as PP.

1.Epidemiology

The prevalence and incidence of the disease vary according to geographical regions and genetic characteristics. PP accounts for 5-26.7% of pediatric uveitis in different series[2, 3-5]. In a retrospective study conducted by Özdal et al. from Türkiye, the main cause of pediatric uveitis was found to be PP (24%)[5]. Soylu et al. found it to be the 3rd most common (9%) cause of pediatric uveitis after Behçet's and toxoplasma uveitis[4]. The typical onset of the disease occurs between the ages of 6 and 10[3, 4]. Symptoms begin on average around age 6, and most patients are diagnosed before age 14[6]. Although both genders can be affected, male gender predominates at young ages and female gender comes to the fore in adolescence[7, 8]. PP is bilateral in 75-80% and may show asymmetric involvement[9].

2.Etiopathogenesis

Histopathological and clinical findings suggest autoimmune etiology. It is thought to be an autoimmune response to ocular antigens that have not yet been identified playing a role in the etiology of the disease. It is thought that the retinal blood vessels, the ciliary body, or the pars plane itself may be the source of these antigens. T-helper cells have been found in retinal vascular infiltrates and snowbank structures. Due to the intense detection of T cells in the vitreous, the role of an autoimmune mechanism in which T cells are dominant is accepted.

3.Genetic factors

A genetic predisposition is believed to exist as a familial relationship is found in approximately 15% of patients and HLA DR2 is present in 50–70% of patients[10]. Associations between PP and HLA-DR2, DR15, B51 and DRB1*0802 haplotypes suggest immunogenetic predisposition. Patients who are HLA-DR15 positive have been reported to have systemic manifestations of other HLA-DR15-related disorders such as multiple sclerosis (MS), optic neuritis, and narcolepsy, indicating a common genetic alteration[11].

4.Clinical characteristics

Symptoms usually begin in one eye and have an insidious onset. It typically starts with mild blurring of vision and floaters. Donaldson and colleagues reported blurred vision in 74% of cases and floaters in 61% at diagnosis[12]. Although more rare, patients may present with red eyes, pain, light sensitivity, vision loss, strabismus and leukocoria. Sometimes the disease has an asymptomatic course and uveitis can be detected during routine eye examination. Especially in young patients; due to the difficulty in expressing complaints, delays in diagnosis and high complication rates at the time of diagnosis are encountered[13]. Especially in younger patients, diagnosis is delayed and the risk of developing complications that may lead to permanent vision loss increases.

PP is a disease that mostly has a bilateral course, but the severity of inflammation may be asymmetrical. Various studies have reported bilateral involvement at rates as high as 92%[3,9]. Typical clinical findings include mild to moderate anterior segment inflammation, diffuse vitreous cells and haze, and snowbanks and snowballs located in the retinal periphery[14]. PP extends from the anterior segment to the posterior segment. Inflammatory cells in the anterior chamber are the most common in anterior segment involvement. Small, round, white keratic precipitates are found on the corneal endothelium in approximately 50% of eyes. Peripheral corneal endotheliopathy which indicates the autoimmune etiology is characterized by peripheral corneal edema and large sheep fat keratic precipitates (KP) at the border of the edematous and normal cornea[15]. As the inflammation becomes chronic anterior segment involvement such as band keratopathy, anterior and posterior synechiae and cataract may be encountered and is more common in childhood than in adults[14].

The posterior segment and vitreous involvement pattern are important clinical features of PP. Characteristic findings include snowbank, snowball, peripheral vasculitis, diffuse cells and haze in the vitreous. Snowballs are yellow-white inflammatory deposits usually found in the middle and lower periphery. Snowbank is defined as exudates on the inferior pars plana. In approximately 60-65% of cases, the snowbank begins inferiorly and can spread and accumulate 360° in front of the peripheral retina. Donaldson et al. found the presence of snowballs in 67.4% and snowbanks in

97.8% of eyes with PP[12]. Although peripheral retinal vasculitis and vein sheathing is seen in PP, its occurrence varies between 17-90% in different clinical studies[31]. Optic disk inflammation is common in PP, its frequency goes up to 70% especially when the screening is done with fundus fluorescein angiography (FFA)[6, 16].

Patients with suspected PP should undergo a careful fundus examination with scleral depression, and the presence of snowball opacity and pars plana exudate should be investigated. In PP, the prevalence of exudate and the presence of more serious vitreous inflammation are often associated with cystoid macular edema (CME). In some cases, intravitreous hemorrhage may occur due to neovascularization of the vitreous base[17].

5.Diagnosis

There is no specific diagnostic test. Diagnosis is made by clinical ophthalmological examination. In a patient with suspected intermediate uveitis, the diagnosis is confirmed after excluding accompanying conditions like infectious (toxocariasis, peripheral toxoplasmosis, Lyme uveitis, tuberculosis, syphilis) and autoimmune (Behcet's disease, sarcoidosis, multiple sclerosis) systemic diseases. Optic coherence tomography (OCT) is widely used because it is fast and easily reproducible. OCT is effective in the follow-up of patients with epiretinal membrane (ERM), vitreomacular traction, and foveal atrophy, as well as macular edema. It is important in visual prognosis prediction as it can provide a detailed evaluation of the retinal layers[18]. In FFA; widespread fluorescein leakage from retinal vessels, optic disc inflammation and hyperfluorescence due to (CME) are observed. While there is no neovascularization, peripheral retinal traction and vasculitic changes on clinical examination, snowbank may show early hyperfluorescence and leakage, and this has been thought to be related to occult neovascularization[19]. Snowbanks located in the peripheral retina may appear as a fibrovascular mass. It is possible to demonstrate this with ultrasonography. Ultrasound biomicroscopy (UBM) shows that the pars plana is thickened and the exudates settled in the peripheral retina and pars plana are homogeneous, medium-density reflective opacities[20].

6.Complication

Pars planitis can lead to permanent damage to ocular structures and blindness due to complications, especially if diagnosis is delayed[21]. Delays in diagnosis and treatment may occur due to its chronic and asymptomatic course. It has been reported that children with uveitis onset at a young age (≤7 years) are more prone to the development of cataracts, glaucoma and vitreous hemorrhage and have a worse visual prognosis compared to older children (>7 years)[22]. Common complications are cataracts, CME, vitreous opacities and optic disc edema. Band keratopathy, amblyopia, ERM formation, vitreous condensation, neovascularizations, retinal detachment (RD) and cyclitic membranes are also seen as a result of long-term PP.

The most common complications are optic disc edema and CME. CME, the most common cause of low vision, is associated with poor visual prognosis. DeBoer et al. reported that it was observed in 44% of children with PP[16]. Ellipsoid zone (EZ) loss on OCT is associated with poor visual acuity in eyes with uveitic macular edema. Other complications include corneal endotheliopathy (corneal graft rejection-like appearance), posterior synechiae, cyclitic membrane, vasculitis, vitreous opacities and inferior peripheral retinoschisis which occurs almost only in children[23]. Optic disc neovascularization has been associated with severe inflammation[11].

Dense vitreous condensations are a cause of leukocoria that may be misdiagnosed as cataracts. Posterior subcapsular cataract is common in children with PP and poses a serious risk for amblyopia[23].

ERM formation was found to be directly related to disease chronicity and the mean time between disease onset and ERM formation was 7-8 years[12]. It has also been reported that the presence of ERM associated with uveitic macular edema is associated with worse visual acuity after treatment[24].

Retinal detachment (tractional, rhegmatogenous or exudative) is rare and has been reported in about 10% of cases in different studies[7,12,25]. The development of retinoschisis and tractional RD in the periphery of the retina is thought to be the result of traction of gliosis caused by the previous snowbank. Peripheral retinoschisis is stable and self-limiting in most cases[26]. Another view focuses on vascular etiology, suggesting that chronic inflammation causes peripheral angiogenesis, which in turn leads to exudative RD, retinoschisis, intraretinal edema and cyst formation[27].

Glaucoma is due to decreased aqueous outflow and blockage, which can develop secondary to many causes such as peripheral anterior synechiae, increased protein concentration in the aqueous humor, trabecular inflammation and damage. Surgical treatment may be required in the presence of high intraocular pressure that cannot be

controlled with topical treatment. The success rate and long-term efficacy of surgery may be limited in uveitic patients. It is a complication seen in approximately 6-8% of patients and requires surgery in half of the cases[11].

Other rare complications include macular hole and macular ectopia.

Amblyopia may occur due to dense band keratopathy, vitreous opacities, vitreous haze, cataracts occluding the visual axis or persistent macular edema.

7.Prognosis

The natural course of PP is variable. According to studies, part of the patients have self-limiting disease while other part of the patients have a prolonged active disease with frequent exacerbations and the rest of the patients have chronic disease after a few exacerbations. PP's chronic and insidious nature and the anterior segment's symptoms' usual quiet characteristics may cause a lot of pediatric patients to have permanent visual loss. In children, PP prognosis is strongly associated with vitreous inflammation's severity. While more severely inflamed eyes are more prone to CME and other macular complications, eyes that developed vitreous bands may result in retinal traction and RD[28]. To improve patients' general prognosis, the main goal is sufficient control of inflammation and rapid detection of disease-associated complications[29]. One of the most important factors that affect visual prognosis is the age at the onset of the disease. In pediatric PP patients, visual acuity at the diagnosis and follow-up is poorer compared to adult patients. It is shown that children who were diagnosed at the age of 7 and younger are more prone to complications and poorer visual prognosis compared to older children[22]. Another study has shown that the onset of disease at 10 years old and before, male gender, apparent vitreous blurriness and macular edema existence are markers for poor prognosis[9].

8.Treatment

Uveitis in pediatric patients is a chronic disease that may have relapses and poor prognosis. It is important to use a multidisciplinary approach with a team consisting of ophthalmologists and pediatricians while managing the treatment[30].

Before starting the treatment, uveitis' relation to systemic diseases and infections should be researched and the mechanism of action and adverse reactions of the therapeutic agents should be known well. Patients must be well informed about the test and the treatment plan and should be followed closely in terms of the side effects.

The main goal of the treatment is to suppress the inflammations acutely and to reduce the frequency and severity of attacks and complications in the long term. The ultimate goal is to provide full remission and to prevent ocular morbidity.

For pediatric patients, conventional treatment for non-infectious uveitis includes topical, periocular, intravitreal or systemic CS and immunomodulator agents (IMT) such as methotrexate (MX), azathioprine (AZA), cyclosporin A (CSA), mycophenolate mofetil (MFM). In recent years, new treatment options which contains biologic agents like anti-TNF-α have become prevalent and used efficiently.

In our PP practice, treatment's first step is the usage of CS which forms the basis of the treatment. When a patient needs long-term therapy with steroids, IMT must be considered. If the patient has refractory uveitis, poor prognostic factors and developed complications at the time of diagnosis, IMTs must be started along with CS without delay as the first-line therapy. IMT agents can be used as monotherapy or combined with other agents. The choice of IMT agent can change according to ophthalmologists' preference and experience, also patient's clinical findings and age.

In conventional immunosuppressive treatment-refractory and uncontrolled uveitis or situations when adverse effects cause treatment discontinuation, biological agents are considered the treatment of choice. Adalimumab (ADA) is the first choice when switching the biological agent treatment. In some cases, when uveitis is very severe and cannot be controlled with anti-TNF-α, tocilizumab (anti-IL 6) treatment can be started.

8.1 Corticosteroids

Corticosteroids are the first-line treatment in PP. Topical CS is mainly used in the treatment of anterior segment inflammation, although its effect is insufficient in the treatment of intermediate and posterior uveitis, especially in phakic cases[31]. Topical CSs are ineffective in posterior segment inflammation because they cannot penetrate the vitreous. In these cases; subconjunctival, peribulbar, intravitreal or systemic CS treatment can be applied. Periocular or subtenon CS injections might be a treatment choice for intermediate and posterior uveitis, specially in unilateral cases and for CME. The most common complications of periocular CS applications are; increased intraocular

pressure, cataracts and aponeurotic ptosis[9]. Others; herpes virus reactivation, delayed healing of corneal wounds, corneascleral thinning, subconjunctival hemorrhages, myopia, central serous chorioretinopathy (CSCR), microcyst formation in the iris/ciliary body.

CS side effects are related to the average dose and duration of treatment. However, serious side effects may occur even with low doses. Systemic CSs are used only for short-term treatment in children due to significant systemic side effects associated with long-term use, such as cushingoid changes, growth retardation, increased appetite, weight gain, restlessness, hypertension, osteoporosis, gastrointestinal upset, psychosis, electrolyte imbalance and pseudotumor cerebri.

The induction dose of oral prednisolone is 1-2 mg/kg. When a faster and stronger effect is required, intravenous methylprednisolone 30 mg/kg may be preferred.

In patients who do not respond adequately to high-dose CS or are dependent on high doses, additional IMT agents should be started. Moreover, in patients who present with serious ocular complications and have risk factors for the development of new complications, IMT agents combined with CS can be started at the first visit.

8.2.Conventional immunomodulatory Treatment Agents

8.2.1Antimetabolites

Methotrexate

Methotrexate is the most commonly used and first-choice IMT agent in children with uveitis. It is a folate analog that inhibits the enzyme dihydrofolate reductase.

MTX is administered to children once a week orally or subcutaneously at a dose of 10-15 mg/m2. At the end of 6-8 weeks, the dose can be safely increased up to 30 mg/m2, depending on the response and tolerance to the drug. The therapeutic effect is usually seen after 6 to 10 weeks[28]. The subcutaneous route is better tolerated in children with nausea or in patients with poor oral bioavailability.

Side effects of treatment depend on the dose and duration of treatment. Since MTX is a folic acid antagonist, it should be used in conjunction with folic acid. Aversion; It is an undesirable side effect that may occur during treatment. Before an oral or subcutaneous dose, children often experience abdominal pain, nausea, and may vomit. if these symptoms significantly affect the child's quality of life; It is important not to insist on treatment and to use alternative agents instead of MTX. However, the most common side effect of MTX is that it affects liver function and increases transaminase levels. Side effects such as gastrointestinal toxicity, liver cirrhosis, hematological toxicity, pneumonia, lung fibrosis and teratogenicity may occur during the use of MTX. In case of inadequate response with MTX, other IMT agents or combined treatment can be started.

Azathioprine

It is a purine nucleotide analog and is given 1-2 mg/kg/day (30-60 mg/m2) orally. The therapeutic effect mainly occurs within 1-3 months of use. Most side effects were in the form of gastrointestinal tract complaints, usually at higher doses, while malignancies were only rarely reported with long-term treatment[32]. The most common side effects are bone marrow suppression with leukopenia, thrombocytopenia and hepatotoxicity. Monthly complete blood count and liver function test (LFT) control should be performed during drug monitoring.

Mycophenolate Mofetil

It is a prodrug. It inhibits the proliferation of human T and B lymphocytes and suppresses the antibody production of B cells[33]. It is better tolerated than AZA. MFM has high oral bioavailability and should be taken on an empty stomach. Antacids reduce the bioavailability of the drug by 15%. The recommended drug dose for uveitis is 2 g/day.

Up to 30% of patients experience nausea, gastrointestinal upset and diarrhea. Less commonly reported side effects of AZA are leukopenia, hair loss and fatigue. Patients should be monitored with a complete blood count once a week for 4 weeks, then twice a month for 2 months, then once a month. LFT should be performed every 3 months.

8.2.2.Calcineurin Inhibitors

Cyclosporine

CsA, a calcineurin inhibitor that suppresses T cell activation, has limited efficacy in pediatric uveitis when used alone. It is usually applied as a combined treatment.

Important side effects associated with cyclosporine use include nephrotoxicity, hypertension, hepatotoxicity, anemia, gingival hyperplasia, hypertrichosis, nausea, vomiting and tremor. It is less nephrotoxic in children than in adults due to higher renal clearance. Patients should be monitored for side effects with kidney and liver

function tests and blood pressure measurements. The recommended dose of CsA is 2.5-5 mg/kg per day[34].

8.3.Biological agents

They provide effective treatment in the immune system by affecting specific molecules (proteins) in the inflammatory process. The majority of these agents are monoclonal antibodies[35]. These drugs are used as next-line therapy in the treatment of uveitis when CS and conventional immunosuppressive therapy fail to suppress ocular inflammation or when steroids must be avoided. They can be used alone or in combination with conventional agents. The most commonly used biologics in the treatment of uveitis are TNF-α inhibitors; Especially ADA and infliximab (IFX) are preferred. Different biological agents such as tocilizumab (anti-IL 6) can be tried in patients resistant to TNF inhibitors.

Inhibition of TNF-alpha has been shown to reduce leukocyte activity, function (rolling, adhesion), and vascular leakage. This mechanism may explain its effectiveness in inflammatory ocular diseases[36]. TNF-α has been found to increase vascular endothelial growth factor (VEGF) production in choroidal endothelial cells and VEGF is responsible for macular edema in patients with uveitis. Anti-TNFs reduce VEGF-α levels in plasma by inhibiting TNF-α production in the treatment of uveitic macular edema[37].

TNF inhibitors can occur in 2 ways; in the form of soluble receptor fusion protein (etanercept) or monoclonal antibodies (IFX, ADA, golimumab, certolizumab). IFX consists of partly human and partly mouse antibodies and is chimeric, whereas ADA is a completely human antibody. Their activities are similar but there are some differences. ADA binds to TNF-α with higher affinity than etanercept or IFX, and therefore its use in treatment has proven to be advantageous[38].

Although TNF-α inhibitors are used in the treatment of sarcoidosis and psoriasis, the reason is not fully explained and they may paradoxically cause sarcoidosis-like involvement in the lungs and psoriatic skin lesions. TNF-α inhibitors are contraindicated in multiple sclerosis. Infections such as tuberculosis, human immunodeficiency virus (HIV), syphilis, HBV, HCV and toxoplasma should be excluded before starting treatment. Common side effects of TNF-α inhibitors include hypersensitivity, more serious side effects include infections, hematological reactions, malignancies and myocardial infarctions.

Patients using TNF-α inhibitors require regular blood evaluations, including complete blood count, LFT, blood urea nitrogen, and serum creatinine levels every 6 weeks.

İnfliximab

Standard practice is intravenous treatment at weeks 0, 2 and 6. Thereafter, it can be given at 4 or 8 week intervals. The half-life of IFX is 10 days; however, its effects may persist for up to 2 months. Due to its chimeric nature, IFX is often given together with MTX or another IMT agent to reduce anti-chimeric antibody formation and increase the duration of drug effectiveness[36]. It is a good option in pediatric uveitis when rapid effectiveness is required and CSs are avoided due to side effects. Pediatric patients may require higher doses or more frequent infusions than adults.

Adalimumab

Adalimumab is a fully humanized monoclonal antibody against TNF-α. Therefore, chimeric antibody formation is not observed. However, some patients may develop antibodies against ADA, which may reduce the effectiveness of the drug over time[36]. Several prospective studies, including the VISUAL I clinical trial, have demonstrated the efficacy and safety of anti-TNF drugs in treating chronic and refractory uveitis and reducing the use of CS[39].

The standard ADA protocol is subcutaneous administration of 80 mg if the patient weighs 30 kilograms or more in the first application, followed by a 40 mg dose 1 week later, and then 40 mg doses every 2 weeks. For patients weighing less than 30 kilograms, the dose is halved.

The most common side effects in adalimumab treatment are injection site reactions and allergic reactions[39]. Cases of cellulitis, pneumonia, appendicitis, herpes zoster, urinary tract infection, gastrointestinal tract abscess and gastroenteritis, and more rarely tuberculosis and opportunistic infections, have been reported with ADA. Other serious side effects such as demyelinating disorders, lupus-like syndrome, and congestive heart failure are rare. The advantage of ADA over other anti-TNF agents is that it can be applied without requiring admission to any hospital or healthcare institution.

In a prospective multicenter case series including 131 patients from different age groups, it was shown that ADA therapy could significantly improve anterior chamber and vitreous inflammation with the ability to reduce CS. Complete resolution of CME was demonstrated in 70% of eyes at 6 months[40]. Studies have shown that ADA and IFX are effective in providing inflammation control; their success and effectiveness are similar[41]. The ease of application of ADA (it can be applied subcutaneously) and the fact that it does not require application to a

healthcare institution are important advantages over IFX. In another study; It has been suggested that ADA will provide a superior response because it binds to TNF-α, which is present not only in the circulation but also on the cell surface and weekly or biweekly administration of ADA will provide less variable serum levels than periodic infusions of IFX[42]. In another study comparing ADA and IFX for the treatment of pediatric chronic non-infectious uveitis, remission rates were similar. However, ADA was found to be more effective than IFX in terms of maintenance of remission. Recently, it has been reported that the use of ADA as the first anti-TNF-α agent in treatment is more effective than its use in cases of IFX failure[43,44].

8.4. Surgical treatment

In complications that develop as a result of a chronic course, surgical interventions may be required in addition to medical treatment. The most important point is that surgical success depends on the complete suppression of ocular inflammation with medical treatment. Therefore, it should be ensured that complete inflammation control is achieved before surgery[45].

Chelation therapy is effective in band keratopathy, but the recurrence rate is high in uveitic eyes. Therefore, chelation therapy is recommended for eyes at risk of amblyopia or serious vision loss[46].

Cataract surgery in pediatric patients may be difficult due to a lack of scleral rigidity and existing ocular complications such as band keratopathy and posterior synechiae. In recent years, in addition to good preoperative inflammation control, modern surgical techniques such as phacoemulsification and the development of foldable hydrophobic acrylic intraocular lenses (IOLs) have resulted in successful visual results after cataract surgery with lens implantation in the capsular bag. Postoperative inflammation control plays a major role in this success. IOL implantation during cataract surgery has been a subject of debate for many years. It was widely believed that IOL implantation after cataract extraction was contraindicated due to the high rate of fibrotic membrane formation around the postoperative IOL[47]. Current studies show the opposite. It has been shown that postoperative complication rates are similar in aphakic and pseudophakic eyes, and long-term postoperative visual outcomes in pseudophakic eyes are better than in aphakic patients[48].

The effectiveness of trabeculectomy in glaucoma may be limited and temporary, especially in the uveitic patient population due to severe postoperative inflammation and fibrosis[49]. Hypotonia or hypertonia may be more common in uveitic patients in the early postoperative period. Glaucoma drainage implant surgery and goniotomy are other surgical methods that can be applied.

Laser photocoagulation can be performed in cases with peripheral neovascularization, retinal traction, and retinoschisis. Pars Plana vitrectomy (PPV) is especially performed in patients who develop vitreous condensation, intravitreous hemorrhage, retinal detachment and ERM. PPV also provides mechanical clearance of inflammatory mediators in patients with active inflammation and CME resistant to medical therapy[31].

Conclusion

PP is one of the most common causes of childhood uveitis. Early diagnosis is made in symptomatic patients with a careful examination. With the introduction of new generation drugs, especially biological agents, disease activity is effectively suppressed and the development of complications is prevented. At the same time, patients should be monitored for ocular and systemic side effects of the drugs during treatment. If diagnosis is delayed and inflammation control is not achieved, complications that may result in blindness may develop.

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Forensic Medical Perspective of Elder Abuse

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ABSTRACT

The issue of elder abuse and neglect is an important public health problem that requires urgent attention from social assistance institutions, health systems, political institutions, and citizens, can create devastating individual and social consequences, and is not unfortunately adequately reported. Elder abuse can cause serious consequences on both mental and physical health, such as injury, death, anxiety, depression, substance addiction, and suicide.

Necessary precautions should be taken to prevent elder abuse. First of all, it is very important to raise awareness of elder abuse and to raise awareness of the entire society on this issue.

Keywords: Elder abuse, neglect, domestic violence, nursing home life, forensic medicine.

Yaşlı İstismarına Adli Tıp Bakış Açısı

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ÖZ

Yaşlı istismarı ve ihmali sosyal yardım kurumlarının, sağlık sistemlerinin, siyaset kurumlarının ve vatandaşların acilen ilgilenmesi gereken aksi takdirde yıkıcı bireysel ve toplumsal sonuçlar yaratabilen, maalesef bildirimi de yeterince yapılmayan önemli bir halk sağlığı sorunudur. Yaşlı istismarı yaralanma, ölüm, anksiyete, depresyon, madde bağımlığı, intihar gibi hem ruhsal hem de fiziksel sağlık üzerinde ciddi sonuçlara neden olabilmektedir.

Yaşlı istismarının önlenmesi için gerekli önerilerin alınması elzemdir. Her şeyden önce, konunun farkındalığının ve tüm toplumun bu konuda bilinçlendirilmesinin sağlanması gerekir.

Anahtar sözcükler: Yaşlı istismarı, ihmal, aile içi şiddet, huzurevi yaşamı, adli tıp.

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Introduction

Abuse, which can be encountered in all societies and cultures at different economic levels, is not limited to the family or the general population but is also a serious social problem that manifests itself in the form of physically and psychologically harming and taking advantage of the elderly, which can be encountered in institutions providing health services and social services[1-4].

World Health Organization (WHO) defined elderly abuse in the Toronto Declaration published at the meeting held with the participation of the Organization for the Prevention of Elder Abuse, Toronto, and Ryerson Universities, to prevent abuse against the elderly on a global scale, as "one or repeated inappropriate behavior that harms or causes stress to the elderly in any relationship with an expectation of trust"[5,6]. According to a definition made by the United States Centers for Disease Control and Prevention, it is the intentional action or failure to act of a caregiver or another person that poses or causes a risk of harm to an older adult in a relationship involving the expectation of trust[7].

Many situations appear to put older people at risk of violence. Some situations may also worsen the older person as a result of stress and frustration as the older person becomes more dependent with strained family relationships. Sometimes, the caregiver's dependence on the elderly person for shelter or financial support can be a source of conflict[8,9].

Older adults may experience with abuse in many different settings. Elder abuse is more likely to occur in the family environment for reasons such as the challenging nature of aging and adapting to changing family dynamics. Elderly people may be abused in public by an acquaintance or caregiver. Elder mistreatment can also occur in institutional settings, such as a hospital, long-term care facility, or nursing home.

Risk factors that affect the abuse of the elderly can be classified into three main groups[10,11]:

1 – Characteristics of the abused elderly

- Being of advanced age,
- Loss of status and power,
- Having a low income,
- Lack of attractive financial resources,
- Presence of functional disability,
- Cognitive impairment or disability,
- Having a mental illness,
- Being dependent on someone,
- Social isolation situation,
- Relationship and dependency with the perpetrator,
- Having a history of abuse/trauma early in life.

2 – Characteristics of the abuser

- Not embracing the care role,
- Lack of necessary knowledge and experience for maintenance,
- Personality problems (inability to control thoughts and behavior),
- Substance use addiction,
- Unemployment/financial insufficiency,
- Perceiving violence as a solution,
- Taking more responsibility than necessary,
- Trying to provide support under bad economic conditions,
- Presence of mental illness,
- Inability to cope with stress,
- Having a history of domestic abuse.

3 – Social factors:

Social factors are the important risk factors for an elderly person to be maltreated. Many older people are isolated due to physical-mental illnesses or the loss of friends/family members.

Age discrimination or negative attitudes leads to prejudice, hostility or social isolation. The experience of abuse may be overlooked, and concerns or disclosures about the abuse may not be taken seriously. The main social factors that encourage abuse are:

- Giving caregivers more freedom in routine care and decision-making,
- High tolerance and acceptance of aggressive behavior,
- The erosion of the concept of family,
- Insufficiency/lack of social policies and support networks,
- Seeing cultural change,

- Transformation from extended family to nuclear family,
- High preference for living together.

Classification of Elder Abuse

Elder abuse is a multidimensional concept that covers physical, psycho-social, economic, sexual abuse, abandonment, and neglect types[6,12].

A. Physical Abuse: Even if there is no traumatic finding, it is the deliberate hitting or rude treatment of an older adult by the individual he or she trusts or is responsible for his or her care. These actions are defined as ecchymosis, whip marks, burn wounds, cut and compression marks caused by behaviors such as slapping, hitting, burning with cigarettes or other hot objects, and are frequently seen and unexplained lesions. These are behaviors such as causing physical harm to the body, causing pain, physical obstruction, being forced to stay in bed, or giving very little medication or physical restriction[10,12-16]. In a study conducted in 1996 on elderly people applying to stay in nursing homes, it was found that approximately one in four people (25.66%) were exposed to physical abuse[17].

Diagnostic elements in physical abuse

- Physical injury such as hitting, burning, pushing, hair loss, abrasion,
- Fractures at different healing stages,
- Hearing loss, confusion,
- Anesthetizing or anesthetizing with various methods,
- Giving too much, too little or wrong medication required for treatment,
- Inconsistency between the stories told and the lesions seen on the body.

Companion's behavior: Medical help is usually sought from different places. Even when seeking medical treatment, shyness and disorientation are noted. In drug abuse, the presence of symptoms such as full alertness may be denied. There may be fear and anxiety in the caregiver or family member[10].

