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EDİTÖRE MEKTUP LETTER TO EDITOR

VOMITING AND METOCLOPRAMIDE

Hatice Şeyma Akça, MD.*

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Dear editor,

We read your case presentation titled 'Metoclopramide-induced dystonia' with interest (1). In patients with gastroenteritis, inflammatory bowel diseases, and neurological symptoms such as seizures, ischemia, and intracranial hemorrhage, vomiting symptom is observed and the physician should stabilize the patient. Although many physicians know that methaclopromide can cause dystonia, it is thought that this effect may occur in higher doses and we do not hesitate to use the drug as a part of the treatment. Metaclopromide is a dopamine antagonist and is also used in hyperemesis gravidarum together with ondansetron, a serotonin receptor antagonist (2,3).

The development of malignant neuroleptic syndrome(4) and an oculogyric crisis in a schizophrenic patient who received anticholinergic therapy after the use of methaclopromide (5) have been reported in the literature.

Medication side effects can occur in different ways, especially in the geriatric and pediatric patient group. Plasma drug levels can be detected at high rates in elderly patients using cardiac drugs, even if they do not have symptoms (6). In addition, symptoms may last longer after drug or substance use in children (7).

Yalçın et al. studied pediatric patients who developed dystonia due to oral methaclopromide use. Of the 20 patients included in the study, 16 had methaclopromide intake in the normal dose range, and the findings became evident 4 hours after taking the drug, and there was a positive significant correlation between biperiden lactate treatment and the recovery period (8).

In the case report of Kılıç et al., we observed that the patient's symptoms started within 2 hours after ingestion of oral metoclopromide solution and regressed within 1 day (1).

We observed from the studies and case reports that we should not ignore the effect of metoclopromide to cause dystonia, but this side effect will not prevent the widespread use of metoclopromide today.

It should be kept in mind that metoclopromide may cause dystonia in children as well as in adults, and patients and their relatives should be informed in patients who are scheduled to be discharged.

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EDİTÖRE MEKTUP LETTER TO EDITOR

NATIONAL EARLY WARNING SCORE AND CHARLSON COMORBIDITY INDEX

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[2]Karamanoğlu Mehmetbey University, Faculty of Medicine, Department of Emergency Medicine, Karaman

Dear editor,

Vital signs are the simplest and probably the most important information collected about hospitalized patients. A vital sign can be defined as any patient feature that can monitor the patient's progress, predict the specific treatment that should be administered to the patient, or monitor the patient. Some patient characteristics, such as date of birth and gender, are fixed, whereas others, including the four traditional vital signs, are dynamic and can change at any time. Several such features have been proposed as additional vital signs. Pain, dyspnea, oximetry, mental status, functional status, and mobility have all been suggested as vital signs (1).

NEWS (National Early Warning Score) was first established in 2012 by The National Early Warning Score Development and Implementation Group, created by the Royal College of Physcians London, in the UK National Health Service to achieve a high standard of patient care, reduce the mortality rate, and improve acute It was developed to standardize the assessment of diseases (2). This scoring system was developed in the first place in order to determine the sudden worsening of the patients hospitalized in the emergency department, service or intensive care unit in the UK hospitals, to reveal the frequency of follow-up of the patients and to determine which patients should be transferred to the intensive care unit. The NEWS scoring system has spread from the UK to the whole world and has been the subject of studies for patient follow-up and triage (3). In one of the retrospective observational studies on NEWS conducted in 2015, patients diagnosed with sepsis and septic shock were evaluated with the SIRS-based approach, and high sensitivity and specificity were found in terms of sepsis diagnosis in those with a score of 3 and above in NEWS (4).

Anamnesis and comorbidities are another important component of the examination. Comorbidities are an independent risk factor for mortality. Charlson Comorbidity Index is a index based on comorbidities. Charlson comorbidity index is a widely used and accepted index for mortality prediction. It is a mortality indicator created by Mary Charlson et al in 1987 to estimate mortality by classifying comorbid disease states and measuring their severity. It was defined by examining 559 patients hospitalized for 1 year in the New York Hospital internal medicine service and associated comorbidities with one-year all-cause mortality (5). While determining the comorbid factors in the list, the comorbid factors with a relative risk above 1.2 were taken into consideration and 1 point if the relative risk is between 1.2-1.5, 2 points between 1.5-2.5, 3 points between 2.5-3.5, and 6 points if the relative risk is higher than 3.5. evaluated as. Although it was origi-

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nally developed for breast cancer patientş, after evaluations, it was shown by Charlson et al. that Charlson Comorbidity Index can be a powerful predictor of disease burden and mortality. The Charlson Comorbidity Index was originally designed to classify prognostic comorbidity in longitudinal studies. The importance of comorbidity was also demonstrated by Greenfield et al. in their study of the comorbidity index, which measures baseline comorbidity severity, acute exacerbations, and patient functional status (6).

The NEWS and Charlson Comorbidity Index are indices calculated with different parameters. A single index may not be sufficient for clinicians to make clinical decisions. Researchers should be encouraged to develop the ideal index for clinical decision making.

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ARAŞTIRMA MAKALESİ ORIGINAL ARTICLE

E-WASTE GOOD OR BAD IN INDIA: SUSTAINABLE FUTURE - OPPORTUNITIES AND CHALLENGES

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ABSTRACT

The use of electronic devices, machinery for work, communication, and increased business operations are all improved by advances in science and technology. In addition to the effects of using electronic equipment, there is also electronic trash (or e- waste) that occurs from not recycling and a lack of disposable processes. It has an impact on people's way of life, health, and the environment's ecosystem and natural resources. The world's most difficult problem at that point was e-waste. The article discusses the pros and downsides of e-waste, factors of managing e-waste for a sustainable future, problems and opportunities in setting up e-waste management, and some innovative ideas for managing e-waste in India. Further, in order to establish a less-carbon, circular frugality, the article emphasizes critical necessity for stakeholders to be aware of consumer behaviour, global obstacles, and opportunities in this area. The paper concludes by emphasizing the value of a general legal work frame, and licenses, for a makeover of an unorganized area, which directly targets the technologies, the duties of many stakeholders, and entrepreneurial prospects to improve the formal capacity. The article fully supports e-waste recycling chains that are transparent, accountable, and traceable in order to foster a more environmentally friendly atmosphere and safeguard our planet and its natural resources for future generations.

Keywords: *E-waste, Health hazards, Future sustainability, Stakeholders, E-waste management.*

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INTRODUCTION

At present situation world has a different type of environmental problems obtaining from manufacturing activities including plastic pollution, industrial waste and electronic waste, etc (Barnes et al., 2009). Recently electronic waste is considered as an important environmental problem (Robinson et al., 2009). E- waste is formed by many aspects (Pant et al., 2012). They are short life cycle of equipment's, poor recycling, sustained enhancing of electronic equipment to reach the demands of developed societies and latest technologies (Tanskanen et al., 2013). In developed countries need to separate the recycled expired electronic equipment which acts as a storage of hazardous chemicals in the environment (Haun et al., 1993).

E-waste used to be regarded as typical rubbish in India. But afterward, the "Hazardous Materials" standards of 2008 were used to treat e-waste (CPCB et al., 2008). Under this, some businesses are developed and engaged in the management of e-waste by scientific and environmentally friendly means by recognized government bodies (Chatterjee et al.2016). Additionally, India's treatment of e-waste is improper due to the involvement of inexperienced workers and the omission of necessary technology as a result of unlawful businesses (Wang et al., 2011). Improper handling of electronic waste leads to severe conditions for both humans and the environment by discharging heavy metals and constituent organics (Cesaro et al., 2017, Rautela et al., 2021, Sankhla et al., 2016, Wath et al., 2010).

With the delivery of E-waste to facilities that are specifically designed to recycle it, technological involvement will give sanitation staff more instruments to promote smooth waste management. In terms of attaining a smart tomorrow in terms of reducing environmental waste, machine learning (ML) applications and robotic automations are seen as the current forerunners. In this article, we look into the employment of a portable, wheeled robot as a garbage truck attachment, with the main objective of sorting and gathering electronic wastes during regular residential trash collection in a city. Individual consumers and civilian houses are the primary targets of our attention. The robot is an addition to the existing labour system, lowering the amount of physical intervention necessary and facilitating simple integration with the city's existing garbage management.

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World Wide E – waste generation

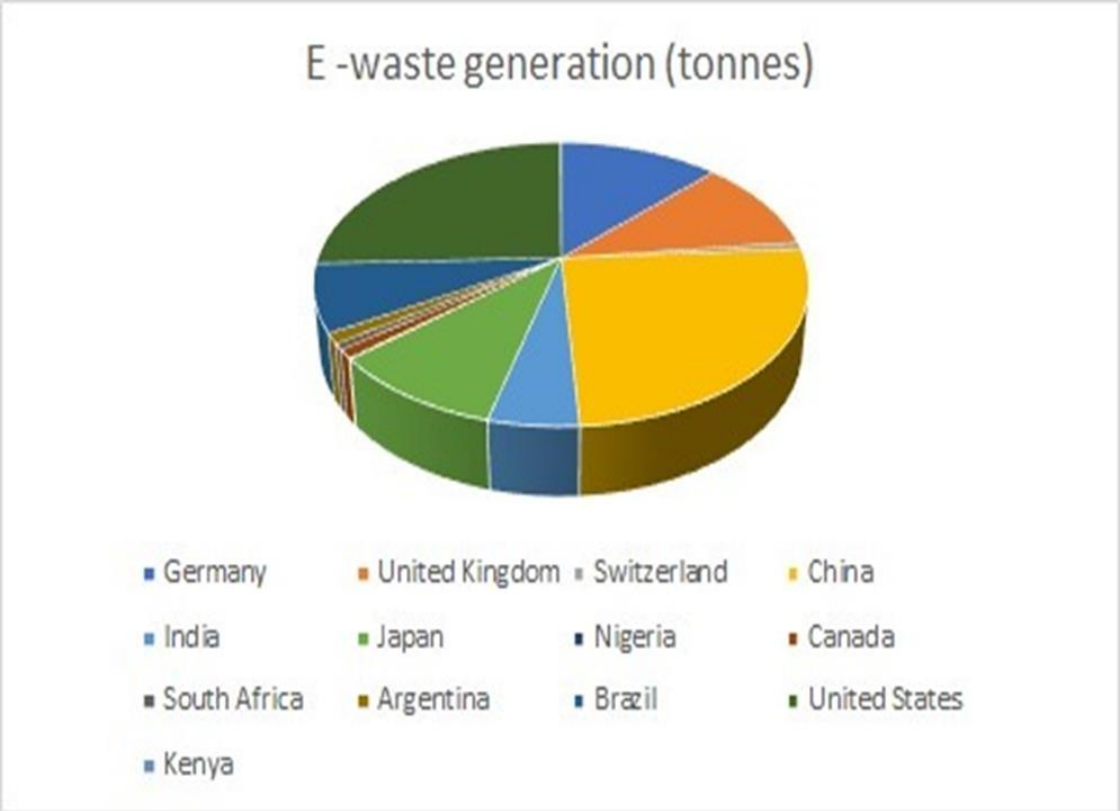

Figure-1: Ilustrates the countries which genetatres tonnes of e-wate

According to research, e-waste exposes the environment to 70% harmful substances and toxics (Hong et al., 2015). Heavy metals like mercury, lead, beryllium, and cadmium are present, along with contaminated PVC plastic and brominated flame retardants that are bad for both human and ecological health. Persistent organic pollutants (POPs), which are also implicated in bioaccumulation and biomagnified food webs, are the primary component of e-waste. (Borthakur et al., 2016).

E-Waste: Good Or Bad?

Now- a-days everyone needs electronic equipment for the purpose of office work, domestic work places like homes, railway stations, bus stations, banks, and other public services. Because it improves the productivity of work, less time taken and get quality products and information. Instead, the consumption of electronics increases dramatically which leads to the accumulation of e-waste (Wu et al., 2011).

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Figure-2: Depicts E-waste importance and harmful effects

Then e-waste is recycled and recycled e-waste not only involved in energy conserve, yet it also recycles natural resources such as copper, silver and aluminum (Borthakur et al., 2016).

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E- waste metals and its value in market

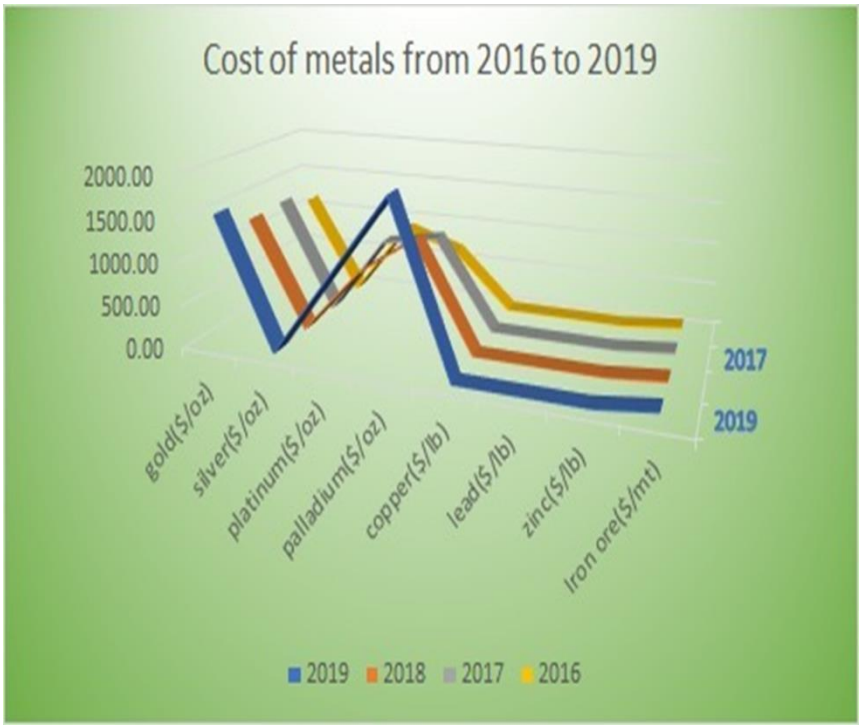

Figure-3: Rare Earth metals existing in electronic waste and its cost

Most of these metals are rare earth metals which are present in electronic waste like gadgets, computers, laptops etc. By recollecting and recycling these rare earth metals helps to decreases the mine works. Recycled e-waste helps to prevent air pollution and water pollution (Rautela et al., 2021).

The electronic waste effects the livelihood, human health and environment. The poisonous chemicals notably mutilate the urinary, respiratory, and digestive system as well as degenerate the immune system resulting in several types of cancers (Osako et al., 2004).

