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Ege Tıp Bilimleri Dergisi

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Makalenin yayımlanması uygun bulunduktan sonra, tüm yazarlardan "Yayın Hakkı Devir Formu" nu imzalamaları istenir: " Biz aşağıda imzaları bulunan yazarlar, sunduğumuz makalenin orijinal olduğunu; başka bir dergiye yayınlanmak üzere verilmediğini; daha önce yayınlanmadığını; eğer, tümüyle ya da bir bölümü yayınlandı ise yukarıda adı geçen dergide yayınlanabilmesi için gerekli her türlü iznin alındığını ve orijinal telif hakkı devri formu ile birlikte Ege Tıp Bilimleri Dergisi Editörlüğü' ne gönderildiğini garanti ederiz."

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Yazar(lar), ticari bağlantı veya çalışma için maddi destek veren kurum varlığında; kullanılan ticari ürün, ilaç, firma vb. ile nasıl bir ilişkisi olduğunu sunum sayfasında Editöre bildirmelidir. Böyle bir durumun yokluğu da yine ayrı bir sayfada belirtilmelidir.

Yazı Türleri

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Orijinal makaleler: 3000 sözcük sayısını aşmamalı, "Özet (250 sözcükten fazla olmamalı), Giriş, Gereç ve Yöntem, Bulgular, Tartışma, Sonuç, Kaynaklar" bölümlerinden oluşmalıdır.

Olgu Sunumu: "Özet, Giriş, Olgu Sunumu, Tartışma, Kaynaklar" şeklinde düzenlenmelidir. En fazla 1000 sözcük ve 15 kaynak ile sınırlıdır. Sadece bir tablo ya da bir şekil ile desteklenebilir.

Editöre Mektup: yayımlanan metinlerle veya mesleki konularla ilgili olarak 500 sözcüğü aşmayan ve beş kaynak ile bir tablo veya şekil içerecek şekilde yazılabilir. Ayrıca daha önce dergide yayınlanmış metinlerle ilişkili mektuplara cevap hakkı verilir.

Yayın Kurulu'nun daveti üzerine yazılanlar dışında derleme kabul edilmez.

Makalenin Hazırlanması

Dergide yayınlanması istenilen yazı için aşağıdaki kurallara uyulmalıdır.

a) Yazı; iki satır aralıklı olarak, Arial 10 punto ile yazılmalıdır. b) Sayfalar başlık sayfasından başlamak üzere, sağ üst köşesinde numaralandırılmalıdır.

c) Online makale sistemine yüklenen word dosyasının başlık sayfasında (makalenin adını içeren başlık sayfası), yazarlara ait isim ve kurum bilgileri yer almamalıdır.

d) Makale, şu bölümleri içermelidir: Her biri ayrı sayfada yazılmak üzere; Türkçe ve İngilizce Başlık Sayfası, Özet, Abstract, Anahtar Sözcükler, Keywords, Giriş, Gereç ve Yöntem, Bulgular, Tartışma, Sonuç, Açıklamalar (varsa), Kaynaklar, Şekil Alt Yazıları, Tablolar (başlıkları ve açıklamalarıyla beraber), Ekler (varsa).

Yazının Başlığı

Kısa, kolay anlaşılır ve yazının içeriğini tanımlar özellikte olmalıdır.

Özetler

Türkçe (Özet) ve İngilizce (Abstract) olarak yazılmalı, Amaç, Gereç ve Yöntem, Bulgular ve Sonuç (Aim, Materials and Methods, Results, Conclusion) olmak üzere dört bölümden oluşmalı, en fazla 250 sözcük içermelidir. Araştırmanın amacı, yapılan işlemler, gözlemsel ve analitik yöntemler, temel bulgular ve ana sonuçlar belirtilmelidir. Özette kaynak kullanılmamalıdır. Editöre mektup için özet gerekmemektedir.

Anahtar Sözcükler

Türkçe Özet ve İngilizce Abstract bölümünün sonunda, Anahtar Sözcükler ve Keywords başlığı altında, bilimsel yazının ana başlıklarını yakalayan, Index Medicus Medical Subject Headings (MeSH)'e uygun olarak yazılmış en fazla beş anahtar sözcük olmalıdır. Anahtar sözcüklerin, Türkiye Bilim Terimleri'nden (www.bilimterimleri.com) seçilmesine özen gösterilmelidir.

Metin

Yazı metni, yazının türüne göre yukarıda tanımlanan bölümlerden oluşmalıdır. Uygulanan istatistiksel yöntem, Gereç ve Yöntem bölümünde belirtilmelidir.

Kaynaklar

Kaynaklar metinde yer aldıkları sırayla, cümle içinde atıfta bulunulan ad veya özelliği belirten kelimenin hemen bittiği yerde ya da cümle bitiminde noktadan önce parantez içinde Arabik rakamlarla numaralandırılmalıdır. Metinde, tablolarda ve şekil alt yazılarında kaynaklar, parantez içinde Arabik numaralarla nitelendirilir. Sadece tablo veya şekil alt yazılarında kullanılan kaynaklar, tablo ya da şeklin metindeki ilk yer aldığı sıraya uygun olarak numaralandırılmalıdır. Dergi başlıkları, Index Medicus'ta kullanılan tarza uygun olarak kısaltılmalıdır. Kısaltılmış yazar ve dergi adlarından sonra nokta olmamalıdır. Yazar sayısı altı veya daha az olan kaynaklarda tüm yazarların adı yazılmalı, yedi veya daha fazla olan kaynaklarda ise üç yazar adından sonra et al veya ve ark. yazılmalıdır. Kaynak gösterilen derginin sayı ve cilt numarası mutlaka yazılmalıdır.

Kaynaklar, yazının alındığı dilde ve aşağıdaki örneklerde görüldüğü şekilde düzenlenmelidir.

Dergilerdeki Yazılar

Kim CH, Cheon JS, Choi WY, Son KM. The efficacy of mobile application use on recall of surgical risks in nasal bone fracture reduction surgery. Arch Craniofac Surg. 2018; 19: 41-47.

Henüz yayınlanmamış online makale

Kurita GP, Højsted J, Sjøgren P. Tapering off long-term opioid therapy in chronic non-cancer pain patients: a randomized clinical trial. Eur J Pain. 2018 May 13. doi: 10.1002/ejp.1241.

Kitap

Bilgehan H. Klinik Mikrobiyoloji. 2. Baskı. İzmir: Bilgehan Basımevi; 1986:137-40.

Kitap Bölümü

McEwen WK, Goodner IK. Secretion of tears and blinking. In: Davson H (ed). The Eye. Vol. 3, 2nd ed. New York: Academic Press; 1969:34-78.

İnternet Makalesi

Abood S. Quality improvement initiative in nursing homes: The ANA acts in an advisory role. Am J Nurs [serial on the Internet] 2002 [cited 12 Aug 2002]. Available from: www.nursingworld.org/AJN/2002/june/wawatch.htm

Web Sitesi

Cancer-pain.org [homepage on the Internet]. New York: Association of Cancer Online Resources [updated 16 May 2002; cited 9 July 2002]. Available from: www.cancer-pain.org

Açıklamalar

Varsa finansal kaynaklar, katkı sağlayan kurum, kuruluş ve kişiler bu bölümde belirtilmelidir.

Tablolar

Tablolar metni tamamlayıcı olmalı, metin içerisinde tekrarlanan bilgiler içermemelidir. Metinde yer alma sıralarına göre Arabik sayılarla numaralandırılıp tablonun üstüne kısa ve açıklayıcı bir başlık yazılmalıdır. Tabloda yer alan kısaltmalar, tablonun hemen altında açıklanmalıdır. Dipnotlarda sırasıyla şu semboller kullanılabilir: *, †, ‡, §, ¶.

Şekiller

Şekil, resim, grafik ve fotoğrafların tümü "Şekil" olarak adlandırılmalı ve ayrı birer .jpg veya .gif dosyası olarak (yaklaşık 500x400 piksel, 8 cm eninde ve en az 300 dpi çözünürlükte) sisteme eklenmelidir. Şekiller metin içinde kullanım sıralarına göre Arabik rakamla numaralandırılmalı ve metinde parantez içinde gösterilmelidir.

Şekil Alt Yazıları

Şekil alt yazıları, her biri ayrı bir sayfadan başlayarak, şekillere karşılık gelen Arabik rakamlarla çift aralıklı olarak yazılmalıdır. Şeklin belirli bölümlerini işaret eden sembol, ok veya harfler kullanıldığında bunlar alt yazıda açıklanmalıdır. Başka yerde yayınlanmış olan şekiller kullanıldığında, yazarın bu konuda izin almış olması ve bunu belgelemesi gerekir.

Ölçümler Ve Kısaltmalar

Tüm ölçümler metrik sisteme (Uluslararası Birimler Sistemi, SI) göre yazılmalıdır. Örnek: mg/kg, µg/kg, mL, mL/kg, mL/kg/h, mL/kg/min, L/min, mmHg, vb. Ölçümler ve istatistiksel veriler, cümle başında olmadıkları sürece rakamla belirtilmelidir. Herhangi bir birimi ifade etmeyen ve dokuzdan küçük sayılar yazı ile yazılmalıdır.

Metin içindeki kısaltmalar, ilk kullanıldıkları yerde parantez içinde açıklanmalıdır. Bazı sık kullanılan kısaltmalar; iv, im, pove sc şeklinde yazılabilir.

İlaçların yazımında jenerik isimleri kullanılmalıdır.

İçindekiler

Orijinal Araştırma / Original Investigation
Aegean J Med Sci 2024;1:1-5

Comparision of The Salt Consumption Habits and Knowledge of The 1st Year and 6th Year Medical Faculty Students

Tıp Fakültesi 1. Sınıf ve 6. Sınıf Öğrencilerinin Tuz Tüketim Alışkanlıkları Ve Bilgi Düzeylerinin Karşılaştırılması

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ÖZET

AMAÇ: Dünya sağlık örgütü günlük en fazla 5 gram tuz tüketilmesi gerektiğini belirtmektedir. Ancak hem ülkemizde hem de dünyada günlük tüketilen tuz miktarı bu rakamın çok üzerindedir. Bizim bu çalışmadaki amacımız tıp fakültesine yeni başlamış 1. sınıf öğrencileri ile tıp fakültesinde 6. sınıfa gelmiş öğrencilerin tuz tüketimi hakkındaki bilgi düzeylerini ve alışkanlıklarını karşılaştırmaktır.

GEREÇ VE YÖNTEM: Toplam 279 katılımcıya yüz yüze sorular sorularak bilgiler elde edilmiştir. Çalışmanın bağımlı değişkeni; fakültemizde eğitim gören dönem 1 ve dönem 6 öğrencilerinin tuz tüketimi hakkındaki bilgi, tutum ve davranışları; bağımsız değişkenleri öğrencilerin fiziksel özelleri, ailenin eğitim düzeyi, kişinin kendisi ve ailesi ile ilgili fazla tuz tüketimine bağlı hastalık geçmişi, sosyo-kültürel düzeyi ve beslenme alışkanlıklarını sorgulayan sorular olmuştur.

BULGULAR: Toplam 279 katılımcının 193 tanesi dönem 1 öğrencisi, 86 tanesi ise dönem 6 öğrencisi idi. Aşırı tuz kullanımının vücuda olan zararlarını bildiklerini söyleyen öğrencilerin oranı dönem 1' de %76 ve dönem 6'da %94 olmasına rağmen restoranlarda tuz kısıtlaması destekleyenlerin oranı sırasıyla %41 ve %65 olarak tespit edildi. Günlük önerilen tuz tüketim miktarını bildiklerini söyleyenlerin oranı sırasıyla %18 ve %48 olarak saptandı. Ancak bildiklerini söyleyenler arasında doğru miktarı bilenlerin oranı sırasıyla %70 iken %75 olarak hesaplandı. Günlük önerilen tuz tüketim miktarına verilen yanıtların ortalaması ise dönem 1 öğrencilerinde 5.7±2.7 g iken dönem 6 öğrencilerinde 4.7±1 g olarak saptandı (p=0.033).

SONUÇ: Sonuç olarak ülkemiz tıp fakültelerinin birinde yapılan bu çalışmada tıp fakültesi öğrencilerinin tuz tüketimi ile ilgili bilinç düzeylerinin 1. sınıftan 6. sınıfa doğru giderken arttığı ancak yine de büyük bir çoğunluğun bu konuda farkındalıklarının az olduğu görülmüştür.

Anahtar Kelimeler: Tuz tüketimi; sodyum alımı; kardiyovasküler risk

ABSTRACT

OBJECTIVE: World Health Organization recommends maximum 5 gr of salt consumption in a single day. However, in our country and all over the World, the salt consumption rate is much more than this value. In this study, our aim was to determine and compare the salt consumption habits and knowledge of 1st year and 6th year medical school students.

MATERIALS AND METHODS: All of the data was gathered from 279 students by face-to-face questionnaire. The dependent variables of the study were knowledge, attitudes and behaviors of students about salt consumption and the independent variables were questions about the physical characteristics, the education levels of their families, medical history of the participants and their families, their socio-cultural levels and nutritional habits.

RESULTS: 193 of the 279 students were 1st year student and 86 of them were 6th year student. Although the proportion of students who said that they knew the harm of excessive salt use to the body was 76% in grade 1 and 94% in grade 6. The proportion of those who supported salt restriction in restaurants was 41% and 65%, respectively. Students who answered that they know the daily salt recommendation were 18% and 48%, however the ratio of the students who knew the correct value was 79% and 75% respectively. The mean average answer given to the daily recommended salt consumption amount was 5.7±2.7 g in the 6th year students and 4.7±1 g in the first year students (p=0.033).

CONCLUSION: As a result, in this study which was conducted in one of the medical faculties of our country, it was observed that the level of consciousness of medical faculty students about salt consumption increased from the 1st grade to the 6th grade, but still, the awareness of the majority of them was low.

Keywords: Salt consumption; sodium intake; cardiovascular risk

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INTRODUCTION

Salt, which is a simple chemical compound, is known systematically as sodium chloride; It is one of the most important foods consumed by people for centuries. Salt increases the durability of many foods and prevents them from rotting, thus allowing them to be stored for a long time, and the taste of the food increases with salt (1). In addition, as an important component of our body, it plays important roles in maintaining fluid-electrolyte balance, regulating blood pressure, and maintaining cell and organ functions (2).

The World Health Organization (WHO) recommends that the amount of salt that healthy adults consume should be no more than 5 g/day (3). However, due to today's lifestyle, food storage conditions, changes in eating habits, increased consumption of fast food and the presence of manufactured products on the shelves, the daily amount of salt consumed by people is highly above the WHO recommendation. In cross-sectional studies on salt consumption in many countries of the world, it has been determined that the daily salt consumption amount is up to 42 g per day (4, 5). In the SALTURK (The relationship between hypertension and salt intake in Turkish population) study, which is the most important study in this context conducted in our country, Turkish peoples' daily salt consumption amount was found approximately 18 g (6). This situation increases the risk of getting many diseases such as cardiovascular diseases, obesity, osteoporosis, diabetes and kidney diseases.

For public health policies, determining the amount of salt consumption in a population and knowing the peoples' awareness levels are very important. Since medical faculty students will be the ones who will raise our public awareness on this issue in the future, their level of awareness should increase during their education. For these reasons, our aim in this study was to compare the knowledge levels of Pamukkale University Faculty of Medicine 1st and 6th class students about WHO's salt consumption recommendation and to determine how they regulate their eating habits in this regard.

MATERIAL & METHODS

The population of this cross-sectional study consists of Pamukkale University Faculty of Medicine 1st and 6th grade students. It was planned to include all of the students in this study, however due to some students could not be reached, only those who were reached were included in the study. Pamukkale University Non-Interventional Clinical Research Ethics Committee approved this study (14.11.2023, E-60116787-020-448906).

Data were collected by asking students face-to-face questionnaire. The dependent variable of the study was knowledge, attitudes and salt consumption habits of the 1st and 6th grade students studying at our faculty. The independent variables were the physical characteristics of the students, the education level of his/her family, the history of diseases related to the student and his/her family due to excessive salt consumption, socio-cultural levels of students and their nutritional habits.

By scanning the literature, a questionnaire form with 30 questions (4 questions about the physical characteristics of the student, 2 questions about the education level of his/her family, 3 questions about the disease history of the student and his/her family, 8 questions about the his/her socio-cultural level, 13 questions about nutritional habits) was created.

The questionnaire was applied by also from medical faculty students determined within the program of Pamukkale University Faculty of Medicine special study module program.

SPSS program (version 22.0, SPSS, Inc., Chicago, IL) was used to analyze the data. Descriptive statistics are written as arithmetic mean ± standard deviation for continuous variables. Chi-square test was used to compare categorical variables. To determine whether the continuous variables were in normal distribution or not, Kolmogorov-Smirnov test was used. Student-t test of independent groups was used to compare parametric variables while Mann-Whitney U test was used to compare nonparametric variables. A post-hoc power analysis was performed by using G-power program and the post-hoc power of our study was found 99.8%. P value <0.05 was considered statistically significant.

RESULTS

A study questionnaire was asked to a total of 279 participants. 193 of the participants were Class 1 students and 86 were Class 6 students. 151 (54.1%) of the participants were women and 128 (45.9%) were men. Body mass index values of 6th grade students were found to be higher than those of 1st class students (p=0.049). Last year students consumed more alcohol and the number of

smokers was significantly higher than first class students. The basic demographic characteristics and social features of the participants are shown in Table 1.

Table 1. *Basic demographic and social characteristics of the participants*

	Class 1 students (n=193)	Class 6 students (n=86)	*p*
Age	18.9±1.0	24.1±1.1	<0.001
Male sex (%)	44.6	48.8	0.508
Height (cm)	171±9	173±8	0.112
Weight (kg)	65.1±14.5	69.3±15.3	0.033
Body mass index	21.9±3.5	22.9±3.5	0.049
Alcohol usage			0.017
Never (%)	50.3	32.6	
Sometimes (%)	44.6	62.8	
Regularly (%)	5.2	4.7	
Smoking			<0.001
Yes (%)	13	38.4	
No (%)	84.5	53.5	
Formers (%)	2.6	8.1	

Data are presented by mean ± standard deviation. Student-T-test and Chi-Square was used for analyses. n: number,

Information about the participants' nutritional habits, salt consumption habits and its relationship with diseases is given in Table 2. When "What do you think about the salt content of the foods you consume?" was asked to the students, approximately 65% of both groups replied "normal". However, those who think that they consumes too salty foods are 3 times more likely among 6th grade students compared to 1st grade students (9.3% vs. 3.1%).

Although it was seen that there is no extra salt consumption at the table in both groups, the consumption of fast food was higher in the 6th grade students. Those who said "yes" to the whether there is an existence of a relationship between salt consumption and cardiovascular diseases were statistically more common among 6th grade students (46.5% vs. 22.8%, p<0.001).