B. Psycho-Social Abuse: It can be in the form of humiliating, insulting, blaming, intimidating, shouting, threatening to send someone to a nursing home, preventing them from making decisions, isolating them, intimidating them, giving harsh orders, or verbal harassment.

Diagnostic elements in psychosocial abuse

- Unexplained, incompatible changes in the elderly person's personality and behavior (such as his glasses being broken),
- Intense somatic complaints, nutritional problems, chronic fatigue,
- Decreased self-esteem,
- Feeling of hopelessness,
- Experiencing post-traumatic stress disorder,
- Having a sleep disorder,
- Verbal aggression,
- Being fearful, anxious and/or depressed,
- Having thoughts of suicide,
- Giving up his decision without any reason,
- Having difficulty concentrating[10].

C. Economic Abuse: WHO defines economic abuse in the elderly as the illegal or inappropriate use and exploitation of the elderly person's funds or resources[18]. It is also known by professionals that economic abuse is accompanied by psychological abuse, which occurs through intimidation, control, and instilling fear.

There are various ways in which economic exploitation occurs. It is the type of abuse most likely to attract the attention of professionals in diverse fields as banking, law, and the welfare industry. Examples such as taking money from the elderly person without permission, using valuable assets, using bank or retirement accounts, their expenses Examples include persistent failure to pay bills and bills, a lower standard of living that is not commensurate with the elderly person's income, the elderly's share of household expenses being too high, and adult children depending on their elderly parents for housing or financial support due to addiction or mental illness, etc. Among the ways economic exploitation is carried out, these include the abuse of powers of attorney, forced changes in wills, unethical trading of property rights, and forcing unauthorized persons to sign documents regarding assets that will provide financial gain to the perpetrator[7].

D. Sexual Abuse: It is the forcing of an individual into any sexual activity without his/her consent. The

number of studies on sexual abuse is quite low. Older women remain vulnerable to sexual assault by their husbands/partners and family members. They may also face threats from service providers they may rely on for general care, health care, and specialty care. Attacks in such environments can be carried out by female personnel as well as male personnel[19]. Symptoms of sexual abuse in the elderly include lacerations in the genital and anal areas that are difficult to explain, ecchymosis, bleeding, torn clothes stained with blood, ecchymosis and bite marks on the chest, and diseases transmitted through sexual intercourse, etc. can be listed as follows.

E. Neglect and Abandonment: It is the failure of individuals responsible for caring for the elderly (family, social institution workers, private caregivers) to meet the daily needs of the elderly or the abandonment of the elderly. It is the situation where the needs of the elderly are not met (nutrition, cleaning, shelter, clothing, health, and medicine supplies). When evaluated together with all these, a decrease in the social relations of the elderly occurs.

Signs of neglect

- Malnutrition in an elderly person who cannot feed without help, excessive weight loss without any disease, and kidney problems due to dehydration.
- Such as the inability of the elderly to access medical treatment and interventions, the inability to meet their physical or mental health needs and to protect themselves from harm that threatens their health and safety, and the failure to provide necessary medications.
- Failure to treat decubitus ulcers in a bedridden elderly patient,
- Poor personal hygiene,
- Ignoring existing symptoms or over-explaining them[20].

EPIDEMIOLOGY

With the decrease in the fertility rate, which started in the twentieth century and continues to the present day, the development of health care services, increased health awareness, and the development of diagnosis and treatment opportunities, people's life expectancy is longer, and the rate of the elderly population is increasing rapidly[21]. Elder abuse causes the situations such as severe physical traumas and chronic psychological problems increased stay in nursing homes, increasing use of emergency services, hospitalization, life-threatening diseases or disability and death, and can have serious consequences for individuals and society [15,21- 25]. Erden and Boz stated that in elderly individuals who have been exposed to abuse, diseases related to psychiatry and neurology increase by 4.7 times, deterioration in general health status increases by 3.5 times, and widespread use of health services increases by 2.1 times[26]. Elder abuse can cause not only physical diseases but also many psychological disorders, including depression and anxiety[15,27,28]. In another study conducted on abused elderly people; It was determined that the risk of depression and anxiety was 2.24 times higher[21]. Additionally, it has been reported that the rate of chronic diseases is higher, especially in older women, and the use of antidepressants and other psychotropic drugs is increasing[29,30].

Elder Abuse in the World

Abuse cases in old age are generally hidden by their families, caregivers, and abusers, or are rarely reported to authorized persons, so abuse cases remain secret[31]. Although the science of gerontology is increasingly becoming an important field of study, there is a serious lack of research on elder abuse[10]. Since the elderly population is increasing rapidly in most countries of the world, it is predicted that the number of people affected by elder abuse will also increase[15,21,32,33]. WHO considers individuals aged 60 and above as elderly. The global elderly population, currently around one billion, is projected to double by 2050. The elderly population is growing both in number and proportion within the general population of many countries in the world[1].

It has been determined that global reporting of elder abuse cases is 4%[33], and the prevalence of elder abuse based on self-report is 15.7%[34]. In corporate areas, it is reported that 64.2% of employees engage in elder abuse[1].

WHO estimates that 15.7% of people aged 60 and over were subjected to abuse in 2019. In 2015, it was observed that one in six elderly people worldwide were exposed to abuse. Elder abuse is reported to be 10% in the USA and 14.2% in Turkey[21]. In the study data on intimate partner violence among older women, it was found to be 27% in those over the age of 65, 30% in the 50-65 age range, and 33% in the 16-49 age group. It is possible that these rates are lower than they should be because many cases of elder abuse are not reported and are hidden[21,23]. In the Netherlands, in 1998, 1.2% of physical abuse, 1.4% of economic

abuse and 0.2% of neglect cases were encountered. Among types of elder abuse in the USA in 2010, 2% of physical abuse, 5% of psychological abuse, 1% sexual abuse, 5% economic abuse and 5% of neglect were determined[35].

Information on the extent of abuse in the elderly population is inadequate, and the few population-based studies conducted indicate that 4% to 6% of the elderly are exposed to some form of abuse at home. Elderly people are also at risk of abuse in institutions such as hospitals, nursing homes, and other long-term care facilities. For example, according to a US survey, 36% of nursing home staff reported witnessing at least one incident of physical abuse of the elderly in the previous year, 10% reported committing at least one act of physical violence, and 40% reported that the elderly were psychologically abused[35].

Elderly Abuse in Our Country

In our country, studies on the abuse and neglect of the elderly are limited, and the size and scope of the problem is not sufficiently known. According to the data of the Turkish Statistical Institute, the population aged 65 and over, which is considered the elderly population in our country, was 6 million 895 thousand 385 people in 2017, and increased by 22.6% in 2022, reaching 8 million 451 thousand 669 people. The proportion of the elderly population in the total population increased from 8.5% in 2017 to 9.9% in 2022. In 2022, 44.4% of the total elderly people were men and 55.6% were women[36]. According to population projections, the elderly population rate is predicted to be 12.9% in 2030, 16.3% in 2040, 22.6% in 2060 and 25.6% in 2080[37]. According to the report of the Association for Aging Studies, 209 cases of abuse, neglect, violence, violation of rights and discrimination against the elderly were detected across the country in September 2021. It is stated that 54% of these cases resulted in death[38]. In 2004, 1.5% of physical abuse, 2.5% of economic abuse and 3.5% of neglect cases were encountered[39].

PROBLEMS IN DIAGNOSIS

The most important factor in elder abuse and neglect is not noticing the problem or missing the diagnosis.

A-Personal Obstacles

• Fear of the elderly person being blamed by his/her caregiver,

• The elder's fear of his/her family's behavior and that he will be treated worse or fear of being sent to an institution, if he reveals the incident,

• Fear that no one will believe him/her,

• Thinking that the situation is his/her own fault,

• Not knowing how and in what way to explain the event,

• Not being socially or economically independent,

• The most important thing is that he/she does not know how and where to get help.

B-Healthcare Professionals and Institutional Obstacles

•The health worker does not know how and what kind of questions to ask to reveal

elder abuse,

• The healthcare professional's lack of knowledge or desire to make notifications and

keep records,

• Have concerns about taking responsibility for evaluation and action,

• Ignoring the problems due to lack of control and various concerns in nursing homes.

The most common place where abuse and neglect occurs is the home environment where the victim lives. The elderly person may be out of the home rarely or not at all, so it may be easy to hide the abuse. According to a study in the USA, it was determined that 90% of those responsible for abuse and neglect were family members, and approximately 2/3 of them were the child or spouse of the individual[40].

Another reason for difficulty in diagnosing abuse is that the hospital staff does not need to question the symptoms such as bruises, signs of malnutrition, introversion, and withdrawal that they see in the elderly person, thinking that they are due to old age. In addition, they are exposed to neglect and abuse in institutional care as a result of nursing homes and rehabilitation centers not responding to their needs, administrators' indifference to the issue, healthy elderly people and mentally ill elderly people being kept in the same environment, and disciplinary punishment being imposed on the elderly.

FORENSIC DIMENSION OF ELDER ABUSE

Responsibility of Healthcare Professionals in Elderly Abuse

According to Turkish Penal Code-Article 280; "It is a crime for healthcare personnel not to report a forensic case admitted to a healthcare center while on duty. Since abuse is considered a judicial case, it is mandatory to report it to the judicial authorities"[41].

Abandonment

According to Turkish Penal Code-Article 97; "Any person who abandons a person who is unable to manage himself due to age or illness and who is therefore under the obligation of protection and supervision, shall be punished with imprisonment. In addition, if the victim suffers from a disease, is injured or dies due to abandonment, he/she will be punished according to the provisions of aggravated crime due to its consequences"[41].

Failure to Fulfill Assistance or Notification Obligations

According to Turkish Penal Code-Article 98; "Any person who does not help a person who is unable to manage himself due to age, illness or injury or for any other reason, to the extent that the circumstances allow, or who does not immediately report the situation to the relevant authorities, will be punished. Additionally, if the person dies, his/her punishment will be increased"[41].

CONCLUSION

As a result of developments in health and technology in the last century, the death rate has decreased. The life expectancy and the proportion of the population over the age of 65 in the total population have increased[16,42,43]. On the other hand, it is a period when the risk of addiction and accidents of individuals in this period increases, their physical and mental abilities decrease, and many chronic diseases are experienced. Therefore, there are difficulties in detecting the phenomenon and presenting the problem in elder abuse or neglect for many reasons. Considering the family as sacred and not intervening in family relations, separating the elderly from society and leaving them at home and not being able to communicate with others, the level of the elderly individual perceiving neglect or abuse as a problem, not being willing to report their family, the lack of awareness of the society in this area, insufficient employment of employees in professional groups related to the elderly can be considered among these reasons[6,12].

The economic, social, physical, and psychological processes that the individual must cope with during the aging period cause significant difficulties in the elderly. In this process, all segments of society, especially families, have great responsibilities in order to provide the necessary support to elderly individuals[44]. Violence is seen as an important problem that tends to increase in today's world. Elderly abuse, the most common type of violence, is a phenomenon related to spousal abuse and domestic violence[45,46,47].

The places where abuse and neglect can occur most include the elderly's own home, hospitals, nursing homes, and day care homes. Studies show that abuse and neglect can occur in every society, at every economic level, ethnic and religious structure[45,48]. In studies evaluating the knowledge level and attitudes of emergency service personnel towards elderly abuse and neglect in our country, it has been observed that emergency care workers have insufficient knowledge about identifying risk factors for elder abuse, taking a focused history, performing a detailed physical examination, knowing their legal obligations and reporting forensic cases, and the majority of them have not received training on this subject before and after graduation[21].

Barriers to Reporting Elder Abuse

•For the victim

<u>Bound by fear.</u>

1-They are afraid that the abuser will do harm to them if they report the abuse,

2-They are afraid that they will be placed in an institution,

3-They think that the police and social institutions cannot help them.

<u>Due to family loyalty</u>

1-The elderly individual wants to protect his loved ones even if he encounters abusive behavior from his family member,

2-They are ashamed to tell anyone that a family member attacked them or stole their money.

<u>Due to disability or lack of control</u>

1-They are completely under the control of the abuser. They depend on them for food, shelter, clothing and healthcare,

2-They cannot do anything to prevent or protect abuse due to physical or cognitive disabilities.

•For family members

As a family dynamic

1-They do not want to talk about the issue due to their family structure,

2-Adults do not want abuse incidents to be reported.

Due to lack of information

1-They may not know who to tell,

2-They cannot predict what to do,

3-They do not believe that anything can be done.

•Service providers

Bound by fear

1-Service personnel serving the elderly may be afraid of the abuser and of entering the home after the abuse is reported,

2-They do not make a report because they think that the police cannot help the elderly person because he cannot physically testify in court,

3-They think that the elderly person can deny being abused and therefore nothing will be done.

Due to lack of information

1-They believe that they have a trustworthy relationship with their elderly customers and cannot tell anyone else what is happening in the customer's home,

2-They may not be aware that assault, theft or serious neglect in the family or long-term care home is a crime[10].

Recommendations

It is very important to take suggestions and raise awareness of this situation in order to prevent elder abuse, which is defined as the caregiver or other individuals with whom they should have a trusting relationship behaving in a way that harms the elderly, creating a risk of serious harm, the caregiver not meeting the basic needs of the elderly, and the inability and failure to protect them from harm.

- The elderly must be economically secured,
- Conditions should be created to ensure the active participation of the elderly in the social environment,
- An environment should be created by providing the necessary services to provide the elderly with opportunities for self-improvement and healthy aging,
- The conditions of existing nursing homes should be improved and the number of rehabilitation centers should be increased. Single room systems should be adopted in nursing homes as much as possible, professional staff should be employed and specialization in the field should be ensured,
- Geriatric hospitals providing healthcare services to the elderly should be operational in every city,
- Consultancy and social support services should be provided on communication, treatment and coping with the patient, especially to those who care for the elderly who are diagnosed with high-risk diseases such as Alzheimer's and dementia, which may constitute a basis for abuse and neglect,
- Public education and awareness are important elements in preventing abuse and neglect. The goal of such efforts is to inform the public about the various types of abuse, how to identify signs and symptoms of abuse, and where to get help[6,12].

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Relationship Between Shelterin Proteins and Agmatine in Urinary Tract Infections

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ABSTRACT

The presence of microorganisms in the kidney, collecting system, or bladder with pyuria and clinical symptoms is called Urinary Tract Infection (UTI). UTI is one of the most common diseases in both nosocomial and community-acquired infections and affects millions of people every year. The clinical types of UTI range from cystitis to sepsis. In this study, we aimed to contribute to the literature by comparing the levels of shelterin proteins and agmatine in the serum of patients diagnosed with cystitis, one of the types of UTI, and healthy volunteers without any known medical disorder, and to bring new approaches to issues such as clinical severity, response to treatment, and pathogenesis of the disease.

In this study, 30 individuals diagnosed with cystitis from UTIs and 30 individuals without any systemic disease participated. Serum agmatine levels were measured by a fluorescence detector using the ultra-high-performance liquid chromatography method (UHPLC). Serum shelterin proteins levels were measured using the ELISA method.

When the patients and healthy controls were compared, serum Telomeric Repeat Binding Factor2 (TRF2) levels of the patients were found to be lower than the controls; serum agmatine levels were found to be higher than the controls and statistically significant ($p<0.05$). Other shelterin protein levels were not statistically different between patients and controls ($p>0.05$).

In conclusion, the statistically significant difference in serum TRF2 and agmatine levels between the groups may be associated with oxidative stress. It is thought that the shortening of telomere lengths may be associated with decreased TRF2 levels.

Keywords: Urinary Tract Infections, Cystitis, Telomeres, Shelterin Proteins, TRF2, Agmatine

İdrar Yolu Enfeksiyonlarında Shelterin Proteinleri ve Agmatin Arasındaki İlişki

Süreç

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ÖZ

Piyüri ve klinik semptomlarla birlikte böbrekte, toplayıcı sistemde veya mesanede mikroorganizmanın bulunması, Üriner Sistem Enfeksiyonu (ÜSE) olarak adlandırılır. ÜSE, hem nozokomyal enfeksiyonlar hem de toplumdan kazanılmış enfeksiyonlarda en sık rastlanan hastalıklar arasında yer almaktadır ve her yıl milyonlarca insanı etkilemektedir. ÜSE'nin klinik tipleri, sistitten sepsise kadar değişmektedir. Bu çalışmada, ÜSE türlerinden biri olan sistit tanısı almış hastalar ile bilinen herhangi bir tıbbi bozukluğu olmayan sağlıklı gönüllü kişilerin serumlarında, shelterin proteinleri ve agmatin düzeylerinin karşılaştırılarak hastalığın klinik ciddiyeti, tedaviye yanıt takibi, patogenezi gibi hususlara yeni yaklaşımlar getirilmesi ve literarüre katkı sağlanması amaçlanmıştır.

Bu çalışmada, ÜSE'lerden sistit tanısı almış 30 birey ve herhangi bir sistemik hastalığı olmayan 30 birey katılmıştır. Serum agmatin seviyeleri ultra yüksek performanslı sıvı kromatografi yöntemi (UHPLC) kullanılarak floresans dedektörle ölçülmüştür. Serum shelterin protein düzeyleri ise ELISA yöntemi kullanılarak ölçülmüştür.

Hastalar ile sağlıklı kontroller karşılaştırıldığında, hastaların serum Telomerik Tekrar Bağlanma Faktörü2 (TRF2) düzeyleri kontrollere göre düşük; serum agmatin düzeyleri kontrolllere göre yüksek bulunmuştur ve istatistiksel olarak anlamlıdır ($p<0,05$). Diğer shelterin protein düzeyleri ise hasta ve kontrol arasında istatistiksel farklı hesaplanmamıştır ($p>0,05$).

Sonuç olarak, serum TRF2 ve agmatin düzeylerinin gruplar arasında istatistiksel olarak anlamlı farklılık göstermesi oksidatif stres ile ilişkilendirilebilir. TRF2 düzeylerindeki azalma ile telomer uzunluklarında kısalma olabileceği düşünülmektedir.

Anahtar sözcükler: Üriner Sistem Enfeksiyonları, Sistit, Telomer, Shelterin Proteinleri, TRF2, Agmatin

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Introduction

The presence of microorganisms in the kidney, collecting system, or bladder with pyuria and clinical symptoms is called Urinary Tract Infection (UTI)[1]. UTI is one of the most common diseases in both nosocomial and community-acquired infections and affects millions of people every year[2]. UTI is the most common cause of bacterial infections in adults and can be seen in both sexes and all age groups. Globally, 150 million cases of UTI develop annually and the cost of treating these patients is estimated to be more than 6 billion dollars[3]. These infections are more common in women than in men, and approximately half of the women are reported to have UTI at some point in their lives. The clinical types of UTI range from cystitis to sepsis[4].

Agmatine is an aminoguanidine molecule formed by the release of a CO2 molecule as a result of the decarboxylation of the amino acid L-arginine by the enzyme arginine decarboxylase. Their metabolism has been shown by studies in neurons, kidney cells, and vascular endothelial cells. Agmatine is released into the synaptic gap and provides metabolic activation by binding to various receptors such as N-methyl-D-aspartate (NMDA), imidazoline, and α2-adrenergic. Due to all these aspects, it is considered a novel neurotransmitter in the brain[5,6]. Agmatine is taken back into presynaptic cells by the reuptake system. It participates in the polyamine pathway via putrescine with the enzyme agmatinase. In the kidneys, it is metabolized to guanidino butanoic acid with the help of the diamine hydroxylase enzyme[7].

Telomeres are composed of a large number of non-coding TTAGGG hexanucleotide DNA repeat sequences that cover the end regions of eukaryotic linear chromosomes. These specialized structures are essential for the maintenance of genomic integrity[8,9]. Telomeres protect chromosomes against unwanted end fusion or nucleolytic degradation. In addition to this physical protection of linear chromosome ends, eukaryotic telomeres play important roles in cellular processes such as chromatin organization and control of cell proliferation10. Human telomere DNA consists of 2-15 kb of tandem (TTAGGG)n sequence oriented in the 5'-3' direction at the ends of chromosomes. The telomere region at the ends of chromosomes is divided into a sub-telomeric region composed of heterogeneous DNA repeats and a main telomeric region composed of homogeneous DNA repeats11. The D-loop structure of telomeres, which terminate in large loops, is formed by the insertion of a single strand known as the guanine-rich G-tail into the double-stranded telomere. The T-loop structure is formed by the backward circular curling of the DNA double strand[12,13]. Telomeres protect chromosomes with this T-loop structure. Specialized proteins attached to various regions of telomeres play a role in shaping the telomere ends and maintaining telomere length[14].

The Shelterin complex contains six main proteins composed of different polypeptides. These are Telomeric Repeat Binding Factor1 (TERF1/TRF1), Telomeric Repeat Binding Factor2 (TERF2/TRF2), Repressor/Activator protein1 (TERF2IP/RAP1), TRF1-Interacting Nuclear protein2 (TINF2/TIN2), Telomere Protection1 (POT1) and Tripeptidylpeptidase1 (TPP1)15. In the Shelterin complex, TRF1 and TRF2 are two telomeric DNA-specific homodimeric proteins that bind to double-stranded TTAGGG repeats with Myb/SANT-type DNA-binding domains[16]. RAP1 is a sequence-specific DNA binding protein. It regulates telomere function and is essential for cell growth. RAP1 also provides a mechanism to regulate the signaling cascade in mammals17,18. The TIN2 shelterin subunit causes telomeric shortening by blocking the recruitment of telomerase. It also forms a link between TRF1 and the TRF2/RAP1 complex by incorporating the TPP1/POT1 heterodimer into the complex[15,19]. POT1 is associated with the 3' end of the single helix of telomeric DNA. It suppresses DNA damage through inhibition of the Ataxia-Telangiectasia Mutated (ATM) and Ataxia-Telangiectasia Related (ATR) signaling pathways20. TPP1, encoded by the ACD gene region, plays an important role in the maintenance of telomere integrity, telomerase migration to telomeres, and telomerase function[21].

The aim of this study was to compare the levels of shelterin proteins and agmatine in the serum of patients diagnosed with cystitis, one of the types of UTI, and healthy volunteers without any known medical disorder, to bring new approaches to issues such as clinical severity, response to treatment, the pathogenesis of the disease and to contribute to the literature.

Material Method

In this study, the patients group consisted of 30 individuals without any systemic disease who were

diagnosed with cystitis from UTIs followed up by the Department of Infectious Diseases, Sivas Cumhuriyet University Health Services Application and Research Hospital. Patients were randomly selected without any discrimination in terms of age and gender. Patients with any chronic disease such as cancer, diabetes, or renal failure were excluded from the study. Thirty healthy individuals who were admitted to Sivas Cumhuriyet University Health Services Application and Research Hospital, who was not diagnosed with cystitis from UTIs, who did not have any systemic disease, who had a similar age distribution to the patients group, and who did not discriminate gender, were determined as the control group. All individuals in the control group were included in the study voluntarily.

Approval for the study permission was obtained by Sivas Cumhuriyet University Clinical Research Ethics Committee (2018-06/07). In addition, written informed consent was obtained from all participants.

Collection of blood samples

After the individuals included in the patients and control groups were informed and the informed consent form was read and signed, 5-10 mL blood samples were collected from each of them into sterile biochemistry tubes. These blood samples were centrifuged at 4000 rpm for 15 minutes. The sera obtained were portioned into eppendorf tubes and stored at -80 0C until the study was performed to determine TRF1, TRF2, RAP1, TIN2, POT1, TPP1, and Agmatine levels. In our study, agmatine levels were determined by Ultra high-performance liquid chromatography (UHPLC)6. TRF1, TRF2, RAP1, TIN2, POT1, TPP1 levels were measured through the ELISA method.

Statistical Method

Frequency tables were created to understand the data obtained from our study. Chi-Square tests were performed for the analysis of patients-control groups and categorical variables and difference tests were performed for the analysis of continuous variables. The Shapiro-Wilk normality test was applied to continuous variables to select the correct test. It was understood that the continuous variables in the study were not suitable for normal distribution ($p<0.05$). Since the variables were not parametric, the Mann-Whitney U test was used to reveal the difference between categorical variables. Similarly, the relationship between continuous variables was analyzed with the Spearman correlation test. In the final stage of the analysis, a binomial logistic regression test was performed to reveal the effect of the variables obtained in the study on the patients-control change. Cox-Snell R2 and Nagelkerke R2 statistics were used as critical values to demonstrate causality. The statistics were interpreted at a 95% confidence level. Analyses were conducted using the SPSS 23.0 package program.

Results

In this study, 30 individuals who were diagnosed with cystitis from UTIs followed up by the Infectious Diseases Clinic of Sivas Cumhuriyet University Health Services Application and Research Hospital constituted the patients group. Another 30 individuals without any systemic disease were included in the control group. As a result of the difference analysis performed on the ages of the individuals included in the study, it was determined that there was no statistically significant difference between the study groups (Patients=33.63±14.24; Control=34.27±12.33) ($p=0.584$). The number of men and women in the patients (%Male=66.7; %Female=33.3) and control (%Male=56.7; %Female=43.3) groups were not statistically significantly different ($p=0.426$). The difference in the results of shelterin proteins and agmatine levels according to the study groups is analyzed in (Table 1).

Table 1. Descriptive Statistics of Variables by Groups and Results of Difference Analysis

Variables	Control (n=30) Mean ± SD. (min.-max.)	Patients (n=30) Mean ± SD. (min.-max.)	p (M-W U)
POT1 (pg/mL)	425,63±412,27 (193,0-1962,0)	280,27±72,95 (183,0-458,0)	0,274 (376,0)
TRF1 (pg/mL)	89,27±13,89 (67,68-130,15)	100,36±22 (68,84-135,41)	0,088 (334,50)
TRF2 (pg/mL)	150,18±45,22 (109,14-278,21)	116,11±28,39 (85,32-165,12)	**0,001 (217,50)**
RAP1 (ng/mL)	15,73±9,67 (8,73-53,61)	15,36±11,24 (8,31-61,17)	0,701 (424,0)
TIN2 (ng/mL)	2,65±1,48 (1,13-6,74)	2,59±1,61 (1,16-6,15)	0,712 (425,0)
TPP1 (pg/mL)	3,41±1,34 (2,54-7,47)	3,25±0,95 (2,43-5,90)	0,836 (436,0)
Agmatine (ng/mL)	7,63±4,77 (0,80-17,02)	28,95±12,60 (9,57-59,49)	**$1,62x10^{-9}$ (42,0)**

M-W U: Mann-Whitney U Test Statistics

According to the difference analysis results, TRF2 (pg/mL) (Control=150.18±45.22; Patients=116.11±28.39) and Agmatine (ng/mL) mean levels were statistically significantly different (p<0.05) (Table 1). Other shelterin protein levels were not statistically different between patients and controls (p>0.05). On the contrary, Agmatine (ng/mL) level in the control group was calculated as 7.63±4.77 ng/mL, while the same value was calculated as 28.95±12.60 ng/mL in the patients group. For a better understanding of the numerically obtained and explained results, a visualization is presented in (Figure 1).

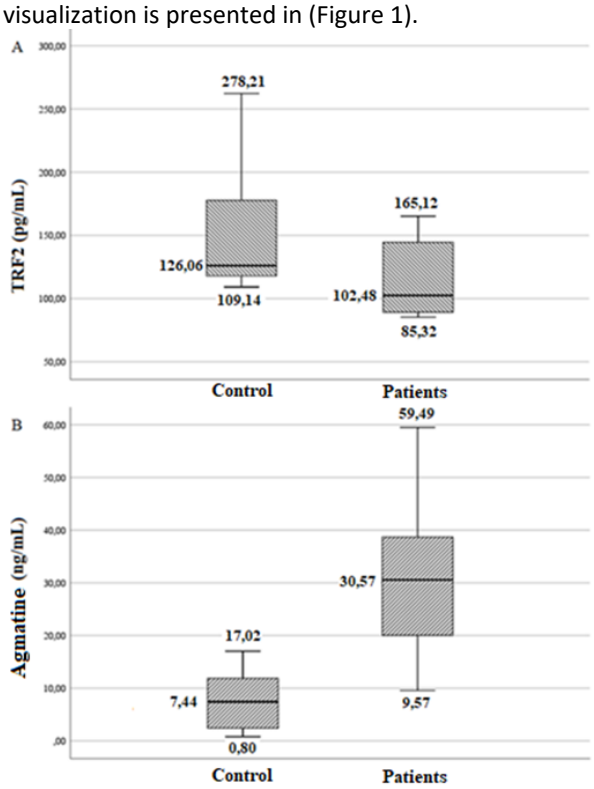

Figure 1. Patients-Control Box Plot for RF2 (pg/mL) and Agmatine (ng/mL)

Table 2. Correlation Analysis Results

Variable	Statistics	TRF1 (pg/mL)	TRF2 (pg/mL)	RAP1 (ng/mL)	TIN2 (ng/mL)	TPP1 (pg/mL)	Agmatine (ng/mL)	Age
TRF1 (pg/mL)	r (p)	-0,051 (0,349)						
TRF2 (pg/mL)	r (p)	**0,483 ($4,7x10^{-5}$)**	-0,131 (0,159)					
RAP1 (ng/mL)	r (p)	**0,394 (0,001)**	0,079 (0,274)	**0,551 ($3,0x10^{-6}$)**				
TIN2 (ng/mL)	r (p)	**0,305 (0,009)**	-0,148 (0,13)	**0,586 ($4,3x10^{-7}$)**	**0,475 ($6,4x10^{-5}$)**			
TPP1 (pg/mL)	r (p)	**0,54 ($4,0x10^{-6}$)**	-0,015 (0,456)	**0,609 ($1,2x10^{-7}$)**	**0,785 ($5,7x10^{-14}$)**	**0,669 ($2,6x10^{-9}$)**		
Agmatine (ng/mL)	r (p)	-0,135 (0,151)	**0,22 (0,04)**	**-0,413 (0,001)**	-0,081 (0,27)	-0,01 (0,47)	-0,085 (0,26)	
Age	r (p)	-0,153 (0,122)	0,15 (0,127)	-0,115 (0,191)	-0,202 (0,061)	-0,025 (0,424)	-0,127 (0,167)	-0,012 (0,46)

Correlation analysis was performed to reveal the relationship between shelterin proteins and agmatine levels (Table 2). The statistically significant results obtained are listed below:

•A moderate positive correlation (r=0.483) was calculated between TRF2 (pg/mL) and POT1 (pg/mL) levels.