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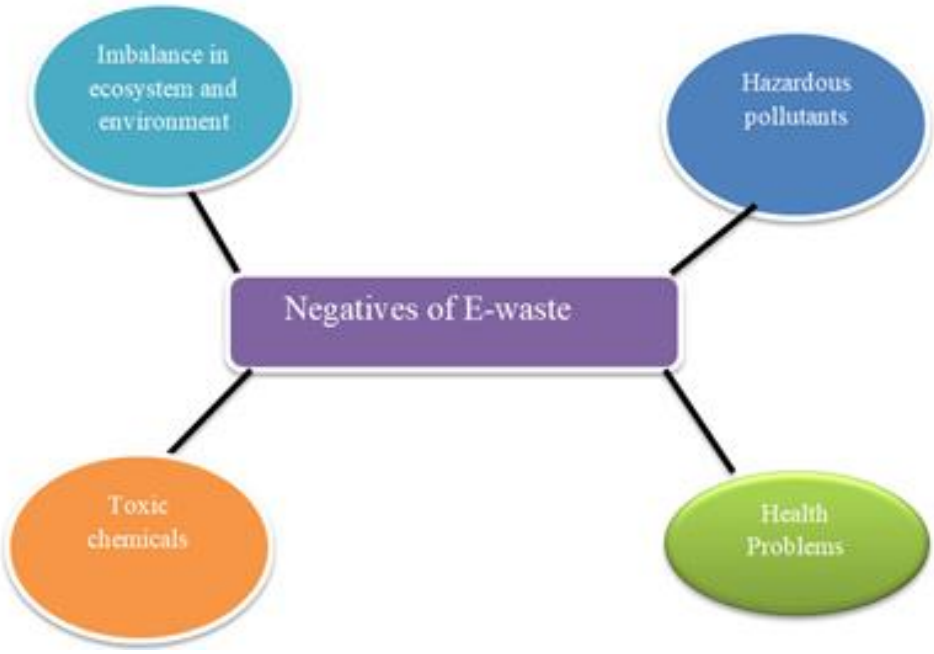

Figure-4: Ilustrates the health problems and toxic chemicals contaminating Earth's Surface

The toxic and hazardous chemicals are present environment around landfills, contaminating local ground water, damaging atmosphere, the surrounding communities and animals are also affected. Because e-waste is acts as a bioaccumulation i.e., uptake of chemicals in organisms' overtime, biomagnification which means enhancing the concentration of chemicals in food chain as a result of ingestion of other organisms which leads to imbalance in ecosystem and environment. Earlier literature reports have depicted higher concentrations of heavy metals such as chromium, cobalt, iron, copper, selenium & zinc in blood (Caravanos et al., 2013),

These are PHAHs (poly-halogenated aromatic hydrocarbons), a family of chemicals [Brouwer 1995]. These organic substances are listed in the Stockholm Convention's list of 11 chemical groups that make up the persistent organic pollutants (POPs) category. POPs are dangerous, extremely stable, not easily broken down, lipophilic, and bio-accumulative in living things. These substances can travel by air, water, migratory animals, and other means. These can build up in animal, terrestrial, and aquatic ecosystems in addition to human bodies [Harrad 2010]. Polychlorinated biphenyls were found in breast milk, especially in female personnel engaged in the management of e-wastes, and PAH metabolites were found in urine (Feldt et al., 2014; Asante et al., 2011).

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Table-1: Hazardous materials existing in e-waste

Substance	Instance in e-waste	Effects on the environment and human health
Halogenated compounds:		
TBBA , PBB, and PBDE	The most extensively used flame retardant for plastics (thermoplastic components, cable insulation), Printed wire boards and casings are currently where you may find TBBA.	**can have detrimental long-term consequences on health and, when burned, is fatal immediately**
CFC	cooling system, foam insulation	**Halogenated material combustion could result in hazardous fumes.**
Heavy metals and other metals:		
Arsenic	Light-emitting diodes contain gallium arsenide in traces..	**severely toxic and harmful to health in the long run**
Barium (Ba)	Cathode Ray Tube (CRT) getters	**if wet, may produce explosive gases (hydrogen).**
Beryllium (Be)	Power supply units with x-ray lenses and silicon-controlled rectifiers	**hazardous if breathed in**
Cadmium (Cd)	NiCd batteries that can be recharged, fluorescent materials (for CRT screens), ink and toner for printers, and drums for photocopier machines	**acutely toxic and harmful to one's health in the long run**
Gallium arsenide	light-emitting diode (LED)	**injurious to health**
Lithium	Li-batteries	**may develop explosive gases (hydrogen) if wetted**
Mercury	LCD backlighting fluorescent bulbs, some alkaline batteries, and mercury wetted switches	**extremely toxic and harmful to the body over the long term**
Nickel	Rechargeable NiCd - batteries or NiMH- batteries, electron gun in CRT	**may cause allergic reactions**
Rare Earth elements	(CRT-screen) Fluorescent layer	**infuriates eyes and skin**
Selenium	Older photocopying-machines (photo drums)	**exposure to high levels may cause adverse health effects**
Zinc sulphide	Rare earth elements are combined inside CRT screens.	**poisonous when breathed in**
PCB	Condensers, Transformers	**Cause cancer and have other negative health effects on the immune system, reproductive system, neurological system, and endocrine system. bio-accumulable and persistent**
Lead	Batteries, printed wiring boards, and CRT screens	**causes learning difficulties in children by causing damage to the neurological system, the circulatory system, and the kidneys.**
PVC	Insulation for cables	**Cables processed at high temperatures may produce chlorine, which is transformed into dioxins and furans.**
Chromium-VI	**Data tapes, floppy-disks**	**Allergies are brought on by substances that are immediately toxic and harmful to health over time.**

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Some neurodevelopment disorders, pregnancy related problems like spontaneous abortions, still births and some studies suggested they observed the DNA damage to the e-workers by expose of toxic chemical substances in e-waste (Kirsten et al., 2013; Wath et al., 2010; Widmer et al., 2005).

Aspects of E-Waste Management for Sustainable Future

Reduce, reuse, and recycle is the primary idea underlying them. By using clever protocols and good maintenance, you may cut down on e-waste as much as feasible (Saoji et al., 2012). Next, try selling or donating any working electronics that are still in working order.

Table-2: E- Waste management and its characteristic features in diverse countries

Country names	Characteristic features				
	Existing System	**E -waste specific**	**Legal restriction on e- waste imports**	**Financial flow**	**Actors in the scene**
South Africa	Partial Authorized	Absence of e -waste specific	Precise laws not properly applied	Metal scrap dealers paper e-waste	Importers, Traders, consumers, authorizers
India	Mostly unauthorized by all phases	Distinct to e-waste by unauthorized	Banned tough not totally applied	Absence of defined system	Importers, Traders, Consumers , Recyclers
China	Mostly unauthorized yet semi authorized in urban areas	Semi authorized not exactly for e-waste	Imports officially banned	Individuals collect e-waste and are paid	Importers, Traders, Consumers, scrap dealers
Switzerland	Highly authorized	No e-waste Specific	Precise laws	Advanced recycling fee	Importers, Traders, Consumers

If an electronic component can't be fixed, it is recycled. Inform the public and the local populations of the features, toxics, dangerous substances, etc. of electronic equipment trash. Some of the solutions to e-waste include minimising the effects on waste management, controlling and reducing the volume helps to prevent e-waste, reducing waste and pollution, using chemical treatments, biological treatments, or incinerators, burying the remaining lifted items, stopping and banning harmful waste exports, taking off the poisons, and designing for longevity upgrade, repair, and reuse. Government assistance is necessary to support e-waste management groups.

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Among the methods used to remove metal are manual sorting, magnetic separation, reverse osmosis, electrolysis, condensation, electrolytic recovery, filtration, and centrifugation (Pinto et al., 2008). These methods are less effective, damaging to both human health and the environment.

Another method, bio hydrometallurgical, uses bacterial leaching to mobilize metals from fine-grained e-waste in order to recover the solution (Harikrushnan et al., 2016). Pb, Cu, and SN are mobilized from printed circuit boards using microbes like bacteria and fungus. More than 90% of the available Cu, Zn, Ni, and Al could be leached by Thiobacillus thiooxidants and Thiobacillus ferrooxidans at electronic scrap concentrations of 5–10g/L in the medium. At a scrap content of 100g/L in the medium, Aspergillus Niger and Penicillium simplicissium were able to mobilize copper and tin by 65% and aluminum, nickel, pb, and zinc by more than 95%. (Brandl et al., 2001). The industries that use them for manufacturing use them as a raw resource (Gupta et al.2008).It helps to prevent and decrease the disposal of electronic waste.

Opportunities And Challenges In The Construction Of E-Waste Management

Providing knowledge about permits and licensures for processing e-waste management companies, organizations, and stakeholders. Then it helps the prevention of accumulation of e-waste and good to the environment (Hong et al.2015). Various countries follow variety of techniques, infrastructure for e-waste management (Huisman et al.2021). So, international leaders are to test the best techniques and implemented them across the globe (Xue et al., 2017).

It will help to create, awareness of their responsibilities and act accordingly without problems. By implementing green policies like information about the products life span, reduce, reuse and recycle in each and every component of products (Huisman et al., 2021). Creating awareness programs to consumers about the toxic, hazardous, and illegal disposal of electronic waste (Xue et al., 2017).

Following all these things helps to overcome the amount of e-waste generated and processed.

Some Ingenious E-Waste Management Techniques in India

- The first business that the government has authorized is **E-Parisaraa**. It is India's scientific e-waste recycling facility, and its objectives are to lessen pollution, reduce garbage sent to landfills, and recover valuable metals, plastics, and glass using environmentally acceptable methods from waste (Saoji et al. 2012).
- **Earth Sense Recycle Private Limited** which is a biomedical waste handling and management company. It is involved in recycling all types of e-wastes.
- **Trishyiraya Recycling private Limited** Indian company which offers a safe and reliable release of e-waste. Its ground-breaking method of recycling e-waste guards against pollution, contaminating the air, water, and noise.

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- **E-Cycling Approaches-**Plug-Into E-Cycling is a collaboration between the Environmental Protection Agency and consumer electronics manufacturers, retailers, and service providers that provide more options for e-cycling unwanted devices through donations and recycling. It also recycled used electronic components and repurposed those components to make new devices. It is involved in the metals' extraction from e-waste. Consequently, it lowers emissions of greenhouse gases, minimizes pollution, and conserves energy and resources for the environment (Saoji et al., 2012.).
- **Bangalore City has e-bins installed.** It is a non-governmental group that led awareness campaigns about e-waste and the need to dispose of it responsibly. By offering toll-free phone numbers to have e-waste collected from homes and recycled, it has done a wonderful service**.**
- **To handle electronic trash in an environmentally friendly way,** the Manufacturer's Association for Information Technology established the Electronic Recycler's Association (MAIT et al., 2010; MAIT et al., 2011-12).

CONCLUSION

The main aim of this article is to develop in the field of science and technology enhances the usage of electronic equipment for good productivity, easy communication, information transformation, boom to business activities, and modern life style in nowadays. Instead, all these activities increase electronic waste. This e-waste is caused by improper handling waste management, low-skilled workers, less advanced equipment and low recycled e-wastes, etc. Then it affects human health such as damaging the respiratory, urinary, and digestive systems, etc., bioaccumulation and biomagnification are involved in toxic and hazardous chemicals being stored which results in abnormalities in the food chain and it is ingestion by animals and surrounding communities finally imbalance occurs in ecosystem and environment. These effects are inhibited by e-waste management by following basic principles like Reduce, Reuse, and Recycle. Conduction of awareness programs to know about the universal laws, life cycled span, toxic and hazards components, implementing Extended Producer Responsibility (EPR) laws to the consumers. To educate stakeholders on the permits and licenses needed for e-waste management. Some proactive businesses, organizations, and government bodies are engaged in e-waste recycling and trash management, which aids in preventing the release of poisonous and dangerous chemicals into the environment and safeguards public health. By taking these actions, you may reduce and even stop the production of electronic trash while also preserving the environment and natural resources for future generations.

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Competing interests

1 The authors declare that they have no competing interests.

2 **Consent for publication**

Not applicable

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ARAŞTIRMA MAKALESİ ORIGINAL ARTICLE

DIAGNOSTIC VALUE OF THE LEUKO-GLYCEMIC INDEX IN CORONARY SLOW FLOW

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ABSTRACT

The leuko-glycemic index (LGI) is an easy-to-calculate and non-invasive index that combines leukocyte count and blood glucose score. Many studies have shown that LGI is a good clinical predictor of atherosclerotic vascular disease[8]. In this study, we aimed to investigate the usability of LGI in determining Coronary Slow Flow (CSF).

This study was a retrospective and observational study. The clinical, demographic and laboratory data of the patients were obtained from the hospital database. A total of 163 patients with 90 slow coronary flow and 73 normal coronary flow were included in the study. LGI was calculated as mg/dl.mm[3] by multiplying both values and dividing by a thousand[12]. Coronary flow rates were calculated using the TIMI frame count (TFC) method[13].

What stands out in all results, the overall logistic regression model was statistically significant (χ_11^2=81.3,p<0.001). The model explained 52.6% (Nagelkerke R^2) of the variance in CSF group and correctly classified approximately 80% of cases. The sensitivity value was calculated as 82.2%, specificity was 76.7% and area under roc curve was 86.9% (AUC: 0.869). LGI score is an effective factor on determination of the existence of CSF with a high odds ratio ($\boldsymbol{odds} = \mathbf{4.22}$; $[\mathbf{1.14}, \mathbf{15.62}]$ $\boldsymbol{CI}$ $\mathbf{95}\%$).

A high LGI was a predictor of CSF patients and was found to correlate with the TFC. The use of this simple and inexpensive index, together with other non-invasive tests before CAG, may provide some knowledge about the CSF.

Keywords: *Coronary Slow Flow, Leukocyte, Glucose, Angiography*

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INTRODUCTION

Coronary slow flow (CSF) is characterized by the slow progression of opaque material applied during coronary angiography into the distal vascular structures without occlusion of the epicardial coronary arteries[1]. The pathophysiology and clinical significance of CSF have not been fully elucidated. Tambe et al. firstly defined this phenomenon in 1972 and suggested that it may be due to abnormalities in coronary microcirculation[2]. Thrombolysis in myocardial infarction frame count (TFC) was used in the diagnosis of CSF and had been found to be associated with insulin resistance in patients with CSF[3].

Hyperglycemia may cause thrombosis and fibrinolysis, which lead to microvascular resistance[4]. Similarly, inflammation is known to trigger endothelial dysfunction and atherosclerotic process[5]. This is evidenced by the demonstration of increased leukocyte levels in many studies. Therefore, leukocyte levels are used as an important indicator in evaluating the risk of cardiovascular disease[6,7].The leuko-glycemic index (LGI) is an easy-to-calculate and non-invasive index that combines leukocyte count and blood glucose score. Many studies have shown that LGI is a good clinical predictor of atherosclerotic vascular disease[8]. In this study, we aimed to investigate the usability of LGI in determining CSF.

MATERIAL AND METHOD

Study populatıons

This study was a retrospective and observational study. Our study was prepared in accordance with the Declaration of Helsinki and was approved by the local ethics committee.

We collected data from the hospital registry system and patients who admitted cardiology clinic due to chest pain and dyspnea in this year were screened and their Coronary angiography (CAG) images were analyzed. A total of 163 patients with 90 slow coronary flow and 73 normal coronary flow were included in the study. Chronic inflammatory disease, obstructive coronary artery disease (≥ 50% stenosis in the left main coronary artery or ≥ 70% in at least one of the epicardial arteries), cerebrovascular events, coronary artery bypass grafting, valvular heart disease, missing data, cardiogenic shock, previously diagnosed with coronary artery disease (CAD), thyroid disorders, hemolytic disease, malignancy, chronic lung diseases, liver diseases, rheumatic disease, chronic kidney failure and history of hemodialysis and non-regulated diabetes mellitus were excluded.. The blood samples at the admission were assessed. The patients were evaluated with the Affiniti 50 echocardiography device before CAG. The left ventricular ejection fraction (LVEF) was calculated using the modified Simpson method. A resting blood pressure ≥ 140-90 mmHg in ≥ 2 measurements or taking antihypertensive medication were considered hypertensive (HT)[9].Patients with fasting blood glucose ≥ 126 mg/dl or postprandial blood glucose ≥ 200 mg/dl or glycated hemoglobin (HbA1c) ≥ 6.5 or taking anti-diabetic drugs were considered as diabetes mellitus (DM)[10]. A low-density lipoprotein cholesterol (LDL-C) level below the European So-

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ciety of Cardiology Guideline threshold or patients who received an anti-lipidemic were considered to have dyslipidemia[11].