76% of Class 1 students and 94% of Class 6 students said that they knew the harms of salt consumption. Despite this, the percentage of those who said that they know the recommended daily salt consumption amount was 18% and 48%, respectively (Table 3). However, ratio of the students who knew the correct amount of WHO's salt consumption recommendation (5 gr/d) was 70% of above students in both groups.

Table 2. *Participants' nutritional habits, salt consumption habits and its relationship with diseases*

	Class 1 students (n=193)	Class 6 students (n=86)	*p*
What do you think about the salt amount of the foods you consume?			0.121
No salty (%)	5.2	2.3	
Low (%)	22.8	23.3	
Normal (%)	68.9	65.1	
High (%)	3.1	9.3	
How often do you eat fast food?			0.007
Never (%)	1.6	4.7	
Sometimes (%)	72	53.5	
Regulary (%)	26.4	41.9	
Do you add salt at the table?			0.648
Yes (%)	19.7	24.4	
No (%)	80.3	75.6	
Do you pay attention to the salt content of packaged foods?	5.7	11.6	0.091
Is there a relationship between salt and cardiovascular diseases?			<0.001
Yes (%)	54.4	89.5	
No (%)	45.6	10.5	
Participant who have a family member with hypertension (%)	22.8	46.5	<0.001
Participant who has a disease related with salt (%)	1.6	1.2	0.799

Data are presented by percentage. Chi-Square was used for analyses.

When students were asked "What is the recommended daily salt consumption amount?", the average of the answers was 5.7±2.7 g in the Class 1 and 4.7±1 g in the Class 6 students (p=0.033) (Figure 1).

Figure 1. *Participants' answers to the question "Recommended daily salt consumption amount"*

d

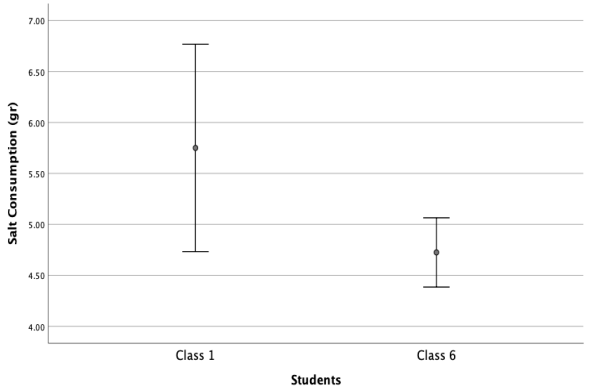

Table 3. *Participants' thoughts and knowledge levels on salt consumption*

	Class 1 students (n=193)	Class 6 students (n=86)	*p*
Do you know the harms of salt consumption?			<0.001
Yes (%)	76.2	94.2	
No (%)	23.8	5.8	
Do you support salt restrictions in restaurants?			<0.001
Yes (%)	40.9	65.1	
No (%)	59.1	34.9	
Is there salt awareness in our country?			0.406
Yes (%)	4.7	7	
No (%)	95.3	93	
Do you know the amount of salt recommendation by WHO?			<0.001
Yes (%)	18.7	47.7	
No (%)	81.3	52.3	
What is the amount of salt (gr) consumption recommendation daily?	5.7±2.7	4.7±1	0.033

Data are presented by mean ± standard deviation. Student-T-test and Chi-Square was used for analyses.

DISCUSSION

In this study, which was conducted to determine the knowledge, attitudes and behaviors of Pamukkale University Faculty of Medicine students regarding salt consumption, we found that 18.7% of the Class 1 students and 47.7% of the Class 6 students knew the correct amount of daily recommended salt by WHO. According to this result, medical school education contributes greatly to raising awareness of salt consumption. However, almost half of the students in the final year of medical school did not know the recommendation and this shows us that the importance of the salt consumption is still not fully understood by the students.

Similar to our study, many studies conducted in other countries have found that the maximum daily salt amount recommended by WHO is not known (7–9). This shows that Turkey is in the same situation as many countries in the world in terms of salt consumption awareness. Similar to our study, a study was conducted on the daily amount of salt consumed by medical school students in Angola, an African country, in 2015 (10). Students were selected as a random sample from each semester and the amount of sodium (Na) in the 24-hour urine was determined. According to the results of urine analysis, the students' average daily salt consumption was 14 g. Looking at the answers given by the students to the survey questions, it was determined that 99% of them knew the harms of salt consumption and 45% of them aimed to reduce their salt consumption by not adding extra salt at the table. However, since our study plan was to directly compare students who have just started medical school with students in their final year, it is acceptable that the knowledge level of first-year students may be low. However, the fact that students in the 6th grade still suffer from the lack of knowledge. This situation clearly demonstrates the necessity of eliminating the knowledge gap on this subject.

According to WHO data, salt consumption ways also change with the development levels of countries. For example, while fast foods and packaged products are the most important sources of salt in America and Scandinavian countries, salt added while cooking is the main source of consumption in many countries in Asia and Africa (11-13). In the SALTurK-2 study conducted in our country, the main source of salt was bread and the salt added while cooking (14). As a result of our study, when we compared the students' eating habits, it was determined that those who ate occasionally fast-food were 72% in Class 1 and 53.5% in Class 6 students. This percentage difference may be due to the fact that 6th grade students spend more time in the hospital and work more intensively.

The percentage of awareness about cardiovascular diseases caused by excessive salt consumption was 54.4% in Class 1 students and 89.5% in Class 6 students. As the level of education and the level of knowledge about medicine increased, effect of salt consumption in human body and its relation with diseases is well known.

According to the SALTurk study conducted in Turkey, the average daily salt intake of men was found to be higher than women (6, 14). The reason for this difference between genders may be due to differences in nutritional habits between men and women, such as men consuming more fast foods, having less habit of cooking at home, and preferring consumption outside the home. Likewise, the living conditions of the students, living apart from their families, inadequate cooking habits and turning to fast food consumption were important factors that affected the results of our study.

Our study has some limitations. First, this study was conducted in a single center with cross-sectional design, so

it does not represent the entire universe. Second, our study population consists of medical faculty students, so we cannot generalize it to other populations. Since each student does not have the same accommodation and food opportunities, their eating habits and salt consumption habits may differ. Third, the amount of salt consumption was not calculated objectively by looking at the salt excretion in the urine or the salt amount of the foods. Salt consumption habits are based solely on self-reports so they cannot be the actual amount of salt.

CONCLUSION

As a result, in this study which was conducted in one of the our medical faculties, it was observed that the awareness level of medical faculty students regarding salt consumption increased from the 1st grade to the 6th grade, but still the majority of them had low knowledge on this issue.

Etik: Çalışmanın geriye dönük olması dolayısıyla hastaların dosyaları taranmasında kurum izni alınmış olup, hastalardan ayrıca izin alınmamıştır. Çalışmaya dâhil edilen tüm hastalarda çalışma öncesinde yapılmış olan cerrahi işlem için bilgilendirilmiş onam formu alınmış olup hastane arşivindeki dosyalarında mevcuttur.

Since the study was retrospective, institutional permission was obtained for reviewing the files of the patients and no further permission was obtained from the patients. Informed consent form was obtained for the surgical procedure performed before the study in all patients included in the study and is available in their files in the hospital archive.

Yazar katkı durumu; Çalışmanın konsepti; SY, GD, RÇ, BK, NT, BBÇ, dizaynı; SY, GD, RÇ, BK, NT, BBÇ, Literatür taraması; SY, GD, RÇ, BK, NT, BBÇ, verilerin toplanması ve işlenmesi; SY, GD, RÇ, BK, NT, BBÇ, istatistik; SY, GD, RÇ, BK, NT, BBÇ, yazım aşaması; SY, GD, RÇ, BK, NT, BBÇ.

Author contribution status; The concept of the study; SY, GD, RÇ, BK, NT, BBÇ, design; SY, GD, RÇ, BK, NT, BBÇ, literature review; SY, GD, RÇ, BK, NT, BBÇ, collecting and processing data; SY, GD, RÇ, BK, NT, BBÇ, statistics; SY, GD, RÇ, BK, NT, BBÇ, writing phase; SY, GD, RÇ, BK, NT, BBÇ.

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REFERENCES

1. Hutton T. Sodium: Technological functions of salt in the manufacturing of food and drink products. British Food Journal. 2002; 104: 126–152.

2. Patel N, Patel D, Farouk SS, Rein JL. Salt and Water: A Review of Hypernatremia. Adv Kidney Dis Health. 2023; 30: 102-109.

3. www.who.int

4. Mozaffarian D, Fahimi S, Singh GM et al. Global sodium consumption and death from cardiovascular causes. N Engl J Med. 2014; 371: 624-634.

5. Öztürk Rİ, Garipağaoğlu M. Tuz tüketimi ve sağlık. Turkiye Klinikleri J Health Sci. 2018; 3: 57-65.

6. Yunus E, Arıcı M, Altun B et al. The relationship between hypertension and salt intake in Turkish population: SALTURK study. Blood Press. 2010; 19: 313-318.

7. Celik I, Bektas M. An Assessment of Turkish Adults' Knowledge Levels About Their Salt and Sugar Consumption, and Their Attitudes Toward Protecting Children from Excessive Salt and Sugar Consumption. J Pediatr Nurs. 2020; 54: e17–e22.

8. Zhang J, Xu AQ, Ma JX et al. Dietary sodium intake: Knowledge, attitudes and practices in Shandong province China 2011. PLoS One. 2013; 8: e58973.

9. Haji Yusuf, Abdurahmen J, Paulos W. Knowledge and Perception of Consumption of Iodized Salt Among Food Handlers in Southern Ethiopia. Food Nutr Bull. 2017; 38: 92-102.

10. Land MA, Webster J, Christoforou A et al. The association of knowledge, attitudes and behaviours related to salt with 24-h urinary sodium excretion. Int J Behav Nutr Phys. 2014; 11: 47.

11. Magalhães P, Sanhangala EJ, Dombele IM, Ulundo HS, Capingana DP, Silva AB. Knowledge, attitude and behaviour regarding dietary salt intake among medical students in Angola. Cardiovasc J Afr. 2015; 26: 57-62.

12. Marakis G, Tsigarida E, Mila S, Panagiotakos DB. Knowledge, attitudes and behaviour of Greek adults towards salt consumption: A Hellenic food authority project. Public Health Nutr. 2014; 17: 1877-1893.

13. WHO. Reducing salt intake in populations. WHO forum and technical meeting proceedings. 5-7 Ekim 2006, Paris, France.

14. Erdem Y, Akpolat T, Derici Ü et al. Dietary Sources of High Sodium Intake in Turkey: SALTURK II. Nutrients. 2017; 9: 933.

Orijinal Araştırma / Original Investigation
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The Relationship Between Immune Inflammation Index and Major Cardiovascular Adverse Events in Patients with Heart Failure with Reduced Ejection Fraction

Azalmış Ejeksiyon fraksiyonlu Konjestif Kalp Yetersizliği Hastalarında İmmun İnflamasyon İndeksi ile Major Kardiyovasküler Olay Sıklığı Arasındaki İlişki

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ÖZET

AMAÇ: Sistemik immün inflamasyon indeksi (SII)'nin, düşük ejeksiyon fraksiyonuna sahip Kalp yetmezliği (HFrEF) hastalarında, exitus, stroke ve hospitalizasyon gibi majör kardiyovasküler olayları öngörmede, prognozu belirlemede prediktif değeri olup olmadığını araştırmayı amaçladık.

GEREÇ VE YÖNTEM: Çalışmaya Ocak 2019- Ocak 2022 arası kardiyoloji ve acil polikliniğine başvuran 18 yaş üstü, HFrEF'li (Ejeksiyon Fraksiyonu <% 40) tanısı olan hastalar retrospektif olarak tarandı. Güvenilir klinik verileri olan 597 hasta analiz edilmek üzere çalışmaya grubu olarak kabul edildi. Hastaların ilk başvuru sırasındaki sosyodemografik özellikleri, kronik hastalıkları, sigara kullanımı ve hemogram, biyokimya parametreleri, sol ventrikül ejeksiyon fraksiyonları kullandığı ilaçlar kaydedildi. Tam kan sayımları ve biyokimyasal parametreleri incelendi. Sistemik immün inflamasyon indeksi hesaplandı. Major kardiyak olaylar ile SII arasındaki ilişki değerlendirildi. Major kardiyak olaylar olarak exitus, inme ve hospitalize olma durumu olarak kabul edildi.

BULGULAR: HFrEF'li hastalarda, SII indeksi açısından gruplar karşılaştırıldığında exitus olan grupta (1504,34±1722,74) exitus olmayan gruba göre (893,94±972,13) anlamlı olarak daha yüksek bulundu (p=0,014). Stroke olan ve olmayan, hastaneye yatış olan ve olmayan gruplar SII indeksi açısından karşılaştırıldığında anlamlı bir fark bulunamadı (tablo 2). Exitus varlığı, stroke varlığı ve hastaneye yatış varlığı ile SII indeksi arasında korelasyona bakıldığında exitus varlığı ile SII indeksi arasında anlamlı pozitif korelasyon bulundu (r=0.165 p<0,001) . SII indeksi 697,29 değeri kalp yetmezliği hastalarında Exitusu %604 sensivit, %607 spesivite ile pretikte ettirdiği saptandı (AUC: 0.621, 95%CI 0.539-0.704, p=0.04).

SONUÇ: HFrEF'lı hastalarda, kolayca bakılan bir tam kan sayımındaki lenfosit, trombosit ve nötrofil sayısından kolayca hesaplanabilen, SII indexinin mortaliteyi, predikte ettirdiğinin saptanmasıdır. Bu indexin HFrEF hastalarında prognostik önemi olduğu, özellikle yaşlı ve ISS indexi yüksek hastaların daha yakın izlenmesinin faydalı olabileceğini düşündürmektedir.

Anahtar Kelimeler: immün inflamasyon indeks, kalp yetmezliği

ABSTRACT

OBJECTIVE: We aimed to investigate whether systemic immune inflammation index (SII) has a predictive value in predicting prognosis and major adverse cardiovascular events such as exitus, stroke and hospitalization in heart failure patients with reduced ejection fraction (HFrEF).

MATERIALS AND METHODS: Patients over the age of 18 who applied to the cardiology and emergency outpatient clinics between January 2019 and January 2022 and diagnosed with HFrEF (Ejection Fraction <40%) were retrospectively screened. A total of 597 patients with reliable clinical data were included in the study.The relationship between major adverse cardiovascular events and SII was evaluated. Exitus, stroke and hospitalization were accepted as major adverse cardiovascular events.

RESULTS: In patients with HFrEF, SII index was found to be significantly higher in the Exitus (+) group (1504.34±1722.74) when compared with the Exitus (-) group (893.94±972.13) (p=0.014). On the other hand, SII index was not found to be different between the patients with or without stroke and between those with or without hospitalization. When the correlation between the SII index and presence of exitus, stroke, and hospitalization was evaluated, a significant positive correlation was found between the presence of exitus and SII index (r=0.165 p<0.001). A SII index value of 697.29 was found to predict exitus with 604% sensitivity and 607% specificity in heart failure patients (AUC: 0.621,95%CI 0.539-0.704, p=0.04).

CONCLUSION: SII index, which can be calculated easily from lymphocyte, platelet and neutrophil counts, predicts mortality in patients with HFrEF. This index has prognostic significance in patients with HFrEF, suggesting that closer monitoring of elderly patients with a high SII index may be beneficial.

Keywords: immune inflammation index, heart failure

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INTRODUCTION

Heart failure (HF) is a complex clinical syndrome, characterized by ventricular systolic or diastolic dysfunction and is the leading cause of mortality and morbidity worldwide(1). HF is a major public health problem and the incidence of HF increases with increasing age. Despite advanced modern treatment approaches, mortality rates are still high. Moreover, since HF is a chronic disorder with acute exacerbations, hospitalizations and medications for HF take place near the top in the health spendings.

Recently, a new classification of HF defined by the European Society of Cardiology (ESC) based on left ventricular ejection fraction (LVEF), clinical manifestations, and myocardial changes has received increasing attention. (2) . This classification includes HF with preserved ejection fraction (HEpEF, LVEF>50%), HF with mildly reduced ejection fraction (HFmrEF, LVEF 41-49%), and HF with reduced ejection fraction (HFrEF, LEVF < 40%)(2) .

Remarkably, HFrEF is responsible for almost half of all heart failure cases(3). The main pathological mechanisms causing HFrEF include incompatibility of the neurohormonal system and hyperactivation of the renin-angiotensin aldosterone system (4). In addition, some systemic inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6) levels were found to be high in HFrEF patients (5). This inflammatory process can induce myocardial damage, resulting in progression and exacerbation of HFrEF.

The systemic immune inflammation index (SII) is a new inflammatory parameter that includes neutrophil (N), platelet (P) and lymphocyte (L) counts. SII has been previously studied in cancer patients, and it has been found that patients with high SII have a higher risk of death in long-term follow-up (6). In addition, the predictive value of this index was evaluated in predicting mortality in patients with coronary artery disease and acute coronary syndrome (7,8). . In this study, we aimed to investigate whether SII plays a role in predicting prognosis and major adverse cardiovascular events such as death, stroke and hospitalization in patients with HFrEF.

MATERIAL & METHODS

Patients over the age of 18 and diagnosed with HFrEF (Ejection Fraction <40%) in the cardiology and emergency outpatient clinic between January 2018 and January 2021 were retrospectively screened. Initially, a total of 616 patients were included in the study. The data at the first admission including sociodemographic characteristics, haematological and biochemical parameters, medical history, smoking status and echocardiographic parameters were recorded. Fourteen patients were excluded from the study because reliable clinical data were not available. In addition, 5 patients with concurrent active infection were excluded from the study. Finally, analysis was performed in the remaining 597 patients.

Complete blood counts and biochemical parameters were examined in the venous blood samples taken from the antecubital vein. The systemic immune inflammation index was calculated using the neutrophil X platelet / lymphocyte formula.(9).

All patients included in the study undervent 2D transthoracic echocardiographic (TTE) evaluation performed by an experienced cardiologist. (Philips, iE33, the Netherlands). Echocardiographic evaluation was performed in accordance with the recommendations of the American Society of Echocardiography. Left ventricular (LV) end-diastolic and end-systolic diameters, interventricular septum and posterior wall thickness were measured using M-mode in the parasternal long axis view. LVEF was calculated using the modified Simpson's method on apical two-chamber and four-chamber views.

Exitus, stroke and hospitalization were taken as major adverse cardiovascular events. Stroke and hospitalization within 1 year were recorded from the file records. The National Death Notification System was used to evaluate survival status of each case. The study protocol was evaluated and approved by the local ethics committee.

Statistical analysis

Data were tested for normality with the Kolmogorov-Smirnov test and for homogeneity of variance with the Levene test. Groups were compared with Welch's t-test, Mann-Whitney U test and student-t test. The numeric variables were expressed as mean ± SD and median [min-max] while the categorical variables were expressed as percentage. Point biserial correlation test was used to evaluate the correlation between presence of exitus and SII index. Binary logistic regression analysis was used to find parameters that predict exitus. Roc curve analysis was performed to calculate the SII index cut-off value. All statistical analyzes were performed using SPSS v25 (IBM Inc., Chicago, IL, USA) statistical software. The results were

evaluated at the 95% confidence interval and the significance level was p<0.05.