•There was a weak positive correlation between RAP1 (ng/mL) and POT1 (pg/mL) levels (r=0.394) and a moderate positive correlation between TRF2 (pg/mL) levels (r=0.551).

•There was a weak positive correlation between TIN2 (ng/mL) and POT1 (pg/mL) levels (r=0.305) and a moderate positive correlation between TRF2 (ng/mL) (r=0.586) and RAP1 (pg/mL) (r=0.475) levels.

•A moderate positive correlation was calculated between TPP1 (pg/mL) and POT1 (pg/mL) levels (r=0.540); a strong positive correlation was calculated between TRF2 (ng/mL) (r=0.609), RAP1 (ng/mL) (r=0.785) and TIN2 (pg/mL) (r=0.669) levels.

•A weak positive correlation between agmatine (ng/mL) and TRF1 (pg/mL) levels (r=0.220) and a moderate negative correlation between TRF2 (pg/mL) levels (r=-0.413) were calculated.

Table 3. Logistic Regression Analysis Results

Variable	B	Std. Err.	Wald	p	Exp.(B)	95% Confidence Interval	
						Lower Limit	Upper Limit
TRF2 (pg/mL)	-0,037	0,11	11,709	0,001	0,963	0,943	0,984
Agmatine (ng/mL)	0,323	0,099	10,719	0,001	1,382	1,139	1,677

Due to the presence of a dependent variable consisting of two groups, it was decided to apply the binomial logistic regression technique. It is possible to examine the values calculated as a result of the analysis in (Table 3). To calculate the significance of the model with all variables (shelterin proteins and agmatine), the back-feedback Wald technique was used. The mathematical model obtained as a result of the model was determined as.

$$[\mathbf{0},\mathbf{1}] = \mathbf{0},\mathbf{323} \cdot (\boldsymbol{Agmatine}) - \mathbf{0},\mathbf{037} \cdot (\boldsymbol{TRF2}) \quad \rightarrow \quad \mathbf{0} = \boldsymbol{Control}; \mathbf{1} = \boldsymbol{Patients}$$

As a result of the analysis, it was calculated that the risk of high agmatine level was 1.382 times higher in the patients group. Similarly, the risk of having a low TRF2 (pg/mL) level was 0.963 times higher in the patients group. The agmatine (ng/mL) level calculated as a risk factor is effective between 1.139-1.677 times, while TRF2 (pg/mL) level is effective between 0.943-0.984 times.

It is understood that the results obtained by calculating the Cox-Snell R2 value of 0.603 will be similar in 60.3% of the population and the results obtained by calculating the Nagelkerke R2 value of 0.805 will be similar in 80.5% of the population. The following crosstabulation table (Table 4.) shows the classification results including the actual and LR (Logistic Regression) prediction values.

Table 4. Cross Table of Actual and Estimated Values

	Group	Estimate	
		Control	Patients
serve	Control	28	2
	Patients	4	26

As can be seen from (Table 4), it is clear that the effect of TRF2 (pg/mL) and Agmatine (ng/mL) levels is quite successful in separating the patients and control groups. The control group can be correctly predicted at 93.3% and the patients group 86.7% of the time. Overall, 90.0% of successful classification is achieved. Based on this, a person who is not sick can be predicted not to be sick according to the variables in the model with a 93.3% Positive Predictive Value (PPV), and a person who is sick can be predicted to be sick with 86.7% Negative Predictive Value (NPV).

Discussion

In this study; shelterin proteins and agmatine levels were evaluated in the sera of patients diagnosed with cystitis, one of the types of UTI, and healthy volunteers without any known medical disorder.

UTI is an infection of any part of the urinary system, such as the kidneys, ureters, bladder, and urethra. Most infections involve the lower urinary tract. UTI is a common transmission between men and women but is more common in women due to their physiology. UTI, whose clinical types vary from cystitis to sepsis, is one of the most common infectious diseases in outpatients and inpatients with high social costs [4,22].

The Shelterin complex is found in the telomeric end structures of DNA as tandem repeats of the TTAGGG sequence. Six members, consisting of TRF1, TRF2, TIN2, POT1, TPP1, and RAP1, associate with double-stranded and single-stranded DNA repeats at telomeres to form this complex25. Shelterin proteins contribute to telomere protection from unwanted DNA damage control-specific responses by aiding telomere stability[29]. Alterations in the structure or function of any of these proteins trigger unwanted DNA damage responses and trigger cellular aging and death processes[24]. It has been stated that telomeres can be protected against the DNA damage response that may occur at chromosome ends through the specific functions of each subunit of the shelterin complex, therefore, changes in the structure/function of the shelterin complex during the development and aging processes are an area of intense research30. In this context, when the relevant literature studies on shelterin proteins, which is a very important research topic, are examined; it is observed that the proteins are explained by associating them with different variables[24,25,30]. The ultimate role of the shelterin complex is to maintain telomere homeostasis, which is critical for genome stability and cell fate. Furthermore, the shelterin complex is described as multifunctional due to its involvement in various cellular processes such as replication, mitosis, meiosis, heterochromatin stability, immunity, and oxidative stress[24,30]. These functional processes of the shelterin complex led us to question the contributions of the whole complex versus its subunits and the individual functions of the six main proteins that make up the complex in order to bring new approaches to the pathogenesis of UTI.

Within the scope of the findings obtained in our study, it was concluded that TRF2 (pg/mL) and Agmatine (ng/mL) levels were statistically significantly different between the patients and control groups ($p<0.05$), while other shelterin proteins POT1 (pg/mL), TRF1 (pg/mL), RAP1 (ng/mL), TIN2 (ng/mL) and TPP1 (pg/mL) levels were not statistically significantly different ($p>0.05$). It is evaluated that TRF2 (pg/mL) level may be expected to decrease in case of cystitis from UTIs. When the literature is examined, there is no study showing shelterin proteins in the sera of patients with cystitis from UTIs. This situation reveals the scientific contribution and importance of the study in terms of Shelterin Proteins. On the other hand, there are a number of studies on shelterin proteins in cancer, viral infections, molecular and animal modeling.

TRF2 expression, one of the subunits of the Shelterin complex, has been reported to be

increased in various human cancers[31,32]. In a study, it was reported that protein expressions of TRF1, TRF2, and TIN2 were significantly higher in gastric cancer tissues at different stages compared to normal gastric mucosal tissues[26]. In another study involving acute myeloid leukemia patients, increased TRF2 expression correlated with poor prognosis and suggested that TRF2 has prognostic significance[33]. Despite these studies, there are studies in the literature in which TRF2 levels are decreased. In one study, it was revealed that TRF2 depletion cannot suppress ATM pathway activation and may initiate genomic instability by causing chromosome fusions mediated by the non-homologous end joining (NHEJ) pathway[35]. In a study investigating the ability of SARS-CoV-2 infection to affect DNA damage response and telomere stability, it was reported that TRF2 expression was decreased in infected Vero E6 kidney cells. In the study, it was shown that decreased TRF2 expression destabilizes telomeres, initiates telomere fusions, and causes genomic instability[36]. The contributions of the Shelterin proteins TRF1 and TRF2 to the maintenance of genomic integrity and telomeric stability are invaluable. This complex is known to play a regulatory role in telomere length and telomerase enzyme. Depending on the presence of TRF1 or TRF2 in the environment, the stimulatory and restrictive functions of the shelterin complex are shaped in opposite directions. If TRF1 protein is present in the medium, the complex can be found as TRF1-TIN2-TPP1-POT1 form, while in the presence of TRF2, it can be found in TRF2-RAP1-TIN2-TPP1-POT1 subunits. In this context, the significantly lower TRF2 levels in our study compared to the control group can be interpreted in light of the literature. TRF2 is a shelterin subunit required for chromosomal end protection, DNA damage response suppression and to prevent topological stress. Low levels of TRF2 can fail to inactivate enzymes that lead to the DNA damage response when bound to the telomere. This can trigger genomic instability by initiating end-to-end fusions. Failure to maintain telomere structure can shorten telomere lengths. In addition, when TRF2 levels are evaluated in relation to the complex members that affect each other in terms of structure and function; RAP1 failed to strengthen its effect by binding to TRF2, TPP1 failed to increase the activity of the telomerase enzyme, and TIN2 protein failed to ensure that the telomere is firmly attached to the nuclear matrix, as a result, it can be mentioned that these factors may affect the telomere length of cystitis patients in a shortening direction. One of the causes of telomere length shortening is oxidative stress. The failure of TRF2 to inactivate the enzymes that cause the DNA damage response may have led to severe oxidative stress in telomeres due to ROS, as it may cause an increase in reactive oxygen species (ROS) due to UTI. Severe oxidative stress may deplete a homodimeric binding protein, such as TRF2, as it may cause an accumulation of oxidized DNA base products in guanine-rich telomeres. This may lead to the shortening of telomere length[34,37-47]. All these results are consistent with the hypothesis of our study.

Agmatine, a biogenic polyamine, is a metabolite of the amino acid L-arginine produced by decarboxylation with the ADC enzyme and hydrolyzed to putrescine by the enzyme agmatinase[27]. The metabolism of agmatine in neurons, kidney cells, and vascular endothelial cells has been elucidated by studies. In cell culture studies, it has been reported that agmatine suppresses apoptotic signaling pathways and shows a protective effect against oxidative damage[5,6,56]. Studies showing differences in the levels of agmatine in various diseases have been reported[28,48]. In light of the given information, it was aimed to evaluate agmatine in terms of bringing new approaches to the pathogenesis of UTI. According to these results, it is expected that the level of agmatine (ng/mL) will be increased in case of cystitis from UTIs. When the literature is reviewed, there is no study measuring Agmatine levels in the serum of patients with cystitis from UTIs. As with Shelterin proteins, the lack of any evaluation of Agmatine levels in the literature reveals the importance of this study. In contrast, there are a number of comprehensive studies on agmatine under various titles. In a study evaluating the effects of agmatine supplementation against nephrotoxicity in rats, it was noted that agmatine supplementation reduced oxidative stress-related kidney damage by reducing free oxygen radicals and lipid peroxidation, restoring NO levels to normal levels and inhibiting inflammatory mediators such as TNF-α[49]. In another study in which enzymatic activities of NOS isoforms were determined in the brain, macrophage, and endothelial cells, agmatine was shown to be a potent NOS inhibitor with an antioxidant effect[50]. In a metabolomics study conducted for the diagnosis of UTI, it was observed that infections caused by Enterobacterales, Klebsiella, and Citrobacter species, such as E. coli, which cause the most prominent UTI, were associated with high agmatine levels[51]. In another urine analysis study, a significant increase in agmatine levels was observed in patients infected with at least one of Escherichia coli, Proteus mirabilis, and Citrobacter species. Therefore, it has

been reported that the presence of agmatine is considered a strong indicator of UTI[52]. In this context, the fact that agmatine levels were significantly higher in our study compared to the control group can be interpreted in light of the literature. Agmatine is known to be a NOS inhibitor and has a strong antioxidant effect. When the uncompensated increase in the number of reactive nitrogen species (RNS) and reactive oxygen species (ROS) in metabolism exceeds the capacity of antioxidant defense mechanisms, it disrupts the oxidative balance and causes oxidative/nitrosative stress. ROS can cause tissue destruction by damaging various macromolecules and may act as signaling molecules in the activation and induction stages of some genes. Agmatine may play a protective role against oxidative damage. In our study, it can be suggested that high agmatine levels may eliminate the oxidant damage caused by severe oxidative stress that may occur with the virulence effect of a uropathogenic in the lower urinary tract caused by UTI with its antioxidant effect. The failure of the decreased TRF2 level in our study to inactivate the enzymes leading to DNA damage response may have led to severe oxidative stress since it may cause an increase in ROS due to UTI. Severe oxidative stress may cause an accumulation of oxidized DNA base products in telomeres, which may shorten telomere length. It can be said that the high agmatine finding in our study may prevent oxidant damage caused by the aforementioned reasons. In addition, the increased activity of the arginine decarboxylase (ADC) enzyme, which is responsible for agmatine synthesis, and the effects of UTI on polyamine metabolism may have caused the high agmatine finding[23,38,39,53-57]. The results of the studies in the given literature support our findings.

According to the data we obtained as a result of the comparison, there are different correlations between cystitis and serum levels of shelterin proteins and agmatine molecules. While positive correlation is noteworthy in the significant correlations between shelterin proteins, TRF1 and TRF2 show positive and negative correlations with agmatine.

In studies examining the relationship between POT1 and TRF2, it has been reported that POT1 and TRF2 interact to form a complex with telomeric DNA and that this interaction is important for telomere length and homeostasis58. In a study similar to our study, TRF1, TRF2, POT1, TPP1, TIN2, and RAP1 levels were compared. As a result of the study, it was shown that there was a strong positive correlation between TRF2, TIN2, TPP1, and RAP1 levels, and TRF2 levels decreased as the disease duration increased. In light of these findings, they reported that the shelterin complex is not present as a whole under telomere length control, but may be formed as different sub-complexes according to the presence of TRF1 or TRF2 homodimeric proteins37. When these results obtained by the researchers are evaluated, it is seen that results compatible with our study were obtained.

Conclusion

In conclusion, there has not been a study similar to our study in patients diagnosed with cystitis from UTIs. Thanks to this study, the serum levels of shelterin proteins and agmatine molecules were determined together for the first time in the sera of patients diagnosed with cystitis from UTIs and healthy volunteers without any medical disorder.

Our study has some limitations. These include the absence of urine analyses, the measurement of telomere length using different methods and with larger sample groups, and the limitation of the scope of the universe. Considering these limitations, if the results of this study are supported by future research, it is believed that, in addition to evaluating whether these molecules can be a factor or biomarker affecting the pathogenesis of the disease, they may also provide guidance on the clinical severity of the disease and the response to treatment.

Conflict of interest

The authors declare no conflict of interest.

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The Relationship Between Postpartum Anxiety and Maternal Function in Mothers

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Reasearch Article

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ABSTRACT

This descriptive and relationship-seeking study aimed to determine the relationship between postpartum anxiety and maternal function in mothers with 6-10 weeks old babies.

The study was carried out with 258 mothers who were 6-10 weeks postpartum. The data were collected using the Personal Information Form, Postpartum Specific Anxiety Scale (PSAS), and Barkin Index of Maternal Functioning (BIMF).

It was determined that the majority of the mothers participating in the study were between the ages of 27-34, high school graduates, not working, having health insurance, having a moderate income, living with a nuclear family, and married for 2-6 years. The majority of mothers had babies who were 8-9 weeks old, had a vaginal delivery, experienced 2-3 pregnancies, had assistance with postpartum care, and received education/information about postpartum care. The mean PSAS score for the mothers was determined to be at a moderate level (83.71±21.71), while the mean BIMF score was above a moderate level (71.49±13.89). It was found that there was a moderate, negative significant relationship between the PSAS total score and the BIMF total score, and it was determined that the level of maternal functioning decreased as postpartum anxiety increased (r=-0.616, p=0.05).

It has been determined that the mother's anxiety during the postpartum period negatively affects maternal function. Therefore, it is crucial for healthcare professionals to comprehensively assess the mother's physical, psychological, and social well-being during the postpartum period and identify potential issues early on.

Keywords: Anxiety, Functional Status, Maternity function, Midwifery, Postpartum Period

Annelerde Postpartum Anksiyete ve Annelik Fonksiyonu Arasındaki İlişki

Süreç

Geliş: 07/09/2022
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ÖZ

Bu araştırma, 6-10 haftalık bebeği olan annelerde postpartum anksiyete ve annelik fonksiyonu arasındaki ilişkinin belirlenmesi amacıyla tanımlayıcı, kesitsel ve ilişki arayıcı olarak yapılmıştır.

Araştırma postpartum 6-10 hafta da olan 258 anne ile gerçekleştirilmiştir. Veriler Kişisel Bilgi Formu, Postpatum Spesifik Anksiyete Ölçeği (PSAÖ) ve Barkin Annelik Fonksiyonu Ölçeği (BAFÖ) kullanılarak toplanmıştır.

Araştırmaya katılan annelerin çoğunluğunun 27-34 yaş aralığında, lise mezunu, çalışmayan, sağlık güvencesine olan, gelir durumu orta, çekirdek aile ile birlikte yaşadığı ve 2-6 yıldır evli olduğu belirlenmiştir. Annelerin çoğunluğunun bebeğinin 8-9 haftada olduğu, normal doğum yaptığı, 2-3 gebelik geçirdiği, doğum sonrasında yardımcı bir kişinin olduğu, doğum sonrası bakıma yönelik eğitim/bilgi aldığı belirlenmiştir. Annelerin PSAÖ puan ortalamasının 83,71±21,71 orta düzeyde olduğu, BAFÖ puan ortalamasının 71,49±13,89 orta düzeyin üzerinde olduğu belirlenmiştir. PSAÖ toplam puan ile BAFÖ toplam puan arasında orta düzeyde, negatif yönlü anlamlı bir ilişki olduğu saptanmış olup, postpartum anksiyete arttıkça annelik fonksiyonu düzeyinin azaldığı saptanmıştır (r=-0,616, p=0,05).

Postpartum dönemde annenin anksiyeteli olma durumunun annelik fonksiyonunu olumsuz yönde etkilediği belirlenmiştir. Bu nedenle sağlık profesyonellerinin postpartum süreçte anneyi fiziksel, ruhsal ve sosyal yönden bütüncül olarak değerlendirilmesi, oluşabilecek sorunları erken dönemde tespit etmesi oldukça önemlidir.

Anahtar sözcükler: Anksiyete, Fonksiyonel Durum, Annelik Fonksiyonu, Ebelik, Postpartum Dönem

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Introduction

Pregnancy, childbirth, and the postpartum period are times when women's healthcare needs significantly increase, and they are affected both physically, mentally, and socially [1]. The postpartum period is a critical crisis period in which many developments or tensions are experienced, the mother and family encounter many stressors in keeping up with these changes and have a significant place in protecting and improving the health of the mother-baby and the family as a whole [1-3].The postpartum period covers 6-8 weeks after birth and causes many physiological and psychological changes in the mother [1, 4, 5] .

The postpartum period, especially the first six weeks, is exposed to many stressors for mothers in terms of establishing an emotional bond with the baby, establishing a balance between the baby's needs, and bringing their emotional-mental state to a good level [6]. Due to these stressors, there is an increased risk of psychiatric issues such as maternal sadness, postpartum anxiety, postpartum depression, and postpartum psychosis in mothers [6, 7].

It is reported that the prevalence of postpartum anxiety varies between 13% and 40% in a systematic review [8]. In another systematic review, it was stated that the prevalence of postpartum anxiety was 33.8% during COVID-19, and it was reported that the prevalence of postpartum anxiety increased 2.56 times compared to studies conducted before COVID-19 [9].Extensive research has been conducted on postpartum depression, while anxiety during pregnancy and postpartum anxiety have been relatively neglected [10, 11]. Anxiety, defined as a situation with an unknown source that causes a person to experience apprehension and depression, can have particularly negative effects on women, especially during the postpartum period when it is at a high level. Anxiety can also exacerbate depression and increase the risk of suicide [7]. Postpartum anxiety can cause negative perinatal outcomes in both mother and baby [12]. In particular, it can seriously disrupt mother-infant interaction [13]. Therefore, correct diagnosis and treatment are vital in protecting the mental health of the mother in the postpartum period [7, 14].

Since the mother experiences various physiological, psychological, and social changes in the postpartum period, a change in her functioning is also expected [15]. In the postpartum period, functional status is defined as the mother's infant care, self-care, mother-infant bonding, mother's emotional state, social support, housework, and adaptation to the motherhood role [16]. In addition, it was emphasized that the psychological state of the mother should be especially evaluated when considering the functioning of the mother [15].

In the postpartum period, while the mother adapts to her new role, she experiences psychological and physiological changes, her responsibilities increase, and her social life changes [17, 18]. It is considered that these changes experienced by the mother may cause an increase in anxiety and a decrease in the level of maternal functioning. Therefore, this study was conducted to examine the relationship between postpartum anxiety and maternal function in mothers with 6-10 weeks-old babies. In this regard, answers to the following questions were sought in the study.

1. What is the level of postpartum anxiety and maternal function in mothers?

2. Is there a difference between some descriptive and obstetric characteristics of mothers and postpartum anxiety levels?

3. Is there a difference between some descriptive and obstetric characteristics of mothers and the level of maternal function?

4. What is the relationship between postpartum anxiety and maternal function in mothers?

Material Method

Purpose and Type of the Study

This descriptive and relationship-seeking study aimed to determine the relationship between postpartum anxiety and maternal function in mothers with 6-10-weeks-old babies.

Time and Place of the Study

This research was conducted in 6 Family Health Centers (FHC) determined using a cluster sampling method in the city center of Sivas between March 15, 2021, and September 15, 2021.

Universe and the Sample of the Study

The universe of the study consists of mothers registered at the FHC determined in the city center of Sivas between March 15, 2021, and September 15, 2021, who are in the postpartum period between 6-10 weeks. The sample size was calculated to be 236 mothers using the formula $n=(t^2 S^2)\backslash d^2$, with a α=0,05, S=6,28, t=1,96, d= ± 0,8 [19] based on the study conducted by Yıldırım et al., (2011) [20]. Considering the possible data losses, the mothers who met the inclusion criteria were

sampled from the relevant universe by non-probability sampling method and the study was completed with 258 mothers.

Inclusion Criteria: Mothers who could speak Turkish, could read and write, had a single birth, did not have a physical or mental illness in their baby and themselves, did not have a chronic disease, did not have any risk factors during birth and postpartum period, were between 6-10 weeks postpartum, were between the ages of 19-45, and agreed to participate in the study were included in the study.

Do not have any risk factors during birth and postpartum period

Dependent variables: Scores from the Postpartum Specific Anxiety Scale (PSAS) and the Barkin Index of Maternal Functioning (BIMF).

Independent variables: Descriptive and obstetric characteristics of mothers

Data Collection Tools

The study data were collected using the Personal Information Form, PSAS, and BIMF. Data were collected by the researchers via face-to-face interview method.

Personal Information Form

The form was created in line with the literature to determine the descriptive and obstetric characteristics of mothers [7, 15].

Postpartum Specific Anxiety Scale (PSAS)

PSAS was developed by Fallon et al. to measure the postpartum anxiety status of mothers [21]. The validity and reliability study of the Turkish version was conducted by Duran [7]. The scale is of a 4-point Likert type, one-dimensional, and has 47 items. According to the scoring results, a score of 73 or lower indicates a low level of postpartum anxiety, a score between 74 and 100 indicates a moderate level of postpartum anxiety, and a score of 101 or higher indicates a high level of postpartum anxiety. The Cronbach's Alpha value of PSAS was 0.91. In this study, the Cronbach's Alpha value was calculated as 0.93.

Barkin Index of Maternal Functioning (BIMF)

BIMF was developed by, Barkin et al. to measure the functional status of mothers in the postpartum period [16]. The validity and reliability study of the Turkish version was carried out by Aydın and Kukulu [15]. The scale consists of 16 items and is a 7-point Likert-type scale. The scale has 5 sub-dimensions; Self-Care (items 2, 11, and 13), Maternal Psychology (items 8 and 10), Infant Care (items 12, 14, 15, and 16), Social Support (items 6, 7, and 9), and Adaptation to Motherhood (items 1, 3, 4, and 5). The scale has no cut-off points. Evaluation on the scale is made based on total scores. A high score indicates a high level of maternal function. The lowest score that can be obtained from the scale is 0 and the highest score is 96. The Cronbach's Alpha value for BIMF is 0.73, and the Cronbach's Alpha values for the sub-dimensions of the scale are as follows: 0.66 for Self-Care Sub-dimension, 0.71 for Maternal Psychology Sub-dimension, 0.62 for Infant Care Sub-dimension, 0.69 for Social Support Sub-dimension, and 0.50 for Maternal Adaptation Sub-dimension [15]. In this study, the Cronbach's Alpha coefficient for the total BIMF was calculated as 0.91, and the Cronbach's Alpha coefficients for the sub-dimensions of the scale were calculated as 0.84 for Self-Care Sub-dimension, 0.65 for Maternal Psychology Sub-dimension, 0.82 for Infant Care Sub-dimension, 0.86 for Social Support Sub-dimension, and 0.73 for Maternal Adaptation Sub-dimension.

Data Analysis

The data obtained in the study were computerized and statistical analysis was performed using the SPSS 25.0 package software. In the analysis of the data obtained from the Personal Information Form, descriptive statistical criteria were used to determine the mean, standard deviation, minimum and maximum values, and percentage distribution. In the normality analysis conducted to determine the tests to be used in the evaluation of the data, it was found that the skewness and kurtosis coefficients of the PSAS total score and the BIMF total and sub-dimension scores were within the ±2 limits, indicating that the data were distributed within normal ranges [19]. According to this result, independent sample t-test was employed to determine the difference between the means of two independent groups, one-way analysis of variance for more than two independent groups (to determine which group's mean is different from the others, the Tukey test was used when homogeneity was achieved, and the Tamhane's T2 test was used when homogeneity was not achieved), Pearson correlation analysis was used to determine the direction and level of the relationship between the variables, and the error level was taken as 0.05.

Ethical Issues

All stages of the study were conducted following ethical principles. Before starting the study, ethics committee approval was obtained from the

Cumhuriyet University Non-Interventional Clinical Research Ethics Committee (dated 19.02.2020 and decision number 2020-02/41). Institutional permits were obtained from the Sivas Provincial Directorate of Health (Decision dated 01.03.2021 and numbered 2021/03). Permission was obtained from the authors of the scales to be used in the study via e-mail. When the mothers who met the inclusion criteria were invited to participate in the study, the information in the Informed Consent Form was read and their written/verbal consent was obtained. This study was conducted following the principles of the Helsinki Declaration.

Findings

When the descriptive and obstetric characteristics of the mothers were examined, it was found that 45.3% were between the ages of 27-34, 37.6% were high school graduates, 76.0% lived in a nuclear family, 69.8% were not working, 53.9% had a moderate income level, 87.6% had social security, 50.4% had been married for 2-6 years, 69.8% had a baby 8-9 weeks old, 50.8% had a male baby, 67.4% had a normal vaginal delivery, 47.7% had 2-3 pregnancies, 93.8% had a person who would help them after birth. 69.8% of them received training/information on postpartum care, the mean age was 28.70±5.31 (min: 19 – max: 42), the mean duration of marriage was 6.71±5.18 (min: 1 – max: 23), the mean age of the babies was 7.96±1.07 weeks (min: 6 weeks – max: 10 weeks), and the mean number of pregnancies was 2.24±1.25 (min: 1 – max: 6) (Table 1).

It was determined that the mean PSAS score of the mothers was 83.71±21.71, and the mean BIMF score was 71.49±13.89 (Table 2).

When the statistical comparison of the descriptive and obstetric characteristics of the mothers and the mean scores obtained from the PSAS was examined, it was found that there was a significant difference between the variables of age, education level, family type, employment status, income status, social security presence, duration of marriage, baby's age, and number of pregnancies and the score obtained from the scale ($p<0,05$) (Table 3).