Calculation of Leuko-Glycemic Index

Laboratory values of each patient were checked before CAG. Blood glucose was expressed as mg/dl and white blood cell count as the number of cells per mm^3. LGI was calculated as $mg/dl.mm^3$ by multiplying both values and dividing by a thousand[12].

Coronary angiography and thrombolysis in the myocardial infarction frame count calculation

Coronary Angiography was performed via the femoral or radial artery, depending on the operator's experience. A routine Judkins catheter was used in the diagnostic CAG. The left main coronary artery (LMCA), left anterior descending (LAD) and left circumflex artery (LCX) were evaluated from the right and left oblique positions using cranial and caudal angles at a rate of 25 fps. Coronary flow rates were calculated using the TIMI frame count (TFC) method[13].

For TFC measurement, the start and end points were determined separately for LAD, LCX and RCA. The starting point was accepted as the point where the contrast material contacted both sides of the coronary artery and started to progress. Endpoint for LAD, mustache region; The endpoint for RCA was the point at which the first lateral branch was stained with contrast in the posterior lateral artery; For LCX, it is the point where the distal bifurcation of the long branch is visualized. Since LAD lasts longer, the measured value was standardized by dividing it by 1.7. The mean TFC for each participant was calculated by dividing the sum of the TFCs of LAD (corrected), LCX, and RCA by 3. All participants with a corrected TFC greater than 27 (two standard deviations from the published normal range) in at least one of the three epicardial coronary arteries were accepted as having CSF. Those whose TFC fell within the standard deviation of the published normal range were considered as having normal coronary flow.

Statistical analyses

In this study, various statistical methods were applied in order to diagnose the CSF and to determine the factors affecting it. Firstly, the distribution and percentages of qualitative variables on each group are obtained and given in Table 1. The assumptions including the normality, the homogeneity of variance and the linearity required by the tests were checked before applying the statistical analysis. The normality assumption was checked via Kolmogrov-Smirnov test and skewness / kurtosis values with their z-scores, the homogeneity of variance via Levene test and the linearity assumption via scatter plot. Additionally, the possible outliers were observed by using the Box plot and the range [-3,3] of z-scores corresponding to the each variable. As a result of the controls, it was observed that there were no outliers in the data. Appropriate statistical test was determined according to whether other assumptions were met or not.

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RESULTS

In the first step of statistical analysis, descriptive statistics were obtained for qualitative and quantitative variables and the results are given in Table 1 and Table 2, respectively. According to the results of table 2, there was a statistically significant difference in HDL scores between CSF and normal flow with CSF scores $(M = 41.50)$ lower than control $(M = 47.00)$ group $(U = 2649.50, p = 0.034)$. Also, there was a statistically significant difference in PDW scores between CSF and control groups with CSF scores $(\bar{x} = 48.03)$ higher than control $(\bar{x} = 16.06)$ group $(t = 37.894, \boldsymbol{p < 0.001})$. However, there is no statistically significant difference in hemogram scores between CSF and control groups $(t = 0.617, \boldsymbol{p = 0.538})$.

Table 1. The descriptive statistics of qualitative variables

		Group			
		Coronary Slow Flow		Coronary Normal Flow	
		Value	Percentage (%)	Value	Percentage (%)
Gender	Male	62	68.9	29	39.7
	Female	28	31.1	44	60.3
Clinic	Usap	30	33.3	0	.0
	Non-STEMI	14	15.6	2	2.7
	STEMI	5	5.6	0	.0
	Stable Angina Pectoris	29	32.2	71	97.3
	Heart Failure	8	8.9	0	.0
	Arthmia	4	4.4	0	.0
Hypertension	Yes	40	44.4	38	52.1
	No	50	55.6	35	47.9
Diabetes mellitus	Yes	16	17.8	0	.0
	No	74	82.2	72	100.0
Hyperlipidemia	Yes	81	90.0	9	12.3
	No	9	10.0	64	87.7
Cigarette	Yes	42	46.7	12	16.4
	No	48	53.3	61	83.6
Alcohol	Yes	10	11.1	2	2.7
	No	80	88.9	71	97.3
Responsible artery	LAD	37	41.1	0	.0
	LCx	2	2.2	0	.0
	RCA	12	13.3	0	.0
	LAD- LCx	17	18.9	0	.0
	LCx -RCA	1	1.1	0	.0
	LAD-RCA	3	3.3	0	.0
	LAD-LCx-RCA	18	20.0	0	.0
	No	0	.0	73	100.0

Abbreviations:USAP: unstabil anjina pectoris, Non-STEMI:Non- st segment elevation myocardial infarction, STEMI: ST segment elevation myocardial infarction,LAD:Left anterıor descending, LCx: Left Circumflex, RCA: Right coronary artery

Table 2. The comparison results of each variable across to the flow groups

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	Group	N	Mean	Median	SD	SE	Test Statistic	p
Age (year)	CSF	90	56.1	55.00	12.10	1.28	-0.737	0.462
	Control	73	57.4	58.00	10.00	1.17		
Total cholesterol (mg/dL)	CSF	90	189.28	189.50	41.56	4.38	-0.214	0.831
	Control	73	190.64	196.00	39.26	4.59		
LDL (mg/dL)	CSF	90	108.54	105.50	33.59	3.54	-1.001	0.318
	Control	73	113.92	118.00	34.67	4.06		
Hemoglobin (g/dL)	CSF	90	14.24	14.30	1.79	0.19	0.617	0.538
	Control	73	14.08	13.90	1.55	0.18		
Lymphocyte (10^3/L)	CSF	90	2.19	2.10	0.79	0.08	-1.555	0.122
	Control	73	2.37	2.25	0.71	0.08		
PDW (%)	CSF	90	48.03	47.00	7.99	0.84	37.894	<0.001
	Control	73	16.06	16.10	0.40	0.05		
LCX-TFC	CSF	90	24.22	24.00	8.13	0.86	1.689	0.094
	Control	73	22.62	22.00	3.51	0.41		
Hdl (mg/dL)	CSF	90	44.59	41.50	15.18	1.60	2649.50	0.034
	Control	73	47.44	47.00	10.50	1.23		
Triglyceride (mg/dL)	CSF	90	184.22	132.50	155.26	16.37	2.12	0.036
	Control	73	145.95	132.00	64.52	7.55		
Hba1c (mmol/mol)	CSF	90	6.02	5.80	1.19	0.13	1776.50	<0.001
	Control	73	5.28	5.20	0.63	0.07		
Tsh (mIU / L)	CSF	90	2.72	1.90	6.22	0.66	3280.50	0.988
	Control	73	1.98	1.71	1.31	0.15		
Ft3 (mIU / L)	CSF	90	2.97	3.00	0.58	0.06	1688	<0.001
	Control	73	2.32	2.41	0.87	0.10		
Ft4 (mIU / L)	CSF	90	1.33	1.20	0.57	0.06	3086	0.505
	Control	73	1.20	1.18	0.28	0.03		
Hematocrıt (%)	CSF	90	42.60	43.65	6.28	0.66	2963	0.282
	Control	73	41.39	42.20	6.79	0.80		
Platelet (K/uL)	CSF	90	227.78	229.00	76.35	8.05	2490	0.008
	Control	73	250.86	246.00	58.03	6.79		
Rdw (%)	CSF	90	13.92	14.00	1.92	0.20	2.71	0.008
	Control	73	13.14	13.30	1.76	0.21		
LAD-TFC	CSF	90	39.58	38.00	11.57	1.22	2066.50	<0.001
	Control	73	34.95	35.00	1.46	0.17		
RCA-TFC	CSF	90	21.26	21.00	2.91	0.34	2289	0.001
	Control	73	17.27	15.00	7.30	0.77		
LVEF	CSF	90	57.50	60.00	10.60	1.12	2461	0.004
	Control	73	58.60	60.00	2.52	0.295		
Glucose (mg/dL)	CSF	90	118.78	105.00	42.25	4.45	2509	0.010
	Control	73	101.85	99.00	14.68	1.72		
Leukocyte (µl/ml)	CSF	90	8.31	8.18	2.45	0.26	3279	0.984
	Control	73	8.15	8.20	1.77	0.21		
Leucoglycemic index	CSF	90	1.01	0.88	0.56	0.06	2.84	0.005
	Control	73	0.82	0.79	0.24	0.03		

Abbreviations: LDL: low-density lipoprotein, PDW: Platelet Distribution Width, LCx- TFC: Left Circumflex-TIMI frame count, HDL:High- density lipoprotein, Hba1c: glycated hemoglobin, TSH: thyroid stimulating hormone,Ft3: free t3, Ft4: free t4, RDW: Red Cell Distribution Width, LAD: Left anterıor descending, RCA; Right coronary artery, LVEF: Left ventricular ejection fraction

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The correlation results was presented in Table 3. Based on these results, it can be said that LAD TFC scores has statistically significant and positive correlation with LCX TFC score for CSF group $(r = 0.551; p = 0.0001)$. Similarly, there was positive and significant correlation between RCA TFC and LCX TFC scores $(r = 0.246, \boldsymbol{p = 0.020})$. These two values tend to increase or decrease together.

Table 3. The correlation analysis results between disease group. LGI and TIMI values

Group			Ladtimi	Lcxtimi	Rcatimi	LGI
CSF	LAD-TFC	Value		0.551	-0.013	-0.004
		p		0.0001	0.902	0.973
	LCX-TFC	Value	0.551		0.246	0.121
		p	0.0001		0.020	0.256
	RCA-TFC	Value	-0.013	0.246		-0.084
		p	0.902	0.020		0.434
	LGI	Value	-0.004	0.121	-.084	
		p	0.973	0.256	.434	
Control	LAD-TFC	Value		0.020	-0.085	0.162
		p		0.865	0.475	0.170
	LCX-TFC	Value	0.020		-0.004	0.144
		p	0.865		0.975	0.223
	RCA-TFC	Value	-0.085	-0.004		0.387
		p	0.475	0.975		0.001
	LGI	Value	0.162	0.144	0.387**	
		p	0.170	0.223	0.001	
All	LAD-TFC	Value		0.522	-0.099	0.056
		p		<0.001	0.209	0.481
	LCX-TFC	Value	0.522		0.162	0.146
		p	<0.001		0.039	0.064
	RCA-TFC	Value	-0.099	0.162		-0.092
		p	0.209	0.039		0.244
	LGI	Value	0.056	0.146	-0.092	
		p	0.481	0.064	0.244	

Abbreviations: LAD: Left anterıor descending, RCA; Right coronary artery, LCx: Left Circumflex, TFC: TIMI frame count, LGI: leuko-glycemic index.

Only the variables which were found as significant in statistical tests were considered in logistic model. Table 4 provides the summary results including the coefficiens, odds ratios and significance values. The confusion matrix and performance criteria based on this matrix were presented in Table 5 and 6, respectively. To observe the performance as visually, the roc curve was given in Figure 1. What stands out in all o these results, the overall logistic regression model was statistically significant $(\chi^2_{11} = 81.3, \boldsymbol{p < 0.001})$. The model explained 52.6% $(Nagelkerke\ R^2)$ of the variance in CSF group and correctly classified approximately 80% of cases. The sensitivity value was calculated as 82.2%, specificity was 76.7% and area under roc curve was 86.9% (**AUC: 0.869**). Besides, it can be seen from the results in Table 4 that LGI, ft3, platelet, RDW,

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LVEF, triglyceride, the usage of cigarette and wall movement disorder situation were found as statistically significant factor on diagnosing the CSF and control groups. The rest of variables were not statistically significant ($p > 0.05$). When the odds ratios were observed, higher LGI scores was associated with an increased likelihood of exhibiting CSF. LGI score is an effective factor on determination of the existence of CSF with a high odds ratio ($odds = 4.22; [1.14,15.62]\ CI\ 95\%$).

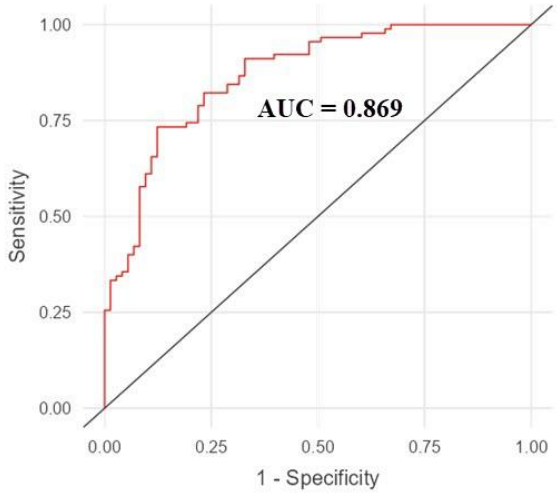
Table 4A. The significance and performance results of binomial logistic regression model

						CI (95%)		Model Fit Measures			
	β	SE	Z	p	$Odds$	Lower	Upper	χ^2	df	p	$R^2_{Nagelkerke}$
Intercept	-13,92	3,51	-3,97	< ,001	<0.001	<0.001	<0.001				
LGI	1,44	0,67	2,15	0,03	4,22	1,14	15,62				
Ft3 (mIU / L)	1,28	0,35	3,69	< ,001	3,58	1,82	7,06				
Platelet (K/uL)	-0,01	<0.001	-2,56	0,01	0,99	0,99	1,00				
Rdw (%)	0,33	0,11	2,87	0,00	1,39	1,11	1,73				
LVEF (%)	0,08	0,04	2,26	0,02	1,08	1,01	1,16	81.3	11	<0.001	0.526
Triglyceride (mg/dL)	0,01	<0.001	2,15	0,03	1,01	1,00	1,01				
Hdl (mg/dL)	0,02	0,02	0,88	0,38	1,02	0,98	1,05				
Hypertension (Yes)	-0,19	0,43	-0,44	0,66	0,83	0,36	1,92				
Cigarette (Yes)	1,18	0,54	2,19	0,03	3,27	1,13	9,44				
Alcohol (Yes)	0,56	1,09	0,52	0,60	1,76	0,21	14,81				

Table 4B. Performance metrics based on the confusion matrix

Accuracy	Specificity	Sensitivity	AUC
0.798	0.767	0.822	0.869

ROC Curve



Abbreviations: LGI: leuko-glycemic index, Ft3: free t3, RDW: Red Cell Distribution Width, LVEF: Left ventricular ejection fraction, HDL:High- density lipoprotein.

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DISCUSSION

In our study, we investigated the relationship between LGI and CSF for the first time. The most important results this study as follows, LGI was significantly higher in the CSF group than control group. According to multivariate regression analysis, LGI' as a predictive marker for CSF with %86.9 accuracy.

Previous studies showed the prevalence of CSF almost 1% in acute coronary syndrome, 7% in patients who underwent elective CAG, and 4% in patients who underwent CAG for unstable angina pectoris[14]. In our study, the rate of CSF was 6%. Considering these rates, there is a need for non-invasive tests with high sensitivity and specificity to predict CSF. Because it will allow early diagnosis and treatment. Insulin resistance, hyperglycemia and inflammation are the main factors that play a role in the pathogenesis of CSF[3]. Therefore, we thought that LGI, which can evaluate both inflammation and glycemia simultaneously, can predict CSF and can be used in non-invasive evaluation.