RESULTS

The average age of the patients included in the study was 65.83±11.45 years. 37 % of patients were females and 63 % were males. In the study population, diabetes was detected in 31.5% and hypertension in 52.6%. Sociodemographic characteristics and laboratory parameters of the patients are given in Table 1. The mean LVEF in the study group was 28.5±6.5 %. Baseline echocardiography parameters are shown in Table 1.

SII index was found to be significantly higher in the Exitus (+) group (1504.34±1722.74) when compared to Exitus (-) group (893.94±972.13, p=0.014). On the other hand, SII index was not found to be different between the patients with or without stroke and between those with or without hospitalization (Table 2). When the correlation between the SII index and presence of exitus, stroke, and hospitalization was evaluated, a significant positive correlation was found between the presence of exitus and SII index (r=0.165 p<0.001) (Table 3).

Age and white blood cell count were found to be higher and platellet count was found to be lower in the Exitus (+) group when compared to Exitus (-) group (p=0.001, p<0.001, p=0.042, respectively). Urea, creatinine and AST values were also significantly higher (p<0.001, p<0.001, p<0.001, respectively). The total cholesterol levels were higher in the Exitus (+) group (p=0.014) while TG levels were lower (p=0.015). BNP and Troponin levels were also higher in the Exitus (+) group (p=0.021, p=0.037, respectively, Table 4)

Binary logistic regression analysis revealed that age (Beta: 0.036 95%CI 1.009-1.065 p=0.009) and SII index (beta 0.000 95%1,000-1,000 p=0.003) can predict exitus in heart failure patients (Table 5).

SII index value of 697.29 was found to predict exitus with 604% sensitivity and 607% specificity in heart failure patients (AUC: 0.621, 95%CI 0.539-0.704, p=0.04) (Figure 1).

Table 1. *Sociodemographical characteristics, laboratory and echocardiographic findings*

Variables		Variables	
Age (year)	65,83±11,45	**HDL (mg/dL)**	40.11±11.78
Gender		**LDL (mg/dL)**	129.14±133.56
Female, n(%)	221 (%37)	**TG(mg/dL)**	146.13±95.93
Male, n(%)	376 (%63)	**BNP (pg/mL)**	3122.99±3272.34
Diabetes Mellitus, n(%)	188 (%31.5)	**Troponin (ng/mL)**	0.176±1.707
Hypertension, n(%)	314 (%52.6)	**Exitus**	53 (%8.9)
Hyperlipidemia, n(%)	111 (%18.6)	**Stroke**	60(%10.1)
Chronic kidney disease, n (%)	33(5.52)	**Hospitalization**	108 (%18.1)
Sigara	133 (%22.3)	**SII**	950.76±1077.07
Rhythm		**Duration of heart failure (month)**	23 (9-35)
Sinus Rhythm (%)	311(52.1)	**Medications (%)**	
Atrial fibrillation, n(%)	292 (48.9)	**ACEI**	
Hgb (g/dL)	13.86±6.12	**ARB**	35
WBC (10^3/µL)	8.57±4.41	**Beta blocker**	25
Plt (10^3/µL)	230.16±84.62	**Digoxin**	75
Neutrophil	5.73±4.95	**ASA**	73.2
Lymphocyte	1.65±0.97	**MRA**	75.5
Fasting glucose (mg/dL)	116.73±50.15	**Anticoagulants**	52
Urea, (mg/dL)	41.85±29.76	**Furosemid**	45
Creatinine (g/dL)	1.24±1.66	**NYHA Class(%)**	40
CRP (mg/l)	8.45±9.77	**I**	
AST,(U/L)	32.14±50.20	**II**	30.5
ALT, (U/L)	29.59±39.92	**III**	35
T. Cholesterol (mg/dL)	187.41±45.64	**IV**	32
Left atrium(mm)	42.5±3.1	**RVDD(mm)**	2.5
Septum(mm)	10.9±2.1	**TAPSE**	29.5±3.5
LVDD(mm)	59.1±8.4	**E wave m/sec**	17.2±3.0
LVSD(mm)	42.3±10.2	**A wave m/sec**	1.5 (0.8-1.9)
Ejection fraction %	28.5±6.5	**E/A**	1.1 (0.9-2.5)
			1.36 (0.9-1.2)

SII: Immune Inflammation Index; ACEI - angiotensin-converting enzyme inhibitor; ASA - acetylsalicylic acid; AST - aspartate aminotransferase; ALT - alanine aminotransferase; A wave- A wave velocity; BNP - brain natriuretic peptide;CRP- C reactive protein; E wave- E wave velocity; LDL - low-density lipoprotein; TG -

triglycerides; LVDD - left ventricular diastolic diameter; LVSD - left ventricular systolic diameter; HDL - high-density lipoprotein; Hgb- hemoglobin; Plt- platelet; MRA - mineralocorticoid receptor antagonist; NYHA- New York Heart Association; RVDD – Right ventricular diastolic diameter; ;T. Cholesterol-Total Cholesterol; TAPSE - tricuspid annular plane systolic excursion; WBC- White blood cell.

Table 2. *Comparision of the groups in terms of SII index*

	Exitus (+)(n=53)	**Exitus (-)(n=544)**	**p**
SII index	1504.34±1722.74 (min 81.53 max 8059.42)	893.94±972.13 (min13.73 max 9601.70)	**0.014***
	Stroke (+)(n=60)	**Stroke (-)(n=537)**	
SII index	805.69 (min 139.054 max 4816.0)	591.58 (min 13.371-9601.706)	0.103**
	Hospitalization (+) (n=108)	**Hospitalization (-) (n=489)**	
SII index	608.46 (min 66.14 max 4251.07)	593.54 (min13.731 max 9601.706)	0.573**

**: Welch's t-test **: Mann- Whitney U test SII- Immune Inflammation Index*

Table 3. Point Biserial Correlation test

	SII index	**p**
Exitus (+)	r=0.165	**<0.001**
Hospitalization (+)	r=0.017	0.687
Stroke (+)	r=0.070	0.096

Table 4. Comparision of Exitus (+) and Exitus (-) groups in terms of age and laboratory parameters

	Exitus (+)	**Exitus (-)**	**P value**
Age, year	70.66±12.02	65.34±11.29	***0.001****
Hemoglobin, g/dl	12.85±2.58	13.96±6.34	0.231*
White blood cell10^3/UL	12.55±9.50	8.17±3.28	***<0.001****
Platelet, 10^3/UL	207.42±80.72	232.38±84.74	***0.042****
C-reactive protein, mg/L	5.10 (0.60-72)	5(0.06-73)	0.776**
Fasting glucose (mg/dL)	115.73±49,29	126.98±57.78	0.123
Urea, mg/dl	48(16-208)	36(6-236)	***<0.001***
Creatinine (g/dL	1.2 (0.6-6.5)	0.93 (0.60-11.2)	***<0.001***
AST,U/L	26 (6-756)	22(3-414)	***<0.001***
ALT, U/L	21 (5-146)	20 (5-453)	0.149
T. Cholesterol (mg/dL)	172.74±33,66	188.84±46,42	***0.014***
HDL(mg/dL)	38.31±15,55	40.28±11.36	0.255
LDL (mg/dL)	115.20(11-892)	116(11-892)	0.914
Triglyceride(mg/dL)	114.64±58.09	149.12±98.28	***0.015***
BNP(pg/mL)	3321(48-21400)	2146(25800)	***0.021***
Troponin(ng/mL)	0.027(0.008-0.67)	0.013(0.001-12)	***0.037***

**: Student T testi **: Mann- Whitney U test AST - aspartate aminotransferase; ALT - alanine aminotransferase; HDL - high-density lipoprotein; LDL - low-density lipoprotein; TG - triglycerides; BNP - brain natriuretic peptide*

Table 5. *Independent predictors of Exitus in heart failure patients in binary logistic regression analysis.*

	Beta	**Exp(Beta)**	**95% confidence interval**	**p**
Age	0.036	1.036	1.009-1.065	***0.009***
BNP	0,000	1.0	1.000-1.000	***0.063***
Troponin	-0.186	0.83	0.376-1.834	0.645
SII index	0,000	1.0	1.000-1.000	***0.003***

BNP:Brain natriuretic peptide, SII: Immune Inflammation Index

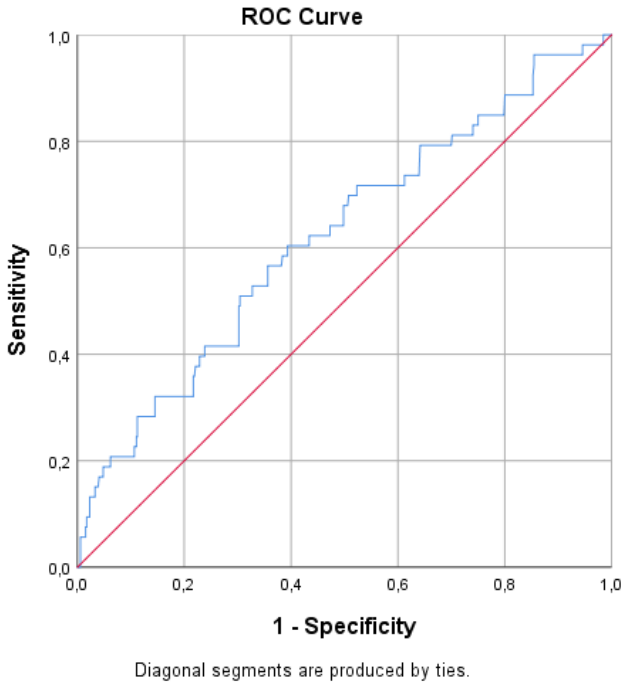

Figure 1. Roc curve analysis; SII index value of 697.29 was found to predict exitus with 604% sensitivity and 607% specificity in heart failure patients (AUC: 0.621, 95%CI 0.539-0.704, p=0.04)

DISCUSSION

The most remarkable outcome of our study is that the SII index, which can be easily calculated from the lymphocyte, platelet and neutrophil counts, can predict mortality in patients with HFrEF. This index has prognostic significance in patients with HFrEF, suggesting that closer monitoring of elderly patients with a high SII index may be beneficial.

It is well known that inflammation has an important role in the pathogenesis of atherosclerosis and cardiovascular diseases (10). The role of inflammation in heart failure has been demonstrated in many previous studies. The heart failure syndrome is mainly due to the imbalance between inflammatory and anti-inflammatory processes (11).

Systemic inflammatory indices which are calculated by platelets, inflammatory activators (neutrophils/monocytes) and inflammatory regulators (lymphocytes), are considered as effective indicators of systemic inflammation and immune balance, and play an important role in the prognostic and therapeutic evaluation of various diseases.

SII is an index calculated using platelet, lymphocyte and neutrophil counts. SII can be considered as a modified and reliable version of the previously described platelet-lymphocyte ratio (PLR) and neutrophil-lymphocyte-ratio (NLR). NLR has prognostic value in HF patients with reduced or preserved ejection fraction (12,13). Similarly, recent studies have confirmed the prognostic value of PLR in different cohorts of HF patients (14,15).

Elevated inflammatory marker levels are associated with poor outcome in heart failure, as in many chronic diseases. Increased inflammatory stimulus causes secretion of many inflammatory cytokines such as TNF-alpha, IL-6 and CRP. These inflammatory cytokines cause detrimental effects on the myocardium, leading to decreased left ventricular function and heart failure (10,11). In a study, it was found

that patients with decompensated heart failure had higher NLR and PLR values. Moreover, these parameters were found to have an impotant role in predicting heart failure decompensation (16). These findings about the association between HF and inflammation are also consistent with the results of our study.

In a recent study, SII was found to be an independent predictor for both long-term mortality and requirement of ICD therapy in patients with HFrEF(17). In our study, the fact that SII was associated with mortality but not with hospitalization may suggest that this robust association between SII and mortality results from arrhythmic events.

There is a 2 to 5-fold increased risk of stroke in patients with heart failure(18). A higher incidence of ischemic stroke is observed in patients with chronic HF when compared to general population (8-11% vs. 1%) (19). There was no significant difference in the incidence of stroke between HFrEF, HFmrEF and HFpEF subgroups. On the other hand, stroke risk was found to be higher in the elderly patients and those with atrial fibrillation(20,21).

It is well known that patients with HFrEF have a prothrombotic state due to platelet hyperactivity, increased thrombin production and impaired fibrinolysis (22). The presence of hypercoagulation has also been reported in patients with HFpEF (23). As a result, the presence of HF carries a risk of stroke regardless of its subgroup.

Endothelial dysfunction observed in patients with chronic heart failure leads to decreased endothelial-derived nitric oxide formation and myocardial microvascular activity leading to sub endocardial damage, which ultimately leads to the development of thromboembolic complications.(24,25). The main pathophysiological mechanisms causing progression of HFrEF such as activation of sympathetic and renin-angiotensin-aldosterone systems and systemic inflammation, further increase the risk of stroke in these patients. In our study, lack of a correlation between SII and stroke was an unexpected finding. Although the frequency of stroke was high, a clear relationship between SII and stroke could not be determined. This may be secondary to intensive use of antiaggregant or anticoagulant therapy in patients with HFrEF.

CONCLUSION

SII index, which can be calculated easily from lymphocyte, platelet and neutrophil counts, predicts mortality in patients with HFrEF. This index has prognostic significance in patients with HFrEF, suggesting that closer monitoring of elderly patients with a high SII index may be beneficial.

Study limitations

Limited number of patients and single-center and retrospective design can be considered as the limitations of our study. On the other hand, all consecutive patients with sufficient data were included in the study. Since the exact cause of mortality in our study population is unclear, it was also not possible to distinguish between cardiac and non-cardiac mortality.

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REFERENCES

1. Ardahanli I, Celik M. Serum Uric Acid Levels among Patients who Died in Recent Year due to Heart Failure with Reduced Ejection Fraction. J Coll Physicians Surg Pak. 2020 Aug;30(8):780-7doi: 10.29271/jcpsp.2020.08.7PMID: 32893785.

2. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure. EurHeartJ. 2021;42(36):3599-37doi: 10.1093/eurheartj/ehab3

3. Savarese G, Lund LH. Global public health burden of heart failure. Card Fail Rev.2017;3(1):7-doi: 10.15420/cfr.2016:25:2

4. Hartupee J, Mann DL. Neurohormonal activation in heart failure with reduced ejection fraction. Nat Rev Cardiol. 2017;14(1):30doi: 10.1038/nrcardio.2016.163.

5. Adamo L, Rocha-Resende C, Prabhu SD, Mann DL. Reappraising the role of inflammation in heart failure. Nat Rev

Cardiol. 2020;17(5):2692doi: 10.1038/s41569-019-0315-x.

6. Yang R, Chang Q, Meng X, Gao N, Wang W. Prognostic value of systemic immune-inflammation index in cancer:ameta-analysis. J Cancer. 2018;9(18):3295-3302 doi: 10.7150/jca.25691.

7. Yang YL, Wu CH, Hsu PF, et al. Systemic immune-inflammation index (SII) predicted clinical outcome in patients with coronary artery disease.Eur J Clin Invest.2020;50(5):e132doi: 10.1111/eci.13230.

8. Su G, Zhang Y, Xiao R, Zhang T, Gong B. Systemic immune inflammation index as a promising predictor of mortality in patients with acute coronary syndrome: a real-world study. J Int Med Res. 2021;49(5):30006052110162doi: 10.1177/03000605211016274

9. Yurdam FS, Kış M. The Predictive Role of Systemic Immune Inflammation Index to the Aortic Valve Calcification in the Elderly Population with Chronic Renal Failure. E J Cardiovasc Med 2023;11:11-16

10. Güzel T, Kış M. Correlation Between Coronary Lesion Severity Detected in Fractional Flow Reserve with Systemic Immune Inflammation Index and Atherogenic Plasma Index 10.4274/BMB.galenos.2022.2022-04-036.

11. Oikonomou E, Tousoulis D, Siasos G, Zaromitidou M, Papavassiliou AG, Stefanadis C. The role of inflammation in heart failure: new therapeutic approaches. Hellenic J Cardiol 2011; 52: 30-PMID: 21292605.

12. Uthamalingam S, Patvardhan EA, Subramanian S, et al. Utility of the neutrophil to lymphocyte ratio in predicting long-term outcomes in acute decompensated heart failure. Am J Cardiol. 2011;107(3):4334doi: 10.1016/j.amjcard.2010.09.039.

13. Curran FM, Bhalraam U, Mohan M, et al. Neutrophil-to-lymphocyte ratio and outcomes in patients with new-onset or worsening heart failure with reduced and preserved ejection fraction. ESC Heart Fail. 2021;8(4):3168-31doi: 10.1002/ehf2.13424.

14. Demir M, Duyuler PT, Guray U, Celik MC. Platelet to lymphocyte ratio on admission and prognosis in patients with acute cardiogenic pulmonary edema.JEmergMed.2018;55(4):465-4doi: 10.1016/j.jemermed.2018.06.021

15. Heidarpour M, Bashiri S, Vakhshoori M, et al. The association between platelet-to-lymphocyte ratio with mortality among patients suffering from acute decompensated heart failure. BMC Cardiovasc Disord. 2021;21(1):454 doi: 10.1186/s12872-021-02260-7.

16. Durmus E, Kivrak T, Gerin F, Sunbul M, Sari I, Erdogan O. Neutrophilto-Lymphocyte Ratio and Platelet-to-Lymphocyte Ratio are Predictors of Heart Failure. Arq Bras Cardiol 2015; 105: 606-13 doi: 10.5935/abc.20150126.

17. Hayıroglu M˙I, ÇınarT, Çinier G, et al. Evaluating systemic immune-inflammation index in patients with ICD for heart failure with reduced ejection fraction. Pacing Clin Electrophysiol.2022;45:188–1https://doi.org/10.1111/pace.14436

18. Adelborg, K.; Szépligeti, S.; Sundbøll, J.; et al. Risk of Stroke in Patients With Heart Failure: A Population-Based 30-Year Cohort Study. Stroke 2017, 48, 1161–11doi: 10.1161/STROKEAHA.116.016022.

19. Pullicino, P.M.; Halperin, J.L.; Thompson, J.L. Stroke in patients with heart failure and reduced left ventricular ejection fraction. Neurology 2000, 54, 288–2doi: 10.1212/wnl.54.2.288.

20. Sartipy, U.; Dahlström, U.; Fu, M.; Lund, L.H. Atrial Fibrillation in Heart Failure with Preserved, Mid-Range, and Reduced Ejection Fraction. JACC Heart Fail. 2017, 5, 565–574 doi: 10.1016/j.jchf.2017.05.001.

21. Pullicino, P.M.; Halperin, J.L.; Thompson, J.L. Stroke in patients with heart failure and reduced left ventricular ejection fraction. Neurology 2000, 54, 288–2doi: 10.1212/wnl.54.2.288.