When the statistical comparison of the descriptive and obstetric characteristics of the mothers and the total mean scores obtained from the BIMF was examined, it was found that there was a significant difference between the variables of age, income status, presence of social security, baby's age, type of delivery, presence of a person who helped after birth, and education/information status for postpartum care and the score obtained from the scale ($p<0,05$) (Table 3).

The relationships between mothers' PSAS scores and BIMF total and sub-dimensions scores were examined, and according to the correlation analysis conducted, the highest correlation was found between maternal psychology sub-dimensions and the total BIMF score. This correlation was very high, significant, and positively oriented. The lowest correlation was between the PSAS total score and the self-care sub-dimension of the BIMF. This correlation was very weak, significant, and negatively oriented. In general, it was determined that there was a moderate-level, significant, positive relationship between the BIMF sub-dimensions ($p < 0.05$).

According to the correlation analysis between the sub-dimensions of the scales, it was determined that there was a significant relationship between the total and all sub-dimensions of BIMF and PSAS. Accordingly, it was determined that as the level of anxiety increased, the level of self-care, maternal psychology, infant care, social support, and adaptation to motherhood decreased.

It was found that there was a moderate, negative significant relationship between the PSAS total score and the BIMF total score, and it was determined that the level of maternal functioning decreased as postpartum anxiety increased ($p<0,05$).

Table 1: Distribution of Mothers According to Descriptive and Obstetric Characteristics (n=258)

Characteristics	n	%
Age		
19-26	99	38.4
27-34	117	45.3
35-42	42	16.3
Educational status		
Primary school	72	27.9
High school	97	37.6
Associate Degree	47	18.2
Undergraduate and graduate	42	16.3
Family Type		
Nuclear family	196	76.0
Extended family	62	24.0
Employment Status		
Employed	78	30.2
Unemployed	180	69.8
Income Status		
High	98	38.0
Moderate	139	53.9
Low	21	8.1
Presence of social security		
Yes	226	87.6
No	32	12.4
Duration of marriage		
1 year	23	8.9
2-6 years	130	50.4
7-11 years	62	24.0
12 years and more	43	16.7
Baby's age		
6-7 weeks	49	19.0
8-9 weeks	180	69.8
10 weeks	29	11.2
Sex of the baby		
Female	127	49.2
Male	131	50.8
Delivery method		
Normal vaginal delivery	174	67.4
Cesarean delivery	84	32.6
Number of pregnancies		
First pregnancy	94	36.4
2-3 pregnancies	123	47.7
4 and more pregnancies	41	15.9
Presence of a helper after childbirth		
Yes		
No	242	93.8
	16	6.2
Education/information status on postnatal care		
Yes	180	69.8
No	78	30.2

Table 2: Comparison of Mothers' PSAS, BIMF Total, and BIMF Sub-Dimension Mean Scores (n=258)

Scales	X̄	SD	Min	Max
PSAS	83.71	21.71	47	151
BIMF	71.49	13.89	2	96
Self-care	10.12	3.97	0	18
Maternal psychology	9.09	2.12	0	12
Infant care	20.51	3.20	0	24
Social support	12.84	4.26	0	18
Adaptation to motherhood	18.92	3.65	2	24

PSAS: Postpartum Specific Anxiety Scale, BIMF: Barkin Index of Maternal Functioning

Table 3: Comparison of Mothers' Descriptive and Obstetric Characteristics and PSAS and BIMF Total Mean Scores (n=258)

Characteristics	PSAS Total Score	BIMF Total Score
	x̄ ± SD	**x̄ ± SD**
Age		
19-26	85.38±22.59[a]	68.76±14.43[a]
27-34	85.42±21.19[b]	72.32± 13.35
35-42	75.02±19.26[ab]	75.62±13.06[a]
Test value*/p	***4.116/0.017***	***4.068/0.018***
Educational status		
Primary school	77.78±19.36[a]	68.65± 15.92
High school	84.67± 21.40	71.42± 12.29
Associate Degree	84.17± 22.56	74.30± 13.97
Undergraduate and graduate	91.17±23.23[a]	73.36± 13.12
Test value*/p	***3.621/0.014***	1.913/0.128
Family Type		
Nuclear family	85.22± 22.82	72.33± 13.28
Extended family	78.94± 17.03	68.84± 15.49
Test value/p**	***2.322/0.022***	1.729/0.085
Employment Status		
Employed	90.79± 24.62	73.13± 14.58
Unemployed	80.64± 19.61	70.78± 13.57
Test value/p**	***3.225/0.002***	1.249/0.213
Income Status		
High	79.94±22.16[a]	77.21±12.13 [ab]
Moderate	84.60± 21.04	69.28±13.83 [ac]
Low	95.48±19.90[a]	59.38±9.94 [bc]
Test value*/p	***4.818/0.009***	***20.822/0.000***
Presence of social security		
Yes	84.94± 22.17	72.55± 12.74
No	75.06± 15.78	64.00± 18.87
Test value/p**	***3.129/0.003***	***3.319/0.001***
Duration of marriage		
1 year	87.96± 26.51	70.91± 14.99
2-6 years	86.64±22.54[a]	70.16± 15.16
7-11 years	82.82± 19.90	73.50± 12.07
12 years and more	73.88±15.57[a]	72.91± 11.51
Test value*/p	***4.204/0.006***	0.990/0.398

Baby's age		
6-7 weeks	76.08±23.22[a]	77.31±13.94[a]
8-9 weeks	87.41±20.42 [ab]	69.26±12.70[a]
10 weeks	73.66±20.96[b]	75.48± 17.32
Test value*/p	***9.318/0.000***	***8.242/0.000***
Sex of the baby		
Female	83.34± 22.29	71.77± 13.20
Male	84.08± 21.20	71.21± 14.58
Test value/p**	-0.272/0.786	0.322/0.748
Delivery method		
Normal vaginal delivery	83.59± 21.37	70.16± 13.83
Cesarean delivery	83.98± 22.50	74.25± 13.69
Test value/p**	-0.135/0.893	***-2.235/0.026***
Number of pregnancies		
First pregnancy	91.21±24.96 [ab]	70.53± 13.98
2-3 pregnancies	79.78±18.70[a]	72.44± 14.48
4 and more pregnancies	78.32±17.39[b]	70.17± 11.74
Test value*/p	***9.480/0.000***	0.842/0.432
Presence of a helper after childbirth		
Yes	83.37± 21.77	72.14± 13.89
No	88.88± 20.74	61.56± 9.68
Test value/p**	-0.982/0.327	***2.995/0.003***
Education/information status on postnatal care		
Yes		
No	82.80± 22.57	74.00± 12.84
Test value/p**	85.82± 19.54	65.69± 14.57
	-1.026/0.306	***4.578/0.000***

*F: One Way Anova test was used, ** t: Independent Sample t-test was used, a-c: There is a significant difference between variables with the same letter within the group, PSAS: Postpartum Specific Anxiety Scale, BIMF: Barkin Index of Maternal Functioning

Table 4: Relationships between mothers' PSAS total, BIMF total, and BIMF sub-dimension scores

		PSAS Total	Self-care	Maternal psychology	Infant care	Social support	Adaptation to motherhood	BIMF total
PSAS Total	r	1	***-0.621***	***-0.565***	***-0.421***	***-0.380***	***-0.528***	***-0.616***
	p		***0.000***	***0.000***	***0.000***	***0.000***	***0.000***	***0.000***
Self-care	r		1	***0.594***	***0.528***	***0.507***	***0.569***	***0.804***
	p			***0.000***	***0.000***	***0.000***	***0.000***	***0.000***
Maternal psychology	r			1	***0.734***	***0.599***	***0.727***	***0.867***
	p				***0.000***	***0.000***	***0.000***	***0.000***
Infant care	r				1	***0.425***	***0.710***	***0.811***
	p					***0.000***	***0.000***	***0.000***
Social support	r					1	***0.434***	***0.756***
	p						***0.000***	***0.000***
Adaptation to motherhood	r						1	***0.833***
	p							***0.000***
BIMF total	r							1
	p							

*Pearson Correlation Analysis was used, PSAS: Postpartum Specific Anxiety Scale, BIMF: Barkin Index of Maternal Functioning

Discussion

The findings of the study conducted to examine the relationship between postpartum anxiety and maternal function in mothers whose babies are 6-10 weeks old are discussed in light of the literature.

In this study, it was determined that the mean PSAS score of the mothers was moderate level. In a previous study, the mean score obtained from PSAS was moderate level [22], which supports the findings of this study. In Karademir's study using the Beck Anxiety Scale, it was determined that the anxiety level of the participants was low [23]. Di Paolo et al., found that the COVID-19 pandemic has increased the anxiety level of mothers [24]. The modarete level of postpartum anxiety in this study is considered to be attributed to the fact that the study was conducted during the COVID-19 pandemic, the use of a scale specific to the postpartum period.

In this study, it was determined that the mean total BIMF score and sub-dimensions of mothers was above the moderate level. In Palancı's (2019) thesis, the total mean score of BIMF and sub-dimension averages were above the moderate level [25]. Karataş and Ejder Apay compared maternal functioning by birth methods and found that the mean total BIMF score for mothers who had a normal and cesarean section delivery was above the moderate level [26]. Similarly, in these studies in the literature, maternal function and its sub-dimensions were determined to be above the medium level.

When the statistical comparison of the descriptive and obstetric characteristics of the mothers and the mean scores obtained from the PSAS was examined, it was found that there was a significant difference between the variables of age, education level, family type, employment status, income status, social security presence, duration of marriage, baby's age, and number of pregnancies and the score obtained from the scale. The findings of the literature are similar to the findings of this study [8, 22, 27-34].

When the statistical comparison of the descriptive and obstetric characteristics of the mothers and the total mean scores obtained from the BIMF was examined, it was found that there was a significant difference between the variables of age, income status, presence of social security, baby's age, type of delivery, presence of a person who helped after birth, and education/information status for postpartum care and the score obtained from the scale. The findings of the literature are similar to the findings of this study [35-38].

In this study, it was determined that there was a significant negative relationship between the mothers' PSAS total score and BIMF total score. In a previous study, a negative significant relationship was found between the postpartum anxiety level in the sixth week of postpartum and the functional status, social activities, and self-care activities of the mothers [39]. Aktan (2010) determined a negative relationship between postpartum anxiety and the functional status of the mother [40]. In another study, a significant and moderate negative correlation was determined between anxiety and the functional status in the postpartum period in mothers who gave birth by cesarean section [41]. In a study conducted in East India, a relationship between functional status and anxiety was determined in the sixth week of birth, and it was found that mothers with no anxiety or mild anxiety had higher functional status [42]. Gholizadeh, Shamasbi, et al. (2020) found a positive significant correlation between a mother's mental health and the total score and sub-dimensions of maternal function during the postpartum period and determined that as the mental health of mothers increased, the level of maternal function also increased [43]. In the literature and in this research, it is seen that having a psychological problem such as postpartum anxiety in mothers affects the functional status of mothers in the postpartum period.

In this study, it was determined that there was a significant negative relationship between the mothers' PSAS total score and BIMF sub-dimensions total score. According to a systematic review, women's postpartum self-care needs include aspects of their emotional well-being, such as adapting to a new role as a mother [44].Karademir (2021) found a negative relationship between the anxiety level of mothers and their self-confidence levels towards newborn care [23]. A study conducted in Northern Jordan found that mothers who perceived high levels of information support from health professionals were significantly associated with lower levels of postpartum anxiety related to practical infant care [45]. Dol et al., determined that social support was negatively associated with postpartum depressive symptoms and anxiety symptoms [46]. A previous study indicated that postpartum anxiety can arise in mothers due to various factors; therefore, comprehensive support and care are needed in the postpartum maternal adaptation process [47]. In the literature and in this research, it is seen that the presence of postpartum anxiety in the mother negatively affects maternal psychology, self-care of the baby and mother,

social support and adaptation to motherhood, making it difficult for the mother to adapt to the postpartum process.

Conclusion and Recommendations

In this study, it was determined that the mean PSAS score of the mothers was moderate level and the total mean BIMF score was above the moderate level. It was found that there was a moderate, negative significant relationship between the PSAS total score and the BIMF total score.

It has been determined that the mother's anxiety during the postpartum period negatively affects maternal function. For this reason, it is important for health professionals to evaluate the mother as a complete whole, physically, spiritually and socially, in the postpartum period. If postpartum anxiety is present, the functional status of the mother should be increased by taking necessary interventions.

In order to reduce the anxiety levels of expectant mothers and enable them to use their motherhood functions effectively during the postpartum period, pregnancy training classes and consultancy services are to be made widespread. It is crucial for midwives particularly working in primary healthcare to evaluate the physical condition of mothers, as well as their psychological and social conditions during the postpartum period. When evaluating mothers psychologically, anxiety scales related to the postpartum period are to be used in particular. Mothers with a higher level of postpartum anxiety should be determined during the early phase. These mothers should be supported both psychologically and socially and necessary precautions are to be taken. In addition, trainings should be provided to strengthen the functional condition and alleviate the adaptation to motherhood. In line with the results of this study, it is recommended that scales specific to the postpartum period be used and similar studies with larger sample groups be conducted in different areas.

Ethics Committee Approval: Ethics committee approval was obtained from Cumhuriyet University Non-Interventional Clinical Research Ethics Committee (dated 19.02.2020 and decision number 2020-02/41)

Informed Consent: The participants were provided with information about the purpose of the study and their informed consent was obtained before they started filling out the questionnaire.

Remarks: This study was produced from the thesis study on the Relationship between Postpartum Anxiety and Maternal Function in Mothers.

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Conflict of interest: The authors declare that they have no competing interests.

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Limitations of the Study The fact that this study was conducted during the COVID-19 pandemic and the limited number of studies related to the subject have posed limitations to the discussion of the findings. This study can be generalized to mothers who are between 6-10 weeks postpartum in the determined primary care clinic region.

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The Medicolegal Evaluation of Occupational Injury Cases Applied to Emergency Department of Cumhuriyet University Hospital

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ABSTRACT

Work accidents are of great concern to society because they directly affect the health and life of workers and the production process of the enterprise, as well as creating significant social and economic costs for workers, employers, the country's economy and society. In this study, the total of 1.048 occupational injury cases who applied to Emergency Department of Cumhuriyet University Faculty of Medicine between 2011-2015 was evaluated.

In this study; frequency, chi-square and percentage tests were used in the analysis of data. 1.034 (98.7%) of the cases was male and the rest was female. The cases were more often between the ages of 25-34 (36.2%). 64.2% of applications to emergency were occured between 08:01-17:00. The accidents were more often at metal/machine industry (20.8%). It was seen that it was not mentioned whether the injuries could be resolved with simple medical intervention in 84.4% of the reports. There wasn't an alcohol evaluation at most (92%) of the cases. Most of the injuries were located at upper extremity (39.6%). The most observed lesion was soft tissue damage (35.3%). 624 of the cases (59.6%) were discharged after treatment in emergency department. It was determined that the number of cases applied to the Department of Forensic Medicine by the prosecutor's office or court decision after occupational accident was 29 (2.8%); in 79.3% of cases, the injuries could be resolved with simple medical intervention; in 24.1%, there was life-threatening; in 3.4%, there was declining function; in 6.9%, there was loss of function.

Inadequacies in the writing of forensic reports will cause serious legal problems. In addition, it was concluded that it is important to raise awareness for all healthcare personnel, especially emergency physicians, and to provide up-to-date training for forensic case reporting and proper-complete preparation of forensic reports.

Keywords: Occupational injury, emergency, forensic medicine, medicolegal report, death.

Cumhuriyet Üniversitesi Hastanesi Acil Servisine Başvurulan İş Kazası Olgularının Adli Hukuki Değerlendirilmesi

Süreç

Geliş: 18/10/2023
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ÖZ

İş kazaları, işçinin sağlığı ve hayatı ile işletmenin üretim sürecini direkt olarak etkilemesinin yanında işçi, işveren, ülke ekonomisi ve toplum açısından önemli sosyal ve ekonomik maliyetler yaratması nedeniyle toplumu yakından ilgilendirmektedir. Bu çalışmada 2011 ve 2015 yılları arasında Cumhuriyet Üniversitesi Tıp Fakültesi Hastanesi Acil Servise iş kazası nedeniyle başvuran 1.048 olgunun tamamı incelendi.

Bu çalışmadaki verilerin analizinde frekans, yüzde ve ki-kare testleri kullanıldı. Olguların 1.034'ü (%98.7) erkek ve sıklıkla 25-34 yaş grubunda (%36.2) olduğu saptandı. Kazaların %64.2'sinin 08:01-17:00 saatleri arasında gerçekleştiği, en çok (%20.8) metal/makine endüstrisinde olduğu belirlendi. Acilde düzenlenen adli raporların sonuç bölümünde %84.4'ünde yaralanmanın basit bir tıbbi müdahaleyle giderilebilecek nitelikte hafif olup/olmadığının belirtilmediği, %92.0'sinde alkol değerlendirilmesinin yapılmadığı saptandı. En fazla yaralanmanın üst ekstremitelerde (%39.6) olduğu, en fazla görülen lezyon tipinin (%35.3) yumuşak doku yaralanması olduğu, 624'ünün (%59.6) acil serviste tedavilerinin ardından taburcu edildiği saptandı. Kesin adli rapor için Adli Tıp Anabilim Dalı'na başvuran olgu sayısının 29 (%2.8) olduğu, yaralanma bulgularının %79.3'ünde basit bir tıbbi müdahaleyle giderilebilecek ölçüde hafif olmadığı, %24.1'inde yaşamsal tehlikeye neden olduğu, %3.4'ünde duyu veya organlarının işlevinde sürekli zayıflamaya neden olduğu, %6.9'unda duyu veya organlarının işlevinde yitirilmesine neden olduğu tespit edildi.

Adli raporlarda yetersizliklerin görülmesi ciddi sorunlar doğuracaktır. Konuyla ilgili çok sayıda yapılacak araştırma bulgularının ayrıntılı incelenmesi iş kazalarının asıl nedenlerinin tespit edilmesi ve önlenmesinde önem taşımaktadır. Bununla birlikte, özellikle acil hekimler olmak üzere tüm sağlık personeline farkındalığın sağlanmasının, adli olgu ihbarı ve adli raporların düzgün-eksiksiz düzenlenmesi için güncel eğitimler verilmesinin önem taşıdığı sonucuna varıldı.

Anahtar sözcükler: İş kazası, acil servis, adli tıp, adli rapor, ölüm.

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Introduction

The World Health Organization defines the work accident as "an unplanned event that often leads to personal injuries, damage to machines, tools and equipment, and a temporary stoppage of production"[1]. With the rapid advancement of technology, occupational accidents have been increasing recently due to reasons such as taking the necessary precautions in workplaces incompletely or not at all, not giving due importance to occupational safety, and expecting much more production in a short time from employees in order to get better efficiency[2-4]. The occupational accidents, which are frequently encountered in emergency services and cause personal and social material and moral losses, are one of the urgent health problems that should be emphasized[5].

According to International Labor Organization data; every 15 seconds in the world, a worker dies due to work accidents or occupational diseases, while 160 workers have a work accident. Almost 6,400 worker die every day due to work accidents or occupational diseases. There are 270 million work accidents every year and more than 313 million workers have non-fatal work accidents[6].

Although occupational health and safety is considered an important issue in our country as well as in the world, every year many worker are injured or even lose their lives due to work accidents that could have been prevented. Work accident is one of the biggest risks that an employee may encounter in business life; It affects not only the employee but also his family financially and psychologically, and also it brings with it various problems that concern the employer and the state[7-10]. As in the majority of developing countries, there are difficulties in accessing actual data on work accidents in our country. Although there are many work accidents in our country and the material and moral damages are increasing day by day, studies and research on work accidents are limited. Keeping full and complete work accident reports is an important step in preventing future grievances and loss of rights. Disability and deaths due to work accidents are also encountered in forensic medicine practices. Due to deficiencies in the reports, we encounter problems in evaluating the results of the incident. In this study, it is aimed to emphasize the importance of work accidents for society, to evaluate the sociodemographic characteristics of those who had a work accident as well as the characteristic features of the accidents, to identify the deficiencies and errors in the forensic reports and hospital registry system, to draw attention to the development of the recording system and the importance of medical records related to work accidents.

Materials and Methods

This research is a descriptive study conducted to determine the sociodemographic characteristics of the forensic cases who applied to the Emergency Department of Sivas Cumhuriyet University Hospital due to a work accident in the five-year period between 01.01.2011 and 31.12.2015, how the incident occurred, in which line of work it was, whether a forensic report was kept and the content of the report, examination findings, alcohol level, social security, whether there is an application to the Department of Forensic Medicine after a work accident, final report findings, disability rate, whether a death has occurred due to a work accident. In this research, the data recorded in the hospital automation system and patient files were used.

The population of this research consisted of cases (n=1,263) who applied to Sivas Cumhuriyet University Hospital Emergency Department with work accident between 01.01.2011 and 31.12.2015, and no sample selection was made. It was aimed to evaluate all cases, but a total of 214 cases with insufficient and incomplete data in the hospital file, whose diagnosis was mistakenly entered as a work accident in the automation system, and one case who did not consent to the study were excluded from the study, and a total of 1,048 cases were included in the study. Limitations of the study are that this study was conducted only with work accident cases who applied to Sivas Cumhuriyet University Hospital Emergency Department, the data was obtained through records, and most important data (educational status, time spent in the sector, size of the place of work, etc.) could not be accessed.

The data in our study were uploaded to the SPSS (ver:22.0) program and the Chi-Square Test was used for statistical evaluation. When the assumptions regarding the Chi-Square distribution could not be met, the Monte Carlo model and Fisher Exact test, which are among the Chi-Square Exact tests, were used. The data are stated in the tables as the number of individuals and percentages, and the error level is taken as 0,05. A value of $p<0,05$ was considered significant. Ethics committee approval was received for this research from Cumhuriyet University Non-Interventional Clinical Research Ethics Committee with decision number 2016/09 dated 25.03.2016.

RESULTS

In this study, 98.7% of those who had a work accident were male, and the average age of the cases at the time of admission to the hospital was 33.44±9.83 (minimum:15, oldest:69). It was determined that the most cases were in the 15-24 age group, with 22.0%. It is seen that the number of occupational accidents experienced decreases significantly in people aged 45 and over, and the majority (91.9%) have health insurance (Table 1).

Table 1. Distribution of Cases According to Some Demographic Characteristics.

Gender	n	%
Woman	14	1,3
Man	1.034	98,7
Total	**1.048**	**100,0**
Age Groups		
15-24	231	22,0
25-29	175	16,7
30-34	204	19,5
35-39	152	14,5
40-44	143	13,6
45-49	83	7,9
50-54	39	3,7
55-59	12	1,1
60 age and above	9	0,9
Total	**1.048**	**100,0**
Health Insurance		
No	85	8,1
Available	963	91,9
Total	**1.048**	**100,0**

Of the cases who had a work accident and whose line of business specified facts, 20.8% were in the metal/machinery sector, followed by the construction sector (building works) with 13.7 % (Table 2).

Table 2. Distribution of Cases According to Their Business Lines.

Business Lines	n	%
Chemical matter	14	1,3
Metal/Machine	218	20,8
Construction (Building works)	144	13,7
Mine-sand-quarry	68	6,5
Transportation	8	0,8
About health	1	0,1
Food industry	20	1,9
Power plant	33	3,1
Textile	2	0,2
Tunnel and road construction	19	1,8
Train	15	1,4
Agriculture	5	0,5
Wood work	23	2,2
Communication	3	0,3
Vehicle repair	1	0,1
Natural gas	2	0,2
Other-Unspecified	472	45,0
Total	**1.048**	**100,0**

It was determined that the most work accidents occurred on Wednesday with 184 cases (17.6%), on Tuesday with 165 cases (15.7%) and on Monday with 159 cases (15.2%). It is seen that 719 (75.5%) of the total 1.048 work accidents occurred on weekdays and 257 (24.5%) occurred on weekends (Figure 1).

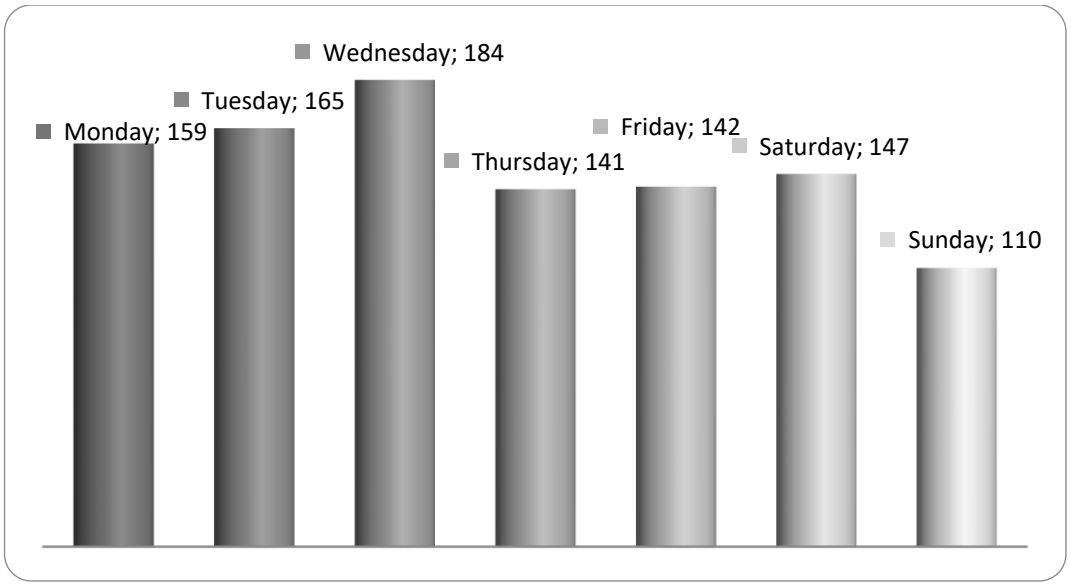

Figure 1. Distribution of Cases According to Application Days.

36.7% of applications to the emergency department as a result of work accidents occur between 12:01 and 17:00, 28.6% between 17:01 and 00:00, and 27.5% between 08:01 and 12:00. It was determined that the minimum application with 7.2% was between 00:01 and 08:00 hours (Figure 2).

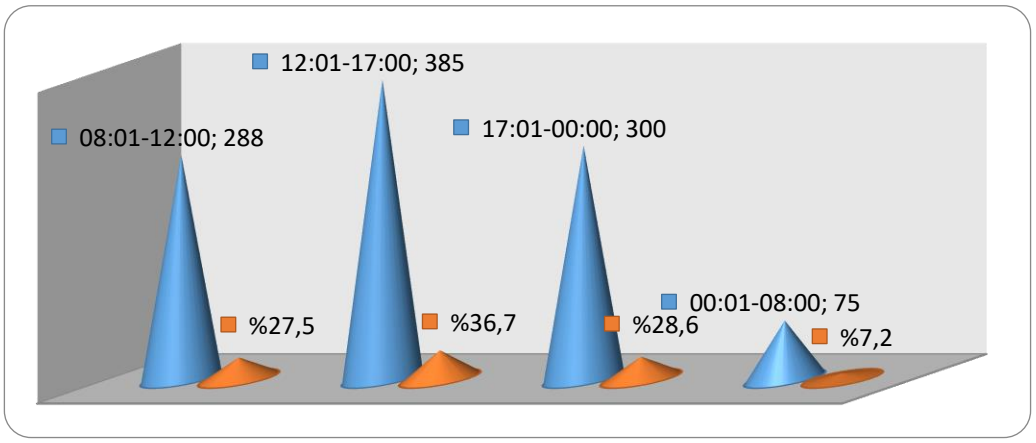

Figure 2. Distribution of Cases According to Application Times.

According to Table 3; It was found that out of 417 cases who applied to the emergency department after a work accident and for whom a forensic report was issued. In 352 reports (84.4%), it did not indicate whether the condition was mild enough to be resolved with a simple medical intervention, and in 408 reports (97.8%) it was stated whether it was life-threatening or not.

Table 3. Distribution of Findings in Forensic Reports Prepared in the Emergency Department.

	n	%
Determining whether the condition is mild enough to be treated with simple medical intervention.		
No	352	84,4
Yes	65	15,6
Total	**417**	**100,0**
Indicating whether or not there is a danger to life		
No	9	2,2
Yes	408	97,8
Total	**417**	**100,0**

Among the types of accidents, injuries caused by machinery/materials are the most common (36.8%), falling (22.1%) is the second most common type of work accident, and injuries caused by machinery/materials and cutting tools are the third most common with 13.3% (Table 4). In work accident cases, the most injured area is the upper extremity (39.6%), and the head-neck region (17.3%) is the second most injured area (Table 5). Considering the individual lesion type seen in the cases (Table 6); it was determined that the most common injuries were soft tissue injuries such as injury and tenderness at the skin-subcutaneous level (35.3%), followed by bone fractures (21.1%) and sub/total amputations (9.3%).