LGI was first described by Quiroga Castro et al[15]. They evaluated the prognosis in patients with a diagnosis of acute myocardial infarction (AMI). They found a significant association with poor prognosis as the LGI value increased. In addition, many other studies have been published investigating its association with in-hospital mortality in AMI. Caldas et al. and Garcia Alvarez et al. also conducted studies investigating the relationship between LGI and mortality in ischemic stroke[16,17]. Our study shows that the LGI value is a strong marker for CSF estimation.

CSF is defined as a microvascular disorder characterized by slow progression of the opaque material administered during CAG to the distal vascular structures, without obstruction in the epicardial coronary arteries[1]. Loss of morphology and histopathological findings of small vessel disease such as pycnosis are shown. However, the components affecting the microvascular structure have not been fully elucidated[18]. Hyperglycemia, insulin resistance and inflammation are thought to be effective[1-4]. We also demonstrated the independent correlation of leuko-glycemia with the presence of CSF.

There was also a positive correlation between LAD TFC, LCX TFC and RCA TFC and LGI Higher TFC values shows more slow coronary flow. Therefore, we may say that as the LGI values related with the severity of slow flow.

In our study, while there were 60.3% men in the control group, it was observed that it was 68.9% in the CSF group. In addition, 90% of the patients in the CSF group were diagnosed with hyperlipidemia. However, our results are similar to the literature.

There are some limitations. First, it is a retrospective, cross-sectional and single-center study. Considering the number of patients and their data, the results cannot be generalized. Second, due to the limited literature on this subject, it is necessary to undertake further research. So we need further and larger studies. Finally, the study design does not give us prognostic knowledge.

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CONCLUSION

A high LGI was a predictor of CSF patients and was found to correlate with the TFC. The use of this simple and inexpensive index, together with other non-invasive tests before CAG, may provide some knowledge about the CSF. Prospective studies are needed to clarify the LGI and CAD severity prognostic relationship in terms of future cardiovascular events.

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ARAŞTIRMA MAKALESİ ORIGINAL ARTICLE

CAN CRP/ALBUMIN RATIO PREDICT IN-HOSPITAL AND 30-DAY MORTALITY IN ACUTE ISCHEMIC STROKE PATIENTS

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ABSTRACT

Purpose: Inflammation plays a pivotal role development of both acute ischemic stroke(AIS) and atherosclerosis. It has been shown that the CRP (C-reactive protein (CRP)/albumin ratio (CAR), calculated by dividing CRP by albumin, is a good indicator of the level of inflammation. In this study, we planned to investigate whether CAR has an effect on in-hospital and 30-day major adverse cardiovascular events(MACE) in AIS patients.

Methods: We retrospectively enrolled 209 AIS patients. The patient group was classified into two groups according to CAR levels. These groups were compared in terms of C-reactive protein, albumin, CAR, and other hematologic inflammatory parameters. In-hospital and 30-day MACE was recorded.

Results: In-hospital and one-month follow-up, a total of 35 MACE was developed. In-hospital and 30- day MACE was significantly higher in high CAR patients with high CRP values and low albumin levels.

Conclusion: Our study demonstrated that a high CAR value is an independent predictor of in-hospital and 30-day mortality in patients with AIS.

Keywords: *Acute ischemic stroke, CRP/albumin ratio, Major adverse cardiovascular event*

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INTRODUCTION

Acute ischemic stroke (AIS) is one of the major causes of death and disability worldwide [1]. Ischemic stroke accounts for approximately 90% of all strokes [2]. In the last decades, as a result of advances in diagnosis and interventional treatment, a decrease in AIS mortality and morbidity rates is observed. Chronic inflammation has a significant role in the pathophysiology of AIS [3]. Inflammatory biomarkers predict the development of atherothrombotic events and short and long-term mortality after acute stroke.

Increased C-reactive protein (CRP) levels have been shown to predict both the risk of future stroke and the risk of death after stroke [4]. Albumin decreases as a negative acute phase reactant in acute illnesses including AIS [5]. Albumin also shows the nutritional status of AIS patients and decreases as a result of malnutrition [6]. For these reasons, decreased albumin levels were shown with poor outcomes in AIS patients [7].

CRP/ albumin ratio (CAR) was calculated by dividing the serum CRP level to the serum albumin level. The level of CRP increases in proportion to the inflammation in the serum, and the level of albumin decreases, which causes an increase in CAR. Increased CAR was found an increased 90- day mortality risk in AIS patients [8]. The relationship between both CRP and albumin levels and in-hospital were shown separately in AIS patients. However, CRP to albumin ratio (CAR), a newly defined inflammation and nutrition-based risk score, has not yet been sufficiently studied. In this study, we planned to investigate the possible relationship between CAR level and in-hospital and post-hospital 30-day mortality in AIS patients.

MATERIAL AND METHOD

Study populatıons

Between September 2019 and January 2022, 209 consecutive patients with acute ischemic stroke (age 18–90 years) were retrospectively enrolled. Acute stroke was defined as the presence of occlusion in the vessels supplying blood flow to the brain, with imaging findings on magnetic resonance imaging (MRI) or computed tomography (CT) scans, and a new neurological defect that develops within 24 hours. The patient group in our study was divided into two groups according to the development of mortality or not. CAR score was calculated according to the admission C-reactive protein and serum albumin level. Exclusion criteria were: age under 18 years, changes in inflammatory or immune markers other than CVE (e.g., autoimmune diseases, sepsis, trauma, recent major surgery, active malignancy), glomerular filtration rate <30 ml/min, receiving thrombolytic therapy, and pregnancy. Our study was carried out in full compliance with the Declaration of Helsinki. Ethics committee approval was obtained for our study [Decision number 09-2022/5].

Demographic characteristics of patients such as age, gender, and individual risk factors were scanned from hospital records.

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Blood sample test analysis

Fasting blood samples were taken from arm veins. Cobas 6000 Roche was used to measure fasting glucose level, cholesterol panel, and renal function tests. The auto hematology analyser (BC6800 Mindray Medical Electronics Co. Shenzhen, China) was used to measure the complete blood count parameters This formula was used to calculate SII index: (SII=platelet count × neutrophil count /lymphocyte count). This formula was used to calculate the neutrophil-lymphocyte ratio (NLR): neutrophil counts /lymphocyte counts (NLR).

Transthoracic echocardiography

Echocardiography was performed using the Vivid 5 device ((Vivid 5; GE Healthcare, Inc. Chicago, IL, USA) with a 2.5 MHz transducer. All axes including parasternal long and short axis, and apical views were used to assess cardiac structures. The modified Simpson method was used to assess ejection fraction (EF).

Follow-up and study endpoints

Clinical endpoints in the study included all-cause mortality and major adverse cardiovascular event (MACE). We assessed in-hospital mortality (during the hospital stay). All-cause mortality was the primary endpoint of the study. The major adverse cardiovascular event (MACE) composite of rehospitalisation for severe heart failure, nonfatal MI, and nonfatal stroke. New York Heart Association (NYHA) stage 4 heart failure patients were classified as advanced heart failure. European Society of Cardiology guidelines including the non-ST elevation myocardial infarction (NSTEMI) guideline published in 2020 and the ST-elevation myocardial infarction (STEMI) guideline published in 2017 was used to diagnose of acute myocardial infarction [9, 10].

All-cause mortality was defined as death from any cause in-hospital follow-up. Hospital records and national patient records were reviewed to assess primary clinical outcomes and mortality.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows 18.0 (IBM Corp., Armonk, NY, USA). CAR cut-off value was determined as 0.01752 according to the receiver operating characteristic curve (ROC) analysis. Accordingly, patients with >0.01752 were in group 1; patients with <0.01752 were included in group 2. Kruskal Wallis test was used to assess the normality of the distribution of the variables. Normally distributed numerical variables were expressed as mean ± standard deviation., while those with non-normal distribution were expressed as the median (min-max). The categorical variables were expressed as numbers and percentages. The non-normally distributed variables were assessed with the Mann-Whitney U test, while normally distributed variables were assessed with an independent sample Student's t-test.

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The categorical variables were analysed with a chi-squared test. $P < 0.05$ was taken as statistical significance

RESULTS

A total of 209 patients (mean age: 66.74±12.61 years) were included in this study. Patients were divided into two groups according to CAR levels. CAR cut-off value for predicting MACE was determined as 0.017 according to the receiver operating characteristic curve (ROC) analysis (Figure 1). During in-hospital and one-month follow-up, 35 patients developed MACE. In-hospital MACE was observed in 22 patients. In 1-month follow-up, additionally 13 patients developed MACE. The demographic and clinical characteristics of the patients are listed in table 1. The patients with high CAR were older and there were more males when compared to patients low CAR group (p=0.087 and p= 0.085, respectively). The presence of diabetes mellitus, hypertension, congestive heart failure, peripheral vascular disease, and stroke/transient ischemic events were not statistically different between the two groups ($p > 0.05$ for all parameters). The laboratory tests and trans thoracic echocardiography results of the groups are listed in table 2. In the high CAR group, cholesterol parameters were significantly higher compared to low CAR group. There were no statistically significant differences in patients with high and low CAR in whole blood parameters, including white blood cell, haemoglobin, neutrophil, and platelet (P) count. Neutrophil/lymphocyte ratio(NLR) and serum immune inflammation(SII) index were found significantly higher and lymphocyte count was significantly lower in the high CAR group. CRP, albumin, and CRP/albumin level were significantly higher in high CAR patients compared to low CAR patients (p<0.001). There were no statistically significant differences in atrial fibrillation, paroxysmal atrial fibrillation, CHA2DS2- VASc score, and carotid artery lesion between patients with high and low CAR ($p > 0.05$ for all parameters). The left ventricle ejection fraction was similar in the two groups.

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Table 1. Demographic and clinical characteristics of the groups.

	Total (209)	High CAR (n=87)	Low CAR (n=122)	*p*
Male	117(56%)	54 (62.1%)	63 (51.6%)	0.087*
Age	66.74±12.61	64.48±11.36	67.92±13.86	0.085**
Smoking	38 (18.3%)	15 (17.4%)	23 (18.9%)	0.472*
History of CAD	30 (14.4%)	14 (16.3%)	16 (13.1%)	0.328*
HT	145 (69.7%)	61 (70.9%)	84 (68.9%)	0.435*
HL	19 (9.1%)	10 (11.6%)	9 (7.4%)	0.210*
DM	94 (45.2%)	36 (41.9%)	58 (47.5)	0.252*
CHF	18 (8.7%)	7 (8.1%)	11 (9)	0.516*
Prior CVE	40 (19.2%)	20 (23.3 %)	20 (16.4%)	0.145*
Carotid artery lesion	33 (15.9%)	15 (17.4%)	18 (14.9%)	0.378*
CHA2DS2- VASc	4.4±1.31	4.37±1.31	4.44 ± 1.31	0.706
Atrial fibrillation	46 (22.2%)	20 (23.3%)	26 (21.5%)	0.445*
Paroxysmal atrial fibrillation	35(16.9%)	14 (16.3%)	21 (17.4%)	0.497*
In-hospital mortality	21 (10.6%)	15 (17.4)	6 (4.9%)	0.003*
In-hospital MACE	22 (10.1%)	16 (18.6%)	6(4.9%)	<0.001
In-hospital mortality day	6.06 ± 1.8	4.33±0.51	6.48±0.79	0.260**
First-month mortality	9 (4.3%)	6 (7%)	3 (2.5%)	0.110
First-month mortality day	1.24±0.31	0.34±0.04	2.94±0.74	<0.001**
First-month MACE	13	10 (11.6%)	3 (2.5%)	0.008

CAD: Coronary artery disease; CHA_2DS_2-VASc score=congestive heart failure, hypertension, age, diabetes mellitus, prior stroke or TIA or thromboembolism, vascular disease, age, sex category; CHF: Chronic heart failure; CONUT: Controlling Nutritional Status; CRF: Chronic renal failure; CVE: Cerebrovascular events; DM: Diabetes mellitus; HL: Hyperlipidemia; HT: Hypertension; MACE: Major advers cardiovascular event.

*: Fisher's Exact Test.

**: Independent sample T test

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Table 2. Laboratory tests and trans thoracic echocardiography results of the groups.

	High CAR (n=87)	Low CAR (n=122)	*p*
Glucose (mg/dL)	129.56 ± 50.52	140.76±68.83	0.209*
Total cholesterol (mg/dL)	168 (160-221.75)	149 (143-204.5)	0.002**
LDL (mg/dL)	123 (89.75-149.6)	105 (75.3-138.0)	0.026**
Serum creatinine (mg/dL)	1.04 ±0.37	0.87±0.21	<0.001*
WBC ($\times10^3/\mu L$)	9.54±2.99	8.77±2.58	0.055*
Neutrophil ($\times10^3/\mu L$)	5.69 (4.66-7.28)	5.34(4.35-6.95)	0.183**
Lymphocyte ($\times10^3/\mu L$)	1.97 (1.51-2.44)	2.15 (1.68-2.99)	0.009**
NLR	2.93 (2.23-3.87)	2.37 (1.74-3.43)	0.004**
SII	693.83 (518.02-1070.27)	561.90 (399.58-832.52)	0.003**
Hemoglobin (g/dL)	13.1 (11.65-14.6)	13.4(12.4-14.6)	0.209**
Platelets ($\times10^3/\mu L$)	250.05±66.44	244.59±60.64	0.538*
CRP (mg/dL)	2.69±0.32	0.28±0.046	<0.001*
Albumin (g/L)	38.68±4.33	41.29±4.07	<0.001*
CRP/Albumin ratio	0.320 (0.235-0.554)	0.052 (0.037-0.055)	<0.001**
Ejection Fraction (%)	60 (60-60)	60 (57-60)	

CRP: C-reactive protein; dL: deciliter; g: Gram; HDL: High density lipoprotein; ıqr: Interquartile range; L: Liter; LDL: Low density lipoprotein; mg: Miligram; uL: microliter; NLR: Neutrophils-to-Lymphocytes ratio; SII: Systemic immune-inflammation index, WBC: White blood cells.

*: Independent sample T-test

**: Mann Whitney U test

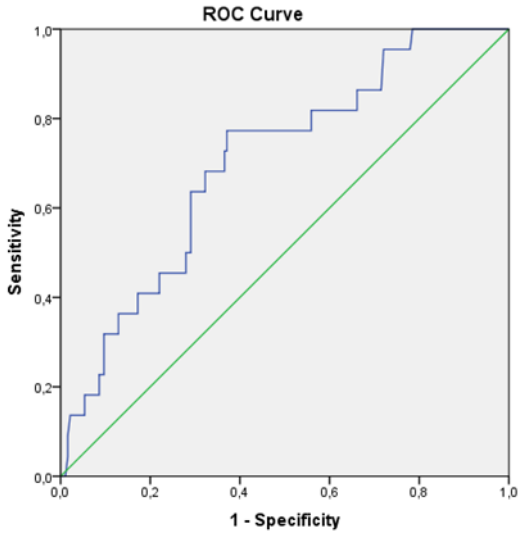

Figure. 1 Receiver operating characteristic curve to determine the optimal threshold for CRP-to-albumin ratio in patients with SVO in-hospital mortality (AUC: 0.702 p: 0.002 [CI:0.594-0.811]; 68.2% sensitivity, 65.6% specificity; CRP/Albumin = 0.017)

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DISCUSSION

In this study, we investigated the prognostic role of CRP/albumin ratio(CAR) in AIS patients. Our study showed that high levels of CAR at admission were significantly associated with intra-hospital and first-month MACE in patients with AIS. This study also showed that higher CRP and lower albumin levels were associated with high MACE rates in AIS patients.