22. Paolillo, S.; Ruocco, G.; Filardi, P.P.; et al. "Right and Left Heart Failure Study Group" of the Italian Society of Cardiology. Direct oral anticoagulants across the heart failure spectrum: The precision medicine era. Heart Fail. Rev. 2020, doi:10.1007/s10741-020-09994-0.

23. Jug, B.; Vene, N.; Salobir, B.G.; Sebestjen, M.; Sabovic, M.; Keber, I. Procoagulant state in heart failure with preserved left ventricular ejection fraction. Int. Heart. J. 2009, 50, 591–6doi: 10.1536/ihj.50.591.

24. Jekell, A.; Kalani, M.; Kahan, T. The interrelation of endothelial function and microvascular reactivity in different vascular beds, and risk assessment in hypertension: Results from the Doxazosin-ramipril study. Heart Vessels. 2019, 34, 484–4doi: 10.1007/s00380-018-1265-7.

25. Scherbakov, N.; Sandek, A.; Martens-Lobenhoffer, J.; et al. Endothelial dysfunction of the peripheral vascular bed in the acute phase after ischemic stroke. Cereb. Dis. 2012, 33, 37–doi: 10.1159/000332809.

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Global DNA Methylation Analysis of Imatinib Resistant and Sensitive K562 Cells

İmatinibe Dirençli ve Duyarlı K562 Hücrelerinin Global DNA Metilasyon Analizi

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ÖZET

AMAÇ: Kronik miyeloid lösemi (KML), Philadelphia kromozomunun (Ph+) varlığı ile bilinen hematolojik bir hastalıktır. BCR-ABL proteini Ph+ kromozomu tarafından ifade edilir ve sürekli olarak artmış tirozin kinaz aktivitesi göstermektedir. İmatinib (IMA), KML'de ilk basamak tedavi olarak kullanılan bir tirozin kinaz inhibitörüdür (TKI). Tedavinin bir noktasında IMA direncinin ortaya çıkması tedavi başarısızlığına yol açar. DNA metilasyonu en stabil epigenetik değişiklik olarak kabul edilir ve epigenetik değişikliklerin ilaç direncinde rol oynayabileceği çeşitli çalışmalarda gösterilmiştir. Bu çalışmada, IMA'ya karşı gelişen dirençte ve bu direnç nedeniyle fenotipte görülen değişimde epigenetik yeniden programlamanın rol alıp almadığını belirlemek amacıyla, IMA'ya duyarlı K562S, IMA'ya dirençli K562R ve IMA'ya dirençli ve yapışan K562R (K562R-adh) hücrelerinin global metilasyon profilini araştırdık.

GEREÇ VE YÖNTEM: Bu çalışmada, global DNA metilasyon profilini analiz etmek için morfolojik olarak farklılık gösteren, IMA'ya karşı duyarlı K562S ve 5μM IMA'ya karşı dirençli K562R ve K562R-adh in-vitro KML hücre modelleri kullanılmıştır. Hücrelerden DNA izole edildikten sonra, eşit miktardaki DNA'lar kullanılarak ELISA yöntemi ile global 5mC DNA metilasyon profilleri araştırılmıştır.

BULGULAR: K562R'nin global metilasyonu K562S'ye göre kıyaslandığında, DNA metilasyon profilinde artış saptanırken, metilasyondaki bu artış istatistiksel olarak anlamlı bulunmamıştır. Buna karşılık, K562R-adh ile K562S ve K562R-adh ile K562R kıyaslandığında, K562R-adh hücrelerinin global DNA metilasyon profilinde K562S ve K562R hücrelerinine göre istatistiksel olarak anlamlı derecede artış saptanmıştır.

SONUÇ: K562S, K562R ve K562R-adh hücre hatlarında CpG adalarındaki 5metil-Sitozin (5mC)'de gözlemlediğimiz farklılıklar, dirençli hücrelerdeki DNA metilasyon değişikliğinin fenotip değişimine kısmen katkıda bulunabileceğini düşündürmektedir.

Anahtar Kelimeler: kronik miyeloid lösemi, imatinib direnci, global metilasyon, EMT

ABSTRACT

OBJECTIVE: Chronic myeloid leukemia (CML) is a hematological disease which is known for the presence of Philadelphia chromosome (Ph+). BCR-ABL protein is expressed by Ph+ chromosome, represents constant increased tyrosine kinase activity. Imatinib (IMA) is a tyrosine kinase inhibitor (TKI) which is utilized as a first line treatment in CML. Emergence of IMA resistance at some point of therapy leads to treatment failure. DNA methylation is considered to be the most stable epigenetic change and several studies have shown that epigenetic changes may play a role in drug resistance. In this Study, we investigated the global methylation profile of IMA-sensitive K562S, IMA-resistant K562R and IMA-resistant and adherent K562R (K562R-adh) cells to determine whether epigenetic reprogramming is involved in the resistance to IMA and the change in phenotype due to this resistance.

MATERIALS AND METHODS: In this study, morphologically distinct, IMA-sensitive K562S and 5μM IMA-resistant K562R and K562R-adh in-vitro CML cell models were used to analyze the global DNA methylation profile. After DNA was isolated from the cells, global 5mC DNA methylation profiles were investigated by ELISA using equal amounts of DNA.

RESULTS: Compared to K562S, the global methylation of K562R showed an increase in DNA methylation profile, but this increase in methylation was not statistically significant. Whereas, a slight hypermethylation was observed in the DNA of the K562R-adh vs K562S and K562R-adh vs K562R which is statistically significant. We observed slight hypermethylation in IMA-resistant cells lines versus to the IMA-sensitive cell line.

CONCLUSION: Our observed differences in 5methyl-Cytosine on CpG islands (5mC) in K562S versus K562R and K562R-adh cell lines suggest that the DNA methylation alteration in resistant cells may partly contributed in phenotype switching.

Keywords: chronic myeloid leukemia, Imatinib resistance, Global methylation, EMT

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INTRODUCTION

Chronic myeloid leukemia (CML) is a type of hematological malignancy which is known to impact hematopoietic stem cells. The Philadelphia chromosome's (Ph+) presence is the hallmark of CML (1, 2). The reciprocal translocation of chromosomes 9 and 22 results in the generation of the BCR-ABL fusion protein production. The protein is expressed by Ph+ chromosome, represents constant increased tyrosine kinase activity (2). Imatinib (IMA) is a tyrosine kinase inhibitor (TKI) which is used as a first line therapy to overcome the constitutive tyrosine kinase activity of BCR-ABL protein in CML (3). Although IMA treatment is successful in clinical routine, patients develop IMA resistance at some point of therapy (4). In most cases IMA resistance caused by the mutations of the kinase domain and /or the amplification of BCR-ABL gene (5). Different BCR-ABL independent mechanisms, including overexpression of efflux transporters, inhibition of apoptosis pathway, aberrant epigenetic modification and dysregulation of microRNA expression are involved in IMA resistance (6, 7). Phenotype switching is the mechanism which is contributed to drug resistance in different cancer types (8). One of the processes causing the epithelial-to-mesenchymal transition (EMT) is probably epigenetic regulation (9).

Epigenetic processes are categorized in three classes: DNA methylation, histone modifications and noncoding RNAs (10). In CML, aberrant DNA methylation frequently occurs, with gene hypermethylation predominately over hypomethylation (11). DNA methylation is considered as the most stable epigenetic alteration (11). This process related to the attachment of a methyl group (CH_3) at the 5'carbon position of cytosine residues in CpG islands (12). There are studies reported that, DNA methylation in hematological diseases including CML can happen regardless of genetic background (13). Considering DNA methylation's significant role in leukemogenesis, it can be a valuable biomarker for leukemia prognosis and treatment response prediction (14).

In our previous study, we showed that constant exposure of IMA-resistant K562R cells to 5 µM IMA led adherent phenotype development (15).

In this study, to determine epigenetic reprograming of each cell type on cell morphology, we analyzed the global methylation pattern of IMA-sensitive K562S, IMA-resistant K562R and K562R-adh cells.

MATERIAL & METHODS

Cell Culture

The CML cell line K562S (IMA-sensitive K562) cells were cultured in RPMI 1640 (Sigma-Aldrich, St. Louis, MO, USA) media at 37°C under 5% CO_2 supplemented with 10% fetal bovine serum (Sigma-Aldrich, St. Louis, MO, USA). The same media supplemented with 5 µM IMA (Santa Cruz Biotechnology, Santa Cruz, CA, USA) was used to sustain the K562R (IMA- resistant K562) cells (6). The stock solution of IMA was prepared at a final concentration of 10 mM since IMA is soluble in water. Every month, it was prepared fresh and kept at -20°C. Every three days, the cell line was passaged and the IMA-containing medium was added.

A subpopulation of adherent cells (K562R-adh) is generated when 5 µM IMA is present in the medium of K562R cells. Adherent cells grew in the presence of IMA for 18 months after discarding the K562R suspended cells (15).

DNA extraction

Using the Quick-DNA TM Miniprep Plus Kit, genomic DNA was isolated from $5x10^6$ cells of the K562S, K562R and K562R-adh using (Zymo research/Irvine, CA, USA) according to the manufactures' instructions. Cells were centrifuged at 500g for 2 min. Then, supernatant was discarded and the pellets were suspended in 1 ml PBS. Later, cells were centrifuged at 500 g for 5 min and resuspended in 200 µl of BioFluid & Cell buffer. In the next step, cells were treated with 20 µl of Proteinase K for 10 min at 55°C. Genomic binding buffer (1 volume) was added to the sample and mixed for 10-15 sec. Later, the mixture was transferred to the Zymo-SpinTM IIC-XLR Column in a Collection Tube. The cells were centrifuged at 12000 g for 1 min. Spin column transferred to the new collection tube and incubated with DNA Pre-Wash Buffer (400 µl). Then, the cells were centrifuged at 12000 g for 1 min. Cells were washed with g-DNA Wash Buffer (200 µl) and centrifuged at 12000 g for 1 min, this step repeated twice. The flow-through collection tube was disposed of. Spin columns were transferred to the lean microcentrifuge tube and 50 µl DNA Elution Buffer was added to each sample. A spectrophotometer was used for quantity and quality assessment of the isolated DNA (BioTek Instruments, Inc./Winooski, VT, USA).

Global DNA Methylation Analysis

To analyze global methylation level in K562S, K562R and K562R-adh cell, we utilized the 5-mC DNA ELISA Kit (Zymo Research/ Irvine, CA, USA). The global DNA methylation level analysis according to the manufacturer's protocol. For analysis, 100 ng of each DNA sample was used.

The absorbance values of seven standards that were created by combining the positive and negative controls included with the kit were used to create the standard curve.

The absorbance of each sample was measured at 405 nm using an ELISA plate reader (BioTek Instruments, Inc. / Winooski, VT, USA).

Statistical analysis

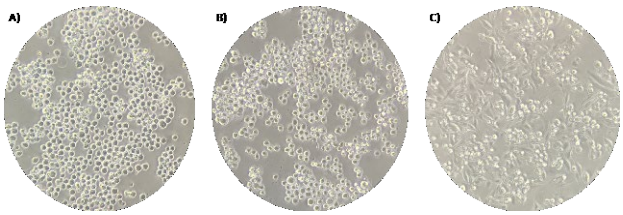
Statistical software Graph Pad Prism was utilized for the analysis of the differences between the K562S, K562R and K562R-adh cells. The sample means were compared using a one-way ANOVA, and the groups that were significantly different were compared pairwise using the Tukey Multiple Comparison test. The results were represented as mean ±SD. $P < 0.05$ was considered as statistically significant.

RESULTS

Global DNA Methylation in CML Cell lines

The mean global level of DNA methylation in K562S, K562R and K562R-adh cells (Figure 1) were 1.2% ± 0.014, 1.305% ± 0.035, and 1.63% ± 0.084 respectively. The mean methylation levels of K562R-adh cells is slightly higher than K562S, K562R cells, which are statistically significant $p < 0.05$ (Figure 2).

Figure1. *Phase-contrast microscopic images of CML cells before DNA isolation (magnification 400). A) K562S cells; B) K562R cells; C) K562R-adh cells.*

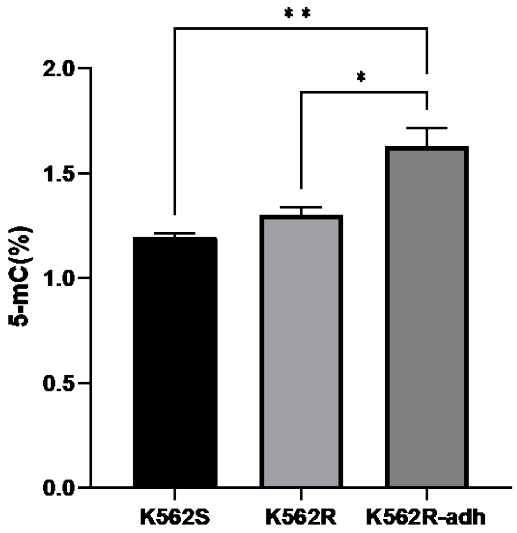


DISCUSSION

CML is a hematopoietic disorder, which is distinguished by the presence of BCR-ABL fusion protein (16). In addition to the BCR-ABL dependent mechanisms, there are BCR-BL independent mechanisms, which are involved in IMA resistance in CML (6). Phenotype switching is one of the alternative mechanism which was reported by Kemper and colleagues in 2014 (8).

DNA methylation profile changes based on the differentiation stage and type of the cell. For instance, compared to lymphoid cells, myeloid progenitors exhibit lower levels of global DNA methylation, which inhibits the myeloid differentiation pathway (17). DNA methylation suppresses gene transcription and cytosine residues at promoter regions in CpG islands (10). There are some studies have reported that epigenetic modifications accompany the phenotypic changes underlying EMT(18, 19). DNA methylation is one of the well- characterized mechanisms of epigenetic gene regulation and it may also play a role in EMT regulation (18). Moreover, gene hypermethylation and loss of function are frequently associated to drug resistance (5).

Figure 2. *5-mC (%) Global methylation level in K562S, K562R and K562R-adh. * P < 0.05 and **P < 0.001*



In this study, by using IMA sensitive and resistant CML cell line models, which are different in morphology, we aimed to evaluate the role of DNA methylation in IMA resistance and phenotype switching of the IMA resistant cells.

Several studies, which reported the increased methylation, profile in early phase of CML (17). In cancer, abnormalities in DNA methylation can be correlated with aberrant gene expression. Ko and colleagues performed a methylation analysis and RNA-seq analysis on CD^{34+} isolated from peripheral blood and bone marrow samples of healthy, CP (Chronic phase) and BP (Blast phase) of CML patients (20).

They reported that DNA hypermethylation events (>80%), frequently at promoters, are the main characteristic of BC transformation (20). Another study reported the aberrant promoter methylation of DAPK1, RASSF1A, p14ARFARF, RIZ1 and P16INK4A genes which have a strong association with poor IMA response, poor overall survival rates, and CML progression to advanced clinical stages (21).

In the study by Kaehler and colleagues, genome wide methylation analysis represented a slight increase in total methylation in IMA resistance K562 cells, which are resistant to 0.5 and 2 µM IMA. According to their study, PDE4DIP (phosphodiesterase 4D interacting protein), BCL2 (B-cell lymphoma 2), NMU (neuromedin U), IFI30 (gamma-interferon-inducible lysosomal thiol reductase) and DNASE2 (deoxyribonuclease-2-alpha) were identified as potential genes that were downregulated in IMA resistance-potentially by DNA methylation in their promoter region (7). Based on our results, there is not significant changes in the DNA methylation profile of K562R vs K562S. Whereas, a slight hypermethylation was observed in the DNA of the K562R-adh vs K562S, K562R-adh vs K562R. This slight increase which is observed between these groups is statistically significant. In our previous study, we performed bioinformatics analysis on the GSE120932 dataset. Based on our analysis and data reported by Baykal-Kose and colleagues, there were not dramatic differences in the number of the upregulated and down regulated genes between K562R vs K562S, K562R-adh vs K562S and K562R-adh vs K562R (15, 22). We did not observe dramatic changes in DNA methylation comparing resistant cells lines versus control CML cell line. Nevertheless, our observed differences in 5mC in IMA sensitive K5652S versus IMA resistant cell lines K562R and K562R-adh cell lines suggest that the DNA methylation alteration in resistant cells may partly contribute in phenotype switching.

Our results suggested that, in addition to the drug concentration, which is crucial in methylation patterns of the cells, switching the shape of the cells which can be caused by the induction of EMT or DNA hypermethylation in these cells.

CONCLUSION

It is not clear whether the observed epigenetic modifications are causally underlying the phenotype switching, or whether phenotype switching is merely a consequence of epigenetic modifications. Different mechanisms could involve in the methylation changes. In the future studies, the methylation profile of DNA, both on promoter sequences of EMT-related genes can be analyzed.

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Author contribution status; The concept of the study; YH, design; YH, literature review; YH, collecting and processing data; YH, statistics; YH, writing phase; YH,

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REFERENCES

1. Groffen J, Stephenson JR, Heisterkamp N, de Klein A, Bartram CR, Grosveld G. Philadelphia chromosomal breakpoints are clustered within a limited region, bcr, on chromosome 22. Cell. 1984;36(1):93-9.

2. Ansari S, Verma M. Control of Ph(+) and additional chromosomal abnormalities in chronic myeloid leukemia by tyrosine kinase inhibitors. Med Oncol. 2023;40(8):237.

3. Bugler J, Kinstrie R, Scott MT, Vetrie D. Epigenetic Reprogramming and Emerging Epigenetic Therapies in CML. Front Cell Dev Biol. 2019;7:136.

4. Loscocco F, Visani G, Galimberti S, Curti A, Isidori A. BCR-ABL Independent Mechanisms of Resistance in Chronic Myeloid Leukemia. Front Oncol. 2019;9:939.

5. You R-I, Ho C-L, Hung H-M, Hsieh Y-F, Ju J-C, Chao T-Y. Identification of DNA methylation biomarkers in imatinib-resistant chronic myeloid leukemia cells. Genomic Medicine, Biomarkers, and Health Sciences. 2012;4(1-2):12-5.

6. Hekmatshoar Y, Ozkan T, Altinok Gunes B, Bozkurt S, Karadag A, Karabay AZ, et al. Characterization of imatinib-resistant K562 cell line displaying resistance mechanisms. Cell Mol Biol (Noisy-le-grand). 2018;64(6):23-30.

7. Kaehler M, Litterst M, Kolarova J, Bohm R, Bruckmueller H, Ammerpohl O, et al. Genome-wide expression and methylation analyses reveal aberrant cell adhesion signaling in tyrosine kinase inhibitor-resistant CML cells. Oncol Rep. 2022;48(2).

8. Kemper K, de Goeje PL, Peeper DS, van Amerongen R. Phenotype switching: tumor cell plasticity as a resistance mechanism and target for therapy. Cancer Res. 2014;74(21):5937-41.

9. Urbanova M, Buocikova V, Trnkova L, Strapcova S, Kajabova VH, Melian EB, et al. DNA Methylation Mediates EMT Gene Expression in Human Pancreatic Ductal Adenocarcinoma Cell Lines. Int J Mol Sci. 2022;23(4).