Table 4. Distribution of Cases According to Types of Work Accidents.

Type of Work Accident Occurrence	n	%
Injury by Machinery/Material	386	36,8
Fall*	232	22,1
Injury by Machinery/Material and Cutting Tool**	139	13,3
Injury with a Cutting Tool	95	9,1
Injury by Chemical Substance (Solid-Liquid-Gas)	39	3,7
Electric shock	31	3,0
Explosion	30	2,9
Traffic accident	28	2,7
Injury with a Pointed Object	28	2,7
Fire	9	0,9
Electric Shock and Fall	7	0,7
Being trapped under rubble	5	0,5
Other	19	1,8
Total	**1.048**	**100,0**

*Falls from height and falls from the same level are taken together.

**This type of injury occurred with machines that have cutting features such as sawmills, saws and spiral machines.

In terms of hospitalization duration of cases receiving inpatient treatment (Table 7), out of a total of 418 cases, those who were treated for 1-3 days are in the first place with 162 cases (38.8%), and the second place is 105 cases (25.1%) who were treated for 4-6 days. However, one of these cases died on the fourth day of hospitalization. It was determined that in 92% of the cases admitted with a work accident, alcohol measurement evaluation was not performed and the measurements were made only with a breathalyzer device. In this study, it was determined that 1,017 (97.2%) of the 1,046 cases, excluding the two cases that lost their lives, did not apply to the Department of Forensic Medicine, while 29 cases (2.8%) applied (Table 8). It was determined that in 23 (79.3%) of the 29 cases who applied to the Department of Forensic Medicine, the injuries were not so mild that they could be resolved with a simple medical intervention, and in 22 (75.9%) the injuries did not cause a life-threatening situation.

According to Table 9; among the 29 cases who applied to the Department of Forensic Medicine after a work accident, the number of cases that did not receive a disability rate was 12 (41.4%), and the number of cases that received a disability rate between 10-50% was three (10.3%) and this situation was found to be statistically significant ($p<0.05$). The disability rates of three cases with disability rates between 10-50% were determined as 11%, 18.2% and 31%, in order of proportion.

Table 5. Distribution of Cases According to Injury Regions Due to Work Accidents.

Injury Site	n	%
Upper Extremity	415	39,6
Head-Neck	181	17,3
Lower Extremity	144	13,7
Three or More Body Parts	61	5,8
Chest	51	4,9
Head-Neck and Upper Extremity	42	4,0
Back	33	3,1
Upper and Lower Extremities	21	2,0
Abdomen	19	1,8
Head-Neck and Back	14	1,3
Upper Extremities and Back	13	1,2
Head-Neck Region and Lower Extremity	13	1,2
Chest and Back	11	1,0
Lower Extremities and Back	8	0,8
Lower Extremities and Abdomen	8	0,8
Head-Neck and Chest	8	0,8
Upper Extremity and Abdomen	6	0,6
Total	**1.048**	**100,0**

Table 6. Distribution of Cases According to Lesion Types Caused by Work Accidents.

Lesion Types	n	%
Skin-Subcutaneous Level Injury*, Sensitivity	370	35,3
Bone Fracture	221	21,1
Sub/Total Amputation	97	9,3
Burn	67	6,4
Eye Injuries**	48	4,6
Crush Style Injury	47	4,5
Muscle-Tendon Injury	42	4,0
Lesion Not Specified	31	3,0
Internal Organ Injury and Bone Fracture	31	3,0
Internal Organ Injury	19	1,8
Muscle-Tendon Injury and Bone Fracture	18	1,7
Nerve Injury and Bone Fracture	7	0,7
Muscle-Tendon Injury and Burn	7	0,7
Nerve Injury	5	0,5
Sprain-Dislocation	4	0,4
Ear Injuries***	4	0,4
Major Vascular and Nerve Injury	4	0,4
Major Vascular Injury and Bone Fracture	4	0,4
Major Vascular Injury	2	0,2
Other Injuries	20	1,9
Total	**1.048**	**100,0**

*Lesions such as abrasions and abrasions
**Lesions such as Foreign Body in the Eye - Eye Perforation
*** Lesions such as Acoustic Trauma - Eardrum Perforation

Table 7. Hospitalization Duration of Cases Receiving Inpatient Treatment in Hospital

Hospitalization Duration	n	%
1-3 days	162	38,8
4-6 days	105	25,1
7-10 days	61	14,6
11-15 days	34	8,1
16-20 days	29	6,9
20 days and above	27	6,5
Total	418	100,0

Table 8. Evaluation of Forensic Reports Written in the Department of Forensic Medicine After Their Treatment of Cases Applying to the Emergency Department with Work Accidents.

	n	%
Application to Forensic Medicine Department		
No	1.017	97,2
Yes	29	2,8
Total	**1.046**	**100,0**
Whether the Injury Is Light enough to be Resolved with Simple Medical Intervention		
Not light	23	79,3
Light	6	20,7
Total	**29**	**100,0**
Whether the Injury Causes Life Danger or Not		
Yes	22	75,9
No	7	24,1
Total	**29**	**100,0**
Whether or not it causes permanent weakening/loss of sensory/organ function		
ICZ* availale	1	3,4
LA** availale	2	6,9
ICZ/LA not available	12	41,4
Undetermined	14	48,3
Total	**29**	**100,0**

* ICZ: Persistent weakening of function
**LA: Loss of function

Table 9. Distribution of Disability Rates Received by Cases Applying to Forensic Medicine Department.

Disability Rate	Application to Forensic Medicine Department Due to Work Accident					
	Not available		Available		Total	
	n	%	n	%	N	%
%0	0	0,0	12	41,4	12	1,1
%0-9	4	0,4	0	0,0	4	0,4
%10-50	2	0,2	3	10,3	5	0,5
>%50	5	0,5	0	0,0	5	0,3
Unknown	1.006	98,9	0	0,0	1.006	96,2
Undetermined	0	0,0	14	48,3	14	1,3
Total	**1.017**	**100**	**29**	**100**	**1.046**	**100**

X^2=254,54 p=0,0001 p<0,05 important

DISCUSSION

In this evaluation of the cases applicable to Cumhuriyet University Hospital Emergency Department due to work accident, the male rate among those was found to be 98.7%. In research on work accidents, the rates of men who have a work accident vary between 83.8% and 100.0%[2,5,9,11-13]. Studies conducted in our country and other countries find that male rates are higher in work accident cases, the reasons of that are due to the fact that men are employed in heavy jobs that require more active and physical strength in working life, and is due to the fact that women workers work in relatively lighter jobs.

The average age of the cases was 33.44±9.83 and most (36.2%) were in the 25-34 age group. This was followed by those in the 15-2 4 age group with 22.0%. Çelik et al.[14] was observed in the study conducted at Ankara Numune Training and Research Hospital; The average age of work accident cases was 32.96 ± 5.97 and that it occurred most in the 26-35 age group with 37.0%. In a study conducted by Dağlı and Serinken[5] at Pamukkale University Hospital, the average age of work accident cases applying to the emergency department was 32.7±9.7, and the age group of the cases was mostly in the 25-34 age group with 36.4%. Mehrdad et al.[13] found that the average age of work accident cases was found to be 32.07±9.12 and the maximum age group was 25-34 with 47.6%. It was concluded that young age groups experience more work accidents due to the reasons such as younger age groups are more involved in business life, they are employed more in difficult and demanding jobs, and lack of experience and training in practice.

The cases applying with a work accident are examined in terms of the line of work they work in. It was determined that nearly half (45.0%) were not specified, the metal/machinery industry came first with 20.8%, and then the construction industry came next with 13.7%. According to 2015 Social Security Institution work accident statistics[15]. In Doğanlı's[16] study; it was stated that in the sectoral distribution of occupational accidents, the construction sector ranked first with 21.4%, followed by the machinery industry with 17.1%. While the data in our study are consistent with nationwide statistics, differences were observed in regional studies. It was concluded that these differences may have arisen due to reasons such as regional job opportunities and the development of the regional industry.

Distribution of work accidents according to days; it was determined that the most visits to the emergency department were on Wednesdays (17.6%) and Tuesdays (15.7%). 75.5% of the cases

applied to the emergency department on weekdays and 24.5% on weekends. Sayhan et al.[17] reported that 75.7% of the applications to the emergency department due to work accidents occurred on weekdays and 24.3% on weekends, and Ergör et al.[18] determined that the majority of work accidents occurred on weekdays (79.5%). Since employees are exposed to a continuous and intense work schedule during the mid-week and employers do not give them much opportunity to rest, they have difficulty in concentrating and adapting to the workplace, and their hasty behavior can lead to work accidents.

In this research, it was determined that most of the work accident cases with 64.2% applied to the emergency department during daytime working hours (08:01-17:00). Ulutaşdemir et al.[9] in their study on cases who applied to the emergency department of a private hospital due to a work accident; it was stated that work accidents mostly occurred between 08-17 hours (58.7%), and in the study of Dağlı and Serinken[5], they mostly occurred between 08-10 and 14-16 hours. It was thought that more staff working in the work environment frequently during the daytime was effective, especially in the first working hours, as workers had difficulties in adapting to the working environment, focusing problems or concentrating attention when starting work.

It is a legal obligation that cases exposed to work accidents should be evaluated as "forensic case" and reported to law enforcement. The written findings, wording and conclusion of the forensic report, which has the nature of a notice, must be complete and in a language that the lawyer can understand. When the forensic reports of work accident cases are examined, whether it is stated whether it is mild enough to be resolved with simple medical intervention or not, and whether it is life-threatening or not; it was observed that the concept of whether it could be resolved with simple medical intervention was not stated in 84.4% of the cases, and that it was stated whether there was life-threatening or not in 97.8% of the cases. Bozkurt et al.[19] reported that it was stated in 91.5% whether it was life-threatening or not, and that it was not stated whether it would be resolved with simple medical intervention or not in 33.1%. It is a fact that these concepts are important for a fair trial. We think that doctors are not fully aware of whether it is necessary to indicate whether there is a life-threating situation or not, and whether it is mild enough to be treated with simple medical intervention or not, and that is why they act hesitantly. In this regard, all physicians need to be informed and trained about the guide titled "Forensic Medicine Evaluation of Injury Crimes Defined in the Turkish Penal Code".

The most common type of work accident was machine/material injury (36.8%). While the second occupational accident was falling (22.1%), the third (13.3%) was found to be injured by machinery/materials and cutting tools (such as sawmills, saws and spiral machines). Ergör et al.[18] found that 35.6% of occupational accidents consisted of being trapped under or between heavy objects, 21.0% falling, and 15.3% impact/collision type injuries. In a study conducted by Birgen et al.[20]; of the 59 cases whose type of accident was specified, the first one was due to a limb being caught in the machine in 30 cases (51%), and the second one (n=11, 19%) was caused by an object falling on. Evaluating of work accident cases that apply to the emergency department; Sayhan et al.[17] stated that the rate of injuries caused by sharp objects was 40.6%, injuries by falling were 16.7%, and injuries by being trapped under heavy objects were 11.4%.

When the injury areas resulting from work accidents are examined, the most injured area was the upper extremity (39.6%), followed by the head and neck region (17.3%). Following these, the lower extremity region (13.7%) was ranked third. Özkan et al.[21] in their examination of work accident cases that applied to the emergency department; 56.6% of all injuries are upper extremity injuries, 17.6% are lower extremity injuries, and 10.1% are head and neck injuries. Kekeç et al.[22], in their study on occupational accidents that applied to the emergency department, reported that the body part most injured in accidents was the upper extremity. Çelik et al.[14] ; reported that upper extremity injuries were 53.7%, lower extremity injuries were 15.3%, and head and neck injuries were 13.3%. Karakurt et al.[23] stated that in cases related to work accidents, the most injuries occur on the extremities (62.0%) and in the head (22.0%). Yavuz et al.[24], in the evaluation of work accident cases applying to the emergency department, it was determined that injuries were most common in the upper extremity (46.2%), followed by the lower extremity (19.7%) and head area (18.2%). Upper extremity injuries are more common in work accidents, especially since the upper extremities are used more in most lines of work.

In terms of lesion types, mostly (35.3%) are tenderness, soft tissue injury such as skin-subcutaneous level, bone fracture (21.1%), sub/total amputation (9.3%), burn (6.4%) has been seen. Ulutaşdemir et al.[9] reported that 45.1% had soft tissue trauma and 27.8% had fractures. Özkan

et al.[21] in their study, soft tissue traumas occurred in 36.7% of work accident cases, cuts and lacerations occurred in 26.3%, fractures and dislocations occurred in 11.2%, amputation occurred in 6.9%, and burns occurred in 1.45%. According to Social Security Institution statistics, it has been reported that soft tissue traumas (46.4%) come first as a result of work accidents, followed by dislocations, sprains and strains (14.8%), bone fractures (7.5%) and burn findings (2.5%)[15].

In our study, both cases (0.2%) who died were male. Çelik et al.[14] reported that 0.3% of the cases admitted due to work accidents died; 0,25% in the study by Karakurt et al.[23] and 0.8% in Dağlı and Serinken's[5] study. The majority of the cases admitted with a work accident (Table 7) were discharged after outpatient treatment. This is an indication that injuries due to work accidents are mild enough to require outpatient treatment, meaning that they are generally preventable injuries.

In our study; when the cases receiving inpatient treatment were examined according to the duration of their hospital stay, the most (38.8%) were treated for 1-3 days (Table 7). Beyaztaş et al.[25] on occupational accidents in Sivas province, stated that 35.4% of the cases receiving inpatient treatment received treatment for less than 10 days, and 7.3% received treatment for 10-19 days. Considering time the patients spend in the hospital and the rest period after discharge, it should be emphasized once again that occupational accidents must be prevented in order to prevent such material and moral losses, as they will cause more workday losses.

There are also cases where alcohol measurement is required in work accidents, which is important for compensation. Therefore, not having an alcohol assessment may create a legal problem. In our study, it was determined that alcohol assessment was not performed in 92% of the cases admitted to the emergency department and that the assessment was made only with a breathalyzer device. Budakoğlu et al.[26] in a survey study conducted by regarding the frequency of occupational accidents and the risk factors, stated that the exposure to of workers who use alcohol is higher than those who have never drank, quit drinking, those who drink occasionally. In the majority of cases, alcohol content was not checked. This may be due to technical deficiencies in the hospital, overcrowding in the emergency room, or the fact that the patient did not give the impression that he or she might be drunk.

In this study, the cases that applied to the emergency department due to a work accident were contacted by Department of Forensic Medicine of Cumhuriyet University for an additional report after their treatment, through the prosecutor's office or the court. When the distribution of cases (2.8%) applying to the Department of Forensic Medicine is examined; it was determined that in 79.3% of the cases, the injury was not so minor that it could be resolved with a simple medical intervention, and in 24.1%, the injury was life-threatening. It was determined that it caused permanent weakening of function in 3.4%, caused loss of function in 6.9%, and did not result in 48.3% because re-application was expected after the completion of the recovery process. The disability rates of the cases who applied to the Department of Forensic Medicine, where it was decided whether the function of one of their senses or organs was permanently weakened or lost were as follows; it has been determined that 41.4% have not received an disability rate, 10.3% have received a rate between 10-50%, and 48.3% have not yet been concluded in terms of disability rate. Among those who received a disability rate, the highest rate was found to be 31%. The large difference in the rate between the number of cases applying to the emergency department and the number of applications to the Department of Forensic Medicine, may be due to the fact that the cases are not reflected in the judicial dimension due to reasons such as disruptions, delays in the judicial processes, other hospital preferences, the cases agreeing with the employer or not complaining.

CONCLUSION and RECOMMENDATIONS

Ignoring measures for occupational health and safety due to reasons such as competition in a global world order, rapid changes in technology, and efforts to reduce costs causes an increase in the incidence of occupational accident[27]. Recommendations for preventing occupational accidents, along with supporting training for workers and employers, are as follows:

•In working life; Health screening of people during recruitment, assessing their suitability for the job, providing training on the job they will do, repeating this training with up-to-date information for certain periods of time, and ensuring adaptation to the job at intervals will make serious contributions to a safe working life.

•Individuals should be made aware of the use of personal protective equipment and it should be emphasized that they should use it for their own safety, not out of necessity.

•By performing risk analyzes at regular intervals in businesses, worker and work-related risks can be identified and hazards can be minimized.

•By ensuring that the person who has suffered any kind of work accident, whether heavy or light, applies to a health center, complete and accurate data can be obtained, the real extent of the work accidents can be seen and the necessary precautions can be taken.

•Physicians may be held legally responsible and face criminal and compensation lawsuits as a result of any errors or omissions they make in preparing forensic reports. Therefore, physicians need to know how to approach forensic cases, write reports, and what their responsibilities are.

•In most cases of work accidents, the first physician to see the person must determine whether there is alcohol in the person in order to solve problems that may arise later.

•By ensuring that occupational health and safety training is provided to both employees and employers, accidents will be minimized by taking simple precautions.

•It can be ensured that the safety measures required to be taken in the working environment are audited not only by the company's employees but also by independent auditing institutions.

•Various problems will arise if the event that causes the application of a forensic case is mistakenly entered as a different event in the hospital automation system. In order to prevent loss of time, it is necessary to install warning software for forensic cases in the automation system.

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Thrombophilic gene variants in patients with coronary artery disease and myocardial infarction

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Research Article

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ABSTRACT

Coronary artery disease (CAD) and myocardial infarction (MI) are cardiovascular diseases that occur due to atherosclerosis (plaque formation) or atherosclerotic obstruction of the coronary arteries. Their genetic basis has been under investigation for a long time, and common variant studies link different genetic loci with these diseases. In this study, we investigated the possible association of coronary artery disease and myocardial infarction with thrombophilic gene variants, including MTHFR C677T and A1298C, Beta fibrinogen -455G/A, Factor XIIIV34L and PAI-1 4G/5G single nucleotide polymorphisms (SNPs).

A total of 128 people (64 patients and 64 controls) were included in the study. Genomic DNA was isolated using the EZ1 blood mini kit. The DNA was amplified and PCR was performed using the PyroMark PCR Kit (Qiagen, Germany). Pyrosequencing reaction was completed by processing with PyroMark Q24 instrument.

We found that the PAI-1 4G/5G polymorphism and the 4G allele were significantly associated with coronary artery disease and myocardial infarction (P= 0.01). Although mutant variants were higher in patients, no statistically significant difference was observed between the patient and control groups in terms of FXIII, Beta-fibrinogen and MTHFR variants.

It is clear that the PAI-1 4G allele and the 4G/4G genotype have a significant contribution to the development of coronary artery disease and ultimately myocardial infarction. Prophylactic treatment should be considered in patients with this variant.

Keywords: Coronary artery disease, myocardial infarction, PAI-1, MTHFR, Beta fibrinogen, Factor XIII.

Koroner arter hastalığı ve miyokard enfarktüsü olan hastalarda trombofilik gen varyantları

Süreç

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ÖZ

Koroner arter hastalığı (KAH) ve miyokard infarktüsü (MI), aterosklerozun (plak oluşumu) veya koroner arterlerdeki aterosklerotik tıkanıklığın bir sonucu olarak ortaya çıkan kardiyovasküler hastalıklardır. Bunların genetik temeli uzun süredir araştırılmakta olup, yaygın varyant çalışmaları bu hastalıklarla farklı genetik lokusları ilişkilendirmektedir. Bu çalışmada, metilentetrahidrofolat redüktaz (MTHFR) C677T ve A1298C, Beta fibrinojen -455G/A, Faktör XIIIV34L ve PAI-1 4G/5G tek nükleotid polimorfizmleri (SNP'ler) de dahil olmak üzere trombofilik gen varyantlarının koroner arter hastalığı ve miyokard infarktüsü ile olası ilişkisi araştırıldı.

Toplamda 128 kişi (64 hasta ve 64 kontrol) çalışmaya dahil edildi. Genomik DNA, EZ1 blood mini kit kullanılarak izole edildi. DNA çoğaltıldı ve PCR, PyroMark PCR Kit (Qiagen, Almanya) kullanılarak gerçekleştirildi. Pyrosequencing reaksiyonu, PyroMark Q24 enstrümanı ile işlenerek tamamlandı.

PAI-1 4G/5G polimorfizmi ve 4G alleli'nin koroner arter hastalığı ve miyokard infarktüsü ile anlamlı bir şekilde ilişkili olduğunu bulduk (P= 0.01). Hasta gruplarında mutant varyantlar daha yüksek olmasına rağmen, hasta ve kontrol grupları arasında FXIII, Beta-fibrinojen ve MTHFR varyantları açısından istatistiksel olarak anlamlı bir fark gözlemlenmedi.

PAI-1 4G alleli ve 4G/4G genotipinin koroner arter hastalığının gelişimine ve nihayetinde miyokard infarktüsüne önemli bir katkısı olduğu açıktır. Bu varyanta sahip hastalarda profilaktik tedavi düşünülmelidir.

Anahtar Kelimeler: Koroner arter hastalığı, miyokard infarktüsü, PAI-1, MTHFR, Beta fibrinojen, Faktör XIII.

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Introduction

Coronary artery disease is one of the main cardiovascular diseases caused by genetic and environmental factors and the interactions between them[1]. It is a major cause of death and disability in the world[2]. Myocardial infarction is a concept that refers to the damage of the heart muscles due to the reduction of blood flow to the heart as a result of the formation of plaques on the inner walls of the arteries and lack of oxygen[3]. Coronary artery disease, or coronary atherosclerosis, is a condition characterized by narrowing of the arteries that supply the heart muscle. Coronary angiography is the gold standard for the diagnosis of CAD and percutaneous coronary interventions[4]. Most cases of myocardial infarctions are caused by coronary artery disease. A heart attack is a life-threatening condition that occurs as a result of blockage in one or more coronary arteries and leads to serious tissue damage. The lack of oxygen in the myocardium for a certain period of time results in cell death and necrosis. The genetic basis of coronary artery disease is important for the formation and course of the disease. In this context, the effect of thrombophilic variants on coronary artery disease and myocardial infarction is controversial. For example, Park et al. argue that the 4G > 5G polymorphism located in the Plasminogen activator inhibitor-1 (PAI-1) promoter region is associated with coronary artery disease as well as other atherosclerotic diseases such as venous thromboembolism, ischemic stroke, carotid artery stenosis and renal artery stenosis[5]. The 4G/4G genotype and the 4G allele of the PAI-1 gene are thought to be associated with the risk and morbidity of acute myocardial infarction (AMI). The 4G/4G genotype of PAI-1 may also be associated with mortality from AMI[6]. The association of the PAI-1 4G/5G polymorphism with the plasma concentration of PAI-1 has also been reported in different studies[7]. Methylenetetrahydrofolate reductase (MTHFR) is an enzyme that plays an important role in the breakdown of homocysteine (Hcy), a by-product of cysteine metabolism. High homocysteine levels are associated with an increased risk of myocardial infarction. A clear association between the MTHFR C677T polymorphism and the risk of CAD has been demonstrated in the Chinese population[8]. It is also expressed that homozygous TT variant of MTHFR gene in Eastern Black Sea Turks is a risk factor for MI patients[9]. Rallidis et al. assert that the presence of the A allele for the G-455A polymorphism of the β-fibrinogen gene has a protective effect against the development of non-fatal acute MI in the Greek population aged ≤35 years[10]. The FXIII-V34L variant is claimed to reduce the risk of thrombosis[11]. It has also been suggested that the FXIIIA V34L polymorphism may be protective for MI in Caucasians[12]. Based on these discussions and similar considerations, the aim of this study was to analyze the relationship between coronary artery disease-myocardial infarction and MTHFR C677T, MTHFR A1298C, PAI-1 4G/5G, Beta fibrinogen G-455A, FXIII V34L gene polymorphisms.

Material Method

Study Population

The study included CAD patients diagnosed with electrocardiogram (ECG), exercise ECG and/or coronary angiography at Sivas Cumhuriyet University Research Hospital and heart attack cases treated in the emergency department of the same hospital between 2006 and 2022. In this research, 64 CAD patients, 12 of whom had MI were analyzed together with 64 healthy controls. This study was approved by the ethics committee of Sivas Cumhuriyet University (Decision no: 2023-07/01 Date: 20.07.2023).

Laboratory Analysis

Genomic DNA was isolated using the EZ1 blood mini kit and polymerase chain reaction (PCR) was performed using the PyroMark PCR Kit (Qiagen, Germany). After 15 min activation at 95°C, The DNA was amplified for 45 cycles under the following conditions: 30 sec at 94°C for denaturation, 30 sec at 60°C for annealing and 30 sec at 72°C for extension. PCR was completed with 10 min final extension at 72°C. PCR products (10 µL) were mixed with streptavidin-conjugated sepharose material in binding buffer (70 µL). They were collected using a vacuum workstation and added to the sequencing primer and annealing buffer in Q24 plate and kept at 80°C for 2 minutes. Pyrosequencing reaction was performed through PyroMark Q24 instrument (Qiagen, Germany).

Statistical Analysis

Statistical analysis was performed with SPSS 22.0 program (SPSS Inc., Chicago, IL, USA). Independent Samples t Test was used for the comparison of mean age. In this comparison, data were presented as mean ± SD. All genotypes and alleles frequencies of patients and controls was compared by x2 test. The odds ratios were calculated at 95% confidence interval and P value < 0.05 was accepted statistically significant.

Results

Sixty-four CAD-MI patients and 64 healthy controls were evaluated for polymorphisms of MTHFR C677T, MTHFR A1298C, FXIII V34L, Beta fibrinogen G-455A and PAI-1 4G/5G. The age was higher in the patient group (P: 0.001). The mean age of the patients was 66.6 years and that of the control group was 49.8. The number of males was higher in the patient group than in the control group and there were much more smokers in the patient group. Twenty-eight of the patients also had hypertension. (Table 1). There was a statistically significant difference between the patient and control groups in terms of PAI-1 4G/5G genotype and 4G allele frequencies (Table 2). The 4G/4G genotype and 4G allele frequency were significantly higher among patients compared to the control group (P=0.01). Although mutant alleles for MTHFR C677T, MTHFR A1298C, Beta fibrinogen and FXIII variants were higher in the patient group, there was no statistically significant difference between the patients and control group (Table 3-5).

Discussion

Prospectively, genetic testing may identify subgroups of patients at high risk of CAD for the therapeutic or prophylactic approach[13]. A number of gene polymorphisms affecting hemostasis have been identified, and among these, β-fibrinogen−455 G/A and PAI1 4G/5G gene polymorphisms have been associated with both myocardial infarction and CAD[14]. Plasminogen activator inhibitor-1 (PAI-1) is a serine protease inhibitor, that suppresses fibrinolysis by inhibiting both tissue-type and urokinase-type plasminogen activator[15]. It has been suggested that the 4G allele is more active than the 5G allele. In other words, PAI-1 concentrations tend to be higher in the presence of the 4G allele compared to the 5G allele. In this context, homozygous 4G/4G polymorphism has been associated with increased PAI-1 activity and increased risk of thrombosis[16]. Therefore, Zhang et al. suggested that PAI-1 4G/5G polymorphism may be a possible biomarker for the risk of venous thromboembolism[17]. In a study conducted in Brazil, it was found that PAI-1 was independently associated with CAD, and PAI-1 levels were higher in patients with the 4G/4G genotype[18]. In our study, PAI-1 4G allele and 4G/4G genotype were significantly associated with coronary artery disease and myocardial infarction (P:0.01). MTHFR is a major enzyme in homocysteine metabolism that catalyzes the reduction of 5-10-MTHF to 5-MTHF, a circulatory form of folate that is effective in the remethylation of homocysteine to methionine. MTHFR gene mutations affect Hcy level and may contribute to hyperhomocysteinemia, decreased folate levels, and various cardiovascular diseases[19]. While Shivkar et al. observed a statistically significant hyperhomocysteinemia in carriers of the T allele for MTHFR C677T genotype in the young coronary artery disease group, they could not establish such a link for the MTHFR A1298C polymorphism[20]. Friso et al. state that the 1298C allele is not associated with increased plasma homocysteine, regardless of folate status[21]. On the other hand, high Hcy levels with the T allele of MTHFR C677T polymorphism and the A allele of A1298C polymorphism has been linked with AMI and massive and sub massive pulmonary thromboembolism[22]. In a study by Husemoen et al., the risk of ischemic heart disease was higher in individuals with the MTHFR TT genotype, independent of folate status[23]. Although mutant alleles were more common in the patient group, no significant association was found between coronary artery disease and MTHFR C677T-A1298C polymorphisms in the current study. FXIII is a protein that catalyzes the formation of covalent cross-links between fibrin monomers to stabilize the clot[24]. FXIII-A V34L has been associated with a protective effect in relation to thrombotic disease. Some studies assert that FXIII-A V34L may be linked with a reduced risk of myocardial infarction and coronary artery disease[25]. Various factors are known to affect plasma fibrinogen concentrations. These include the β-fibrinogen -455G/A gene single nucleotide polymorphism, and the A allele in this SNP has been shown to be associated with high plasma fibrinogen levels[26]. In the study of Lu et al., the A allele frequency of the G-455A polymorphism of the β-fibrinogen gene was significantly lower in MI cases than controls, in Chinese Han population[27]. This suggests that the A allele may be protective for MI. Conversely, Chen et al. claim that the -455G/A polymorphism of β-fibrinogen gene may be associated with the propensity for coronary artery disease in China and the A allele of this polymorphism increases susceptibility to this disease[28]. No significant difference was observed between the patient group and the control group in terms of FXIII and beta fibrinogen gene variants in our study.