We found few studies in the literature that determined the relationship between CAR and clinical outcomes in patients with acute stroke. In a study of 260 patients with acute ischemic stroke, high CAR levels were found to be an independent predictor of 90-day mortality [8]. In the study of Bai et al. in 236 patients with acute ischemic stroke, CAR was found to be an independent risk factor for 30-day mortality and demonstrated that it can be used in the evaluation of mortality in patients with acute ischemic stroke [11]. Elevated serum CAR levels were shown to predict symptomatic intracranial haemorrhage in AIS patients undergoing endovascular therapy [12]. To our knowledge, our study is the first to compare the relationship between in-patient and post-hospital 30-day mortality and CAR.

Studies have found that increased CRP or high-sensitive CRP levels are related with poor outcomes in AIS patients [13,14]. In the study conducted with Chinese patients, increased hs-CRP levels independently predicted the risk of all-cause death within 3 months [15]. Increased hs-CRP levels were also found to be associated with long-term mortality in AIS patients [16,17]. When only CRP levels were evaluated in our study, it was found to be a predictor for in-hospital mortality in proportion to CAR level.

Decreased albumin levels secondary to reduced malnutrition were found to be related with poor outcomes in AIS patients [18]. In the study conducted with 13 618 patients, low serum albumin levels predicted poor functional outcomes and mortality in patients with AIS or TIA [7]. In a study by Babu et al. in 560 ischemic stroke patients, they showed that relatively high albumin levels reduced adverse outcomes [19]. There was also found a correlation between low albumin levels and the development of atrial fibrillation which can cause cerebrovascular events [20]. In the presented study, a correlation was found between low albumin levels and increased mortality risk in AIS patients.

CAR, which is formed by dividing CRP into albumin, is thought to have higher prognostic accuracy than the use of these two parameters one by one. Elevated CAR levels were found to be associated with poor outcomes in other acute neurological pathologies and cardiovascular diseases besides acute ischemic stroke. CAR was found to be an independent risk factor for mortality in acute traumatic brain injury [21]. In a study of 379 patients with spontaneous intracerebral hemorrhage, increased CAR was found to be associated with in-hospital mortality [22]. CAR was found to correlate with disease severity and poor outcome in aneurysmal subarachnoid hemorrhage [23]. In a study conducted with 652 patients with the acute coronary syndrome, it was

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determined that increased CAR levels were associated with in-hospital and short-term major adverse cardiovascular events [24]. Plasma CAR levels have also been shown to predict clinical outcomes in patients with ST-elevation myocardial infarction [25].

Hematologic inflammatory parameters such as neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and serum inflammation index, which are other indicators of increased inflammation with CAR, were also found to be high in AIS patients with high mortality [26]. In a meta-analysis of 27124 acute stroke patients, an increased neutrophil-lymphocyte ratio was shown to be significantly associated with poor outcomes [27]. Like the neutrophil-to-lymphocyte ratio, the platelet-to-lymphocyte ratio is was also found to be associated with poor outcomes after acute stroke [28,29]. Our study also found that high neutrophil-lymphocyte ratio, and serum inflammation index were associated with higher intra-hospital mortality, which is in line with other researches.

There are some limitations in this study. Our study was conducted in a single center and with a relatively small number of patients. It was made in a retrospective design. In our study, albumin and CRP levels were measured only at the beginning, but their levels may change over time, which may change their prognostic value.

CONCLUSION

CAR may be a risk score that can be used to predict in-hospital mortality in AIS patients based on both inflammation and nutrition. The CAR can provide important prognostic information in determining the mortality risk relative to CRP and albumin separately. Additional studies are needed to compare CAR levels with larger patient populations and long- and short-term mortality in AIS patients.

DECLARATIONS

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Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

The study was approved by Karamanoğlu Mehmetbey University local ethics committee (09-22/05).

Availability of data and material

Not applicable.

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Contributions

All authors contributed to: (1) substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data, (2) drafting the article or revising it critically for important intellectual content, and, (3) final approval of the version to be published.

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ARAŞTIRMA MAKALESİ ORIGINAL ARTICLE

IS THE LYMPHOCYTE/ C-REACTIVE PROTEIN RATIO RELATED TO LONG-TERM MORTALITY IN ACUTE CORONARY SYNDROME PATIENTS?

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ABSTRACT

INTRODUCTION: Atherosclerotic coronary artery disease (CAD) is one of the most common chronic diseases that cause mortality and morbidity in the world. Many risk models have been described so far in the estimation of mortality after CAD. In this study, we aimed to investigate the relationship between mortality and lymphocyte/C-reactive protein ratio (LCR) in patients with the acute coronary syndrome (ACS) in long-term follow-up.

METHODS: A total of 718 patients admitted to the emergency department of our hospital with chest pain and equivalent symptoms and followed up in the coronary intensive care unit with the diagnosis of ACS were included. LCR and other laboratory parameters of each patient were recorded. The patients were followed up for an average of 36 months and mortality was recorded. The relationship between LCR and long-term mortality was investigated.

RESULTS: Among 718 patients, 64 deaths were observed at 36 months of follow-up. Patients were divided into two groups: group 1 survivor and group 2 death group. LCR was found significantly lower in the death group (<0.001). In univariate analysis, age, CAD, creatinine, and LCR were found as significant predictors of mortality. All parameters were added to multivariable linear regression analysis and showed that age (OR: 1.094, 95% CI: 1.063-1.127; p<0.001) and LCR (OR: 0.770, 95% CI: 0.621-0.956; p=0.018) are the only significant predictors of mortality.

CONCLUSION: We found a significant relationship between LCR and mortality in ACS patients. It can be used in clinical practice because it is inexpensive, easy to apply, and has a stronger prognostic prediction in follow-up after ACS.

Keywords: *Coronary artery disease, mortality, lymphocyte, C-reactive protein*

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INTRODUCTION

Atherosclerotic coronary artery disease (CAD) is one of the most common chronic diseases that cause mortality and morbidity (1). Approximately 17 million people die each year due to CAD (2). It is a multifactorial disease. The most common causes are obesity, diabetes mellitus, hypertension, lipoprotein metabolism disorders, smoking, sedentary life, and family history (3). According to the latest data from the World Health Organization; stress and poverty is also effective in the emergence and progression of CAD (4). With each passing day, the incidence and prevalence of CAD increase, and the chronic disease burden of countries increases. This causes additional financial burden. When considered in terms of cost-effectiveness; the mortality and morbidity management strategies of both WHO and national health organizations focus on stratifying the patient according to their risk and using a low-cost, rapid, specific, non-invasive, and predictive prognostic factor.

It is known that inflammation is one of the basic elements that play a role in the atherosclerotic process (5,6). Current studies suggest that vascular inflammation plays an important role in the initiation, progression, plaque instability, and eventual rupture of atherosclerosis (7). Inflammatory hematological parameters such as neutrophil, lymphocyte, monocyte, platelet, and C-reactive protein predict immunological counts. In particular, several studies have shown that the neutrophil/lymphocyte ratio (NLR), lymphocyte/monocyte (LMR) ratio, and platelet-lymphocyte ratio (PLR) are important in the prognostic assessment of coronary heart disease (8-10). The systemic inflammation index (SII) is a new inflammatory marker that combines NLR with platelet. It is emphasized that SII is more promising than NLR, LMR, and PLR (11,12).

Okugawa et al. reported that the lymphocyte/CRP ratio (LCR) can be used to predict prognosis in colorectal cancers (13). Chen K. et al. also showed that LCR is an independent factor affecting the occurrence and severity of CAD (14). Although lymphocyte and CRP levels are used separately in the evaluation of prognosis, the ratio of lymphocyte/CRP in cardiovascular diseases has not yet been determined. In this study, we aimed to investigate the relationship between mortality and LCR in long-term follow-up after acute coronary syndrome (ACS).

MATERIAL AND METHODS

Our study is a retrospective, observational study. Approval was obtained from the local ethics committee. It was in line with the Declaration of Helsinki. A total of 718 patients admitted to the emergency department of our hospital with chest pain and equivalent symptoms and followed up in the coronary intensive care unit with the diagnosis of ACS were included. The clinical characteristics and laboratory data of the patients and long-term follow-up results were accessed from the hospital database and recorded. Patients were diagnosed with ACS according to the principles of the 4th universal definition of AMI as defined by the European Society of Cardiology (ESC) (11). Sepsis or local infection, major surgery, bleeding, aortic dissection, myocarditis, cardiomyopathy, acute pulmonary embolism, and stroke were excluded. In addition, patients

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with missing data, those with only medical follow-up, and those with missing long-term follow-up were not included.

The admission venous blood samples were taken for total blood count, and CRP. Biochemistry parameters except CRP were taken after overnight fasting. Complete blood count values, kidney function values (urea, creatinine), lipid (Total cholesterol, HDL-C, LDL-C, TG) parameters, and C- reactive protein were recorded. The LCR of each patient was calculated. Mortality was recorded in the long-term follow-up. The relationship between LCR and long-term mortality was investigated.

Statistical Analysis

All statistical analyzes were performed using SPSS 25.0 (IBM SPSS Statistics 25 software (Armonk, NY: IBM Corp.)). Continuous variables were defined as mean ± standard deviation, and categorical variables were defined as numbers and percentages. Kolmogorov Smirnov and Shapiro Wilk tests were used to determine the normal distribution. Independent samples t test was used when parametric test conditions were met for independent group comparisons and Mann-Whitney U test was used when parametric test conditions were not met. The difference between categorical variables was analyzed by Chi-Square analysis. Logistic regression (LR) analysis was used to find the predictors of in-hospital mortality in NSTEMI. Univariate analysis was performed in the first step. Independent variables found as statistically significant (p-value less than 0.05) and clinically important parameters were added to binary multivariable logistic regression.

RESULTS

The results of 718 patients with ACS were analyzed. In 36 months' follow-up, 64 patients died. The mean age of the patients who died was higher (65 (56-73) years, 77 (72-87) years, **p<0.001**). The female sex ratio (183 (28), 26 (40.6), **p=0.043**) and the incidence of CAD (111 (17), 4 (6.3), **p=0.030**) were statistically significantly higher in the living group (Table 1). There was no statistical difference between the two groups in terms of DM, HT, HL, and smoking (Table 1). In the group with death in long-term follow-up, Lymphocyte (2.2 (1.5-3),1.6 (1-2.2), **p<0.001**) and LCR (0.54 (0.26-1.12), 0.19 (0.05-1.00), **p<0.001**) was lower. Additionally, WBC (9.4 (7.6-11.5), 13.2 (12.2-15.7), **p=0.001**), creatinine (0.90 (0.79-1.10), 1.04 (0.88-1.28), **p=0.002**), CRP(1.7 (0.5-5.1), 7.4 (2.4-20.2), **p<0.001**) was higher (Table 1). In univariate analysis, age, CAD, creatinine, LCR were found as significant predictors of mortality (Table 2). All parameters were added to multivariable LR and multivariable LR analysis showed that age (**OR: 1.094, 95% CI: 1.063-1.127; p<0.001**) and LCR (**OR: 0.770, 95% CI: 0.621-0.956; p=0.018**) are the only significant predictors of mortality.

Table 1. Demographic Characteristics of The Study Population

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	Survivors (N=654)	Nonsurvivors (N=64)	P Value
Age (years)	65 (56-73)	77 (72-87)	<**0.001**
Gender (Female), n(%)	183 (28)	26 (40.6)	**0.043**
Smoking, N(%)	194 (29.7)	13 (20.3)	0.147
HT, N(%)	299 (45.9)	28 (43.8)	0.793
DM, N(%)	177 (27.1)	21 (32.8)	0.379
CAD, N(%)	111 (17)	4 (6.3)	**0.030**
HL, N(%)	195 (29.9)	24 (37.5)	0.204
CRD, N(%)	4 (0.6)	2 (3.1)	0.093
WBC (10^9/l)	9.4 (7.6-11.5)	13.2 (12.2-15.7)	**0.001**
HGB (mg/dl)	13.6±1.9	13.2±2	0.119
Neutrophil (10^3/L)	6.2 (4.3-8)	7.9 (6.7-10.4)	0.210
Lymphocyte (10^3/L)	2.2 (1.5-3)	1.6 (1-2.2)	<**0.001**
Platelet (10^3/L)	224 (193-271)	275 (196-356)	0.207
Triglyceride (mg/dl)	155 (115-208)	119 (109-187)	0.709
Total Cholesterol (mg/dl)	197±97	193±60	0.733
HDL-C (mg/dl)	40 (34-53)	38 (35-58)	0.622
LDL-C (mg/dl)	117±41	110±40	0.182
Creatinine (mg/dl)	0.90 (0.79-1.10)	1.04 (0.88-1.28)	**0.002**
CRP (mg/dl)	1.7 (0.5-5.1)	7.4 (2.4-20.2)	<**0.001**
LCR	0.54 (0.26-1.12)	0.19 (0.05-1.00)	<**0.001**

Continuous variables were summarized as mean ± SD, categorical variables were summarized as count and percentages. **Abbreviations:** HT: Hypertension, DM: Diabetes Mellitus, CAD: Coronary artery disease, HL: Hyperlipidemia, CRD: Chronic Renal Disease, WBC: White blood cell, HGB: Hemogram, HDL-C: High density lipoprotein cholesterol LDL-C: Low density lipoprotein cholesterol, , CRP: C-reactive Protein, LCR: Lymphocyte to C-reactive Protein ratio.

Table 2. Independent Predictors of long term hospital mortality

Variables	Univariate analysis		Multivariable analysis	
	OR (95% CI)	p	OR (95% CI)	p
Age (years)	1.117 (1.083-1.151)	<0.001	1.094 (1.063-1.127)	<0.001
CAD	0.326 (0.116-0.916)	0.033		
Creatinine	1.459 (0.994-2.143)	0.054		
LCR	0.646 (0.499-0.836)	0.001	0.770 (0.621-0.956)	0.018

Abbreviations: CAD:Coronary artery disease, LCR: Lymphocyte to C-reactive Protein ratio.

DISCUSSION

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This study is the first to investigate the relationship between in-long term follow-up mortality and LCR in ACS patients. According to the results of our study; LCR is a strong predictor of mortality at long-term follow-up after ACS.

Many studies are ongoing on the pathophysiology of coronary heart disease (CHD) (15). Especially in the last 20 years, it has been increasingly accepted that atherosclerosis is an active inflammatory disease (16). Inflammation plays an important role in the formation, progression, and rupture of atherosclerotic plaque (16). Neutrophil and platelet are cells of innate immunity while lymphocyte represents acquired immunity (17,18). In many studies, the effect of the immune system on prognosis was investigated by using neutrophil, lymphocyte, and platelet cells.

Studies have shown that increased early CRP levels can be used to predict long-term cardiovascular events in ACS patients (19, 20). In addition, hematological inflammatory parameters with low lymphocyte levels were found to be an independent predictor of prognosis in ACS patients (21). LCR is the ratio of lymphocyte count to CRP. Rather than evaluating lymphocyte and CRP separately, evaluating lymphocyte and CRP together may provide a better prognostic contribution. In a study, it was determined that high lymphocyte level and low CRP level had a protective effect on atherosclerosis (8). On the other hand, LCR can provide stronger prognostic information by reducing bias. To our knowledge, there is no prognostic study of LCR in cardiovascular diseases. The only cardiac study in the literature examined the relationship between LCR and CAD severity (14). In this study, low LCP level was found to be significantly associated with the severity of coronary artery disease. However, there are many studies in malignancy patients and it has strong predictive value in this patient group (22-24). In our study, we investigated the predictor of mortality of LRC in long-term follow-up after ACS. We found that LRC has a strong predictive value.