10. Koschmieder S, Vetrie D. Epigenetic dysregulation in chronic myeloid leukaemia: A myriad of mechanisms and therapeutic options. Semin Cancer Biol. 2018;51:180-97.

11. Leo E. DNA Methylation in Chronic Myeloid Leukemia. Journal of Molecular and Genetic Medicine. 2016;10(02).

12. Deaton AM, Bird A. CpG islands and the regulation of transcription. Genes Dev. 2011;25(10):1010-22.

13. Byun HM, Eshaghian S, Douer D, Trent J, Garcia-Manero G, Bhatia R, et al. Impact of Chromosomal Rearrangement upon DNA Methylation Patterns in Leukemia. Open Med (Wars). 2017;12:76-85.

14. Jiang D, Hong Q, Shen Y, Xu Y, Zhu H, Li Y, et al. The diagnostic value of DNA methylation in leukemia: a systematic review and meta-analysis. PLoS One. 2014;9(5):e96822.

15. Hekmatshoar Y, Karadag Gurel A, Ozkan T, Rahbar Saadat Y, Koc A, Karabay AZ, et al. Phenotypic and functional characterization of subpopulation of Imatinib resistant chronic myeloid leukemia cell line. Adv Med Sci. 2023;68(2):238-48.

16. Bhamidipati PK, Kantarjian H, Cortes J, Cornelison AM, Jabbour E. Management of imatinib-resistant patients with chronic myeloid leukemia. Ther Adv Hematol. 2013;4(2):103-17.

17. Lebecque B, Bourgne C, Vidal V, Berger MG. DNA Methylation and Intra-Clonal Heterogeneity: The Chronic Myeloid Leukemia Model. Cancers (Basel). 2021;13(14).

18. Galle E, Thienpont B, Cappuyns S, Venken T, Busschaert P, Van Haele M, et al. DNA methylation-driven EMT is a common mechanism of resistance to various therapeutic agents in cancer. Clin Epigenetics. 2020;12(1):27.

19. Tam WL, Weinberg RA. The epigenetics of epithelial-mesenchymal plasticity in cancer. Nat Med. 2013;19(11):1438-49.

20. Ko TK, Javed A, Lee KL, Pathiraja TN, Liu X, Malik S, et al. An integrative model of pathway convergence in genetically heterogeneous blast crisis chronic myeloid leukemia. Blood. 2020;135(26):2337-53.

21. Guru SA, Sumi MP, Mir R, Beg MMA, Koner BC, Saxena A. Aberrant hydroxymethylation in promoter CpG regions of genes related to the cell cycle and apoptosis characterizes advanced chronic myeloid leukemia disease, poor imatinib respondents and poor survival. BMC Cancer. 2022;22(1):405.

22. Baykal-Kose S, Acikgoz E, Yavuz AS, Gonul Geyik O, Ates H, Sezerman OU, et al. Adaptive phenotypic modulations lead to therapy resistance in chronic myeloid leukemia cells. PLoS One. 2020;15(2):e0229104

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Evaluation of Readability and Reliability of Turkish Websites on Low Back Pain

Bel Ağrısı ile İlgili Türkçe Web Sitelerinin Okunabilirliği ve Güvenilirliğinin Değerlendirilmesi

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ÖZET

AMAÇ: Bu çalışmada bel ağrısı konusunda bilgilendirme içeren Türkçe internet sitelerinin okunabilirlik ve güvenilirlik düzeylerini ortaya koymayı amaçladık.

GEREÇ VE YÖNTEM: Şubat 2022'de Google'ın arama motoruna (https://www.google.com) "bel ağrısı" kelimesi yazılarak arama yapıldı. Ticari siteler, reklam siteleri, sohbet siteleri, forum siteleri, magazin siteleri, sadece resim veya video içeren siteler ve 10 cümleden az cümle içeren siteler çalışma dışı bırakıldı. Ortalama hece sayısı, ortalama 4 ve daha fazla heceli kelime sayısı ve Ateşman ve Bezirci-Yılmaz okunabilirlik, JAMA ve DISCERN skorları ile güvenilirlik değerleri hesaplanmıştır.

BULGULAR: Ortalama hece sayısı ve 4 ve daha fazla heceli ortalama kelime sayısı sırasıyla 2,78 (1,68-3,20) ve 3,74 (0,36-6,31)'dir. Median Ateşman, Bezirci-Yılmaz, okunabilirlik değerleri sırasıyla 56,10 (29,77-100,00) ve 12,80 (1,88-20,01); JAMA ve DISCERN güvenilirlik skorları sırasıyla 1.06 (0-2), 43,00 (26,00-67,00) idi.

SONUÇ: Bu çalışma sonucunda bel ağrısı ile ilgili bilgilendirme içeren Türkçe internet sitelerindeki metinlerin okunabilirlik oranı, kalite ve güvenilirliğinin oldukça düşük seviyede olduğu sonucuna ulaşıldı.

Anahtar Kelimeler: bel ağrısı, okunabilirlik, güvenilirlik, internet

ABSTRACT

OBJECTIVE: In this study, we investigated the readability and readability of Turkish websites containing information about low back pain.

MATERIALS AND METHODS: In February 2022, a search was performed by typing the word "low back pain" into Google's search engine (https://www.google.com). Commercial websites, advertising sites, chat sites, forum sites, magazine sites, sites containing only images or videos, and sites with fewer than 10 sentences were excluded from the study. Reliability scores were calculated using the mean syllable count, the mean number of words with 4 or more syllables, and Ateşman's and Bezirci-Yılmaz's scores for readability, JAMA, and DISCERN.

RESULTS: The mean number of syllables and words with 4 or more syllables was 2.78 (1.68-3.20) and 3.74 (0.36-6.31), respectively. The mean Ateşman, Bezirci-Yılmaz, and readability scores were 56.10 (29.77-100.00) and 12.80 (1.88-20.01), respectively, and the JAMA and DISCERN reliability scores were 1.06 (0-2) and 43.00 (26.00-67.00), respectively.

CONCLUSION: As a result of this study, it was found that the readability, quality, and reliability of texts on Turkish websites containing information about low back pain are at a very low level.

Keywords: low back pain, readability, reliability, internet

INTRODUCTION

Low back pain usually occurs between the bottom of the ribs and the top of the lower gluteal folds, often accompanied by leg pain. It is seen at a high rate of 70-80% during life (1,2). It can recur in 70% of patients (3). Low back pain affects not only patients but also the whole society, as it leads to a loss of working capacity(4). Due to the complex anatomical structure, neighborhood, and functional characteristics of the waist, many etiologic factors can cause pain. In addition to mechanical, infectious, and malignant causes, reasons such as job dissatisfaction and psychological stress can also lead to low back pain (5,6). Clearly, the prognosis and treatment of low back pain, which can occur for a variety of reasons, vary.

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In light of technological developments, as our daily lives change, so do the ways in which we obtain information. As of December 2018, it is known that there were over 4.1 billion Internet users in the world (7). People have started to use the Internet frequently in the field of health to get information about diseases, learn about the diagnosis and treatment process, evaluate/control the doctor's recommendations in own perceptual world, and clarify many questions and doubts in their minds (8). It has been reported that more than half of the adult population in the United States and Germany use the Internet for health information (9,10).

It is not easy for individuals to process general, non-patient-specific information on the Internet and adapt it to their own health status. For this information to be useful in the boot, it must be understandable and reliable. Unreliable, unintelligible, and unreadable information without any controls or monitoring mechanisms does more harm than good and leads to difficulties in the doctor-patient relationship (10,11). Studies of the reliability of health information on the Internet have found that the degree of reliability is low (10,12).

Information on the internet must be readable and understandable as well as reliable. The value of medical information provided for informational purposes depends on the ability of patients to understand it. Readability is a concept that expresses the 'ease or difficulty of understanding' texts by readers. Readability, which is a language-specific situation, is directly related to an individual's level of education and health literacy. Factors such as sentence length, number of syllables, and frequency of synonym use affect readability. In a study conducted in Türkiye in 2014, it was found that 64.6% of the population had inadequate health literacy. According to the report published in 2019, the average duration of education in Turkey was reported to be 7.7 years (13,14). In studies that analyzed the degree of readability of Turkish texts on various health-related topics according to the readability formula of Ateşman and Yilmaz-Bezirci, it was reported that the degree of readability of websites is insufficient (13,15-17).

There is no study in the literature that investigates the status of Turkish websites related to low back pain. In this study, we aimed to determine the degree of readability and reliability of Turkish websites with information about low back pain. If these websites are found to be inadequate in terms of readability and reliability, this should be revealed and remedial studies should be conducted in this regard.

MATERIAL & METHODS

Approval for the study was obtained from the Scientific Ethics Committee of the University of Health Sciences, Hamidiye Faculty of Medicine (Ethics Committee Protocol No: 21/674). Using the keyword "low back pain" in the Google search engine (www.google.com), a total of 150 websites were scanned in the first 15 pages in February 2022, as in previous similar studies (10). Commercial sites, sites with chat forms, advertising sites, magazine sites, sites containing only pictures or videos, news sites that did not contain information about the disease, and sites with fewer than 10 sentences were excluded. The websites to be included in the study were divided into two groups depending on the creator: 1.) Hospitals, universities, health professionals, created by health-related associations or other official institutions 2.) News sites, others (blog, anonymous, etc.).

It was investigated whether information on the definition, causes, clinical features, and treatment of low back pain could be found on the websites accessed with the given keyword. In addition, the average number of words, the average number of syllables, and the average number of words with 4 or more syllables were calculated using a computer program. The readability formulas of Ateşman and Bezirci-Yılmaz were used to calculate the degree of readability of the information texts on the websites, and the ratings of the Journal of The American Medical Association (JAMA) - Quality Criteria for Consumer Health Information (DISCERN) were used to evaluate the reliability of the information.

Ateşman readability value:

It is a formula developed by Ateşman by adapting the Flesch Reading Ease (18) formula into Turkish and based on the length of syllables, words, and sentences in the text (15).

Readability value: 198,825-40.175x(total syllables/total words)-2,610x(total words/total sentences).

According to Ateşman, the readability ranges in Turkish are as follows:

• **Ateşman Value**	**Readability Range**
• 90-100	Very easy
• 70-89	Easy

- 50-69 Moderate
- 30-49 Difficult
- 1-29 Very difficult

Bezirci-Yilmaz readability value:

Bezirci and Yilmaz; developed a new readability formula in 2010 based on previously developed readability scales and specific features of the Turkish language (16). It is calculated based on the sentence lengths in the texts (the number of words in the sentences) and the number of syllables in the words. The readability of the texts decreases when the sentence lengths in the texts and the number of syllables in the words increase. The values obtained from the formula correspond to a certain year of education in our country.

YOD: √OKS* ((H3*0.84) + (H4*1.5) + (H5*3.5) + (H6*26.25))

YOD: New Readability Value

OKS: Average number of words in a sentence

H3: Average number of three-syllable words in a sentence
H4: Average number of four-syllable words in a sentence
H5: Average number of five-syllable words in a sentence H6: Average number of six-syllable words in a sentence.

JAMA Criteria:

The JAMA benchmark criteria are used to measure the reliability, relevance, transparency, and usefulness of manuscripts (19). The assessment examines 4 parameters: 1) author details 2) source statement, reference, and citations 3) date, last update information 4) whether there are any related disclosures (sponsorship, conflicts of interest, partnerships with for-profit organizations, etc.). 0 (none), depending on whether each criterion is present or not; It is scored 1 (yes) point. The total score ranges from 0-4; a score of 3 or more indicates high reliability, while less than 2 points indicates low reliability.

DISCERN Score:

DISCERN was created by a group of experts from England to assess the reliability and quality of texts and the appropriateness of treatment options (20). It consists of three parts, in the first part there are 8 questions to measure reliability and dependability, in the second part there are 7 questions about the adequacy of treatment options. The last question in the third part is: it asks about overall quality independent of the other 15 questions. Each question is scored from 1 to 5, from "no" to "yes." An absolute affirmative will earn 5 points, an absolute negative will earn 1 point, or 2-4 points depending on how many times you answered the corresponding question. A score of 63-75 is excellent, a score of 51-62 is good, a score of 39-50 is moderate, a score of 27-38 is inadequate, and a score of 16-26 is very unsatisfactory.

Statistical Analysis

SPSS® 21 software (IBM Inc, USA) was used for data analysis. Descriptive statistics of categorical data in the study were presented using frequency and percentage values, and numerical data were presented using median (min-max) values. Whether the groups in the study were normally distributed was determined using the Shapiro-Wilks Test. Mann-Whitney U Test was used for numerical data comparisons between independent groups, and the Chi-Square test was used for categorical data comparisons. All statistical analyzes used in the study were performed bilaterally, with a 5% significance limit and 95% confidence interval.

RESULTS

Of the total 150 sites, 79 sites were included in the study because they met the inclusion criteria. Of these sites, 55 (69.6%) were in the first group and 24 (30.4%) were in the second group.

When the readability ranges of all sites included in the study are examined according to Ateşman, 3 (3.8%) of them were "very difficult", 24 (30.4%) were "difficult", 48 (60.8%) were "moderate", 2 (2.5%) were classified as "easy", and 2 (2.5%) were classified as "very easy". There was no statistically significant difference between the readability intervals of the study groups according to Ateşman (p=0.099) (Table 1).

Table 1*. Evaluation of the readability ranges of the study groups according to Ateşman*

Ease of read	Group 1 n(%)	Group 2 n(%)	p
Very difficult + difficult	22 (%40,0)	5 (%20,08)	
Medium + easy + very easy	33 (%60,0)	19 (%79,2)	0,099

p: Chi square test p value

The median average number of words in a sentence of all sites included in the study was 13.04 (2.75-23.84), the median number of syllables in a word was 2.78 (1.68-3.20), four or more syllables in a sentence median was 3.74 (0.36-

6.31), Ateşman readability median was 56.10 (29.77-100.00), Bezirci-Yılmaz readability median was 12.80 (1.88-20, 01)' (Table 2), JAMA median value was 1.06, DISCERN part 1 median was 26.00 (15.00-33.00), DISCERN part 2 median was 17.00 (7.00-30.00), the median of DISCERN total value was 43.00 (26.00-67.00) (Table 3). The Ateşman readability range of all sites included in the study was classified as "medium" difficulty. The Bezirci-Yılmaz readability score of all the sites included in the study corresponds to the undergraduate level in the Turkish education and training system.

***Table** 2. Comparison of the readability values of the study groups*

	Group 1 (n=55)	Group 2 (n=24)	p
Average word count in sentence	13,25 (9,06-23,84)	12,28 (2,75-23,84)	0,314
Average number of syllables in words	2,79 (1,68-3,20)	2,76 (1,68-2,93)	0,270
The average number of words containing four or more syllables in the sentence	3,76 (2,19-6,31)	3,36 (0,36-5,38)	0,164
Ateşman	53,54 (29,77-74,38)	59,74 (34,55-100,00)	0,065
Bezirci-Yılmaz	12,89 (7,59-20,01)	11,45 (1,88-20,01)	0,201

Mann-Whitney U Test

***Table 3:** Comparison of DISCERN and JAMA values of study groups*

	Group 1 (n=55)	Group 2 (n=24)	p
Discern 1. Part*	24 (15-33)	29 (16-33)	0,019
Discern 2. Part*	16 (7-27)	19 (7,0-30)	0,191
Discern Total[1]	42 (26-60)	48 (26-67)	0,071
JAMA** 0 JAMA** 1 JAMA** 2	9 (%16,4) 37 (%67,3) 9 (%16,4	1 (%4,2) 17 (%70,8) 6 (%25,0)	

**Mann-Whitney U Test, results are expressed as median (minimum-maximum) ** Chi square test, results are expressed as n (%)*

The average number of words in the sentence (p=0.314), the average number of syllables in the words (p=0.270), the average number of words with four or more syllables in the sentence (p=0.164), Ateşman readability scores (p=0.065), Bezirci- Yılmaz readability scores (p=0.201) were not significantly different (Table 2).

DISCUSSION

Low back pain is a health problem that affects the general population, leading to absenteeism from work and frequent use of health services. In studies conducted in our country, a lifetime prevalence of 51-86.30% was found (21-24).

With technological development, health information provided by physicians and medical personnel have become available from many different sources {25,26). The Internet and television, which are widely used in daily life, are the main sources for obtaining health information (27). With the widespread use of the Internet, information seekers encounter not only information provided by a single source but also user-produced content. Among the various sources of information, people may be confused about their diseases and treatment methods. The readability of text on websites should be correlated with people's level of education. The reliability of information available from a variety of sources is important to people when making decisions about their health status and treatment.

In the study in which Çiftçi et al. evaluated the readability of Turkish websites on drug addiction, they found that the degree of readability of the texts was "difficult" according to Ateşman and "undergraduate" according to Bezirci-Yılmaz (28). In the study in which Solak et al. evaluated the readability of Turkish websites about smoking cessation, they found that the readability range of the texts on the websites was "difficult" according to Ateşman, and "undergraduate" according to Bezirci-Yılmaz, and these results were significantly higher than the educational level of our people. stated that {29). In the study of Deniz et al., in which they evaluated the readability and content of the information texts via the triple test, the readability level of the websites was found to be moderate (57.6) according to the Ateşman formula; it was found to be at the undergraduate level according to the Bezirci-Yılmaz formula (30). In Solak's study, in which he investigated the readability of websites with information about colorectal cancer, he found that the readability of the texts on the websites was above the recommended health literacy and academic level in our country, and the texts were difficult to understand (31). In our study, the readability of the websites containing information about low back pain was found to be at moderate level of difficulty according to the Ateşman formula and at the undergraduate level according

to the Bezirci-Yılmaz formula. In the study by Ayvat et al., it was found that 70.50% of patients with low back pain had primary education or less and 29.50% had high school education or higher (32). According to these results, Turkish websites with information about low back pain are above the educational level of most patients

In their study, Yüksek and Miniksar examined the quality and reliability of websites providing information on sepsis using the ratings JAMA and DISCERN. The mean score of DISCERN was found to be 36 and the median score of JAMA was found to be 2. It was found that the quality and reliability of Internet-based information on sepsis was poor (33). Ceyhan et al. evaluated the reliability of Turkish resources on diagnosis and treatment of anterior cruciate ligament rupture and reported that Turkish resources accessed through search engines on this topic were insufficient to inform patients (17). In the study of Yılmaz and Eden, in which the information on dental trauma accessed through the Internet was evaluated using the DISCERN score, they concluded that the information provided was insufficient (34). In the study of Gökay and Görürgöz, in which Turkish websites containing information on lamellar dental veneers were evaluated with the scores DISCERN and JAMA, the average score of DISCERN was 28.1, and it was found that the quality and reliability were weak (35). In the study of Pamukçu and Izci Duran, in which they examined the videos with information about gout on the Internet, the average DISCERN score was 44.43, the average JAMA score was 2.54, and it was found that the content was of low quality (35). In our study, it was found that the average DISCERN score of the websites that contained information about low back pain was 43, and the average JAMA score was 1.06, which is consistent with the literature, and it was found that the information was inadequate.