In conclusion, we were unable to establish an association between MTHFR C677T, MTHFR A1298C, β-fibrinogen -455G/A and FXIII V34L

variants with coronary artery disease and MI. However, PAI-1 4G/5G gene polymorphism was significantly associated with coronary artery disease. We believe that the 4G allele and 4G/4G genotype of this marker contribute to coronary artery disease and thus MI cases remarkably. It would be meaningful to consider prophylactic antithrombophilic treatment in cases with this variant in risk groups.

Table 1. Characteristics of CAD-MI patients and controls

	Patients	Controls
Age	66.6 ±12	49.8±11
Sex	49 M (76.6%) 15 F (23.4%)	36 M (56.3%) 28 F (43.7%)
Smoking	44 (68.8%)	12(18.8%)
Hypertension	28 (43.8%)	-

Table 2. The distribution of PAI-1 4G/5G genotypes and allele frequencies in CAD-MI cases and control groups

PAI-1 4G/5G Genotype&Allele	CAD-MI n:64	Control n: 64	P value
5G/5G	5 (7.8%)	17 (26.6%)	
4G/5G	40 (62.5%)	37 (57.8%)	P= 0.01 P<0.05
4G/4G	19 (29.7%)	10 (15.6%)	
5G	50 (39%)	71 (55.5%)	P= 0.01
4G	78 (61%)	57 (44.5%)	P<0.05
Odds ratio	0.515 (0.31-0.85) %95 CI		

Table 3. The distribution of MTHFR C677T genotypes and allele frequencies in CAD-MI cases and control groups.

MTHFR C677T Genotype&Allele	CAD-MI n:64	Control n: 64	P value
CC	30 (7.8%)	32 (26.6%)	
CT	27 (62.5%)	27 (57.8%)	P= 0.82 P>0.05
TT	7 (29.7%)	5 (15.6%)	
C	87 (39%)	91 (55.5%)	P= 0.59
T	41 (61%)	37 (44.5%)	P>0.05
Odds ratio	0.863 (0.51-1.47) %95 CI		

Table 4. The distribution of MTHFR A1298C genotypes and allele frequencies in CAD-MI cases and control groups.

MTHFR A1298C Genotype&Allele	CAD-MI n:64	Control n: 64	P value
AA	22 (34.4%)	27 (42.2%)	
AC	31 (48.4%)	29 (45.3%)	P= 0.59
CC	11 (17.2%)	8 (12.5%)	P>0.05
A	75 (39%)	83 (55.5%)	P= 0.30
C	53 (61%)	45(44.5%)	P>0.05
Odds ratio		0.767 (0.46-1.27) %95 CI	

Table 5. Distribution of Beta-fibrinojen -455 G>A & FXIII allele frequencies in CAD-MI cases and control groups.

Beta-fibrinojen -455 G>A	CAD-MI n:64	Control n: 64	P value
G	101 (78.9%)	103 (80.5%)	P= 0.75
A	27 (21.1%)	25 (19.5%)	P>0.05
Odds ratio		0.908 (0.49-1.67) %95 CI	
FXIIIV34L	MI/KAH n:64	Control n: 64	P value
V	99 (77.3%)	103 (80.5%)	P= 0.54
L	29 (22.7%)	25 (19.5%)	P>0.05
Odds ratio		0.829 (0.45-1.51) %95 CI	

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Evaluation of the Effect of Smoking on Nesfatin-1 Level

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Research Article

History

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ABSTRACT

Abstract

Nesfatin-1 is a recently discovered adipocytokine that is believed to regulate food intake and is linked to body mass index. While its precise mechanism of action remains unclear, a deeper understanding of how nesfatin-1 interacts with metabolic diseases, inflammation, and insulin resistance could have significant implications for the treatment of a wide range of conditions, including cardiovascular disease. Smoking is a complex issue with roots in social, cultural, and economic factors that can contribute to nicotine addiction. Additionally, nicotine's ability to stimulate the mind and promote feelings of relaxation can create a positive feedback loop that makes it difficult to quit. Unfortunately, there is limited research on the effects of smoking on Nesfatin-1 levels. However, one study found that women who smoke tend to have lower levels of Nesfatin-1. To build on this finding, the present study aims to further investigate nesfatin-1 levels in both smokers and non-smokers.

A total of 70 participants, smokers (n=35) and non-smokers (n=35), were included in the study. The participant's gender, age, height and weight, body mass index, and nesfatin-1 levels were measured and compared. The SPSS 23.0 program was used to evaluate the data statistically. Data were evaluated with a t-test. The error level was taken as 0.05.

Serum Nesfatin-1 levels were significantly higher in smokers (13.73± 3.11) than in non-smokers (8.63 ± 0.91) (t=-9.315, p<0.01). No significant difference was found between other parameters in the smoker and non-smoker groups.

The study has shown that individuals who smoke display higher levels of Nesfatin-1 compared to non-smokers, indicating a correlation between smoking and Nesfatin-1. However, further investigation is required to understand the mechanism behind this increase. It is hoped that continued research will unveil the potential of Nesfatin-1 in treating human obesity.

Keywords: Smoking, Nesfatin, Nutrition

Sigara Kullanımının Nesfatin-1 Düzeyi Üzerine Etkisinin Değerlendirilmesi

Süreç

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ÖZ

Nesfatin-1, besin tüketimini düzenleyen ve vücut kitle indexi ile ilişkili bulunan yeni bir anoreksojenik adipositokindir. Nesfatin-1'in vücutta ne şekilde etkili olduğu yeterince incelenmemiştir. Nesfatin-1'in metabolik hastalıklar, insülin rezistansı ve enflamasyondaki rolü tam olarak anlaşılması durumunda başta kardiyovasküler hastalıklar olmak üzere birçok hastalığın tedavisine katkı sağlayabilir Sigara içme, özellikle nedenleri açısından önemli bir ruhsal-toplumsal sorundur. Toplumsal, kültürel ve ekonomik etmenler nedeniyle nikotin bağımlılığı sık gelişmektedir. Nikotinin aynı zamanda ruhsal açıdan uyarıcı nitelik taşıyan bir madde olması, duygu durumunu olumlu yönde değiştiren, rahatlatıcı etkisinin olması, bir yanda kullanımını artırmakta, diğer yandan sigaranın yarattığı sonuçlara duyarsızlık yaratmakta, bırakma çabalarını azaltmaktadır. Sigara kullanımının Nesfatin-1 üzerine etkisiyle ilgili eldeki veriler çok sınırlıdır. Yapılan bir çalışmada sigara içen kadınlarda Nesfatin-1 düzeyi düşük bulunmuştur. Bu amaçla sigara kullanan ve kullanmayan kişilerde Nesfatin-1 düzeylerini değerlendirmek için bu çalışma planlanmıştır.

Verilerin istatistiksel analizinde SPSS 23.0 programı kullanıldı. Elde edilen veriler t testi ile değerlendirildi ve yanılma düzeyi 0.05 olarak alındı. Araştırmaya sigara içen (n=35) ve sigara içmeyen (n=35) toplam 70 kişi dahil edildi. Katılımcıların cinsiyet, yaş, boy kilo, beden kitle indeksi ve nesfatin-1 düzeyleri ölçüldü ve karşılaştırıldı.

Serum Nesfatin-1 düzeyleri sigara içenlerde (13,73± 3,11) sigara içmeyenlere (8,63 ± 0,91) göre önemli ölçüde daha yüksekti (t=-9,315, p<0,01). Sigara içen ve içmeyen grupta diğer parametreler arasında önemli bir fark bulunmamıştır.

Sigara içen kişilerde sigara içmeyenlere göre serum Nesfatin -1 değerleri yüksektir. Bu Nesfatin-1 ve sigara arasındaki ilişkiyi göstermektedir. Sigaranın hangi mekanizma ile nesfatin-1 seviyesinde artmaya neden olduğunu açıklayabilmek için daha ileri araştırmalara gerek olmakla birlikte obezite tedavisinde nesfatin-1 uygulaması yapılabilir.

Anahtar sözcükler: Sigara, Nesfatin, Beslenme

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Introduction

Adipose tissue serves as both a fat storage and an endocrine organ, secreting various substances. Adipocytokines, or cytokines secreted within fat tissue, are divided into two types. Adiponectin is believed to have an anti-inflammatory effect, while adipocytokines like tumor necrosis factor alpha (TNF α), interleukin (IL)-6, monocyte chemoattractant protein 1 plasminogen activator inhibitor-1 have an inflammatory effect. Both types of adipocytokines need to be balanced in the body to prevent the development of diseases such as obesity, hypertension, diabetes-related vascular complications, and atherosclerosis. While recently discovered adipocytokines like omentin, visfatin, nesfatin, vaspin, and chemerin are not yet fully understood, nesfatin-1 is thought to have a contractile effect on vascular structures and could impact blood pressure [1].

Nesfatin-1 is a novel adipocytokine with anorexogenic properties that modulates food intake and is linked to body mass index. While several cytokines, including TNF alpha, are involved in atherosclerosis and systemic inflammation, the precise mechanisms by which nesfatin-1 exerts its effects remain insufficiently understood[2]. Interestingly, existing research suggests that nesfatin-1 may also contribute to the inflammatory response[3,4].

Similar to conditions such as Type 2 Diabetes Mellitus, obesity, insulin resistance, hypertension, and metabolic syndrome, smoking is a significant risk factor for atherosclerosis and systemic inflammation. A comprehensive understanding of nesfatin-1's role in metabolic diseases, insulin resistance, and inflammation could potentially aid in treating various ailments, particularly cardiovascular, neurovascular diseases, and it can be used as biomarker[3-5].

Currently, there is a lack of sufficient research regarding the evaluation of nesfatin-1 levels in smokers and non-smokers. Our study aims to assess nesfatin-1 levels in both smokers and non-smokers.

Materials and Methods

This study was conducted at Cumhuriyet University Faculty of Medicine Research and Practice Hospital and involved a volunteer patient group. The patients had a history of smoking for at least one year and were not discriminated against based on age or gender. We also included a control group of healthy, non-smoking volunteers. To ensure the study's validity, we excluded patients with previous chronic diseases or current active infections. Hemogram and CRP results were obtained through routine examinations, and Nesfatin-1 levels were studied in blood samples taken from a sufficient number of patients. We did not exclude any patients against their will, and the study was concluded once we reached our target number of 35 volunteer smokers and 35 healthy non-smoker control groups. Patient and control group information was accessed from patient files or created patient forms. Blood samples were taken from patients who had fasted overnight, and Nesfatin-1 levels were determined after centrifugation and storage at -80 °C. The researcher covered the expenses for Nesfatin-1.

Nesfatin-1 levels were analyzed at the Biochemistry Laboratory of Cumhuriyet University Faculty of Medicine Research and Application Hospital using commercial Elisa kits (Cat no: EK-067-52, lot no: 603894; Phoenix Pharmaceuticals, Belmont, CA, USA). The analysis was concluded upon reaching the target file scan. Statistical analysis of patient group data was performed using SPSS 23.0 software, and a t-test was used to evaluate the data. The significance level was set at 0.05

Ethics Committee Approval

Prior to conducting the research, ethics committee approval was obtained from Cumhuriyet University Interventional Clinical Research Ethics Committee (decision number 2019-03/02). In this manner, individuals provided informed consent before their participation.

Results

The findings indicate that serum nesfatin-1 levels were notably elevated in smoking patients (13.73 ± 3.11) when compared to the non-smoking control group (8.63 ± 0.91) ($t=-9.315$, $p<0.01$). However, there were no significant differences observed in other parameters between the smoker and non-smoker groups, as presented in Table 1.

Grup	Smokers (n=35) (X±SD)	Non-smokers (n=35) (X±SD)	Test Result
Nesfatin-1	13,73 ±3,11	8,63±0,91	t=-9,315, p<0,01
Age	37,37±12,23	35,49±11,42	t=-0,667, p>0,05
Height	171,63±7,27	171,49±8,52	t=-0,075, p>0,05
Weight	73,23±12,78	73,49±10,59	t=0,092, p>0,05
BMI	25,48±3,50	25,50±3,28	t=0,028, p>0,05

Discussion

While there has been some research on the impact of smoking on nesfatin-1, the available data is limited. Nesfatin-1 is a promising therapeutic agent for various diseases, but its potential role in addressing the obesity epidemic is particularly interesting. Obesity is a major health concern both domestically and globally, and understanding the biochemical mechanisms that influence our eating behaviors is critical. One such mechanism is nesfatin-1, a peptide that suppresses appetite[6]. Interestingly, nicotine, the primary metabolic component of smoking, has also been shown to suppress appetite, potentially suggesting a link between the two[7,8].

Numerous studies have explored the correlation between nesfatin-1 levels and various biochemical parameters. Early research indicated that adipokines have a regulatory effect on energy metabolism and may be linked to obesity-related metabolic disorders as well as inflammatory diseases[9,10]. Additionally, adipokines have been linked to inflammatory lung conditions[11], with most studies focusing on the role of leptin and adiponectin in these diseases. Some studies have shown that asthma can be predicted independently of obesity by high leptin and low adiponectin, while low leptin and high adiponectin are associated with stable COPD[12]. However, there are still conflicting results regarding the relationship between COPD and adipokines, and certain adipokines linked to chronic inflammatory diseases have not yet been studied[13]. One particular study found that serum nesfatin-1 levels were significantly lower in patients with obstructive sleep apnea syndrome (OSAS) than in healthy controls and that intravenous administration of nesfatin-1 to rats increased blood pressure and eliminated the decreases in blood pressure caused by sodium nitroprusside[14].

Furthermore, Zhao et al. reported that plasma nesfatin-1 levels were significantly higher in hypertensive patients. Studies conducted on control groups, significantly overweight/obese hypertensive patients, indicate that nesfatin-1 plays a role in gonadal development, as it increases during the pubertal transition period and premature thelarche[15]. Finally, Park et al. found that while smoking reduced plasma testosterone levels and caused a decrease in sexual function, it did not significantly decrease estrogen levels in women[16].

Although the role of nesfatin-1 in obesity is not yet fully understood, it is believed to interact with other molecules that regulate appetite, particularly leptin or melanocortin. Research has shown that nesfatin-1 is secreted from neurons in the brain regions that control energy balance. This appetite-regulating effect is independent of many transmitter systems but is related to the melanocortin system[17].

Several studies have explored the relationship between nesfatin-1 levels and BMI. For example, a study by Abacı et al.(2013) found that serum nesfatin-1 levels were significantly lower in obese children than in the control group. Ramanjaneya et al.'s (2010) study of adults showed a positive correlation between plasma nesfatin-1 levels and BMI. However, this study did not find a significant statistical difference between BMI and nesfatin-1 levels.

Conclusion

Nesfatin-1 has shown promise as a valuable target for developing non-toxic drug therapies to aid in the treatment of obesity and preventing weight gain after smoking cessation. Further comprehensive studies are needed to explore its effectiveness in controlling the increase in appetite that occurs after quitting smoking and other similar habits, as well as investigating all of its metabolic and endocrine

effects. With continued research, nesfatin-1 may prove to be a helpful tool in the fight against human obesity.

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Is the Safe Cholecystectomy Technique Really Safe?

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Research Article

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ABSTRACT

Abstract

This study aims to present the results of a single surgeon's experience to demonstrate the effectiveness of the 'Critical View of Safety' (CVS) technique in preventing bile duct injuries in clinical practice.

We retrospectively reviewed the records of 899 patients who underwent cholecystectomy using the CVS technique performed by a single surgeon at the Sivas Cumhuriyet University Hospital General Surgery Department between 2018 and 2023. Ethical approval for the study was obtained. Cholecystectomy cases were scanned retrospectively. The patients' age, gender, drain placement, surgery indications, and reason for switching to open cholecystectomy were recorded.

Among the 899 patients reviewed, 312 were male (34.70%), and 587 were female (65.30%). The average age was 55.10 for males and 51,65 for females. It was determined that 7(0.77%), cases converted to open cholecystectomy. The most common indication for cholecystectomy was elective gallbladder stone removal, accounting for 47.05% of cases. No major bile duct injuries were detected..

The safe cholecystectomy technique can be safely applied to avoid bile duct injuries in laparoscopic cholecystectomy

Keywords: Cholecystectomy, Bile duct injuries, Critical View of Safety

Güvenli Kolesistektomi Gerçekten Güvenli mi?

Süreç

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Kabul: 27/12/2023

ÖZ

Bu çalışma, klinik pratikte safra yolu yaralanmalarının önlenmesinde 'Eleştirel Güvenlik Görüşü' (CVS) tekniğinin etkinliğini göstermek için tek bir cerrahın deneyiminin sonuçlarını sunmayı amaçlamaktadır.

2018-2023 yılları arasında Sivas Cumhuriyet Üniversitesi Hastanesi Genel Cerrahi Anabilim Dalı'nda tek cerrah tarafından CVS tekniği kullanılarak kolesistektomi yapılan 899 hastanın kayıtları retrospektif olarak incelendi. Çalışma için etik onay alındı. Kolesistektomi olguları geriye dönük olarak tarandı. Hastaların yaşı, cinsiyeti, dren yerleşimi, ameliyat endikasyonları ve açık kolesistektomiye geçiş nedenleri kaydedildi.

İncelenen 899 hastanın 312'si (%34,70) erkek, 587'si (%65,30) kadındı. Erkeklerde yaş ortalaması 55,10, kadınlarda ise 51,65' idi. Olguların 7'sinin (%0,77) açık kolesistektomiye dönüştüğü belirlendi. Kolesistektominin en yaygın endikasyonu safra kesesi taşının elektif olarak çıkarılmasıydı ve vakaların %47,05'ini oluşturuyordu. Majör safra kanalı yaralanması tespit edilmedi.

Laparoskopik kolesistektomide safra yolu yaralanmalarını önlemek için güvenli kolesistektomi tekniği güvenle uygulanabilir.

Anahtar sözcükler: Kolesistektomi, Safra yolu yaralanmaları, Güvenliğe Eleştirel Bakış

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Introduction

Over the past three decades, laparoscopic cholecystectomy has become a widely practiced method for gallbladder removal. Still, it has been associated with an increase in major bile duct injuries compared to open cholecystectomy[1-4]. Presently, among 1,000 patients undergoing laparoscopic cholecystectomy, two to four experience major bile duct injuries necessitating biliary reconstruction[5]. Despite the global acceptance of the 'Critical View of Safety' (CVS) for identifying critical anatomical structures such as the cystic duct, common bile duct, and cystic artery, major bile duct injuries continue to occur[6]. These injuries have serious consequences, including extended hospital stays, multiple invasive procedures, reduced quality of life, and increased mortality[7]. One of the significant factors leading to these complications during laparoscopic cholecystectomy is the adhesions that often result from prior or ongoing cholecystitis, causing challenges for surgeons and potential legal implications.

The CVS technique, conceptualized in 1995, has emerged as a critical and reproducible step to ensure safe cholecystectomy[8]. It involves three key components: (i) clearing all fibrous and fatty tissue from the hepatocystic triangle, (ii) dissecting the distal one-third of the gallbladder, and (iii) completely exposing the anatomy of the cystic duct and cystic artery. Various international guidelines have emphasized the importance of CVS as a fundamental step in safe cholecystectomy[9,10]. The primary focus of these guidelines is on the precise identification and dissection of critical anatomical structures related to the gallbladder.

This study aims to present the results of a single surgeon's experience to demonstrate the effectiveness of the CVS technique in preventing bile duct injuries in clinical practice.

Materials and Methods

We retrospectively reviewed the records of 899 patients who underwent cholecystectomy using the CVS technique performed by a single surgeon at the Sivas Cumhuriyet University Hospital General Surgery Department between March 2017 and March 2022. Ethical approval for the study was obtained.

In this technique, uniform principles were applied to all patients. As the initial step, the procedure involved clearing the Calot's triangle of fat and fibrous tissue and separating the gallbladder from the lowest part of the gallbladder bed (Figure 1). The second step focused on dissecting the lower end of the gallbladder, ensuring that only two structures, the cystic duct and cystic artery, remained(Figure 1). All cutting and ligating procedures were performed after achieving clear visibility of the entire anatomy at this stage. The final step involved using cautery to remove the lower part of the gallbladder from the gallbladder bed, completing the cholecystectomy.

The patient records were examined retrospectively, with evaluations based on age, gender, the use of drains, surgical indications, reasons for open conversion, and the development of complications.

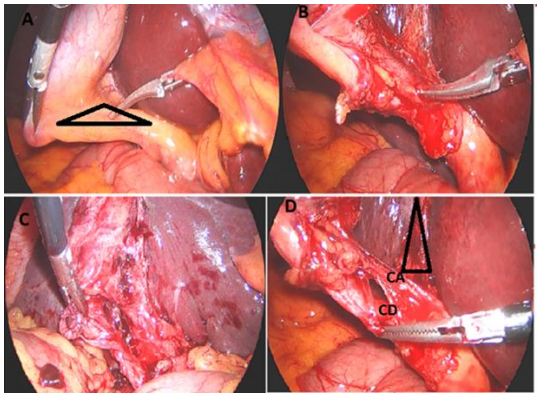

Figure 1:A: Calot's triangle. B, C: Clearing the Calot's triangle of fat and fibrous tissue and separating the gallbladder from the lowest part of the gallbladder bed. D: It ensures that only two structures (cystic duct and cystic artery) enter the gallbladder. CA: Cystic artery, CD: Cystic duct.

Results

Among the 899 patients reviewed, 312 were male (34.70%), and 587 were female (65.30%). The average age was 55.10 for males and 51,65 for females.

The most common indication for cholecystectomy was elective gallbladder stone removal, accounting for 47.05% of cases. Other indications included a history of pancreatitis or choledocholithiasis, acute cholecystitis (early cholecystectomy), gallbladder empyema, and gallbladder perforation (with percentages of 18.02%, 14.12%, 14.79%, 3.11%, and 1.44%, respectively).

Among the seven cases (0,77%) that required open conversion, two cases (28.57%) had severe inflammation, two cases (28.57%) had strong adhesions, two cases (28.57%) had anatomical irregularities, and one case (14.28%) involved bleeding.

After laparoscopic cholecystectomy, drains were placed in 402 patients (44.7%).

Table 1. Table of age and drainage catheter use according to cholecystectomy indications

Indication	Male	Female	total	Drein		
				No	Yes	Total
Planned Surgery	145	278	423	237	186	423
Dyspeptic Complaints	50	112	162	100	62	162
Pancreatitis, Choledocholithiasis	46	81	127	74	53	127
A Cholecystitis (Early Cholecystectomy)	47	86	133	65	68	133
Gallbladder Empyema	11	17	28	6	22	28
Gallbladder Perforation	7	6	13	2	11	13
Celiacystitis Planned Surgery	312	587	899	497	402	899
Total	145	278	423	237	186	423

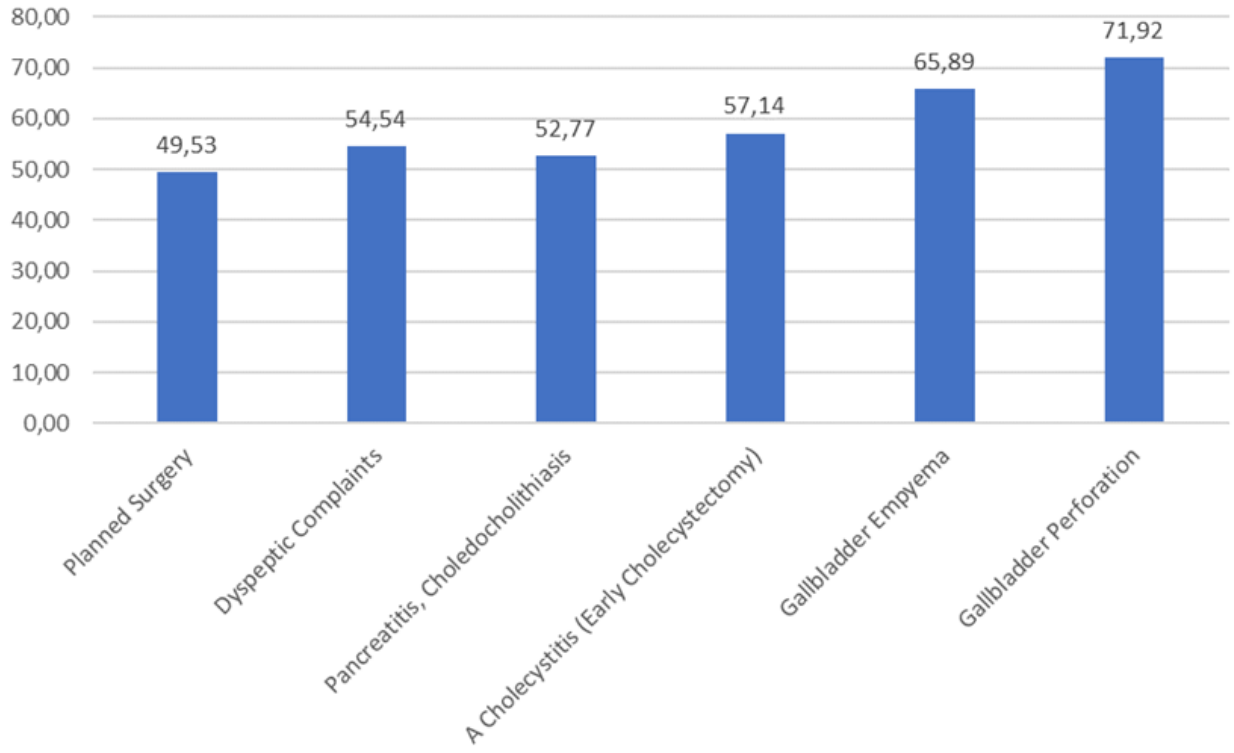

Figure 2. Figure of age according to cholecystectomy indications.

Discussion

Laparoscopic cholecystectomy is widely recognized as the gold standard for the surgical treatment of cholelithiasis. Nevertheless, the associated complications have been linked to mortality rates of up to 18%[11]. Factors contributing to these complications include inadequate surgical experience and insufficient dissection, which may result from challenges posed by anatomical variations and adhesions associated with previous cholecystitis[12,13].

The adoption of laparoscopic techniques as the gold standard in cholecystectomy has not only led to an increased complication rate but has also altered the nature of bile duct injuries, with more severe complications such as complete bile duct transections, thermal injuries, and central injuries caused by incorrect dissection of the hepatic hilum[15].

Various surgical techniques have been described in the literature to ensure the safe identification of ductal structures in laparoscopic cholecystectomy[16,17]. These techniques share the common goal of establishing an objective surgical method for recognizing the anatomical structures in this region.

While intraoperative cholangiography has been presented as an effective method for preventing bile duct injuries[18-19], it has not provided the expected level of protection. Moreover, it is known to present technical challenges and increase both the duration and cost of the operation.

The safe critical view technique, introduced by Strasberg in 1995[8], has been widely adopted by many surgeons. In this study, where our own cases were presented, we applied this technique to all patients, irrespective of whether their cases were elective or emergency. A single experienced surgeon performed these cases. Similar to the findings of Avginos[15], no major bile duct injuries were encountered.

The absence of bile duct injuries and the consistency in the surgical approach performed by the same surgeon underscore the significance of the surgical experience. Some studies in the literature highlight the decrease in the rate of injuries after a surgeon's first 50 cases, emphasizing the importance of factors based on experience, such as familiarity with anatomical variations, safe dissection techniques, and making the correct decisions regarding open conversion, as the number of cases increases[20,21].

Result: The safe cholecystectomy technique can be safely applied to avoid bile duct injuries in laparoscopic cholecystectomy

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Endoscopic Transcanal Stapes Surgery: Our Audiological and Surgical Results

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ABSTRACT

The aim of this study is to investigate the intraoperative and postoperative results of endoscopic stapes surgery performed at our institution.

A total of 25 patients with 28 ears (14 right, 14 left ears) who underwent endoscopic stapes surgery between 2018 and 2022 were analysed for postoperative hearing outcomes and surgical complications at the 6-month follow-up.