It was determined that the ratio of these hematologic inflammatory cells to each other (NLR, PLR, LMR, and SII) had a stronger predictive value in the cardiovascular area. NLR, PLR, and SII have been shown to correlate with the severity and prognosis of CAD. In a study conducted with 300 ACS patients in 2021, both PLR and NLR affected prognosis, and a positive correlation was found between the increase in the combination of PLR-NLR and the increase in major adverse cardiac events (25). In a meta-analysis published in 2018, NLR was found to be an indicator of hospitalization and long-term prognosis after interventional treatment in patients with ST-segment elevation myocardial infarction (26). In a study of 400 patients, SII was found to be an independent risk factor for the occurrence and severity of CAD (11). Furthermore, SII is a potential indicator for predicting clinical endpoints for elderly patients with ACS undergoing interventional treatment (27).

The limitations of our study; the results cannot be generalized due to the single-center study and the limited number of patients. Our study is not prospective. it is retrospective. Therefore, the results we have obtained should be supported by multicenter and large-participant prospective

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studies. Some patients were excluded because of missing clinical data and/or laboratory variables. Finally, the presence of multiple comorbidities and vulnerabilities may affect in-hospital mortality.

In conclusion, our study is a study comparing LCR and in long-term follow-up mortality in ACS. In multivariate regression analysis, we found a significant relationship between LCR and in long- term follow-up mortality. It can be used in clinical practice because it is inexpensive, easy to apply, and has a stronger prognostic prediction in follow-up after ACS

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ARAŞTIRMA MAKALESİ ORIGINAL ARTICLE

COMPARING HEALTH LITERACY LEVEL IN TURKEY BEFORE AND AFTER THE COVID-19 PANDEMIC

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ABSTRACT

Background and Objectives*: The aim of this study is health literacy before and after the COVID-19 epidemic is compared. The effect of the pandemic on health literacy is highlighted in this study.*

Materials and methods*: The study made use of the Turkish Health Literacy scale, which was created using the European Health Literacy scale's Turkish validity and reliability(1). The scale were administered to a random sample (N= 332). The scale's allowed for the calculation of the health literacy score value. The data of the study were analyzed by using T-test and one-way analysis of variance test using SPSS 25 program. Significance level was accepted as <0.05. The outcomes of data collected before and after the pandemic were compared.*

Results*: The study indicated that the health literacy score was 29.5 prior to the pandemic and 41.8 post-pandemic. The study indicated that people between the ages of 25 and 44, people with high levels of education, people who work in the health field, people who receive social security, and those whose income is higher than their outgoings all had higher average health literacy scores than the rest.*

Conclusions*: The research shows that there is a considerable impact of the pandemic on the level of health literacy when the index values before and after the pandemic are compared. The degree to which participants understand health-related information decreases as they age. Those who were health workers showed greater levels of access to health-related information, comprehension, and knowledge evaluation than did participants from other categories. Additionally, it was discovered that when participants' educational levels rise, it gets simpler to access, comprehend, and assess knowledge of health-related topics. Our study also found that as income increases, so does people's capacity to access and understand health-related information.*

Keywords*: COVID-19, Pandemic, Health Literacy*

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INTRODUCTION

The world's attention was drawn to Wuhan, China's Hubei province, on December 1, 2019, when several cases of pneumonia of unknown origin were reported there. After the virus first appeared in China and quickly spread to 18 other nations, the World Health Organization (WHO) declared an emergency on January 30, 2020. Covid-19 was declared a pandemic on March 11 as it spread to 113 nations following the declaration of an emergency (2). According to data from Covid-19 show that about 80% of patients have mild illnesses, 20% need hospitalization, and about 5% need intensive care (3). Mortality rates have been noted to be higher in people over 60 and most frequently in those with hypertension, diabetes, and cardiovascular disease (4). In order to combat the virus, hygiene precautions like hand washing, wearing a mask, and keeping a physical distance have been very successful. Health literacy levels play a major role in the variation in these straightforward virus prevention methods (5).

Since the beginning of defining and assessing the functional literacy requirements of the adult population, the idea of health literacy has evolved. With these changes, it is now acknowledged that complex literacy abilities are becoming more and more necessary to participate in society. Low literacy negatively affects health and access to health care (6). Making decisions about people's health services, disease prevention, health promotion, and protection of health quality are all part of health literacy. The ability to access, comprehend, evaluate health information to make decisions about one's own health is also included (7). Terminology in health-related information causes to low health literacy, which makes it challenging to discriminate between reality and fiction. Many individuals with limited health literacy view the challenges they have in comprehending and applying knowledge of health as an impermeable barrier that existed against their will (8). Access to medical care and treatment is extremely difficult for those who do not endeavor to eliminate this barrier (9).

Health literacy is also described as the capacity of individuals to comprehend health information, make decisions, and select actions within the confines of their culture, language, and system of trust for information (10). Basic reading and writing abilities as well as the capacity to access, comprehend, review, and put into practice health facts are referred to as health literacy (11). Health literacy is typically defined as a person's ability to acquire, process, and comprehend essential health information and services required to make wise health decisions (12). In order to achieve universal health literacy, it is more reasonable to assess open communication methods between the patient and the healthcare provider (13).

Simonds (1974) was the first to suggest health literacy as a strategy that might have an impact on the health system (14). It is claimed that health literacy also has an impact on patient safety, access to healthcare, and the standard of care (15). Health literacy is crucial for accessing and using healthcare services as well as for health education and personal usage of health information. In a similarly, Van den Broucke et al. (2014) pointed out that in order to promote health-related be-

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haviors, educational interventions related to health literacy should be developed (16). Increased community health education can boost health literacy, according to a Japanese study (17). Participants with higher levels of health literacy were found to be more likely to get physicals or cancer screenings. Low cancer screening rates have been linked to low health literacy, according to numerous studies (18;19). Studies have also demonstrated that patients who have higher levels of health literacy use medical services more effectively (20).

MATERIALS AND METHODS

The study was inspired by a PhD thesis. This study was designed to examine the differences in health literacy between Turkey's pre-pandemic era and the COVID-19 process. Data were gathered for the study using a quantitative research methodology, with the comparison model serving as the foundation. The study was conducted in the province of Istanbul, which has the most COVID-19 cases per capita in Turkey. Participation in the study was open to everyone.

The study used the Turkish Health Literacy Scale, whose reliability and validity were examined by Okyay and Abacıgil (2016) prior to the pandemic (1). The degree of health literacy among participants with COVID-19 has been identified. Health literacy scale consists of 2 sub-dimensions; 'treatment and service', 'prevention of diseases/health promotion'.It has 4 processes, each of which defines 2 sub-dimensions: accessing, comprehending, evaluating, and using health-related knowledge. This scale has 32 items related to health literacy, scored on a 5-point Likert scale (strongly agree, agree, have no opinion, disagree, strongly disagree). The scale's allowed for the calculation of the health literacy score value. The data of the study were analyzed by using T-test and one-way analysis of variance test using SPSS 25 program. Significance level was accepted as <0.05. The Cronbach Alpha coefficient was 0.927 in Okyay and Abacgil's (2016) study and 0.779 in our study. The scale's reliabilitythat is more than 0.60 is acceptable.

The study's objective is to identify participants who have gone through the Covid-19 process. Therefore, the research's participation was chosen using a simple random sampling method. A total of 332 voluntarily participating individuals were chosen at random, and their health literacy levels were assessed. It was determined whether the study's sample size was adequate using the Kaiser-Meyer-Olkin (KMO) test. The test's findings revealed that the sample size was adequate. The participant's health literacy results were compared to those from the pre-pandemic health literacy study.

RESULTS

The Findings Regarding Descriptive Characteristics of the Participants:

The majority of the study's participants 53% are aged 25 to 34; men make up 29.8% of the participants while women make up 70.2%. 69% of participants are single, 31% are married, and 33.1% have graduated from high school or an undergraduate program. It was shown that 44.6%

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of the participants had less income than expenses, 51.5% did not have social security, and 41.9% of participants consists of the majority as students.

Analysis of Health Literacy Scale Factors

It was determined using the Kaiser-Meyer-Olkin (KMO) test whether the sample size was appropriate for factor analysis. KMO value is 0.921. It is clear that the sample size is adequate for the data because the statistic is bigger than 0.50 (21). The sample size was determined to be "sufficient" for the factor analysis.

Table 1. Results of the Health Literacy Scale's Explanatory Factor Analysis

Factors	Eigen Value	ExplainedVariance %	CumulativeVariance %	Cronbach Alpha Coefficient
1	10.78	33.70	33.7	0.779
2	2.03	6.34	40.0	
3	1.49	4.65	44.7	
4	1.36	4.27	48.9	
5	1.27	3.98	52.9	

Kaiser-Meyer-Olkin Sample Adequacy: 0.921
the Bartlett's Sphericity Test's Chi-Square Value: 4711,434 Sd= 6 p=0.000
Table 1 factor loads analysis reveals that all items have factor loads greater than 0.30.

Comparison of Health Literacy Distribution

The participants in this study were found to have sufficient health literacy, with a score of 41.8, as opposed to Okyay and Abacıgil's (2016) finding that Turkey's health literacy index average was 29.5 at a low health literacy level. According to the participants in the study by Okyay and Abacıgil (2016), 5.8% had good health literacy, 24.8% had adequate health literacy, 42.2% had restricted health literacy, and 27.2% had insufficient health literacy. 52% of the participants in this study had great health literacy, 43% had good health literacy, and 5% had inadequate health literacy, it was discovered.

Analysis of Quantitative Findings Related to Participants' HL Level:

There is no significant difference gender and marital status between the health literacy subdimensions ($p>0.05$). According to the participants' health insurance, there is a significant difference between the groups in the ANOVA test results between the levels of health literacy ($p<0.05$). Understand information relevant to health regarding social security is significantly different statistically in table 2 ($p<0.05$). The post-hoc Scheffe test was used to determine the cause of the difference. In terms of understand information relevant to health, there is a differ-

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ence between the average of participants with social security (X=4.13) and the average of individuals without social security (X=3.93).

Table 2. Comparison of the HL Scale and Sub-Dimensions of the Gender, Marital Status and Health Insurance

	Factors	**Variable**	**N**	**X**	**SS**	**P**
Gender	Health information access	Male	99	4.16	0.74	.268
		Female	233	4.25	0.69	
	Understanding health information	Male	99	4.03	0.79	.998
		Female	233	4.03	0.81	
	Evaluate health information	Male	99	4.08	0.58	.836
		Female	233	4.07	0.60	
	Access to disease prevention information	Male	99	4.13	0.68	.915
		Female	233	4.13	0.67	
	Evaluating disease prevention information	Male	99	3.85	0.74	.120
		Female	233	3.71	0.71	
Marital Status	Health information access	Married	103	4.22	0.70	.992
		Single	229	4.22	0.71	
	Understanding health information	Married	103	4.08	0.81	.470
		Single	229	4.01	0.80	
	Evaluate health information	Married	103	4.00	0.62	.157
		Single	229	4.10	0.58	
	Access to disease prevention information	Married	103	4.03	0.72	.070
		Single	229	4.18	0.65	
	Evaluating disease prevention information	Married	103	3.72	0.68	.549
		Single	229	3.77	0.74	
	Health information access	No	161	4.23	0.68	.841
		Yes	171	4.22	0.72	
	Understanding health information	No	161	3.93	0.83	**.021***
		Yes	171	4.13	0.76	

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Health Insurance	Evaluate health information	No Yes	161 171	4.07 4.07	0.59 0.59	.933
	Access to disease prevention information	No Yes	161 171	4,09 4.17	0.76 0.59	.273
	Evaluating disease prevention information	No Yes	161 171	3.75 3.76	0.73 0.71	.910

* Significant at the p< 0.05 level1

Only knowing the information about understand information relevant to health and the participants' ages were significantly different (p<0.05) when the sub-dimensions of health literacy were compared to their ages in Table 3. We looked at the post-hoc Scheffe test scores to determine which groups had different knowledge of treatment and services. The mean of the age groups 25–34 and 35–44 (X=4.17) and the group of people aged 45 and older (X=3.58) were found to differ in comprehension the health-related knowledge.

The educational status of the participants and the factors of understand health information, appraising health information, and access information relevant to disease prevention are statistically different (p<0.05). It was determined which groups the difference stemmed from using the post-hoc Scheffe test. The difference between the means of primary school graduates (X=3.50), high school graduates (X=3.95), and postgraduate graduates (X=4.46) was revealed in terms of understand information relevant to health. The difference between undergraduate graduates (X=4.00) and graduate graduates (X=4.36) in the sub-factor of appraise information relevant to health. The averages of primary school pupils (X=3.62) and graduate students (X=4.43) differ in terms of access information relevant to disease prevention sub-factor.

Table 3. Comparison of the HL Scale and Sub-Dimensions of the Age, Educational and Occupation Status

	Factors	**Variable**	**N**	**X**	**SS**	**P**
Age	Health information access	15-24 25-34 35-44 45 over	177 94 43 18	4.24 4.25 4.19 4.04	0.70 0.72 0.64 0.82	.673
	Understanding health information	15-24 25-34 35-44	177 94 43	3.97 4.17 4.17	0.80 0.76 0.71	**.012***

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		45 over	18	3.58	1.07	
	Evaluate health information	15-24	177	4.08	0.56	
		25-34	94	4.09	0.67	.614
		35-44	43	4.07	0.54	
		45 over	18	3.89	0.64	
	Access to disease prevention information	15-24	177	4.13	0.71	
		25-34	94	4.17	0.65	.736
		35-44	43	4.11	0.60	
		45 over	18	3.98	0.67	
	Evaluating disease prevention information	15-24	177	3.78	0.69	
		25-34	94	3.69	0.73	.303
		35-44	43	3.85	0.74	
		45 over	18	3.53	0.69	
Educational Status	Health information access	Primary School	10	3.93	0.87	
		High School	110	4.22	0.65	
		Associate Degree	76	4.28	0.74	.186
		Bachelor's Degree	104	4.15	0.73	
		Postgraduate	26	4.50	0.57	
		PhD	6	4.17	0.86	
	Understanding health information	Primary School	10	3.50	1.25	
		High School	110	3.95	0.73	
		Associate Degree	76	3.99	0.89	**.008***
		Bachelor's Degree	104	4.06	0.75	
		Postgraduate	26	4.46	0.69	
		PhD	6	4.50	0.55	
	Evaluate health information	Primary School	10	3.82	0.82	
		High School	110	4.03	0.55	
		Associate Degree	76	4.13	0.59	**.029***
		Bachelor's Degree	104	4.00	0.60	

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		Postgraduate	26	4.36	0.55	
		PhD	6	4.37	0.39	
	Access to disease prevention information	Primary School	10	3.62	1.23	
		High School	110	4.08	0.73	
		Associate Degree	76	4.21	0.61	**.020***
		Bachelor's Degree	104	4.09	0.59	
		Postgraduate	26	4.43	0.56	
		PhD	6	4.33	0.45	
	Evaluating disease prevention information	Primary School	10	3.45	0.91	
		High School	110	3.79	0.69	
		Associate Degree	76	3.77	0.80	.105
		Bachelor's Degree	104	3.64	0.65	
		Postgraduate	26	4.02	0.71	
		PhD	6	4.04	0.87	
Occupation	Health information access	Worker	30	3.23	0.70	
		Civil Servant/Retired	58	4.01	0.83	
		Student	139	4.25	0.67	
		Health Manager	13	4.36	0.63	.070
		Academician	11	4.45	0.43	
		Doctor	5	3.93	0.68	
		Nurse/Midwife	27	4.09	0.84	
		Health Technician	49	4.41	0.55	
	Understanding health information	Worker	30	3.77	0.91	
		Civil Servant/Retired	58	4.05	0.81	
		Student	139	3.92	0.85	
		Health Manager	13	4.46	0.48	**.008***
		Academician	11	4.23	1.03	
		Doctor	5	4.90	0.22	
		Nurse/Midwife	27	4.09	0.52	