Limitations:

The study has several limitations. The results reflect this time period because the pages on the site are scanned in a given month. Since the number of sites included in the study is small, it may not be possible to generalize to the entire country.

CONCLUSION

As a result of this study, it was found that the readability, quality, and reliability of text on Turkish websites containing low back pain information are at a very low level. We believe that it would be more beneficial if the texts on Turkish websites containing information about low back pain were of high quality, reliable and at a readable level that can be understood by the general public according to the average educational level of society.

Etik: Bu çalışmanın etik kurulu alınmıştır (No: 21/674).

Ethics committee approval had been taken (No: 21/674).

Yazar katkı durumu; Çalışmanın konsepti; EA, SK, RY, HY, İS, dizaynı; EA, SK, RY, HY, İS, Literatür taraması; EA, SK, RY, HY, İS, verilerin toplanması ve işlenmesi; EA, SK, RY, HY, İS, istatistik; EA, SK, RY, HY, İS, yazım aşaması; EA, SK, RY, HY, İS.

Author contribution status; The concept of the study; EA, SK, RY, HY, İS, design; EA, SK, RY, HY, İS, literature review; EA, SK, RY, HY, İS, collecting and processing data; EA, SK, RY, HY, İS, statistics; EA, SK, RY, HY, İS, writing phase; EA, SK, RY, HY, İS.

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REFERENCES

1. Fitzmaurice C, Allen C, Barber R, Barregard L, Bhutta Z, Brenner H, et al. A systematic analysis for the global burden of disease study. JAMA Oncol. 2017;3(4):524-48. DOI: 10.1001/jamaoncol.2016.5688

2. Karahan AY, Sahin N, Baskent A. Comparison of effectiveness of different exercise programs in treatment of failed back surgery syndrome: A randomized controlled trial. J Back Musculoskelet Rehabil. 2016 Jun 17. doi: 10.3233/BMR-160722. PMID: 27341641

3. Becker A, Held H, Redaelli M, Strauch K, Chenot JF, Leonhardt C, et al. Low back pain in primary care: costs of care and prediction of future health care utilization. Spine. 2010;35(18):1714-20. PMID: 21374895

4. Chung JW, Zeng Y, Wong TK. Drug therapy for the treatment of chronic nonspecific low back pain: systematic review and meta-analysis. Pain physician. 2013;16(6):E685-704. PMID: 24284847

5. Deyo RA, Jarvik JG, Chou R. Low back pain in primary care. Bmj. 2014;349. PMID: 25030632

6. Yıldırım P, Basol G, Karahan AY. Pilates-based therapeutic exercise for pregnancy-related low back and pelvic pain: A prospective, randomized, controlled trial. Turk J Phys Med Rehabil. 2022 Nov 24;69(2):207-215. doi: 10.5606/tftrd.2023.11054. PMID: 37671372; PMCID: PMC10475913.

7. Bujnowska-Fedak MM, Węgierek P. The impact of online health information on patient health behaviours and making

decisions concerning health. International journal of environmental research and public health. 2020;17(3):880. PMID: 32023828

8. Lu X, Zhang R. Impact of physician-patient communication in online health communities on patient compliance: cross-sectional questionnaire study. Journal of medical Internet research. 2019;21(5):e12891. PMID: 31094342

9. Wollmann K, van der Keylen P, Tomandl J, Meerpohl JJ, Sofroniou M, Maun A, et al. The information needs of internet users and their requirements for online health information—A scoping review of qualitative and quantitative studies. Patient Education and Counseling. 2021;104(8):1904-32. PMID: 33563502

10. Yurdakul OV, Kilicoglu MS, Bagcier F. Evaluating the reliability and readability of online information on osteoporosis. Archives of Endocrinology and Metabolism. 2020;65:85-92. PMID: 33166440

11. Balatsoukas P, Kennedy CM, Buchan I, Powell J, Ainsworth J. The role of social network technologies in online health promotion: a narrative review of theoretical and empirical factors influencing intervention effectiveness. Journal of medical Internet research. 2015;17(6):e3662. PMID: 26068087

12. Kothari M, Moolani S. Reliability of "Google" for obtaining medical information. Indian journal of ophthalmology. 2015;63(3):267. PMID: 25971176

13. Solak İ, Kozanhan B, Ay E. Readability of Turkish Websites Containing COVID-19 Information. The Anatolian Journal of Family Medicine. 2021;4(1):57. DOI: 10.5505/anatoljfm.2020.21939

14. Conceição P, Kovacevic M, Mukhopadhyay T. Human Development: A Perspective on Metrics. Measuring Human Capital: Elsevier; 2021. p. 83-115. 10.1016/B978-0-12-819057-9.00007-X (DOI)

15. Ateşman E. Measuring readability in Turkish. AU Tömer Language Journal. 1997;58(2):171-74.

16. Bezirci B, Yılmaz AE. A software library for measurement of readability of texts and a new readability metric for Turkish. DEÜ FMD. 2010;12(3):49-62.

17. Ceyhan E, Gurhan U, İnci F, Karaismailoğlu E, Yavuz İA, Koçak C, et al. Türkçe İnternet Sitelerindeki Ortopedik Hastalıklar Hakkındaki Bilgilerin Değerlendirilmesi: Ön Çapraz Bağ Rüptürü Üzerine Pilot Bir Çalışma. SDÜ Tıp Fakültesi Dergisi. 2021. doi: 10.17343/sdutfd.595351. https://doi.org/10.17343/sdutfd.595351

18. Flesch R. A new readability yardstick. Journal of applied psychology. 1948;32(3):221. PMID: 18867058

19. Silberg WM, Lundberg GD, Musacchio RA. Assessing, controlling, and assuring the quality of medical information on the Internet: Caveant lector et viewor—Let the reader and viewer beware. Jama. 1997;277(15):1244-5. PMID: 9103351

20. Charnock D, Shepperd S, Needham G, Gann R. DISCERN: an instrument for judging the quality of written consumer health information on treatment choices. Journal of Epidemiology & Community Health. 1999;53(2):105-11. PMID: 10396471

21. Özdemir F, Karaoğlu L, Özfırat Ö. Malatya il merkezinde yaşayan bireylerde boyun, sırt ve bel ağrısı prevalansları ve etkileyen faktörler. 2013. PMID: 23588867

22. Altinel L, Kose KC, Ergan V, Isik C, Aksoy Y, Ozdemir A, et al. The prevalence of low back pain and risk factors among adult population in Afyon region, Turkey. Acta Orthop Traumatol Turc. 2008;42(5):328-33. PMID: 19158453

23. ARSLANTAŞ D, METİNTAŞ S, KALYONCU C, ÜNSAL A, IŞIKLI B. Eskişehir kırsal kesimi erişkinlerinde bel ağrısı sıklığı. Medical Network Klinik Bilimler ve Doktor. 2003;9(4):391-5. ISSN: 1300-4743

24. Esen ES, Toprak D. Bel ağrısı sıklığı ve ilişkili faktörlerin değerlendirilmesi. Ankara Medical Journal. 2018;18(4):460-9. doi.org/10.17098/amj.497473

25. AVCI AGİB, SÖNMEZ AGMF. SAĞLIK İLETİŞİMİ BAĞLAMINDA BİREYLERİN TELEVİZYONDA YAYINLANAN SAĞLIK PROGRAMLARINI İZLEME ALIŞKANLIKLARI VE MOTİVASYONLARI: ELAZIĞ ÖRNEĞİ. Gümüşhane Üniversitesi İletişim Fakültesi Elektronik Dergisi. 2013;2(2).

26. Basch CH, MacLean SA, Romero R-A, Ethan D. Health information seeking behavior among college students. Journal of community health. 2018;43(6):1094-9. PMID: 29779074

27.

28. Luth W, Jardine C, Bubela T. When pictures waste a thousand words: analysis of the 2009 H1N1 pandemic on television news. PloS one. 2013;8(5):e64070. PMID: 23691150

29. ÇİFCİ HKK, Kozanhan B, Solak İ. Madde Bağımlılığı İle İlgili Türkçe İnternet Sitelerinin Okunabilirliğinin Değerlendirilmesi. Bağımlılık Dergisi. 2020;21(1):56-63.

30. Solak İ, Kozanhan B, Akın A, Gürer N, Ay E, Eryılmaz MA. Evaluation of Readability of Turkish Websites About Smoking Cessation Sigara Bırakma Hakkında Hazırlanan Türkçe İnternet Sitelerinin Okunabilirliğinin Değerlendirilmesi. https://doi.org/10.51982/bagimli.829808

31. Deniz ÇD, Kozanhan B, Tutar MS, Özler S. Üçlü test ile ilgili internet bilgilendirme metinlerinin okunabilirlik ve içeriklerinin değerlendirilmesi. Mersin Üniversitesi Sağlık Bilimleri Dergisi. 2020;13(1):35-44. https://doi.org/10.26559/mersinsbd.569617

32. SOLAK M. Kolorektal Kanser Hakkında Bilgi İçeren İnternet Sitelerinin Okunabilirliği. Harran Üniversitesi Tıp Fakültesi Dergisi. 2019;16(3):509-13. https://doi.org/10.35440/hutfd.623920

33. AYVAT PÜ, AYDIN ON, OĞURLU M. Algoloji polikliniğine başvuran bel ağrılı hastaların risk faktörleri. AĞRI 2012; 24 (4): 165. 2012;70. doi: 10.5505/agri.2012.38258

34. YUKSEK A, Miniksar ÖH. Does the Internet Provide Enough Information About Sepsis for the General Public. Çukurova Anestezi ve Cerrahi Bilimler Dergisi. 2021;4(3):173-81. Doi: 10.36516/jocass.2021.86

35. Yılmaz E, Eden E. Dental Travma ile İlgili İnternet Aracılığıyla Ulaşılan Bilgilerin Niteliğinin Değerlendirilmesi. Ege Üniversitesi Diş Hekimliği Fakültesi Dergisi. 2020;41(3):231-5.

36. GÖKAY GD, GÖRÜRGÖZ C. Laminate Veneer: Türkçe İnternet Sitelerindeki Bilgilerin Kalite Değerlendirmesi. Turkiye Klinikleri Dishekimligi Bilimleri Dergisi. 2021;27(4).

Olgu Sunumu / Case Report
Aegean J Med Sci 2024;1:24-27

Dilde Uyuşma ve Çatlak Şikâyetleri ile Başvuran MTHFR Mutasyonu Saptanan Hasta: Vaka Sunumu

Patient With MTHFR Mutation Presenting With Tingling and Cracking in the Tongue: Case Presentation

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ÖZET

17 yaş erkek hasta dilde uyuşma ve dilinde çatlaklar şikayeti ile başvurdu. Hastanın fizik muayenesi harita dili olması dışında tamamen normaldi. büyümesi ve gelişmesi normaldi. Yapılan laboratuvar incelemelerinde tam kan sayımı ve rutin biyokimya testleri normaldi. B12 düzeyi normal , folik asit hafif düşük saptandı ve homosistein düzeyi yüksek olarak saptandı. Hastada etiyolojiye yönelik yapılan ileri incelemelerde MTHFR geninde homozigot mutasyon tespit edildi ve tedavi başlandı. Hastaya folik asit , B12 ve betain tedavisi verildi. Tedavi ile homosistein düzeyinin kademeli düştüğü gözlemlendi. Dilde yara, harita dili gibi oral lezyonlarda B vitamini eksiklikleri pediatri pratiğinde sık akla gelen nedenlerdendir. Ancak tedavi ile düzelmeyen homosistein yüksekliğinde homosistinüri ve MTHFR mutasyonu da etiyolojide akılda bulundurulmalıdır..

Anahtar Kelimeler: homosistein yüksekliği, MTHFR mutasyonu, harita dili

ABSTRACT

A 17-year-old male patient presented with complaints of tingling and cracks on the tongue. Except for geographical tongue, the physical examination of the patient was entirely normal. His growth and development were also normal. Laboratory investigations including complete blood count and routine biochemistry tests were within normal limits. B12 level was normal, while folate level was slightly low, and homocysteine level was found to be high. Advanced investigations aiming to determine the etiology revealed a homozygous mutation in the MTHFR gene, and treatment was initiated. The patient received folate, B12, and betaine therapy. It was observed that homocysteine levels gradually decreased with the treatment. Oral lesions such as tongue sores and geographical tongue due to B vitamin deficiencies are common considerations in pediatric practice. However, in cases of persistent high homocysteine levels despite treatment, homocystinuria and MTHFR mutation should also be taken into account in the etiology.

Keywords: high homocysteine level, MTHFR mutation, geographic tongue

GİRİŞ

MetilenTetraHidroFolat Redüktaz (MTHFR) enzimi, folat metabolizmasında önemli bir enzimdir (1). İnsan MTHFR geni, kromozom 1p36.3'de lokalize olmuştur ve 656 aminoasitten oluşan MTHFR enzimini kodlar (2).

Homosistein vücudumuz tarafından diğer proteinlerin yapımında yeniden kullanılmak üzere geri dönüştürülebilir. Bu geri dönüşüm için B12, B6 ve folik asit (B9) vitaminlerine ihtiyacımız vardır. Bir kişi B12, B6 veya folik asit eksikliği yaşıyorsa, homosistein etkili bir şekilde geri dönüştürülemez ve bu nedenle kanın içinde birikir (3). Ayrıca, geri dönüşümün etkili olabilmesi için MTHFR enzimine ihtiyaç vardır.

MTHFR C677T polimorfizminde, MTHFR enzimini kodlayan gende 677. nükleotid olan C (Sitozin)'in →T (Timin)'e dönüşmesi sonucu ortaya çıkan bir nokta mutasyonu vardır (4-5). MTHFR enzimini üreten gendeki kalıtsal mutasyonlar, etkin çalışmayan bir enzime yol açabilir ve bu da yükselmiş homosistein seviyelerine neden olabilir (6).

Kan plazmasındaki yüksek homosistein seviyesi, inme, kardiyovasküler hastalıklarla ilişkilidir ve koroner arter hastalığı olan hastalarda artmış mortalite ile ilişkilidir (7). Bir meta-analizde, plazma homosisteinindeki her 5 µmol/l'lik artışın, erkeklerde koroner kalp hastalığı riskini %60, kadınlarda ise %80 artırdığını göstermektedir (8). Homosistein, metiyoninin metil grubunun DNA'ya, proteinlere veya diğer moleküllere transfer edilmesiyle oluşur. Plazma homosisteinin bazal seviyesi, homosisteinin metionine remetilasyonu ile belirlenir (9). Bu reaksiyon, enzim MTHFR tarafından düzenlenir, bu enzim 5,10-

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metilentetrahidrofolatı 5-metiltetrahidrofolata dönüştürür (10). Metiyonin/homosistein dengesindeki bozukluklara, temel koenzimler olan B6, B12 ve folat eksiklikleri ile MTHFR ve sistationin beta sentaz (CBS) genlerindeki nadir mutasyonlar neden olur. Bu genetik defektler, plazmada büyük ölçüde artmış homosistein seviyelerine ve zihinsel gerilik, kemik bozuklukları, inme ve erken aterosklerotik hastalığa neden olur (11). Son zamanlarda, MTHFR geninde yaygın bir C677T (ala-val) polimorfizmi tanımlanmıştır ve bu, metionin/homosistein metabolizmasının daha az ciddi bir bozukluğuna yol açar (12).

OLGU

17 yaşında erkek hasta, dilde uyuşma ve tekrarlayan çatlak şikâyetleri ile hastaneye başvurdu (Foto 1). Daha önce bilinen bir hastalığı olmayan hastanın, büyüme ve gelişmesi yaşı ile uyumluydu. Geliş muayenesi dilde belirgin çatlaklar olması dışında tamamen doğaldı. Tam kan sayımı ve rutin biyokimya testlerinde anormal değer saptanmadı. Dilde yaralarla gelen hastalarda B vitamini düşüklükleri ilk akla gelmesi gereken klinik durumlardan biridir. Ancak hastamızın kan B12 düzeyi normaldi, folat düzeyi hafif düşüktü. İdrar organik asit analizinde ise eser metilmalonik asit atılımı mevcuttu.

Bu hastalarda kobalamin metabolizması bozuklukları, MTHFR mutasyonunun da benzer kliniğe neden olabileceği unutulmamalıdır. Etiyolojiye yönelik ileri incelemelerde homosistein düzeyi 62 µmol/L olup, yüksek saptandı. Kan metiyonin düzeyi ve ardışık kütle spektrometrisinde (tandem mass) C3 propiyonilkarnitin düzeyi normaldi. Hastanın geliş ve takip kanları Tablo 1'de görülmektedir. Hastada kan metiyonin düzeyinin normal olması ve hastanın göz muayenesinin ve ekokardiyografisinin normal olmasından dolayı klasik homosistinüri ön planda düşünülmedi. Kobalamin metabolizması bozukluğu veya MTHFR mutasyonu ön tanı olarak düşünüldü.

Foto 1. *Dilde çatlaklar (harita dili)*

Hastadan tanıya yönelik yapılan ileri genetik incelemelerde MTHFR geninde C677T homozigot değişim tespit edildi. Bu gendeki olası diğer mutasyonlar açısından tüm gen dizi analizi planlandı. Hastaya vitamin B6, B12, folik asit oral olarak ve hidroksikobalamin IM başlandı. Tedavi dozları Tablo 2'de görülmektedir. Homosistein yüksekliği tromboembolik olay açısından risk oluşturduğundan, hastaya oral aspirin tedavisi başlandı.

Tablo 1. *Kan Değerleri*

	Homosistein	B12	Folat	Tandem C3 Karnitin	Metiyonin	İOA MMA
Birim	µmol/L	ng/L	µg/L	µmol/L	µmol/L	mmol/mol/kre
Normal aralık	<15	270-1132	7.8-20	0.28-2.9	12-40	0-0.01
Tedavi öncesi	**62 (Y)**	298	**6.4 (D)**	1.05 (N)	28 (N)	1.28 (eser)
Tedavi sonrası 2. hafta	**26 (Y)**	1094	8.4 (N)			
Tedavi sonrası 4. hafta	12	1200	14.4(N)			

MMA: Metilmalonik asit, N: Normal, D: Düşük, Y: Yüksek C3: Propiyonil Karnitin, B12: Kan Vitamin B12 Düzeyi, İOA: İdrar Organik Asit Analizi

Tablo 2*. Tedavi dozları*

İLAÇ	DOZ
Betain (po)	Henüz başlanmadı
Siyanokobalamin (po)	250 mg/gün
Pridoksin (po)	100 mg/gün
Hidroksikobalamin (im)	1 mg ilk iki hafta haftada 1 kez, sonra ayda 1 kez
Folik Asit (po)	Haftada iki gün 2.5 mg
Aspirin (po)	100 mg/gün

im: intramusküler po: peroral

Hastanın 1 hafta sonraki kontrolünde klinik iyileşme gözlendi, dilde çatlaklar ve uyuşma geçti. Tedaviden 2 hafta sonra homosistein 26 µmol/L'ye düştü. Bir ay sonra kontrol homosistein 12 µmol/L (normal) olarak saptandı.