The average age of the patients was 43.16 years (range, 24-63 years), and 64.0% of the patients were female. The median preoperative air-bone gap decreased from 30.36 dB hearing level (HL) to 18.95 dB HL after surgery ($P < 0.001$). The postoperative air-bone gap was 10 dB or lower in 8 ears (28.6%), 11-20 dB in 10 ears (35.7%), and more than 20 dB in 6 ears (21.4%). Worse hearing outcomes were observed in 4 ears (4.14%). Intraoperative complications included only tympanic membrane ruptures in one patient, which resolved during the initial follow-up. Postoperatively, 10.7% of the subjects complained of changes in taste sensation. One patient developed facial paralysis responsive to steroid treatment one week after surgery.

Endoscopic surgery is particularly suitable for stapedial disorders. Endoscopic stapes surgery is minimally invasive and suitable for surgical training, as surgical anatomy can be easily understood, and both the surgeon and assistant can observe the procedure from the same monitor. The operation should only be performed by experienced surgeons due to the need for single-handed operation and the lack of stereoscopic vision.

Keywords: *Stapes; Stapedectomy; Outcomes; Endoscopic ear surgery*

Endoskopik Transkanal Stapes Cerrahisi: Odyolojik ve Cerrahi Sonuçlarımız

Süreç

Geliş: 11/10/2023
Kabul: 28/12/2023

ÖZ

Araştırmanın amacı, kurumumuzda gerçekleştirilen endoskopik stapes cerrahisinin intraoperatif ve postoperatif sonuçlarını incelemektir. 2018 ile 2022 yılları arasında endoskopik stapes cerrahisi geçiren 25 hasta, 28 kulak (14 sağ, 14 sol kulak) üzerinde yapılan çalışmada postoperatif işitme sonuçları ve cerrahi komplikasyonlar 6 aylık takipte analiz edilmiştir.

Hastaların yaş ortalaması 43.16 yıldı (24-63 yaş aralığı), hastaların %64'ü kadındı. Median preoperatif hava-kemik açıklığı, cerrahiden önce 30.36 dB işitme seviyesindeyken (HL), cerrahiden sonra 18.95 dB HL'ye düştü ($P < 0.001$). Postoperatif hava-kemik açıklığı, 8 kulağın (%28.6) 10 dB veya daha az, 10 kulağın (%35.7) 11-20 dB ve 6 kulağın (%21.4) 20 dB'den fazla olduğu görüldü. Dört kulakta (%4.14) daha kötü işitme sonuçları gözlemlendi. İntraoperatif komplikasyonlar sadece bir hastada timpanik membran yırtıkları içeriyordu ve bu, ilk takipte çözüldü. Postoperatif olarak, katılımcıların %10.7'si tat duyusundaki değişikliklerden şikayet etti. Bir hasta, cerrahiden bir hafta sonra steroid tedavisine yanıt olarak gelişen yüz felci yaşadı.

Endoskopik cerrahi, stapedial bozukluklar için özellikle uygundur. Endoskopik stapes cerrahisi minimal invazivdir ve cerrahi anatomiyi anlamak kolay olduğu için cerrahi eğitim için uygundur; cerrah ve yardımcı aynı monitörden işlemi izleyebilir. Ancak operasyon, tek elle gerçekleştirilmesi ve stereoskopik görüş eksikliği nedeniyle yalnızca deneyimli cerrahlar tarafından gerçekleştirilmelidir.

Anahtar sözcükler: *Stapes; Stapedektomi; Sonuçlar; Endoskopik Kulak Cerrahisi*

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Introduction

Otosclerosis, characterized by bone resorption and sclerotic bone formation in the temporal bone, can result in either conductive or mixed-type hearing loss. It was first described by Valsalva[1].

In 1953, Rosen introduced the original stapes procedure for managing otosclerosis. Since then, various surgical methods, including stapedectomy and stapedotomy, have been described. Traditionally, these surgical procedures have been performed using the operating microscope[2].

Compared to traditional microscopic approaches for middle ear surgery, endoscopic ear surgery (EES) is advocated for its distinct advantages, such as enhanced visualization and access, reduced postoperative pain, expanded experience in surgical education, and the diminished need for cutting the chorda tympani nerve[3,4].

The endoscopic approach, especially in stapes surgery, offers several advantages such as better visualization of the stapes and footplate, reduced bony canal removal, and prevention of endaural incision[5,6]. With these advancements, endoscopic stapes surgery provides similar auditory outcomes when compared to the microscopic technique[2,7].

Additionally, Sproat et al. reported a reduced likelihood of chorda tympani nerve damage, similar procedure durations, and postoperative audiological results between endoscopic and microscopic groups, with endoscopic patients experiencing less postoperative pain[8].

Despite the mentioned advantages, the use of endoscopy in surgery is limited by the fact that it requires the surgeon to operate with one hand while holding the endoscope. Additionally, theoretically, due to the two-dimensional nature of the endoscopic image, it does not provide depth perception. However, this limitation can be overcome by manipulating the endoscope to create a sense of spatial configuration between structures[7].

With the increasing availability of training courses in endoscopic ear surgery, surgical experiences have been globally shared, and endoscopic approaches have become a widespread option worldwide[9]. The purpose of this study is to investigate the intraoperative and postoperative outcomes of endoscopic stapes surgery performed at our institution.

Material And Methods

Population

This study was conducted on patients who presented with complaints of hearing loss to the Ear Nose Throat Clinic of Sivas Republic University between 2018 and 2022. These patients were initially suspected of having otosclerosis based on their medical history, physical examination, audiological, and radiological evaluations. The definitive diagnosis of otosclerosis was established, and surgical treatment was performed by our team. All parameters to be evaluated in the study were accessible from the patient records.

Pure Tone Audiometric Evaluation

Pure tone audiometric evaluations were conducted using the Interacoustics Clinic Audiometry device, AC-40 model (Interacoustics, Assen, Denmark). Audiological assessments were performed before the initiation of treatment and one year after the treatment. Pure tone averages for preoperative and one-year postoperative assessments were recorded. In the audiometric evaluation, air conduction pure-tone thresholds were examined at 250, 500, 1000, 2000, 4000, and 6000 Hz, while bone conduction pure-tone thresholds were examined at 500, 1000, 2000, 4000, and 6000 Hz.

Hearing levels were classified according to the indicator chart provided in Katz's Handbook of Clinical Audiology. Accordingly, patients hearing loss was categorized as follows: mild between 25-40 dB, moderate between 41-56 dB, moderately severe between 57-70 dB, severe between 71-90 dB, and profound for values above 91 dB, indicating severe hearing loss.

In addition to age, gender, and other demographic information, the evaluation of pure-tone threshold averages and air-bone gap (ABG) values was based on the preoperative and postoperative audiometric assessments of patients. The effect of the endoscopic stapedectomy technique on current hearing was determined by classifying the results (ABG<10 dB, ABG<20 dB).

Written and verbal consent was obtained from all volunteers included in the study, and those who agreed to participate were included.

Inclusion criteria for the study required that the cases had undergone surgical treatment with the endoscopic stapedectomy technique, had not used fluoride for medical purposes, and had no

pathologies other than otosclerosis detected during routine Ear Nose Throat examinations.

Surgical Procedure

Endoscopic stapes surgery (EES) was performed under general anesthesia with a transcanal approach in a hypotensive condition. For this surgical procedure, 0-degree endoscope tips with a length of 18 cm and a diameter of 2.7 mm, along with a high-resolution camera system (Karl Storz, Tuttlingen, Germany), were used. After intubation and sterilization, following the infiltration of a local anesthetic (20 mg/mL of lidocaine + 0.0125 mg/mL of epinephrine HCl) to reduce bleeding, a superior and inferior timpanomeatal flap elevation was performed approximately 7-8 mm lateral to the annulus. Care was taken to avoid damage to the chorda tympani while entering the middle ear.

Adequate bone curettage was performed from the scutum to ensure full visibility of the stapes and tendon and to allow for sufficient manipulation. The mobility of the ossicular system in the middle ear was assessed, along with the stability of the stapes footplate or movement of the incudomalleolar joint. The course of the facial nerve and the condition of other middle ear structures were also examined.

After confirming the stability of the stapes footplate, it was separated from the incudostapedial joint, and the stapes tendon was cut. The anterior and posterior crura were fractured to remove the stapes superstructure. A hole was carefully drilled in the footplate using a Microdrill to accommodate the piston. After that, a Teflon piston was hung on the long process of the incus, and the motion system was ensured. In selected cases for piston stability, bone cement was used on the incus and piston, and a fat graft was used around the piston to support it and prevent perilymph leakage. The motion system was checked, and the piston was laid over the tympanomeatal flap to prevent flap lateralization, supported with gel foam. Patients were discharged on the second day postoperatively after head elevation and received ear drops containing ciprofloxacin following external ear canal cleaning one week later. The first audiological evaluation after surgery was performed at 4-6 weeks. Additionally, audiological evaluations were repeated at 6 months and 1 year postoperatively.

Statistical Analysis

For the evaluation of the data obtained in the study, the SPSS (SPSS Inc., Chicago, IL) 23.0 software program was used. Complementary statistics such as arithmetic mean, standard deviation, median, and minimum-maximum values were used for data evaluation. The normality assumption was checked using the Kolmogorov-Smirnov or Shapiro-Wilk test. Parametric tests were used for values that met the normality assumptions, while non-parametric tests were used for values that did not meet the normality assumptions.

The relationship between two variables was examined using Pearson correlation and Spearman rank correlation. Chi-square analyses were used for categorical qualitative variables. A significance level of $p < 0.005$ was considered statistically significant.

Result

A total of 28 ears from 25 patients were included in the study, with 64% (n=16) being female and 36% (n=9) male. The average age of the patients was 43.16±11.44 years (ranging from 24 to 63 years). The average age of female patients was 44.00±11.23 years (ranging from 26 to 63 years), while the average age of male patients was 41.67±12.35 years (ranging from 24 to 58 years). There was no significant difference in age between females and males. Fourteen patients were operated on the right ear, and 14 patients on the left ear.

Changes in both air conduction and bone conduction were found to be statistically significant before and after surgery (Table-1).

Table 1. Changes in air conduction and bone conduction before and after surgery

	Mean	Std.Deviation	Minimum	Maximum	p
AC Pre-Op	54.0714	10.4027	33	80	0.001
AC Post-Op	38.6071	20.4565	10	90	
BC Pre-Op	23.5714	10.1267	12	52	0.010
BC Post-Op	20.0357	15.2352	5	65	

The patients' preoperative and six-month postoperative bone conduction thresholds, air-bone gap, and average postoperative air-bone gap improvement have significantly improved (Table-2).

Table 2. Preoperative and Six-Month Postoperative Bone Conduction Thresholds, Air-Bone Gap, and Average Postoperative Air-Bone Gap Improvement in Patients.

	BC	ABG	ABG.Gain
Preop	23,57±10,13 (12-52)	30,36±7,58 (13-47)	-
Postop	20,04±15,24 (5-65)	18,93±9,5 (5-40)	11,43±11,56 (-12-33)
p	0,01	<0,001	-

The results of the air-bone gap show a significant improvement compared to the preoperative levels ($p < 0.001$). The postoperative air-bone gap was 10 dB or lower in 8 ears (28.6%), 11-20 dB in 10 ears (35.7%), and more than 20 dB in 6 ears (21.4%). Worse hearing outcomes were observed in 4 ears (4.14%) (Figure 1).

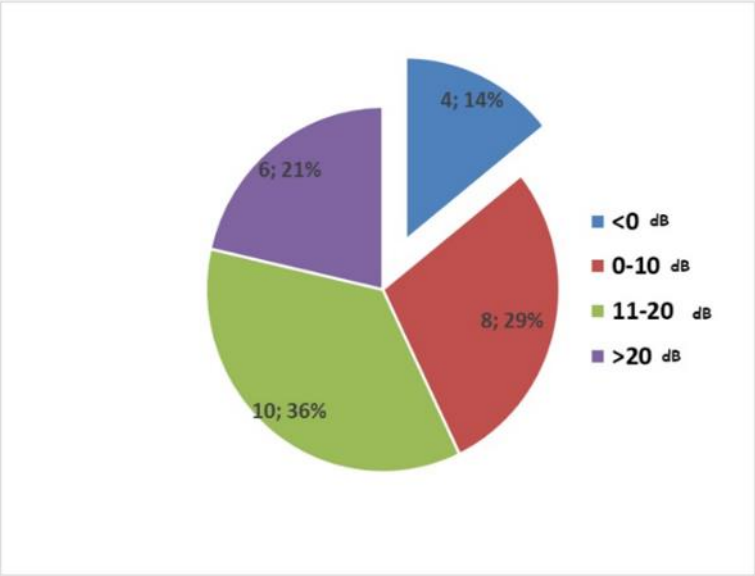

Figure1. Rate of change in the air-bone gap.

Worse hearing outcomes occurred in some patients due to the following reasons:

One patient who underwent surgery on the right ear had a reoperation one year after the initial procedure due to erosion of the prosthesis on the incus neck.

Two patients required reoperation because the prosthesis became dislodged.

Surgery was canceled for one patient who was planned for surgery on the left ear due to an extremely narrow external auditory canal that would not allow passage of the endoscope.

In one patient where the facial nerve was exposed, facial paralysis responsive to steroid treatment developed one week after surgery. In one patient, a perforation of approximately 2x1 mm in the tympanic membrane was closed during surgery using a fat graft harvested from the earlobe, and the postoperative examination showed an intact tympanic membrane. Three patients reported a disturbance in their sense of taste. No patient experienced severe vertigo.

Discussion

Stapes surgery is the gold standard treatment for otosclerosis. Initially, this surgery was performed using a microscope. However, as endoscopic ear surgery became popular among otologists, literature reviews have revealed an increasing number of studies each year, and the amount of data that can be gathered about EES procedures is growing[10].

The first results related to EES were published by Tarabichi in 1999, and they observed a postoperative decrease of <10 dB in ABG in 85% of cases[11]. In the 2000s, due to strong criticism from the otological community and very few published studies on EES, there were almost no results reported. However, in the decade from 2010 to 2020, new studies began to emerge. In 2016, a study by Daeshi et al.[12] reported a <20 dB decrease in ABG in 94% of cases and a <10 dB decrease in 58% of cases. Another study by Hunter et al.[13] showed a 90% reduction in ABG <20 dB. Naik et al. reported outcomes from their series of 20 EES cases, where 55% of patients achieved complete closure of the air-bone gap, 30% had mild conductive hearing loss (up to 20 dB), and 2 cases had mixed hearing loss (BC up to 30 dB and air-bone gap up to 20 dB). They also mentioned a case where a patient initially experienced improvement in hearing after surgery but developed a moderate conductive hearing loss of 35 dB at the 10th week due to adhesions[14]. In our study, we obtained better hearing results with an 86% improvement in ABG. Among these ears, the postoperative air-bone gap was 10 dB or lower in 8 ears (28.6%), 11-20 dB in 10 ears (35.7%), and more than 20 dB in 6 ears (21.4%). In the 4 ears who did not achieve the desired hearing outcome, one had erosion of the prosthesis on the incus neck one year after surgery, two had dislodgement of the prosthesis, and one had worse hearing due to an extremely narrow external auditory canal that would not allow the passage of the endoscope.

In the initial follow-up, postoperative dysgeusia was recorded in 10.7% of patients, a range that falls between 0% to 61.9% as reported for traditional microscopic stapes surgery[15,16]. High rates of postoperative dysgeusia have been noted with minimal chorda tympani nerve manipulation, which is common in endoscopic stapes surgery[17]. Additionally, it is important to note that being close to the light source during surgery can potentially affect the chorda tympani nerve[18]. However, the impact of light intensity on the sense of taste has not yet been researched. Interestingly, the extent of chorda tympani nerve damage does not always align with the degree of changes in taste sensation, as only 50% of patients with chorda tympani nerve sectioning reported alterations in taste sensation[16]. Late facial nerve palsy (House-Brackmann grade 3) occurred in one of the patients one week after surgery. In this patient, there was facial nerve dehiscence. No damage was inflicted on the facial nerve during surgery, and the temporary facial paralysis improved within 1 month after medical. The use of bone cement to stabilize the piston and incus was considered a possible risk factor. Timpanic membrane perforation, as reported by Jacob B. Hunter and colleagues, occurred in approximately 8% of cases. In our case series, only one patient experienced a perforation of approximately 2x1 mm in size during the surgery. This perforation was closed with a fat graft taken from the earlobe during the operation, and postoperatively, the tympanic membrane was found to be intact[18].

All patients who underwent endoscopic surgery experienced mild postoperative dizziness.

Despite the limited number of cases examined in this study, the safety of endoscopic surgery was observed based on the frequency of complications. However, stapes surgery is challenging, and complications can lead to significant sensorineural hearing loss.

Conclusion

Endoscopic surgery, especially for stapedial diseases, is suitable and offers a minimally invasive approach. It is also conducive to surgical education, as surgical anatomy can be easily understood, and both the surgeon and assistant can observe the procedures on the same monitor. However, due to the need for single-handed operation and the lack of stereoscopic vision, it should only be performed by experienced surgeons.

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Is a pathological assessment required following pilonidal sinus surgery? 10-year retrospective analysis

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Research Article

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ABSTRACT

Pilonidal sinus is most often seen in men between the ages of 15-30. It is regarded as a benign condition that most frequently affects the sacrococcygeal area. However, malignant degeneration can occur at a rate of 0.1%. Malignant degeneration patients tend to be older than 50, untreated for a long time, or to have relapsed frequently. Squamous cell carcinoma (SCC) is the most frequent type of cancer to appear on the pilonidal sinus's base. The first course of treatment is surgery. After surgery, local recurrence rates have been estimated at 40%. Adjuvant radiotherapy or chemoradiotherapy has an effect in reducing recurrence. In this study, we looked at the frequency of cancer and potential risks as well as the value of routine pathological evaluation in patients who underwent pilonidal sinus surgery in our clinic during a ten-year period.

We performed a retrospective analysis of 1070 patients who underwent pilonidal sinus surgery at the Recep Tayyip Erdogan University Training and Research Hospital between January 2012 and June 2022.

After a retrospective analysis of 1070 cases, 0.18% (n=2) of them had a malignancy developed on the basis of the pilonidal sinus, and the pathological result of both patients was reported as SCC. Additionally, one patient had histology that revealed tissue from the pilonidal sinus with a high Ki-67 index and significant mitotic activity. The mean age of the two patients with malignancy was 51. Patients with cancer were found to have complained for approximately 20 years. The patient with high Ki-67 index and mitotic activity was 60 years old, and had complaints for about 10-11 years.

Pilonidal sinus has a risk of malignancy in patients with long-term existence, multiple recurrences, and those over 50 years of age. Despite the low rates of malignancy in the pilonidal sinus or the advanced age and long-term disease of the patients with malignancy risk, we advocate pathological examination of all specimens.

Keywords: Pilonidal sinus, malignant transformation, squamous cell carcinoma

Kıl dönmesi ameliyatı sonrası patolojik değerlendirme gerekli midir? 10 yıllık geriye dönük analiz

Süreç

Geliş: 11/11/2022
Kabul: 19/12/2023

ÖZ

Giriş: Pilonidal sinüs, sıklıkla 15-30 yaş aralığında ve erkeklerde görülmektedir. En sık olarak sakrokoksigeal bölgede görülmekte olup benign bir hastalık olarak kabul edilir. Ancak %0.1 oranında malign dejenerasyon da gelişebilmektedir Malign dejenerasyon saptanan hastaların büyük kısmı 50 yaş üstünde, uzun dönem tedavi olmamış veya birçok kez nüks etmiş vakalardır. Pilonidal sinüs zemininde gelişen malignitelerde en sık olarak squamoz sellüler karsinom (SCC) görülmektedir. Tedavide ise cerrahi ilk seçenektir. Cerrahi sonrası lokal nüks oranları %40 düzeylerinde bildirilmiştir. Lokal nüksü azaltmada adjuvan radyoterapi veya kemoradyoterapinin etkisi vardır. Çalışmamızda, pilonidal sinüs nedeniyle kliniğimizde 10 yıllık bir süreçte opere edilen olgularda, malignite insidansını ile olası riskleri saptamak ve rutin uygulanan patolojik incelemenin değerini gözden geçirmek amaçlanmıştır.

Yöntem: Çalışmamızda Ocak 2012- Haziran 2022 tarihleri arasında T.C. Sağlık Bakanlığı Recep Tayyip Erdoğan Üniversitesi Eğitim ve Araştırma Hastanesi Genel Cerrahi Kliniğinde pilonidal sinüs hastalığı nedeniyle opere edişmiş 1070 olgu retrospektif olarak incelenmiştir.

Bulgular: 1070 olgu retrospektif incelenmesi sonrasında %0.18'inde (n=2) pilonidal sinüs zemininde gelişmiş olan malignte mevcuttu ve her iki hastanın patolojik sonucu ise SCC olarak rapor edilmişti. Ayrıca bir hastada da patoloji sonucunda, Ki-67 indeks ve mitotik aktivitesi yüksek olan pilonidal sinüse ait doku saptandı. Malignite saptanan iki hastanın yaş 0rtalaması 51 idi. Malignite saptanan hastaların yaklaşık 20 yıl kadar süredir şikayetlerinin var olduğu saptandı. Ki-67 indeks ve mitotik aktivitesi yüksek olarak saptanan hasta ise yaşı 60 idi ve bu hastanın da yaklaşık 10-11 yıl kadar şikayetlerinin var olduğu saptandı.

Sonuç: Pilonidal sinüs, uzun dönem var olan, çoklu olarak nüks eden ve 50 yaş üzerinde olan hastalarda malignite riskine sahiptir. Pilonidal sinüste malignite oranlarının düşük olması veya malignite riski olan hastaların da ileri yaş ve uzun dönem hastalıklı olmasına rağmen tüm spesmenlerin patolojik incelemesinin yapılması taraftarıyız.

Anahtar sözcükler: Pilonidal sinus, malignant transformation, squamous cell carcinoma

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Introduction

Pilonidal sinus is a disease characterized by chronic inflammation, first described by A.W.Anderson in 1847[1]. It is generally encountered in the 15-30 age range and in male[1,2]. Although it is most commonly seen in the sacrococcygeal region, it can also be detected in many different localizations such as the umbilicus, axilla, penis, and anal canal[3].

Although pilonidal sinus has been accepted as a fairly common benign disease, malignant degeneration can also develop at a rate of 0.1%[4,5]. Most of the patients with malignant degeneration are over 50 years of age, have not been treated for a long time or have relapsed many times[5,6]. Detection of ulceration, seropurulent discharge, and peripheral adenopathy in a long-term pilonidal sinus area should suggest that malignant degeneration may have developed[7]. Continuous and uninterrupted tissue damage due to chronic inflammation is thought to cause malignant degeneration ranging from hyperplasia to invasivecarcinoma[6,8]. Squamous cellular carcinoma (SCC) is most commonly seen in malignancies developing in the pilonidal sinus basis. More rarely, basal cell carcinomas and adenocarcinoma cases have also been reported[3,9].

Although malignancies developing due to the pilonidal sinus show slow growth, local invasion and metastasis tendency are observed (10). Surgery is the first choice in treatment. Reconstructions can be made with wide excision and flap if necessary[10,11]. Local recurrence rates after surgery have been reported as 40%. Adjuvant radiotherapy or chemoradiotherapy have an effect in reducing local recurrence[11].

In our study, it was aimed to determine the incidence of malignancy and possible risks and to review the value of routine pathological examination in patients who were operated for pilonidal sinus in our clinic over a 10-year period.

Material Method

In our study, 1070 patients who were operated for pilonidal sinus disease in the General Surgery Clinic of Recep
Tayyip Erdoğan University Training and
Research Hospital between January 2012 and June 2022 were retrospectively analyzed. Age, gender and pathological reports of the patients were evaluated. Ethics committee approval was obtained from the Ethics Committee of Recep Tayyip Erdogan University Training and Research Hospital, dated November 2022 and numbered 2022/198.

Statistical Analysis

Data IBM SPSS Statistics for Windows Armonk, NY, USA, IBM Corp. analyzed with software. Numerical data obtained in the study are shown with mean and standard deviation values, and categorical data are shown with numbers and percentages. The relationship between age and gender was evaluated with the Mann Whitney U test, $p<0.05$ was accepted as the statistical significance limit.

Results

Between January 2012 and June 2022, 1070 patients who were operated on for pilonidal sinus disease in the General Surgery Department of the Recep Tayyip Erdoğan University Training and Research Hospital were retrospectively analyzed. Of these patients, 0.18% (n=2) had malignancies developed on the basis of the pilonidal sinus, and the pathological result of both patients was reported as SCC. In addition, as a result of pathology, tissue belonging to the pilonidal sinus with high Ki-67 index and high mitotic activity was detected in one patient. Since there was no carcinomatous tissue as a result of the pathology in this patient, it was not classified as a malignancy that developed on the basis of the pilonidal sinus.

Of the 1070 patients evaluated, 84.2% (n=901) were male and 15.8% (n=169) were female. The mean age of the patients was 28.6 (Table 1).

The ages of two patients with malignancy were 50 and 52 years old. The average was 51. When the complaints of two patients with cancer were examined for the duration of their occurrence, it was found that both patients' problems had been present for around 20 years. The patient with high Ki-67 index and mitotic activity was 60 years old, and this patient had complaints for about 10-11 years.

Table 1.Age and gender informationofthepatients

	Male	Female	p
Mean age (±SD)	29.5 (± 9.8)	24.1(± 7.4)	p=0,103
Gender (%)/ (n)	84,2 (n=901)	15,8 (n=169)	p<0.001

Discussion

Pilonidal sinus disease is most common between the ages of 15-30 and is more common in males[2]. Of 1070 patients evaluated retrospectively in our study, 84.2% (n=901) were male and 15.8% (n=169) were female. The mean age of the patients was found to be 28.6 (Table 1) Gender distribution and mean age values were consistent with the literature[5].

Bree et al. reported that 80% of the patients were male and the mean age was 52 years in their study on 59 cases of malignancy developed on the basis of the pilonidal sinus[11]. Another study indicated that individuals with malignant degeneration of the pilonidal sinus were on average 54 years old[12]. In our study, two patients with malignancy were male and the mean age was 51.

Pilonidal disease is a benign condition, however numerous studies have indicated that it has a low malignancy risk of 0.1%. (4,5). Alarcóndel et al. analyzed 3729 cases retrospectively and found malignancy secondary to pilonidal sinus in 4 cases (0.11%)[12]. Boulanger et al. 731, Akin et al. on the other hand, examined 2486 patients retrospectively and stated that they did not detect any malignancy in pilonidal sinus excision materials in their series (13,14). In our study, the incidence of malignant degeneration was found to be 0.18% in pilonidal sinus cases.

While basal cell carcinoma and adenocarcinoma are infrequently observed, up to 94% of malignancies that arise on the basis of the pilonidal sinus are SCC[12]. In our study, SCC was detected in two patients with malignancy. In the literature, it is seen that the disease has been present for at least 10 years in cases with malignancy and the average age of the patient is 50[6,8] Considering the cases with malignancy, it is seen that the disease has not been treated for a long time and/or there are frequent recurrences. Malignant degeneration is thought to develop secondary to chronic inflammation. It is thought that free oxygen radicals released in tissues due to chronic inflammation disrupt DNA repair mechanisms, and then degeneration from hyperplasia to carcinoma develops in the tissues[6]. It was learned that 2 patients with malignancy in our patient group had complaints for about 20 years. A third patient, 60 years old and known to have had the disease for about 10 years, was not reported as malignant, but Ki-67 proliferation index and mitotic activity were found to be high. The surgical margin was found to be clean in the excision material of the patient and close follow-up was recommended in terms of recurrence. The increase in Ki-67 index and mitotic activity is accepted as an indicator of proliferation in tumor lesions[15]. We believe that such a situation in our patient overlaps with the theory in the process of malignant degeneration due to pilonidal sinus.

In the clinical evaluation, a long-term and/or recurrent pilonidal sinus, sinus openings in the gluteal regions on both sides of the midline, ulcerated mass lesion, seropurulent discharge and inguinal adenopathy can be seen[5,10,15]. In our study, two patients with clinical complaints for about 20 years and SCC, and the third patient who had complaints for about 10 years, had multiple sinus openings extending to the bilateral gluteal regions and persistent seropurulent discharge complaints on physical examination. No inguinal lymphadenopathy was detected.