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		Health Technician	49	4.20	0.63	
	Evaluate health information	Worker	30	3.87	0.65	
		Civil Servant/Retired	58	3.93	0.66	
		Student	139	4.09	0.58	
		Health Manager	13	4.15	0.54	.055
		Academician	11	4.33	0.54	
		Doctor	5	4.64	0.54	
		Nurse/Midwife	27	4.13	0.52	
		Health Technician	49	4.13	0.52	
	Access to disease prevention information	Worker	30	3.79	0.94	
		Civil Servant/Retired	58	4.07	0.56	
		Student	139	4.15	0.71	
		Health Manager	13	4.14	0.75	**.010***
		Academician	11	4.29	0.46	
		Doctor	5	4.96	0.09	
		Nurse/Midwife	27	4.08	0.59	
		Health Technician	49	4.26	0.49	
	Evaluating disease prevention information	Worker	30	3.37	0.86	
		Civil Servant/Retired	58	3.76	0.72	
		Student	139	3.79	0.70	
		Health Manager	13	3.77	0.73	**.027***
		Academician	11	4.07	0.54	
		Doctor	5	4.40	0.45	
		Nurse/Midwife	27	3.66	0.77	
		Health Technician	49	3.75	0.64	
Income-expenditure	Health information access	Income less than expenses	148	4.14	0.76	
		Income equals expense	139	4.33	0.60	**.050***
		Income more than expenses	45	4.19	0.75	
	Understanding health	Income less than expenses	148	3.90	0.83	

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	information	Income equals expense	139	4.14	0.72	**.032***
		Income more than expenses	45	4.11	0.91	
	Evaluate health information	Income less than expenses	148	4.00	0.58	
		Income equals expense	139	4.14	0.62	.129
		Income more than expenses	45	4.10	0.52	
	Access to disease prevention information	Income less than expenses	148	4.07	0.73	
		Income equals expense	139	4.16	0.65	.265
		Income more than expenses	45	4.24	0.57	
	Evaluating disease prevention information	Income less than expenses	148	3.70	0.74	
		Income equals expense	139	3.79	0.72	.476
		Income more than expenses	45	3.79	0.65	

* Significant at the p< 0.05 level1

The occupational categories of the participants and the sub-factors of understanding information important to health, accessing information relevant to disease prevention, and disease prevention are statistically different, as shown in ($p<0.05$). The difference's cause was determined using a post-hoc Scheffe test. The test revealed a significant difference in the means for understanding health-related information and accessing information related to disease prevention between the working group (X=3.77) and doctors (X=4.90). Additionally, compared to doctors (X=4.96), the average access information relevant to disease prevention is lower for employees (X=3.79). Employees appraise information relevant to disease prevention is on average lower (X=3.79) than doctors' (X=4.96).

A statistically significant difference between the sub-factors of access information relevant to health and income-expenditure evaluation and understand information relevant to health was identified ($p<0.05$). The post-hoc Scheffe test was used to determine the cause of the difference. The test results show that the averages of those whose income is less than their expenditure (X=4.14) and those whose income is equal to their expenditure (X=4.33) differ from one another in terms of their Access information relevant to health. It can be shown that the averages of participants whose income is less than their expenses (X=3.90) and those whose income is equal to their expenses (X=4.14) differ from one another in how they perceive their understand information relevant to health.

DISCUSSION

Within the context of the COVID-19 pandemic outbreak and in comparison, to pre-pandemic levels, health literacy was assessed in this study. Turkey's level of health literacy was evaluated

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using the "Turkey Health Literacy Scale-32 (TSOY-32)" developed by Abacgil and Okyay (2016) with cooperation from the General Directorate of Health Promotion of the Ministry of Health. We conducted this study following the pandemic, and the results showed that 52% of participants had excellent health literacy, 43% had good health literacy, and 5% had low health literacy. Although Okyay and Abacgil's (2016) study reported that the overall health literacy score was 29.5 before the pandemic, the sample in the study was determined to have a sufficient level of health literacy, with a total health literacy index value of 41.8. It is clear from comparing the two figures that the epidemic has a positive effect on health literacy. The participants' health literacy was distributed as follows: 42.2% problematic, 27.8% inadequate, 24.8% adequate, and 5.8% excellent before the pandemic. Following the pandemic, our study found that 52% of participants had excellent health literacy, 43% had adequate health literacy, and 5% had limited health literacy.

When demographic data and health literacy are compared, contrary to the findings of earlier researchers, there is no evidence of a relationship between gender or marital status and health literacy. However, there was a difference in health literacy levels when age, education, occupation, social security, income, and expenditure were compared. According to Yakar et al. (2019), people with poor vision, married people, people with children, and women with less education than a high school certificate all had lower health literacy levels than the other groups (22). In another study, the Turkish health literacy scale was used, and the individuals who had completed high school or higher education, those who had received prior health education, and men all shown higher health literacy than the other participants. Low education levels are associated with lower levels of health literacy than secondary or higher education levels (24). Participants who are older have less health literacy than patients who are younger (23). Men's health literacy is also substantially lower than women's, and single people's health literacy is significantly lower than that of married individuals. In the study by Do et al. (2020), it was discovered that individuals with high health literacy adhered to infection prevention and control methods better, adopted healthier lifestyles, and were more adept at identifying COVID-19 symptoms (25).

Conclusion: This study reveals pre- and post-pandemic health literacy. The originality of the research is boosted by the lack of studies contrasting health literacy in Turkey before and after the Covid-19 pandemic. The study's most striking finding was that the pandemic had a favorable impact on health literacy. Health literacy has been found to be positively influenced by higher education levels, youth, health professions, social security, and high income. The majority of the sample population is young and female, which is the study's biggest flaw. No statistical difference in the tests was produced by this circumstance. It is advised that future studies in this field take the distribution between groups into account. Additionally, it is believed that the pandemic did not purposefully increase health literacy. In order to improve health literacy in daily life, society's participation should be increased on the basis of voluntarism and awareness-raising. A rise in health literacy will be ensured as a result, aiding in the advancement of public health.

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Abbreviations: HL: Health Lıteracy, phD: Doctorate

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VAKA TAKDİMİ CASE REPORT

ISOLATED SCALP METASTASIS DEVELOPING 10 YEARS AFTER DIAGNOSIS OF BREAST CANCER: A CASE REPORT

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ABSTRACT

Breast cancer is the most common type of cancer in women. Breast cancer is the most common type of cancer that metastasizes to the skin. Isolated scalp metastases are rare in breast cancer. In this study, a breast cancer case with isolated scalp metastasis that developed 10 years after mastectomy is presented.

Keywords*: Breast Cancer, Scalp Metastasis*

INTRODUCTION

Breast cancer is the most common type of cancer in women (1). Breast cancer is the most common type of cancer that metastasizes to the skin(2). However, scalp involvement is very rare in breast cancer (3). In this study, "a rare case of scalp metastasis that developed after 10 years" of a patient who was diagnosed with breast cancer and underwent mastectomy is presented.

CASE REPORT

An 80-year-old female patient was admitted to the outpatient clinic with complaints of swelling and a palpable mass in the right parietooccipital region (Figure 1-2). Brain CT and contrast-enhanced brain MR examinations were performed on the patient (Figure 3). As a result of the examinations, a mass was detected under the scalp of the patient. Contrast enhancement and dural thickening were evident, especially in the cranium adjacent to the mass. Surgical procedure was planned for our patient. It was observed that the scalp tissue on the mass was severely thinned. The flap was raised around the mass and the mass was excised from the inside towards the scalp. Craniectomy was performed on the contrasting cranium. The thickened dura was incised and duraplasty was performed from the fascia lata. The cranial defect was closed with titanium mesh (Figure 4). In the pathology result of the patient who was discharged on the 4th postoperative day, in the examination of the sections, cells that were not related to the epidermis, partially encapsulated, asymmetrical anastomosis of trabeculae and lobules of different diameters, infiltrative in some areas, occasionally showing ductal differentiation, sebaceous differentiation, and

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mild atypia were observed. Mitosis 1/10 BBA was observed. In the immunohistochemical study, diffuse positivity for CK7 and EMA in the tumor; focal positivity with CEA, GATA-3; sporadic staining with p53; 10% positivity was observed with ki-67. Negativity was observed with p16, CK20, CK5/6. The patient had a diagnosis of breast carcinoma 10 years ago and a history of mastectomy, and the result was determined as malignant breast cancer metastasis.

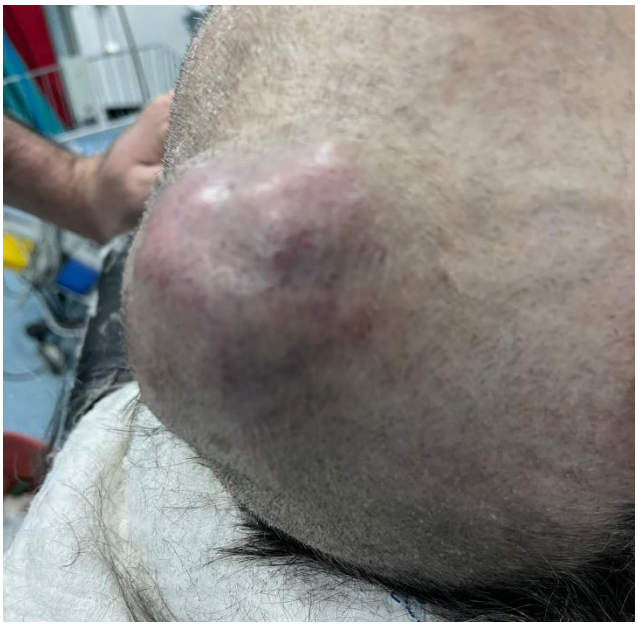

Figure 1. Breast cancer scalp metastasis

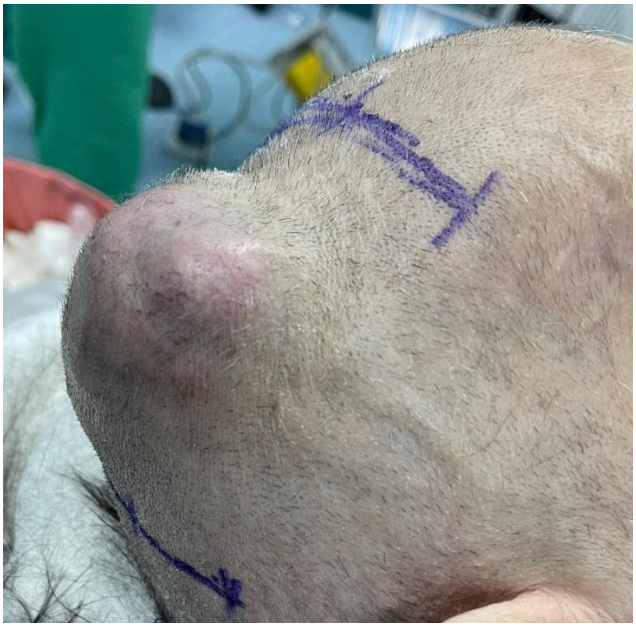

Figure 2. Breast cancer scalp metastasis

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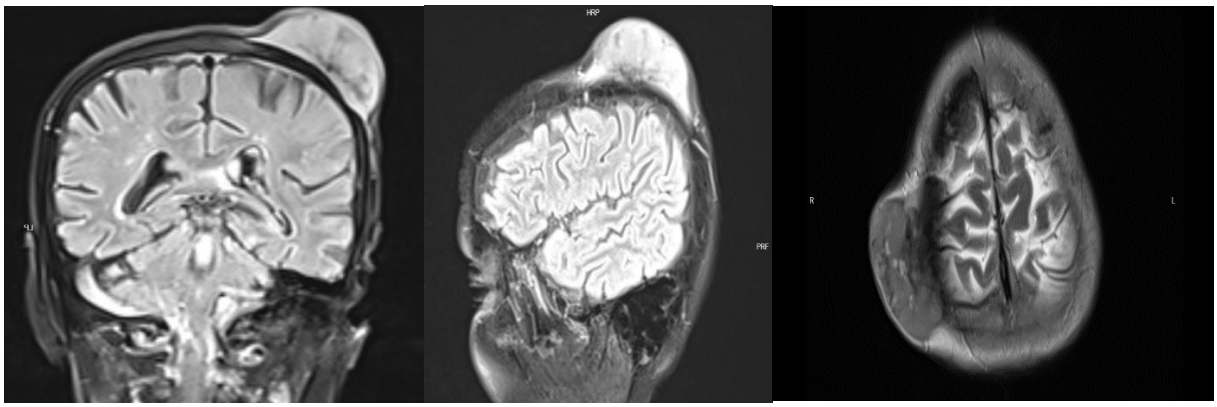

Figure 3. Preop MR image

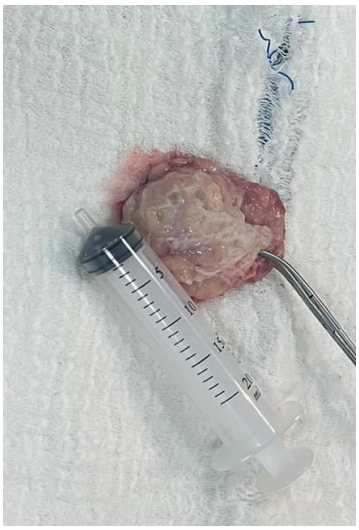

Figure 4. Intraoperatively removed tumor image

DISCUSSION

Breast cancer is the most common malignant tumor worldwide, especially among women. As a matter of fact, approximately 30% of all cancers detected in women are breast cancer (1). In our country, Breast cancer is the most common type of cancer in women. 1 in 4 female cancers is breast cancer. (4). There are 3 treatment methods for breast cancer. These; surgery, radiotherapy and medical treatment(chemotherapy and hormone therapy)(5). Our patient underwent mastectomy 10 years ago and then chemotherapy was applied.

The malignancies that metastasize to the skin in women are, in order of frequency, malignancies of the breast, colon, melanoma, lung, and ovary. Skin metastases are seen in 10% of breast cancer (6). Scalp involvement is very rare in breast cancer (3).

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In patients presenting with a mass in the scalp, biopsy and pathological examinations should be performed from surgical resection materials in terms of cancer risk. Surgical treatment should also be performed in symptomatic cases (severe pain) and lesions that cause aesthetic problems. Extracranial metastases have been reported in the literature as rare case reports for breast cancer. It should be kept in mind that atypically located metastases may be present in breast cancer cases, and it should be kept in mind that curative treatments can be performed in addition to palliative treatments with early diagnosis.