SONUÇ

Dilde uyuşma, perioral yara şikâyeti ile başvuran hastalarda vitamin eksiklikleri hekimlerce ön tanıda sık akla gelen hastalıklardır. Ancak homosistinüri, kobalamin defekti ya da MTHFR mutasyonu gibi metabolik hastalıklar da ayırıcı

tanıda bulundurulmalıdır. Gerek testlerin her laboratuvarda çalışılamaması, gerek hastalıkların görece nadir görülmeleri bu hastalıkların gözden kaçmasına neden olmaktadır. Homosistein yüksekliğinin biyokimyasal ayırıcı tanısını yapabilmek için kan metiyonin düzeyi, tandem mass spektrometri ve idrar organik asit analizine bakılması gerekmektedir. Biyokimyasal belirteçler ışığında genetik doğrulama ile hastanın tanısı konulmalı ve mümkün olan en kısa sürede tedavisine başlanmalıdır.

Tablo 3. *Homosistein yüksekliği ayırıcı tanısı*

	Homosistein	Tandem mass (C3 düzeyi)	İdrar Organik Asit (MMA Düzeyi)	Kan Aminoasit (Metiyonin düzeyi)
Klasik homosistinüri	Y	N	N	Y
Kobalamin Defekti	Y	Y/N	Y/N	D/N
MTHFR mutasyonu	Y	N	Y/N	N/D

Y: Yüksek N: Normal D: Düşük

Tedavide vitamin B12, betain, B6 ve folik asit takviyesi verilmektedir. Betain verilirken yüksek dozlarda retinaya toksik olabileceği ve aralıklı göz muayenesi yapılması gerektiği unutulmamalıdır.

Ayrıca bu hastalarda diyetin de özel bir yeri vardır. Folik asit ve B vitamininden zengin beslenme diyetin temelini oluşturmaktadır. Yapılan çalışmalarda, hiperhomosisteineminin tedavisinde folik asitten zengin beslenmenin homosistein düzeyini düşürdüğü bildirilmiştir (13). Günlük diyetin içerisine 0.5 mg folik asit alımı homosistein seviyeleri %25 oranında düşürülebilmektedir (14).

Homosistein yüksekliğinde tromboemboli için ciddi risk oluşturmaktadır. Bu nedenle bu hastalarda aspirin profilaksisi hayati önem taşımaktadır. Ancak B12 ve folat eksikliğinin de homosistein yüksekliğine neden olabileceği unutulmamalı, bu yüzden tedavi başlanmadan önce vitamin eksikliği yönünden hasta taranmalı ve tedavi ile homosistein düzeyinin düşüşü teyit edilmelidir (15).

Etik; Bu yazıda sunulan olgu için sunulan bilgilerin akademik amaçlı kullanımı hakkında detaylı bilgileri de içeren imzalı "Bilgilendirilmiş onam formu" alınmıştır.

Ethics; For the case presented in this article, a signed "informed consent form" was obtained, which includes detailed information about the use of the information presented for academic purposes.

Yazar katkı durumu; Çalışmanın konsepti; HY, MK, dizaynı; HY, MK, Literatür taraması; HY, MK, verilerin toplanması ve işlenmesi; HY, MK, istatistik; HY, MK, yazım aşaması; HY, MK.

Author contribution status; The concept of the study; HY, MK, design; HY, MK, literature review; HY, MK, collecting and processing data; HY, MK, statistics; HY, MK, writing phase; HY, MK.

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KAYNAKLAR

1. Rosenblatt DS. Methylenetetrahydrofolate reductase. Clin Invest Med, 2001;24:59.

2. Homberger G, Linnebank M, Winter C, et al. Genomic structure and transcript variants of the human methylenetetrahydrofolate reductase gene. Eur J Hum Genet, 2000;8:7729.

3. Selhub J. Homocysteine metabolism. Annual review of nutrition, 1999;19(1):2246.

4. Friedman G, Goldschmidt N, Friedlander Y, et al. Common mutation A1298C in human methylenetetrahydrofolate reductase gene: Association with plasma total homocysteine and folate concentrations. J Nutr, 1999;129:61661. 10.

5. Goyette P, Rozen R. The thermolabile variant 677CT can further reduce activity when expressed in cis with severe mutations for human methylenetetrahydrofolate reductase. Hum Mutat, 2000; 16:1138.

6. Finkelstein J D: The metabolism of homocysteine: pathways and regulation. E ur J Pediatr, 1998; 157 (suppl 2): S4.

7. Nygard O, Nordrehaug JE, Refsum H, Ueland PM, Farstad M, Vollset SE: Plasma homocysteine levels and mortality in patients with coronary artery disease. N Engl J Med, 1997;337:2236.

8. Boushey CJ, Beresford SAA, Omenn GS, Motulsky AG: A quantitative assessment of plasma homocysteine as a risk factor for vascular disease. JAMA, 1995;274:101057.

9. Miller JW, Nadeau MR, Smith D, Selhub J: Vitamin B6 deficiency vs folate deficiency: comparison of responses to methionine loading in rats. Am J Clin Nutr, 1994;59:101039.

10. Mudd SH, Levy HL, Skovby F: Disorders of transsulfuration. In Scriver CR, Beaudet AL, Sly WS, Valle D (eds). The Metabolic Basis of Inherited Disease, 6th edn. New York, 1989;693–734.

11. Frosst P, Blom HJ, Milos R et al: A candidate genetic risk factor for vascular disease: a common mutation in methylenetetrahydrofolate reductase. Nat Genet, 1995;10:111–113.

12. Lowering blood homocysteine with folic acid based supplements: meta-analysis of randomised trials. Homocysteine Lowering Trialists' Collaboration. BMJ, 1998;316:8898.

13. Andreotti F, Burzotta F, Manzoli A, Robinson K. Homocysteine and risk of cardiovascular disease. J Thromb Thrombolysis, 2000;9:21.

14. Pehlivan A, Erduran E, Bahadır A, Reis GP. 18 Yaş Arası Çocuklarda Nütrisyonel Vitamin B 12 Eksikliğinde Oral Kobalamin Tedavisinin Etkinliğinin Retrospektif Değerlendirilmesi. Turkiye Klinikleri Journal of Pediatrics, 2023;32(1).

Olgu Sunumu / Case Report
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Microblading İşlemi Ardından Gelişen Skar Sarkoidozu

Scar Sarcoidosis Developing After Microblading Procedure

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ÖZET

Skar sarkoidozu, eski travma alanlarının üzerinde gelişen, histopatolojik olarak non-kazeifiye granülomatöz reaksiyon ile karakterize, nadir görülen kütanöz sarkoidoz tipidir. Skar sarkoidozu nadir bir klinik olmasının yanı sıra sistemik sarkoidoz açısından klinisyen için uyarıcı olabilmektedir. Bu yazımızda güzellik merkezinde 5 yıl önce kaşlarına microblading işlemi (birkaç küçük iğneden oluşan küçük bir el aletinin cilde yarı kalıcı pigment eklemek için kullanıldığı bir dövme tekniğidir) ardından her iki kaşında diffüz olarak skar sarkoidozu gelişen ve sistemik tutulum açısından yapılan taramalarda pulmoner tutulumun eşlik ettiği öğrenilen otuz beş yaşında kadın bir olgu sunulmaktadır.

Anahtar Kelimeler: sarkoidoz, skar, akciğer, dövme, kaşlar

ABSTRACT

OBJECTIVE: This article aims to provide information about a rare skin condition called scar sarcoidosis by examining a case study, detailing its diagnosis, treatment, and associated risks.

CASE: A thirty-five-year-old female patient was diagnosed with scar sarcoidosis on both eyebrows. The case outlines the diagnostic process, histopathological findings, and treatment plan in detail.

CONCLUSION: Scar sarcoidosis, a rare skin disease, can often be mistaken for keloid or hypertrophic scars. Due to its potential for systemic involvement, it requires careful evaluation. It emphasizes the importance of undergoing aesthetic procedures under medical supervision, necessitating thorough clinical assessment beforehand.

Keywords: sarcoidosis, scar, lung, tattooing, eyebrows

GİRİŞ

Sarkoidoz etiyolojisi tam olarak bilinmeyen [1] , akciğer, deri, sinir sistemi, göz gibi çeşitli organlarda görülebilen ve non-kazeifiye epiteloid hücre granülomları ile karakterize edilen inflamatuar multisistemik bir hastalıktır.[2] Sarkoidoz tanısı alan hastaların dörtte birinde cilt tutulumu gözlenir. Kutanöz sarkoidoz, spesifik ve non-spesifik olmak üzere iki ana kategoriye ayrılır. Non-spesifik lezyonlar arasında en sık görüleni eritema nodosumdur. Spesifik lezyonlar ise lupus pernio, infiltre plaklar, makulopapüler erüpsiyon, subkutanöz nodüller ve skarları içerir. [3] Skar sarkoidozu, kutanöz sarkoidozun en karakteristik ve en nadir görülen klinik formudur.[4] Bu yazıda, microblading işlemi sonrasında her iki kaşında skar sarkoidozu gelişen ve sistemik sarkoidoz için yapılan taramalarla birlikte akciğer tutulumunun eşlik ettiği izlenen bir olgu sunulmaktadır.

OLGU

Otuz beş yaş kadın hasta, son bir yıldır her iki kaşında sarı-turuncu renkli, kaş boyunca uzanan kabarıklıklar nedeniyle tarafımıza başvurdu. Hastanın 5 yıl önce her iki kaşa microblading işlemi yaptırdığı öyküsü alındı. Hastanın özgeçmişinde menometroraji nedeniyle 5 yıl önce histerektomi operasyonu var. Hastanın kronik hastalık ve düzenli kullandığı ilaç bulunmamakla birlikte soy geçmişinde özellik izlenmedi. Hastanın gece terlemesi, kilo kaybı ve ateş şikayeti bulunmamaktaydı. Hastanın fizik muayenesinde solunum sistemi dahil tüm sistemik muayenesinde anormal bir bulguya rastlanmadı. Hastanın dermatolojik muayenesinde her iki kaş lineer hattı boyunca kaş medialinden lateraline kadar devam eden, sarı-turuncu renkli, verrüköz görünümlü papüller izlendi. (Resim 1) Hastanın biyopsi sonrası kaşlarında oluşabilecek iz ihtimali nedeniyle (kozmetik kaygı) ile hastadan shave biyopsi alınmasına karar verildi. Hastanın sağ kaş lateralinden skar sarkoidozu, yabancı cisim reaksiyonu ,keloid ön tanılarıyla alınan shave biyopsi sonucunda epidermisin altından başlayan epiteloid morfolojide histiyosit kümeleri, 1-2 adet Langhans tipi dev hücre oluşumu izlenen granülamatöz

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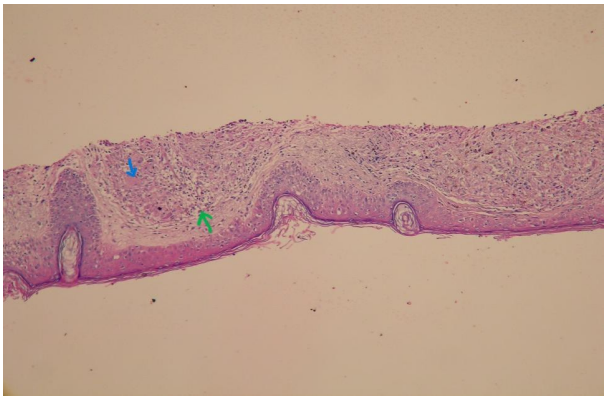
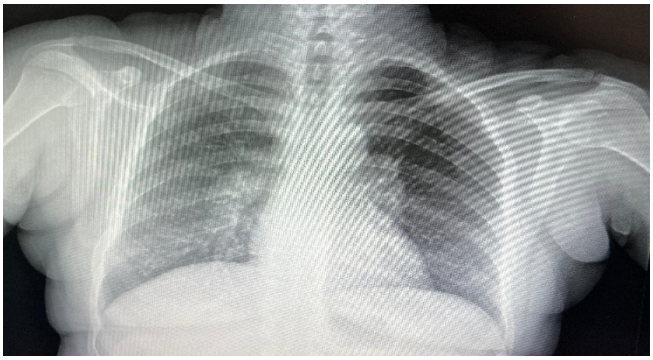
inflamasyon izlendi.(Resim 2). Hastanın yapılan laboratuvar incelemelerinde karaciğer ve böbrek fonksiyon testleri, kan ve idrar kalsiyum düzeyi, tam idrar tetkiki, tiroid fonksiyon testleri normal sınırda izlendi. Hastanın serum "anjiotensin converting enzyme" (ACE) düzeyi 113.28 U/L(8-52 U/L) , hemoglobin değeri 9.7gr/dl (12-16 gr/dl), eritrosit sedimentasyon hızı 62 mm/h (0-20mm/h), CRP değeri 12.43 mg/L(0-5 mg/L) olarak anormal düzeyde oldukları ölçüldü. Hastanıın akciğer grafisinde sağ hiler lenfadenopati izlendi(Resim 3). Hastanın aktif pulmoner yakınması bulunmamasına rağmen pulmoner tutulum açısından göğüs hastalıkları polikliniğine yönlendirildi. Hastanın toraks bilgisayarlı tomografisinde mediastende prevasküler alanda, paratrekeal alanda subkarinal alanda en büyüğü 29x20 mm boyutunda lenfadenopatiler ve lenf nodları izlenmiştir. Hastanın sağ hilusta büyüğü 32x17 mm boyutlarında yumuşak doku dansitesi ,sol hiler bölgede 23x17 mm boyutlarında lenfadenopati, sağ akciğer üst lob posteriorunda ve anterior segmentlerinde santral kesimde büyüğü 5.3 mm boyutlarında çok sayıda nodül ve sol akciğerde üst lob anterior ve lingular segmentlerde santral kesimlerde büyüğü lingular segmentte 7 mm boyutunda çok sayıda nodül dikkati çekmiştir.(Resim 4) Hastaya göğüs hastalıkları tarafından endobronşiyal ultrasonografi planlandı. Hastanın endobronşiyal ultrasonografi sonucunda granülamatöz reaksiyon ve granülomlar içinde asteroid body izlendi. Hastanın her iki kaşına intralezyonel streoid enjeksiyonu(1/9 oranında sulandırılmış triamsinolon asetonid) , oral minosiklin (monondox tablet) ve topikal takrolimus (tacrolin krem) tedavisi verildi. Hasta tedavi sonrasında takiplere gelmediği için verdiğimiz tedavi değerlendirilemedi.

Resim 1. *Her iki kaş medialinden başlayıp tüm kaş boyunca lineer olarak uzanan sarı-turuncu renkli papüller*

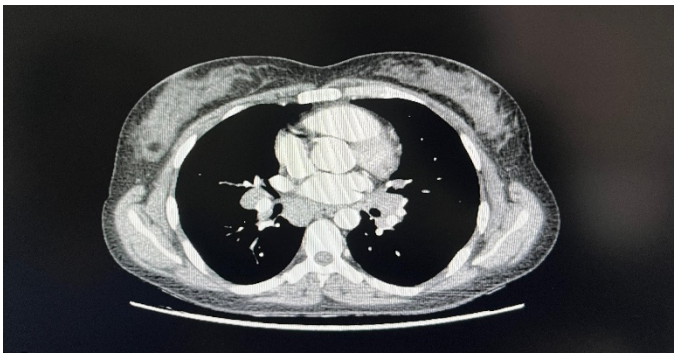
Resim 2. *Mavi ok ile gösterilen dev hücre , yeşil ok ile gösterilen epiteloid hücre grubu, Epidermisin hemen altından başlayan bazıları epiteloid morfolojide histiosit kümeleri, 1-2 adet Langhans tipi dev hücrelerden oluşan granülomatöz inflamasyon(x100 büyütme, hematoksilen & eozin)*



Resim 3. *Postero-anterior akciğer grafisinde sağ akciğerde hiler lenfadenopati*



Resim 4. *Kontrastlı toraks bilgisayarlı tomografisinde parankimde çok sayıda nodül*



SONUÇ

Sarkoidoz etiyolojisi halen aydınlatılamamış kronik granülamatöz bir hastalıktır. [5] Sarkoidoz sıklıkla akciğer tutulumunun izlendiği ancak deri, lenf nodu, karaciğer, sinir sistemi ve göz gibi herhangi bir organı tutabilen sistemik bir hastalıktır. [4] Yapılan çalışmalarda kadınlarda erkeklere göre 5 kat daha sık görüldüğü bulunmuştur. [6] Hastalığın İskandinav insanlarında en yüksek insidansta bulunduğu

tespit edilmiştir. Hastaların yaklaşık %25' inde sistemik hastalıkla beraber cilt tutulumu izlenmiştir. [4] Sar-koidozun kutanöz tutulumu histopatolojik olarak non-kazeifiye granülomları içeren spesifik deri lez-yonları ve granülom içermeyen reaktif bir inflamatuar süreç sonunda oluşan non-spesifik lezyonlar olarak sınıflandırılmaktadır. [3]

Sarkoidozun cilt tutulumları non-spesifik olarak en sık izlenen eritema nodosum, ve spesifik deri lezyonlarından olan lupus pernio, makülopapüler döküntü, infiltre plaklar , subkutan nodül ve skar gibi geniş bir klinik yelpaze göstermektedir. Sarkoidozun kutanöz tutulumu granüloma anulare , lepra, kutanöz tüberkülozis, liken planus gibi hastalıklara benzer cilt tutulumu yapmakta ve buna benzer birçok hastalıkla ayırıcı tanıya girmektedir. [2].Bu nedenle kutanöz sarkoidoz dermatolojik olarak büyük taklitçi hastalıklardan biri olarak kabul edilmekte ve tanının kesinleşmesi için histopatolojik incelemeye ihtiyaç duyulmaktadır.[7]

Tüm biyopsi materyalleri mikobakteriyal ve fungal mikroorganizmaların incelenmesi amacıyla mikrobiyolojik olarak araştırılmalıdır. Ayrıca benzer bir granülamatöz reaksiyona neden olan yabancı cisim reaksiyonunun granülomlarından ayırt edilebilmesi için polarize ışık mikroskobisi ile ek olarak incelenmesi gerektiği unutulmamalıdır. [8]

Skar sarkoidozu , kutanöz sarkoidozun nadir olarak bulunan, ancak hastalığa spesifik , nonkazeifiye epiteloid hücre granülomlarıyla infiltre bir formudur. [4] Skar sarkoidozunun kesin insidansı bilinmemekle birlikte %2.9 ile %13.8 arasında çeşitli oranlarda tespit edildiği raporlanmıştır. [5]

Skar sarkoidozu eski cerrahi skarlar dahil enjeksiyon bölgelerinde(botulinum toksin enjeksiyonu, hyaluronik asit enjeksiyonu), intramüsküler enjeksiyon bölgeleri, aksiller elektroliz bölgeleri, silisyum gibi yabancı maddelerin gömülü olduğu bölgelerde, herpes zoster ve dövme gibi eski travma alanları üzerinde gelişen kutanöz sarkoidoz formudur. [9] Eski skar üzerinde skar sarkoidozu gelişimi 6 ay ile 59 yıl gibi geniş bir periyotta meydana gelebileceği izlenmiştir. [4]

Eski skar alanları üzerinde neden skar sarkoidoz geliştiği net olarak açıklanamamakla beraber genetik olarak yatkınlığı bulunan bireylerin sarkoidoz ile aktive olmuş T lenfositlerin yabancı cisim reaksiyonuna benzer bir granülamatöz reaksiyon neden olduğu tahmin edilmektedir. [1]

Skar sarkoidozu ve diğer kutanöz sarkoidoz tutulumları arasında yapılan çalışmalarda , skar sarkoidozunda pulmoner tutulumun daha sık görüldüğü bulunmuştur. [3] Bu nedenle histopatolojik olarak skar sarkoidozu tanısı alan hastaların pulmoner tutulum ve diğer sistemik tutulumlar açısından daha detaylı bir klinik araştırmaya ihtiyacı vardır.