Due to the low risk of malignancy related to the pilonidal sinus and the fact that malignant degeneration cases are generally over 50 years of age and have been ongoing for at least 10 years, ideas have emerged that pathological examination should not be performed in all patients or that pathologic examination should be performed in selected patients[5,8,18] There are also publications in the literature that there is no malignancy in large case series. During World War II, no malignancy was reported in 86333 young and acutely symptomatic pilonidal sinus patients[17]. Boulanger (731 cases) and Akın (2486 cases) stated that they did not detect

any malignancy in their case series[13,14]. No cancer was detected in the study of Yüksel et al., which involved 905 patients[18]. However, there are also studies reporting that malignant degeneration has been detected. Retrospective analysis of 3729 patients by Alarcón-del et al. revealed 4 cases of cancer at the pilonidal sinus base. (0.11%)[12].The quality of medical care must be maintained while retaining cost effectiveness, even though needless pathological investigation is regarded to negatively affect labor and cost analysis. The management of pathology samples is very important for the patient for the correct diagnosis of the diseases and then for the correct treatment. In addition, it should be kept in mind that the examination of pathological plays is under legal protection with the "Law on Tissue Collection, Storage and Transplantation" in our country[19]. In this context, although the risk of malignancy is low, we believe that routine pathological examination is necessary.

Conclusion

In conclusion, although pilonidal sinus is seen as a benign disease, there is a risk of malignancy, especially in patients with long-term existence, multiple recurrences, and those over 50 years of age. Early treatment of the disease will reduce the risk of developing malignancy. Despite the low rates of malignancy in the pilonidal sinus or the patients at risk for malignancy, advanced age and long-term disease, we advocate pathological examination of all specimens.

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Salivary Gland Ductal Carcinoma of Accessory Parotid Gland

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ABSTRACT

Salivary gland ductal carcinoma (SDC) is a rare, aggressive tumor with a highly malignant course and originates most frequently from the parotid gland among the major salivary glands. The incidence of accessory parotid gland (APG) varies between 21-56% and the incidence of tumor in APG is 1-8% of all parotid tumors. SDC is rarely seen in accessory glands. It was aimed to present our case, which was diagnosed with SDC in APG, in the light of the literature.

Keywords: Salivary duct carcinoma, accessory parotid gland, diagnosis, treatment

Aksesuar Parotis Bezinin Tükürük Bezi Duktal Karsinomu

Süreç

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ÖZ

Tükrük Bezi Kanal Karsinomu (TBKK), nadir, agresif bir tümördür ve genellikle büyük tükrük bezleri arasında parotis bezinden en sık köken alır. Aksesuar parotis bezi (YPB) insidansı %21-56 arasında değişir ve APG'deki tümör insidansı tüm parotis tümörlerinin %1-8'ini oluşturur. TBKK, yardımcı bezlerde nadiren görülür. Bu yazıda, APG'de TBKK tanısı alan vakamızı literatür ışığında sunmayı amaçladık.

Anahtar sözcükler: Tükrük bezi duktal karsinomu, aksesuar parotis bezi, tanı, tedavi

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Introduction

Ductal carcinoma (SDC) is microscopically similar to high-grade ductal carcinoma of the breast in both in-situ and invasive patterns[1]. It is a rare, aggressive salivary gland malignancy with high metastasis and recurrence rates. It was first described in 1968 by Kleinsasser et al[2]. This rare and aggressive tumor has 21 primary subtypes defined by the World Health Organization[3]. SDC accounts for 0.2-9% of salivary gland tumors[4]. Although there are cases reported in the submandibular gland (8%) and minor glands (4%), it often originates from the parotid gland (88%)[5].

Locoregional and distant metastasis rates are high. It is generally observed over the age of 50 (most commonly 60-65 years) and more frequently in men than in women (male/female: 4/1). Clinically, SDC is quite aggressive and typically patients present with a rapidly growing painful mass that often involves the facial nerve[6].

SDC treatment; includes total parotidectomy and ipsilateral neck dissection, followed by adjuvant chemo-radiotherapy or postoperative radiotherapy and targeted therapies[3].

However, the prognosis of SDC is poor and the mortality rate of the cases within 5 years is 60%[4].

There is no standard treatment option for patients with recurrence and metastasis.

The incidence of accessory parotid gland (APG) varies between 21-56%. they are usually less than an inch in diameter. They are located 6 mm anterior to the parotid gland, close to the Stensen canal, between or deep within the zygomatic and buccal branches of the facial nerve[7]. The incidence of tumor in APG is 1-8% of all parotid tumors[7,8]. Patients whose tumors are detected in APG usually apply to clinics with swelling in the cheek area. 26-52% of these masses observed in APG are malignant. SDC in this accessory structure is rarely seen and its incidence is not known for certain[8].

For this reason, it was aimed to present our case who was diagnosed with SDC from APG in the light of the literature.

CASE REPORT

A 76-year-old male patient was admitted to our clinic with the complaint of a painless, hard mass in the left cheek region, which has been growing steadily for two years. In the physical examination of the patient, a firm, fixed and painless mass with irregular borders, approximately 4x3 cm in size, was detected in the zygomatic region, approximately 2 cm lateral from the left preauricular region, adjacent to the masseter muscle. Facial nerve examination of the patient was normal (Figures. 1,2).

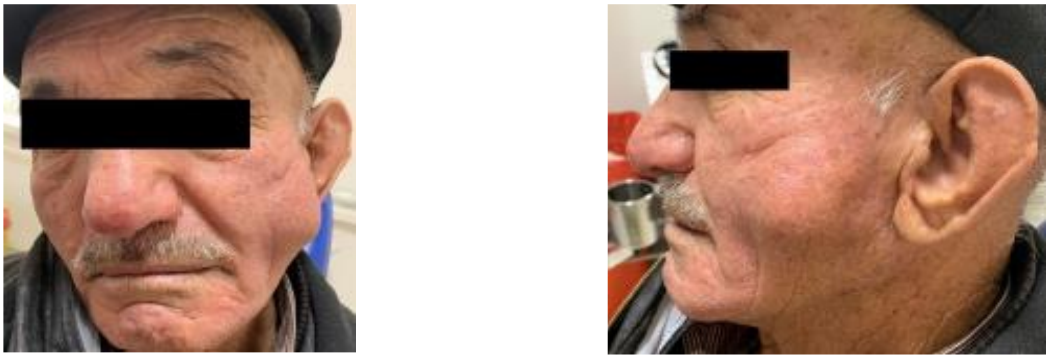

Fig. 1,2. Patient with a 4*3 cm mass in the zygomatic region

Contrast-enhanced neck-diffusion magnetic resonance imaging examination revealed that the left parotid gland is 40x33 mm in size in its widest part, adjacent to the superficial lobe anterior part and masseter muscle, heterogeneous in the T2W periphery with diffusion restriction and intensely contrasting, heterogeneous hypointense in the T2A periphery, and T1A containing cystic necrotic areas in the center, which is thought to be high proteinaceous was observed (Figures. 3, 4). No pathological lymphadenopathy was detected in the neck. Considering the clinical and radiological findings, it was thought that the patient had a pathology originating primarily from the accessory parotid gland. Fine needle aspiration biopsy (FNA) was performed on the patient.

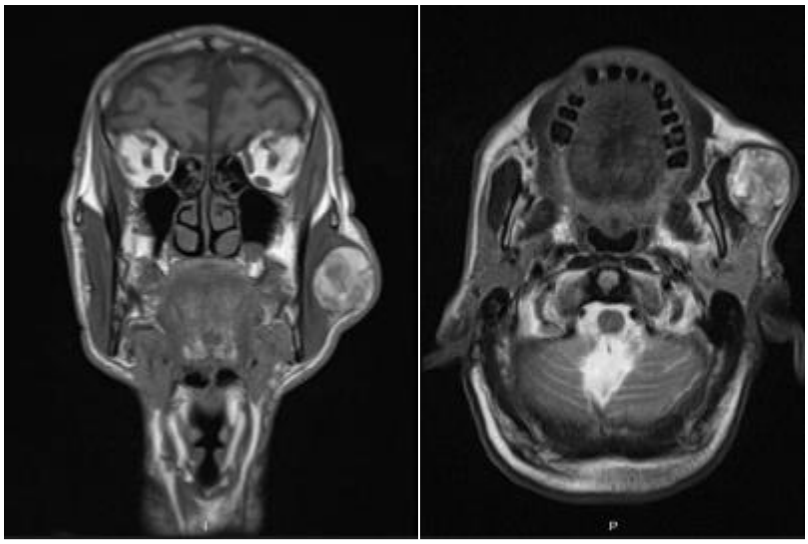

Fig. 3, 4: Contrast-enhanced neck-diffusion magnetic resonance imaging examination of the mass

In the cytopathological examination of fine needle aspiration biopsy (FNAB), atypical epithelial cells with extensive cytoplasm, hyperchromatic eccentric nuclei with prominent nucleoli with increased N/S ratio which formed three-dimensional groups and papillary structures on smears. These features interpreted in the category of "suspected malignancy" according to the salivary gland fine needle aspirations MILAN classification (Fig. 5).

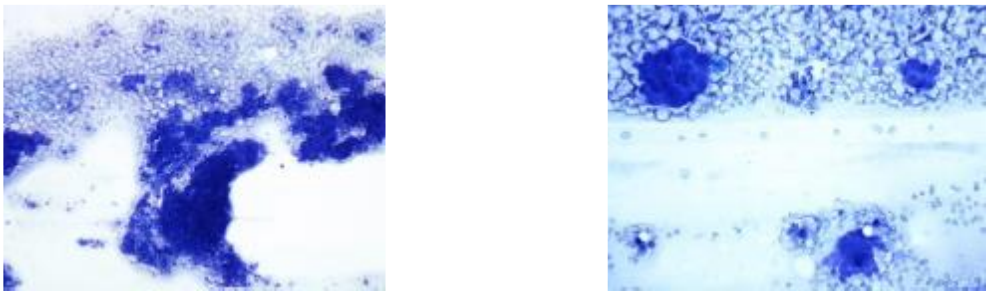

Fig. 5. Hypercellular smears consisting of atypical cells (MGGx100, MGGx200)

The patient was evaluated in the head and neck oncology council. It was decided to remove the mass in the cheek area and perform superficial parotidectomy, and to reevaluate the patient in the oncology council, according to the definitive pathology result.

Macroscopically, it weighs 22 g, measures 4.2x4x3.5 cm, has encapsulated nodular appearance, and consists of gray-white, brown-colored gelatinous areas with lobulation on the section face and heterogeneous yellow-orange-colored areas (Fig. 6). Histopathological examination of hematoxylin-eosin sections with light microscope dilated ductal structures with papillary areas, "Roman-bridge", or solid growth accompanied by comedo necrosis, tubular and cribriform structures with scirrhous pattern, apocrine appearance with large pleomorphic nuclei and abundant eosinophilic cytoplasm seen (Fig. 7). Surgical margins were negative. No perineural and lymphovascular invasion was observed. Immunohistochemical (IHC) stains, HER2 positive (score 3), Androgen (AR) positive, GATA3 positive, GCDFP-15 positive, CK5/6 focal positive, P63 negative were found (Fig. 8). The case was reported as ductal carcinoma of salivary gland with morphological and IHC features.

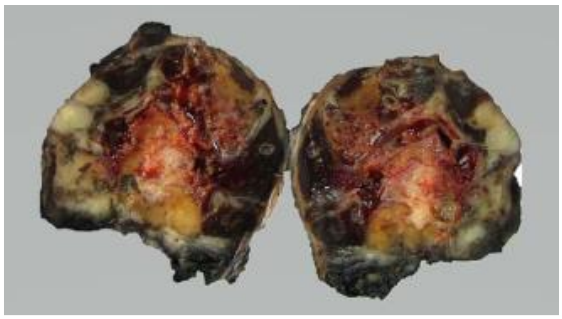

Fig. 6. Filling the entire gland hemorrhagic, grey-white-yellow solid and cystic areas were observed.

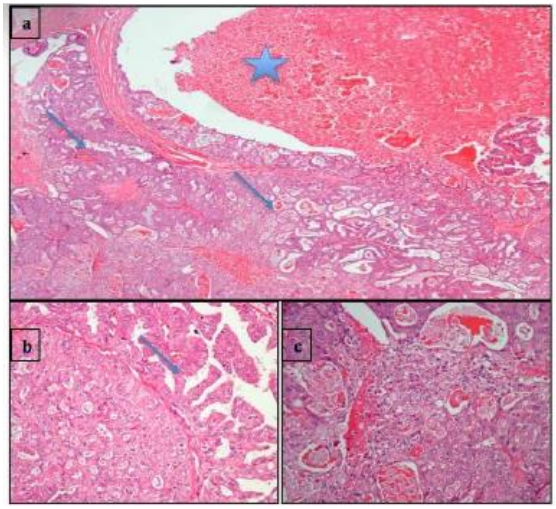

Fig. 7. a Tumor with cribriform ( ), papillary and solid patern and necrosis areas ( ) are observed (HEx40) b. Apocrine appearance and papillary structure ( ) (HEx200) c. There is pronounced pleomorphism and numerous mitoses (HEx200)

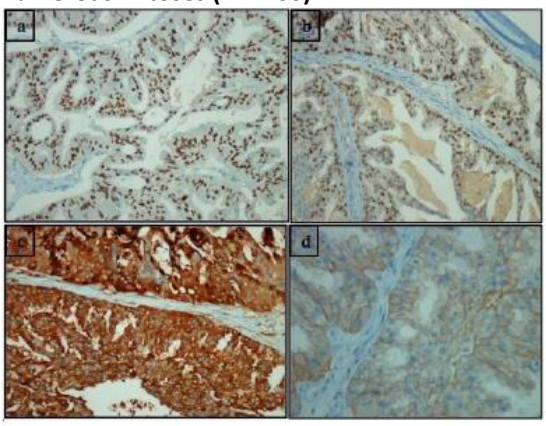

Fig. 8. Significant immunohistochemical stains (X200)
a. Nuclear Androgen expression b. Nuclear GATA 3 expression
c. Cytoplasmic GCDFP 15 positive d. Complete membranous HER 2 expression

Considering the tendency of TDC to make distant metastases, the case was evaluated radiologically. No distant metastases were detected.

The patient was consulted again in the oncology council. Radiotherapy was planned after total parotidectomy and neck dissection. Since the patient did not accept the operation, the treatment was completed as chemo-radiotherapy. After surgery and chemo-radiotherapy, follow-up continues for approximately one year, and no local recurrence and/or distant metastasis were observed during this period. No pathological finding was detected in the radiological follow-ups.

Discussion

SDC arises from the ductal epithelium of the salivary gland tissue and histologically resembles high-grade breast ductal carcinoma[9]. Most cases of SDC develop de novo, but some may arise from pre-existing carcinoma ex

pleomorphic adenoma[1]. Clinically, SDC presents as a firm, painful, rapidly growing mass that causes facial paralysis and tends to metastasize to the temporal bone via perineural spread. Although SDC is most commonly seen in the parotid gland; It can also be seen in the submandibular and sublingual glands, minor salivary glands, larynx, parapharyngeal region and sinonasal region[10]. Patients often present with a rapidly growing mass, facial paralysis, pain and local regional metastases. At the time of diagnosis, 46-60% of the cases have multiple lymph node metastases[11]. Clinically, SDC is characterized by cervical lymph node involvement, high recurrence rate, distant metastasis, and high mortality. Distant metastases are frequently found in the bones and lungs, but liver and brain metastases can also be observed in these cases[12]. Local regional metastases are frequently observed in cervical lymph nodes. Cervical lymph node involvement in SDC at the time of diagnosis varies between 50-82.5% in the series in the literature[13]. It has been 50 years since SDC was first described and numerous cases have been reported in the literature. These case reports generally focused on the clinical features of the cases, diagnosis and treatment approaches, prognosis and genetics of the tumor. In our literature review, SDC studies and case reports, including clinical series, show that the tumor usually involves the parotid gland and that the most prominent clinical symptoms are facial paralysis and pain. SDC also has strong neuronal tropism. Due to this feature, there are case reports in the literature that draw attention to the possibility of metastasis to the mandible and intracranial region by holding the facial nerve or its branches[12-13]. FNA has become widely accepted as an efficient first line diagnostic test in the management of salivary gland lesions. The reported overall sensitivity of salivary gland FNA in most series ranges from 86% to 100%, and the specificity ranges from 90% to 100%[14]. It was evaluated with the MILAN classification, an evidence-based system that associates the FNA diagnostic categories of the case with the risk of malignancy and clinical management strategies. SDC are easily recognized cytologically as high-grade carcinomas, but often require additional methods for more specific classification. The gene expression pattern of SDC is quite similar to that of molecular apocrine breast carcinoma such as AR, HER 2[15]. Masubuchi et al. AR positivity and EGFR positivity were associated with better DFS in patients with SDC, and they stated that anti-AR, anti-HER2 and/or anti-EGFR targeted therapies may be beneficial. In our case, AR, HER 2 positivity was also present[16]. In addition, diagnostically, GATA 3 and GCDFP 15 positivity and p63 negativity are also helpful in diagnosis. The FNAB of our case was evaluated with the MILAN classification, and it was decided by the oncology council to use the histopathological result instead of the FNAB result in the surgical planning, since it was interpreted in the "suspicious malignancy" category. Ductal carcinoma of APG is very rare, so we could not reach an incidence reported in the literature. The biggest problem in APG tumors, which are very rare, is the preoperative diagnosis stage; The most important diagnostic criterion is APG and the physician's suspicion of malignancies in this region[17]. There is currently no consensus on the surgical treatment of APG; however, superficial parotidectomy is a safe surgical procedure with high survival and low morbidity rates[18].

Conclusion

Due to the rarity of salivary duct carcinoma, there is a lack of comprehensive documentation in the literature regarding its clinical features, treatment, and clinical outcomes. In a number of case reports and small case series, it has been pointed out that aggressive clinical behavior, regional lymph node involvement and a tendency to distant metastasis are present. The most important difference of our case from SDC cases in the literature is the diagnosis of SDC of accessory parotid gland while investigating the origin of the fast growing, painless and non-facial paralysis mass detected in the zygomatic region. In addition, the mass did not show neuronal tropism as expected, and it differed from other cases in the literature.

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False positive ecstasy (MDMA) urine drug screening test results due to bupropion use: A case report

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ABSTRACT

Abstract

This case report is about a false positive ecstasy (MDMA) result in the urine substance abuse screening analysis of a person using the antidepressant drugs bupropion and sertraline with a therapeutic indication. Urine drug and stimulant screening analysis of a 25-year-old male patient who is history of bupropion (300 mg/day) and sertraline (100 mg/day) use, followed in the Amatem polyclinic due to the probation law, was performed with Syva® Emit® II Plus kits and immunoassay method. In order to confirm the ecstasy test, which was positive in the screening analysis, the substance analysis was repeated on the same sample with the gas chromatography sequential mass spectrometry (GC-MS) method and ecstasy was not detected in the confirmation analysis. At the same time, the presence of bupropion and sertraline patient declared to use, was confirmed with the LC-MS-Iontrap device. In conclusion, with this case example, we wanted to highlight the potential interaction of bupropion with the Syva® Emit® II Plus urine ecstasy screening tests, which could lead to false positive results. When positive ecstasy values are detected in the urine samples analyzed with the immunoassay method in patients using bupropion, the final decision should be made after a confirmatory analysis.

Keywords: N-methyl-3, 4-methylenedioxy-amphetamine, MDMA, ecstasy, false positive reactions, Enzyme Multiplied Immunoassay Technique, bupropion

Bupropion kullanımına bağlı hatalı pozitif ecstasy (MDMA) idrar uyuşturucu tarama testi sonuçları: Bir olgu sunumu

Süreç

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ÖZ

Bu olgu raporu, terapötik endikasyonla antidepresan etkili ilaçlar olan bupropion ve sertralin kullanan bir kişide yapılan idrarda madde kötüye kullanım tarama analizinde yanlış pozitif sonuçlanmış ekstazi (MDMA) sonucu ile ilgilidir. Denetimli serbestlik yasası nedeniyle Amatem polikliniğinde izlenen, öyküsünde bupropion (300 mg/gün) ve sertralin (100 mg/gün) kullanımı olan 25 yaşında erkek hastanın idrar uyuşturucu ve uyarıcı madde tarama analizi Syva® Emit® II Plus kitleri ile immunoassay yöntemi ile yapılmıştır. Tarama analizinde pozitif olarak sonuçlanan ekstazi testinin doğrulanması için aynı numunede madde analizi gaz kromatografi ardışık kütle spektrometre (GC-MS) yöntemi ile tekrar yapılmış ve doğrulama analizinde ekstazi saptanmamıştır. Aynı zamanda hastanın kullandığını beyan ettiği bupropion ve sertralin varlığı LC-MS-Iontrap cihazı ile doğrulanmıştır. Sonuç olarak, bu olgu örneği ile, bupropionun, Syva® Emit® II Plus idrar ekstazi tarama testleri ile yanlış pozitif sonuçlara yol açabilen potansiyel etkileşimi vurgulanmak istenmiştir. Bupropion kullanan hastalarda immunoassay yöntemi ile analiz edilen idrar örneklerinde pozitif ekstazi değerleri saptandığında, nihai kararın mutlaka bir doğrulama analizinden sonra verilmesi gereklidir.

Anahtar sözcükler: N-metil-3, 4-metilendioksi-amfetamin, MDMA, ekstazi, yalancı pozitif reaksiyonlar, enzim çoğaltılmış immünoassay tekniği, bupropion

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Introduction

N-methyl-3,4-methylenedioxy-amphetamine or 3,4-methylenedioxymethamphetamine (MDMA, ecstasy) is an amphetamine derivative that is abused for stimulating and hallucinogenic purposes. Ecstasy increases the net release of monoamine neurotransmitters and inhibits presynaptic re-uptake of serotonin[1]. In Europe, the prevalence of ecstasy use was 0.61% (0.51-0.83%) in 2018[2]. Ecstasy can be detected in urine with various immunochemical methods such as CEDIA (Clonned enzyme donor immunoassay), DRI (Diagnostic Reagents Incorporated) enzim immunoassay, EMIT (Enzyme mediated immunological technique) and FPIA (Fluorescence polarization immunoassay). Several prescription drugs such as ephedrine, pseudoephedrine and phenylpropanolamine may interfere with EMIT II Plus immunoassay tests and cause false positive ecstasy results[3]. Forensic threshold values are used when reporting urine drug abuse analysis. This value is 500 ng/mL for ecstasy. In this report, we describe a case who had a positive urine drug screen for ecstasy while being treated with bupropion and sertraline.

Case

25 years old male patient was admitted to our Amatem Outpatient Clinic (Illicit Drug Addiction Treatment Center) and received treatment for drug abuse. He was also taking bupropion 300 mg/day and sertraline 100 mg/day for the treatment of depression. Two-level control samples are studied before each ecstasy test. The high-level control value is 500 (400-600) ng/ml with a CV of 2.9%. Low-level control value is 360.0 (288.0-432.0) ng/ml, with a CV of 3.26%. Method performance evaluations for all drug and stimulant analyses are conducted every three months to assess repeatability and accuracy. During the performance evaluation, a sample pool prepared from patient samples in urine matrix is used for repeatability assessment. Intra-assay CV: 5.1%, Inter-assay CV: 4.2%. Ecstasy calibration is performed at five points using calibrators at concentrations of 1000, 750.0, 500.0, 250.0, and 0 ng/ml. The LOQ value for the ecstasy test is 5.0 ng/ml. The urine analysis with Syva® Emit® II Plus immunoassay (SIEMENS Dimension®) gave a positive result for ecstasy (772.0 ng/mL, cut-off value was 500.0 ng/mL). He denied that he had used any illicit drugs. The sample was analyzed with GC-MS for confirmation and the result was negative for ecstasy (<35.0 ng/mL). The presence of bupropion, sertraline and their metabolites in patient's urine was confirmed as qualitatively in LC-MS-Iontrap.

In 2009, using the Emit II method (Dimension, Siemens), in 2012 and 2013, using the Cedia immunochemical method (Thermo Scientific, USA) with the Olimpos automated analyzer at our hospital, tests for amphetamines, ecstasy, cocaine, marijuana, opiates, benzodiazepines, and barbiturates in the patient's urine were found to be negative. In the analysis conducted in 2015, the urine sample was tested using the EMIT immunochemical method (Siemens, Germany) with the Dimension automated analyzer (USA), and ecstasy was detected at a level of 772.0 ng/mL, reported as positive. The patient objected to the ecstasy result and he stated that he used bupropion and sertraline at the same time. The same urine sample underwent re-examination utilizing Gas Chromatography-Mass Spectrometry (GC-MS). After chromatographic separation and sequential mass measurement by GC MS method, it was determined that the ecstasy analyte was not found in the urine sample. In the following year, another urine sample from the same patient was tested in our laboratory, and ecstasy and other screened substances were found to be negative.

Discussion

Several studies, case-reports and the Syva® Emit® II Plus test label (SIEMENS Dimension®) suggest that bupropion may cause false positive results in the urine amphetamine and/or ecstasy tests [4-11]. This effect varies according to the bupropion dose and the selected threshold values of ecstasy or amphetamine which determined the test result is positive or negative. According to Syva Emit II plus Ecstasy kit prospectus[12]; some structurally related compounds like bupropion can produce a positive MDMA result equivalent to the 300 ng/mL and 500 ng/mL MDMA cutoff. Nixon et al. reported that, after the patient was treated with bupropion 300mg/day for 3 weeks, urine EMIT II monoclonal immunoassay of the patient became positive for amphetamines, whereas it was negative for methamphetamine and amphetamine by liquid chromatography[4]. Following the analysis of bupropion and its three major metabolites in monoclonal EMIT II immunoassay, it was reported that all four compounds showed cross reactivity to some extent [4]. In another case report by Vidal et al., following the use of sustained-release formulation of bupropion 150 mg/day for 14 days and 300 mg/day for 7 days, urine CEDIA analysis of the patient was positive for amphetamines/ecstasy. Subsequently, although amphetamine, methamphetamine, or amphetamine derivatives were not detected by GC/MS, bupropion was detected by GC/MS and LC/MS in urine 6. Öztürk et al. reported a positive urine toxicology assay

(repeated twice) for amphetamine and ecstasy in a patient who received risperidone 2 mg/day, mirtazapine 45 mg/day, venlafaxine 150 mg/day, quetiapine 550 mg/day, hydroxyzine 50 mg/day, bupropion 150 mg/day and acamprosate 1998 mg/day. One week after bupropion was discontinued, the urine analysis was negative for amphetamine and ecstasy[8]. In a retrospective study conducted with the patients presented to the emergency department in USA, it was reported that, bupropion had been prescribed to 41% (53/128) of patients whose samples were positive in urine amphetamine screening with Syva EMIT II Plus but were not confirmed by GC[9]. In a study by Marin et al., 100 false-positive EMIT II immunoassay specimens for amphetamine and/or ecstasy were analyzed in the Agilent 6230 time-of-flight (TOF) mass spectrometer to identify compounds that may cause false positive results in immunoassay tests in urine and bupropion was detected in 28 of these specimens[10]. In a retrospective study aimed to evaluate true positive and false positive rates of urine drug screen panels, 174 (2%) of 8825 specimens tested with Syva EMIT II Plus reagents were positive for MDMA, all of which subsequently were confirmed to be false positive by LC-MS-MS. These false positive specimens were tested using LC-MS-MS for the presence of bupropion and/or trazodone; two specimens contained bupropion only, one specimen contained both bupropion and trazadone[11].

In the literature, there is no publication related to the use of sertraline that can cause false positivity in MDMA screening with the urine immunochemical analysis method. In addition, Syva Emit II plus Ecstasy kit prospectus[12] indicated that, sertraline added drug free urine sample 125 µg/mL gave negative MDMA result for either 300 or 500 ng/mL ecstasy cutoff. However, it is indicated in the Syva Emit II plus Ecstasy kit prospectus that bupropion, a compound structurally related to MDMA, can give a positive MDMA result equivalent to the 300 ng/mL and 500 ng/mL MDMA cutoffs[12]. The performance of the ecstasy test during the period of examination of the sample related to the case presented in the study was determined to be acceptable through repeatability and accuracy measurements. The performance evidence of the ecstasy test parameter, with a LOQ value of 5.0 ng/ml and intra-assay and inter-assay CV values of 5.1% and 4.2%, respectively, was found to be below the total acceptable error limits. Therefore, the cause of false positive ecstasy in the urine during concomitant use of bupropion and sertraline in this case was associated with the use of bupropion. However, the patient's urine was not analyzed before and after bupropion medication, which is a limitation of our study.

Conclusion

Bupropion may interfere with Syva® Emit® II Plus urine ecstasy tests and cause false positive results. To make a definitive conclusion, more cases and further studies are required. The most important limitation of this case report was the lack of a negative Syva® Emit® II Plus urine ecstasy test following the cessation of bupropion (dechallenge). For the correct interpretation of urine drug analysis; taking a detailed over-the counter and prescription medication history of the patient is significantly important and further confirmation of the sample with advanced analytical methods such as GC-MS or LC-MS-MS is necessary.

Compliance with Ethical Standards:

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S.A.A. and N.A. worked for the Toksilab. No conflict of interest was declared by the other authors.

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