Skar sarkoidozu tedavisinde uzun dönemde birçok hastada tedaviye rağmen refrakter lezyon gelişebilmekte ya da tedavi sonrası nüks görülebilmektedir. [6] Hastalarda progresif ve tedaviye dirençli sistemik tutulum yoksa, sıklıkla sistemik tedavi tercih edilmemektedir. Lokalize tutulumlarda topikal veya intralezyonel kortikosteroid kullanılmaktadır. İntralezyonel steroidin (triamsinolon asetonid) özellikle 2-3 haftalık aralıklarla tekrar edilmesinin daha efektif bir tedavi olduğu izlenmiştir. [7] Bununla beraber diğer alternatif tedavi seçenekleri ise antimalaryaller(klorokin,hidroksiklorokin), izotretinoin, allopürinol, talidomid, tetrasiklin , metotreksat,, mikofenolat mofetil, anti-TNF inhibitörleri (etanersept, infliksimab, adalimumab) , oral psöralen ile beraber PUVA, karbon dioksid lazer, Q-anahtarlı lazerdir.Bazı çalışmalarda topikal takrolimus , kriyoterapi ve radyoterapinin de kutanöz sarkoidoz tedavisinde başarılı sonuçlar elde ettiği izlenmiştir.[12345678] Küçük lezyonlarda cerrahi eksizyon tercih edilebilir ancak keloidal ya da hipertrofik skar ile rekürrens riski göz önünde bulundurulmalıdır. [6]

Sonuç olarak, skar sarkoidozu, kutanöz sarkoidozun nadir görülen bir varyantıdır ve genellikle keloid veya hipertrofik skara benzeyen cilt lezyonlarıyla kendini gösterir. Dermatolojik olarak pek çok hastalığa benzeyen bu hastalık, büyük bir taklitçi olarak kabul edilir. Bu nedenle, eski skarlar üzerinde gelişen değişikliklerin ayırıcı tanısında göz önünde bulundurulmalıdır. Bizim hastamızda olduğu gibi skar sarkoidozu teşhis edilen hastalarda, her zaman sistemik tutulum olasılığı göz önünde bulundurulmalıdır. Bazen sadece kutanöz tutulum ile semptom veren ve sarkoidoz tanısı alan hastalarda sistemik tutulum açısından taramalar ile sistemik tutulum tespit edilebilir. Sarkoidozun en önemli ipuçlarından birinin sadece kutanöz tutulum olabileceği klinisyen tarafından bilinmelidir.

Bu nedenle, sarkoidoz hastalığını erken teşhis etmek ve tedavi etmek için detaylı klinik sorgulama ve radyolojik görüntüleme gibi yöntemlerin kullanılması gerekmektedir. Sarkoidozun kronik bir hastalık olduğu göz önünde bulundurularak, hastanın sistemik değerlendirmesi tamamlandıktan sonra düzenli aralıklarla klinik kontrollerin yapılması gerektiği hastaya açıkça ifade edilmelidir. Bu sayede hastaların sağlık durumu takip edilir ve gerektiğinde uygun tedavi planları uygulanır.

Bu vakada da anlaşılacağı üzere estetik veya güzellik merkezlerinde yapılan cilt işlemleri, özellikle doktor gözetiminde olmadığında, çeşitli riskler taşıyabilir. Doktor gözetiminde yapılmayan işlemler bir dizi potansiyel komplikasyonla ilişkilidir. Enfeksiyon riski, işlem bölgesinde allerjik reaksiyonlarla beraber keloid ve hipertrofik skar gibi birçok komplikayon izlenebilir. Ayrıca, kişinin genel sağlık durumu, mevcut sağlık durumu, mevcut tıbbi geçmişi, ve kullanılan ilaçlar gibi faktörler de dikkate alınmalıdır, çünkü bu unsurlar yapılan işlemlerin sonuçları üzerinde etkili olabilir. Doktor gözetiminde yapılan işlemler, profesyonel bir değerlendirme içerir. Bu, kişinin sağlık geçmişinin değerlendirilme-sini, potansiyel risk faktörlerinin belirlenmesini ve uygun tedavi seçeneklerinin belirlenmesini içerir. Ayrıca, uzman bir doktor, işlemlerin güvenlik protokollerine uyar ve olası komplikayonları tanımlama ve yönetme konusunda bilgi sahibidir.

Sonuç olarak, güzellik merkezlerindeki estetik işlemler, sadece estetik amaçlar için değil, aynı zamanda kişinin genel sağlığı için de önemli potansiyel riskler içerebilir. Bu nedenle, herkesin bu tür işlemleri düşündüğünde bir doktora danışması ve işlemlerin uzman bir doktor gözetiminde yapılması önerilir. Bu, istenmeyen sağlık sorunlarını önlemeye ve güvenli bir estetik deneyim yaşamaya yardımcı olabilir.

Etik; Bu yazıda sunulan olgu için sunulan bilgilerin akademik amaçlı kullanımı hakkında detaylı bilgileri de içeren imzalı "Bilgilendirilmiş onam formu" alınmıştır.

Ethics; For the case presented in this article, a signed "informed consent form" was obtained, which includes detailed information about the use of the information presented for academic purposes.

Yazar katkı durumu; Çalışmanın konsepti; ÖS, FNK, ÖK, AA, SBÖ, EA, dizaynı; ÖS, FNK, ÖK, AA, SBÖ, EA, Literatür taraması; ÖS, FNK, ÖK, AA, SBÖ, EA, verilerin toplanması ve işlenmesi; ÖS, FNK, ÖK, AA, SBÖ, EA, istatistik; ÖS, FNK, ÖK, AA, SBÖ, EA, yazım aşaması; ÖS, FNK, ÖK, AA, SBÖ, EA.

Author contribution status; The concept of the study; ÖS, FNK, ÖK, AA, SBÖ, EA, design; ÖS, FNK, ÖK, AA, SBÖ, EA, literature review; ÖS, FNK, ÖK, AA, SBÖ, EA, collecting and processing data; ÖS, FNK, ÖK, AA, SBÖ, EA, statistics; ÖS, FNK, ÖK, AA, SBÖ, EA, writing phase; ÖS, FNK, ÖK, AA, SBÖ, EA.

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KAYNAKLAR

1. Bengü Gerçeker Türk, Tuğçe Özkapu, Meltem Türkmen, Alican Kazandı, Can Ceylan. Scar sarcoidosis. . 2013; 47(1): 66-68

2. Xiao A, Falcone LM, English Iii JC. Systemic Sarcoidosis Presenting in a Scar. Case Rep Dermatol Med. 2023 Jan 24;2023:7751754. doi: 10.1155/2023/7751754. PMID: 36733915; PMCID: PMC9889162.

3. Yanardağ H, Pamuk ON, Karayel T. Cutaneous involvement in sarcoidosis: analysis of the features in 170 patients. Respir Med. 2003 Aug;97(8):978-82. doi: 10.1016/s0954-6111(03)00127-6. PMID: 12924527.

4. Hong YC, Na DJ, Han SH, Lee YD, Cho YS, Han MS. A case of scar sarcoidosis. Korean J Intern Med. 2008 Dec;23(4):213-5. doi: 10.3904/kjim.2008.23.4.213. PMID: 19119259; PMCID: PMC2687677.

5. Singal A, Vij A, Pandhi D. Post herpes-zoster scar sarcoidosis with pulmonary involvement. Indian Dermatol Online J. 2014 Jan;5(1):77-9. doi: 10.4103/2229-5178.126041. PMID: 24616865; PMCID: PMC3937498.

6. Selim A, Ehrsam E, Atassi MB, Khachemoune A. Scar sarcoidosis: a case report and brief review. Cutis. 2006 Dec;78(6):418-22. PMID: 17243430.

7. Katta R. Cutaneous sarcoidosis: a dermatologic masquerader. Am Fam Physician. 2002 Apr 15;65(8):1581-4. PMID: 11989634.

8. Berna Aksoy, Hasan Mete Aksoy, Onat Akın, İsmail Yüksekol. Scar Sarcoidosis with an ExcelleResponse to Treatment with Topical Tacrolimus. . 2011; 45(4): 219-221

9. Bahar Sevimli Dikicier , Cutaneous Sarcoidosis. Güncel Dermatoloji Dergisi 2018;3(1):2587-1692.

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The Disregard for the Use of Standardized Keywords in Turkish Medical Publishing: A Brief Critique

Türk Tıp Yayıncılığında Standardize Edilmiş Anahtar Kelime Kullanımının Göz Ardı Edilmesi: Kısa Bir Kritik

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Introduction

A keyword is a word or group of words that represent the text in an article in a concise form. Selecting appropriate keywords is essential for ensuring that articles remain accessible on the internet. Well-chosen keyword ensures that the article is discoverable over time (1,2).

In Turkish medical literature, the English and Turkish keywords need to convey the same meaning. To synchronize these keywords, the preference is to use the Medical Subject Headings (MeSH) search engine. The MeSH search engine is used to align these terms effectively. MeSH thesaurus is a controlled and hierarchically organized vocabulary produced by the National Library of Medicine (NLM). It is used for indexing, cataloging, and searching for biomedical and health-related information. MeSH includes the subject headings appearing in MEDLINE/PubMed, the NLM Catalog, and other NLM databases. (3) The MeSH database serves as a potent tool for conducting precise searches by utilizing MeSH headings and subheadings. MeSH terms function as a thesaurus encompassing all the concepts found within medical literature. (4) Because its terms are defined by multiple terminologies, it allows researchers to quickly and easily access numerous articles with minimal information.

There are no studies in contemporary Turkish medical academic literature evaluating the scope of keywords in articles and the compatibility of English equivalents with MeSH. The purpose of this study is to determine and report the extent to which keywords used in the examined articles are equivalent to MeSH.

Methods

This study was conducted within the “DergiPark” system, which significantly supports national academic publishing. The scanning was carried out between September and December 2023 by two researchers. The research focused on publications between January 1, 2022, and December 31, 2022, encompassing a total of 43 journals and 1743 articles. Selection criteria for journals included a minimum of 3 years of academic publishing, issuance of at least 3 editions in 2022, printing of a minimum of 4 original articles per issue, and having English abstracts and keywords. Only those adhering to eligibility criteria in the scanned journals and publications were included in the study.

Three types of articles were examined: original articles, case reports, and reviews. The study investigated factors such as the language of the article and whether MeSH compliance was based on the journal's own spelling rules. Each keyword in these scanned articles was individually searched in the MeSH database, directly following the author's spelling format. For example, if all keywords matched MeSH terms, 100% compatibility was noted; otherwise, if any of these keywords did not match MeSH, the compatibility was considered zero. At the end of the study, the proportion of keywords that were MeSH compliant was determined according to article and journal specifications. Evaluating the language of the articles is crucial for ensuring harmonization between English and Turkish articles. Many journals require keyword alignment with MeSH as part of their spelling rules. The exploration of MeSH compliance in the journal's spelling rules serves as a measure of whether or not authors are attentive to the journal's guidelines. The study aims to comprehensively evaluate all these variables.

Statistical Analysis

The descriptive statistical analysis of collected data was analyzed with IBM SPSS Statistics 17 (SPSS Inc. Released 2008. SPSS Statistics for Windows, Version 17.0. Chicago: SPSS Inc.). Frequencies, means and standard deviation were calculated. Pearson's chi-squared test was used to test whether the difference between the two groups and the p-value is less than or equal to 0.05 was accepted as the level of significance.

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Results

In this study, 43 journals have been scanned (Table 1). Journal characteristics are provided in Table 2. Of the 1743 articles included in the study, 376 were identified as 100% compatible with MeSH. The MeSH compatibility of articles in journals is shown in Table 3. Of the 376 articles compatible with MeSH, 185 are in English and 191 are in Turkish. It has been determined that the coherence of the articles written in Turkish exceeds the MeSH compliance of the articles written in English (Table 3). Meanwhile, 43 of the 30 journals have specified a framework rule in the spelling regulations of MeSH compliance, and it has been found that 280 articles in these journals comply with the aforementioned spelling framework.

Table 1. *The names of scanned journals*

Abant Medical Journal
Acıbadem University Health Sciences Journal
Acta Media Alanya
Acta Medica Nico Medica
Ahi Evran Medical Journal
Akdeniz Medical Journal
Aksaray University Journal of Medicine
Anatolian Clinic the Journal of Medical Sciences
Anatolian Journal of Emergency Medicine
Archives of Clinical and Experimental Medicine
Archives of Current Medical Research
Atatürk University Faculty of Medicine Journal of Surgical Medical Sciences
Aydın Journal of Health
Balıkesir Health Science Journal
Black Sea Journal of Health Science
Bozok Medical Journal
Dokuz Eylul University Medical Journal
Duzce Medical Journal
Eskisehir Medical Journal
ESTUDAM Public Health Journal
Fenerbahce University Journal of Health Sciences
Hippocrates Medical Journal
Institute of Health Sciences Journal
Journal of ANKEM
Journal of Contınuing Medical Education
Journal of Cukurova Anesthesia and Surgical Sciences
Journal of Dependence
Journal of Harran University Medical Faculty
Journal of Integrative and Anatolian Medicine
Kafkas Journal of Medical Sciences
Maltepe Medical Journal
Manisa Celal Bayar University Journal of the Faculty of Education
Medical Journal of Gaziosmanpasa University
Medical Journal of Ankara Training and Research Hospital
Medical Journal of Mugla Sitki Kocman University
Medical Journal of Western Black Sea
Mersin University School of Medicine Lokman Hekim Journal of History of Medicine and Folk Medicine
ODU Medical Journal
Phoenix Medical Journal
The Journal of Geriatric Science
The Turkish Journal of Forensic Medicine
Tıp Eğitimi Dünyası
Troia Medical Journal

Table 2: *Evaluated characteristics of scanned journals*

SCANNED JOURNALS FEATURES		***PERCENTAGE (%)***
Indexing in TR INDEX	*Yes*	**55.81 %**
	No	**44.18 %**
Sustainability of a journal (Publishing lifespan)	*Less than 15 years*	**76.74 %**
	More than 15 years	**23.25 %**
Journals asking about MeSH compatibility as a writing rule or format	*Yes*	**69.76 %**
	No	**30.23 %**
Issue released in 2022	*Three*	**83.72 %**
	More than three	**16.27 %**

Table 3: *MeSH compatibility percentages according to characteristics of the scanned articles*

SCANNED ARTICLE FEATURES *(n: number of articles)*	***Showing compatibility with the MeSH (%)***	***p-value***
Indexing in TR INDEX		**0.237**
Yes (1212)	21.20 %	
No (531)	22.41 %	
Language of the article		**0.231**
Turkish (862)	22.15 %	
English (881)	20.99 %	
Journals asking about MESH compatibility as a writing rule or format		**0.188**
Yes (1277)	21.92 %	
No (466)	20.60 %	
Journal articles according to the number of issues released in 2022		**0.245**
At least 3 (1408)	21.59 %	
More than 3 (335)	21.49 %	

Discussion

A regulated vocabulary created by the NLM is the MeSH thesaurus. In contrast to keyword searching, which often instructs a database to look for specific keywords in the titles and abstracts of papers (or other user-specified fields), MeSH terms let users locate articles in PubMed or MEDLINE that are on a given topic.

To better comprehend psychosocial MeSH terms and to provide guidance on whether to include both search strategies in an information literacy session or how much time should be spent on teaching each search strategy, De Mars et al. compared the recall and precision of MeSH-term versus text-word searching. The findings of their study demonstrated the advantages of MeSH search techniques for precision and recall. However, if an author is writing a manuscript or developing an idea for which there is no

MeSH term yet, or if they have reason to believe that not much has been written about the subject, then there is likely no MeSH term, and over 1.5 million articles in PubMed are not indexed with MeSH for MEDLINE. (5) We can now conclude that MeSH words are only largely sufficient if MeSH expands its breadth and is updated yearly.

According to the results of our search; considering the statistical data, 1367 of the 1743 articles, which were scanned on the DergiPark site, found no MeSH compliance. The aim of this study is to determine and report the extent to which keywords used in the examined articles are equivalent to MeSH. Based on this aim, it was determined that some medical-oriented journals in DergiPark in 2022 did not pay due attention to keyword selection. Some journals did not prioritize compliance with the MeSH indexing. The continuation of these results in the following years may lead to reduced accessibility, limited analysis of the literature, information clutter, and decreased readability of the article.

Limitation

The keywords of Turkish and English articles were searched using the MeSH search engine. Keywords for Turkish articles have not been additionally queried in the TBT (Turkish Science Terms) search engine. This could be considered a limitation.

Conclusion

Therefore, it is recommended that authors utilize relevant MeSH terms related to the topic. Understanding the significance of using terms mapped to MeSH terms and employing the PubMed search technique will help Turkish readers maximize the use of available MeSH terms, ultimately leading to more effective and well-informed searches.

Explanations Section

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

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REFERENCES

1. Bahadoran, Z., Mirmiran, P., Zadeh-Vakili, A., Hosseinpanah, F.,Ghasemi, A.The Principles of Biomedical Scientific Writing: Results. International journal of endocrinology and metabolism, 2019;17(2): e92113. https://doi.org/10.5812/ijem.92113

2. Karahan, AY. Letter to Editor, Comments on "Scientificity and H-Index.". Acta Med. Alanya 2020;4(2):203-204. doi:10.30565/medalanya.670263

3. nlm.nih.gov.Medical Subject Headings (updated January 5,2024; cited May-September,2022). Available from: https://www.nlm.nih.gov/mesh/meshhome.html

4. Chang, A. A., Heskett, K. M., Davidson, T. M.. Searching the Literature Using Medical Subject Headings versus Text Word with PubMed. Laryngoscope.2006;116: 336-340.

5. Mondal, H., Mondal, S.,Mondal, S. How to choose title and keywords for manuscript according to medical subject headings. Indian Journal of Vascular and Endovascular Surgery. 2018;5(3):141-144.