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VAKA TAKDİMİ CASE REPORT

A CASE OF TYPE 1 NEUROFIBROMATOSIS WITH CORPUS CALLOSUM AGENESIS

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ABSTRACT

Erythema multiforme (EM) is an acute inflammatory hypersensitivity reaction involving the skin and mucous membranes that develops due to infection and drugs and can be seen at any age. Although it is mostly a self-limiting disease, it has a distribution that can go up to the formation of Stevens Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN). A seven-year-old male patient applied with the complaint of rash on the face and hands that started 2 days ago. The patient was diagnosed with Type 1 Diabetes Mellitus (DM) at the age of 2 years and had therefore been using 1U/kg/day insulin (short-medium-acting) for 5 years. On physical examination, his general condition was good, and his body temperature was 36.5 °C. There were typical and atypical target lesions on the cheeks and erythematous maculopapular lesions on the dorsum of the hand. The patient was diagnosed with erythema multiforme developing after herpes simplex. In the treatment, oral valacyclovir at a dose of 20 mg/kg/day 2x1 for 5 days and topical corticosteroids were planned on the lesions. Oral care solutions containing antihistamine for itching and analgesic for oral lesions were given. The patient's skin and mucosal lesions began to regress on the 3rd day after treatment.

Key Words: *Erythema multiforme, Diabetes Mellitus, Valacyclovir*

INTRODUCTION

Erythema multiforme (EM) is an acute inflammatory hypersensitivity reaction involving the skin and mucous membranes that develops due to infection and drugs and can be seen at any age. Although it is mostly a self-limiting disease, it has a distribution that can go up to the formation of Stevens Johnson Syndrome (SJS) and toxic epidermal necrolysis (TEN) (1, 2). Herpes simplex virus (HSV) is known to be the most common cause of recurrent types among infectious agents in etiology.

CASE

A seven-year-old male patient applied with the complaint of rash on the face and hands that started 2 days ago. It was learned that these complaints had recurred from time to time for six

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months, and vesicles had formed on the lips before. The patient was diagnosed with Type 1 Diabetes Mellitus (DM) at the age of 2 years and had therefore been using 1U/kg/day insulin (short-medium-acting) for 5 years. There was no history of recent infection or vaccination. On physical examination, his general condition was good, and his body temperature was 36.5 °C. There were typical and atypical target lesions on the cheeks and erythematous maculopapular lesions on the dorsum of the hand (Fig 1 and Fig 2). Minimal crusting was observed on the lips. In the laboratory examination, complete blood count, peripheral smear, electrolyte and transaminase levels, kidney function tests, sedimentation rate, complete urine analysis and viral serological examination were normal. The patient was diagnosed with erythema multiforme developing after herpes simplex. In the treatment, oral valacyclovir at a dose of 20 mg/kg/day 2x1 for 5 days and topical corticosteroids were planned on the lesions. Oral care solutions containing antihistamine for itching and analgesic for oral lesions were given. The patient's skin and mucosal lesions began to regress on the 3rd day after treatment.

Fig. 1. Papules and plaques with erythema around the face, some in the form of typical targets

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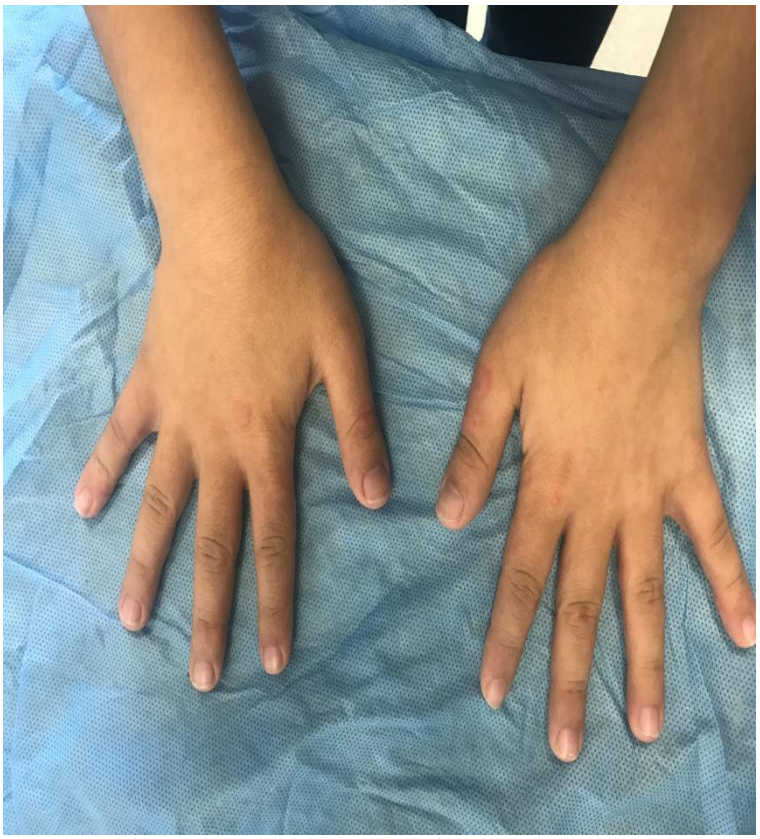

Fig 2. Atypical target lesions on the dorsum of the hand

DISCUSSION

Erythema multiforme (EM) is a mucocutaneous hypersensitivity reaction characterized by target lesions on the skin. It is examined in two subgroups depending on whether there is mucosal involvement: While no involvement is found in the EM minor subgroup, EM major is characterized by mucosal involvement. HSV infection is the most common cause of EM minor development. HSV-associated EM occurs within days or weeks following HSV infection. Both types of HSV (types1-2) have been associated with EM. The lip is the region where lesions are most common (3). In our case, we observed that target lesions were formed on the extremities two days after vesicular lesions appeared on the lip. As in our case, the lesions can be seen as papules in EM minor, or they can enlarge and form typical target lesions characterized by erythema surrounding the pale area in the middle. 20-60% of patients diagnosed with EM in the pediatric and adult groups are defined as EM major. Oral mucosal involvement is the most common in this group (4,5). In EM minor, where mucosal involvement is not usually seen, skin lesions are generally in the extremities and have a symmetrical distribution The dorsum of the hand, palms, and soles are frequently involved (6) In addition, erosive lichen planus, pemphigus, chicken pox, stomatitis, herpetic gingivostomatitis. Kawasaki syndrome, drug eruption, acute hemorrhagic

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edema should be considered in the differential diagnosis of patients with EM major (7). EM is rarely seen in children and often occurs due to infection. EM can be very mild as a minor, or it can be fatal at a rate of 5-15%, such as Steven-Johnson syndrome. An increase in HSV-1-related entities has been reported in adult patients with type 1 DM (8, 9). Although there is not enough data in pediatric cases, since we think that it may be a trigger for the development of erythema multiforme after herpes labialis, Type 1 DM should be considered as one of the possible causes in pediatric patients with EM, along with other reasons, and the patient should be examined in this regard.

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VAKA TAKDİMİ CASE REPORT

KORPUS KALLOZUM AGENEZİSİ İLE BİRLİKTELİK GÖSTEREN TİP 1 NÖROFİBROMATOZİS OLGUSU

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ÖZET

Nörofibromatozis tip 1 (NF1, von Recklinghausen hastalığı) deri, merkezi sinir sistemi, endokrin sistem, iskelet sisteminin ve diğer organların tutulumuyla karakterize kalıtsal bir nörokutanöz sendromdur. Otozomal dominant kalıtım paterni gösterir. On dokuz yaşında kadın hasta, koltukaltında lekeler ve vücutta şişlikler nedeniyle Dermatoloji polikliniğine başvurdu. Bilinen sistemik bir hastalığı olmayan hastanın dermatolojik muayenesinde bilateral aksiller bölgelerde hiperpigmente maküler lezyonlar,gövde ön yüzde papüler lezyonlar, sol servikal cilt bölgesinde kahverengi yamalar sırtta birkaç adet deri renginde solid, deriden kabarık nörofibrom ile uyumlu lezyonlar, tespit edildi. Hastanın kranial MR incelemesinde Korpus kallozum posterior kesiminin gelişmediği, buna bağlı olarak lateral ventriküllerin ayrı durduğu ve hafif kolposefali olduğu raporlandı. NF1 de en sık gözlenen ortak bulgular ; sütlükahve lekeler, Lisch nodülleri, nörofibromlar, aksiller ve inguinal çillenme olması ve beyinde hamartamatöz değişiklikler olmasıdır. Bunlara ek olarak öğrenme güçlükleri , endokrin patolojiler, hipertansiyon gibi sistemik durumlara da rastlanabilir. Bizim vakamızda aksiller çillenme, kahverengi yamalar ,nörofibromlar, öğrenme güçlüğü bulunmaktaydı. Nörofibromatoziste beyin MR incelemelerinde en çok görülen patoloji, T2A serilerde farklı lokalizasyonlarda rastlanan hiperintens lezyonlardır.

Anahtar Kelimeler: *Korpus Kallozum Agenezisi, Nörofibromatozis, Sütlü Kahve Lekeleri*

GİRİŞ

Nörofibromatozis tip 1 (NF1, von Recklinghausen hastalığı) deri, merkezi sinir sistemi, endokrin sistem, iskelet sisteminin ve diğer organların tutulumuyla karakterize kalıtsal bir nörokutanöz sendromdur. Otozomal dominant kalıtım paterni göstermekle birlikte bazı vakalarda yeni gelişen mutasyonlar olduğu görülmüştür. Hastalığın görülme sıklığı 1/2700' dir(1) . Birden fazla sistemi etkileyebilen sendromda tanımlı kriterlerden en az ikisinin görülmesi ile tanı kesinleştirilir. Erken belirlenen muayene bulguları olan cafe au lait lekeleri ve nörofibromlar ile çoğunlukla hastalara çocukluk çağında tanı konmaktadır. Bu yazıda 19 yaşında NF1 tanısı alan bir hasta sunulmuştur.

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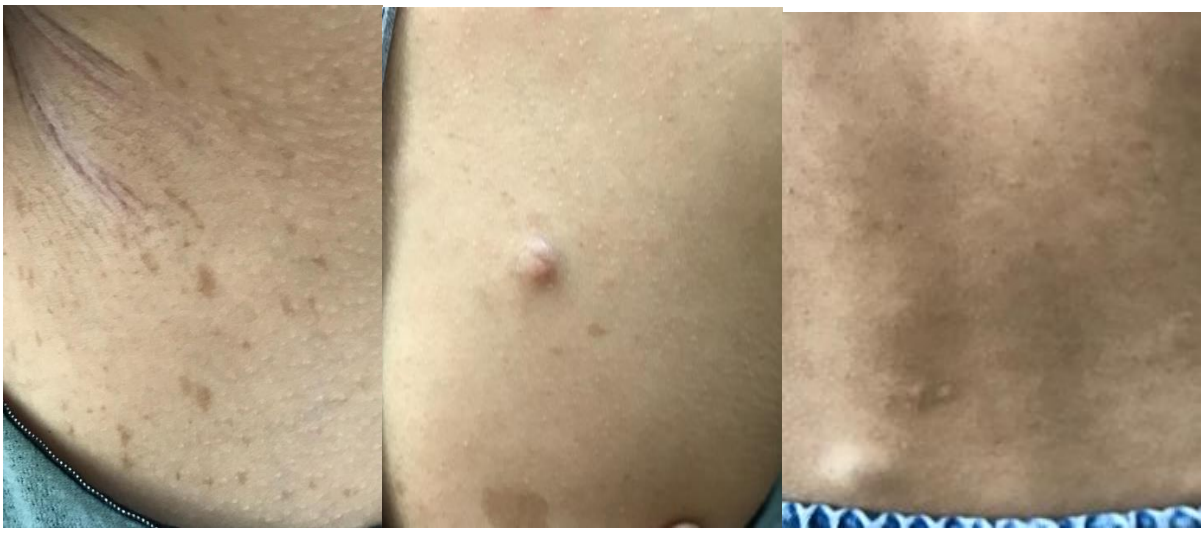
OLGU SUNUMU

On dokuz yaşında kadın hasta, koltukaltında lekeler ve vücutta şişlikler nedeniyle Dermatoloji polikliniğine başvurdu. Ayrıntılı anamnezde unutkanlık ve sinirlilik şikayetlerinin bulunduğu öğrenildi. Bilinen sistemik bir hastalığı olmayan hastanın dermatolojik muayenesinde bilateral aksiller bölgelerde hiperpigmente maküler lezyonlar,gövde ön yüzde papüler lezyonlar, sol servikal cilt bölgesinde kahverengi yamalar sırtta birkaç adet deri renginde solid, deriden kabarık nörofibrom ile uyumlu lezyonlar, tespit edildi (Şekil 1-3). Soygeçmişinde, hastanın halasına daha önce NF tanısı konduğu öğrenildi. Karın ve sırt bölgesindeki nörofibromların ergenlik döneminde ortaya çıktığı ve giderek sayılarının arttığını belirtti.



Şekil 1. Sol aksiller bölgede dağınık yerleşimli maküler hiperpigmente lezyonlar
Şekil 2. Gövde ön yüzde deri renginde solid, deriden kabarık nörofibrom ile uyumlu lezyon
Şekil 3. Sırtta deri renginde solid, deriden kabarık nörofibrom ile uyumlu lezyon

NF1 düşünülen hastanın tam kan sayımı, karaciğer ve böbrek fonksiyon testleri, tam idrar tahlilleri normal sınırlardaydı. Abdominal USG ve uzun kemik direk grafi incelemeleri normal olarak sonuçlandı. Nöroloji ve göz hastalıkları görüşü istendi. Gözde Lisch nodülleri gözlenmeyen hastanın kranial MR incelemesinde Korpus kallozum posterior kesiminin gelişmediği, buna bağlı olarak lateral ventriküllerin ayrı durduğu ve hafif kolposefali olduğu raporlandı (Şekil 4-6).

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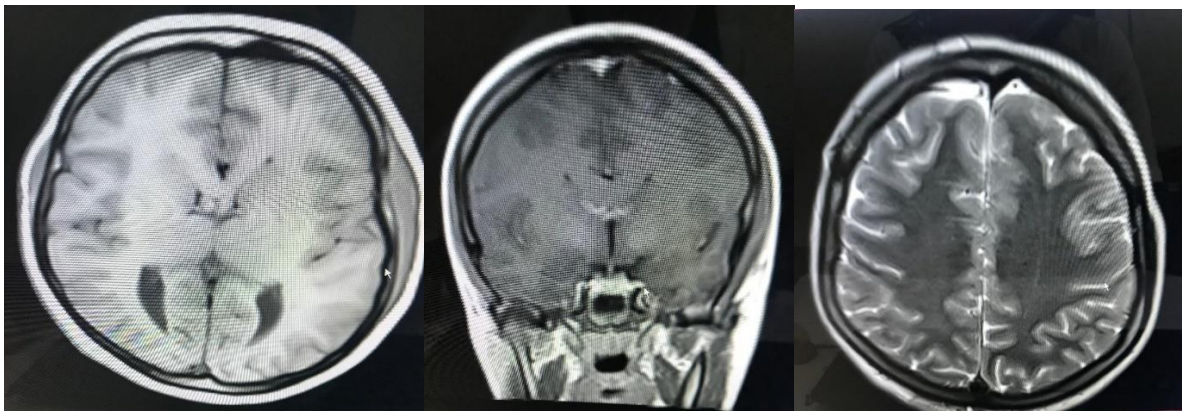

Şekil 4. Aksiyel kraniyal MR kesitinde lateral ventriküllerde ayrışma
Şekil 5. Koronal düzlemde kraniyal MR'da posterior korpus kallozum kesiminde agenezi
Şekil 6. Transvers kesit Kranial MR'da hafif kolposefali

TARTIŞMA

Nörokutanöz hastalıklar içinde en fazla görülen nörofibromatozis (NF-1) tip 1 otozomal dominant geçiş gösterir (2). NF-1 geni 17. kromozomun 11p12 bölgesinde bulunur ve Nörofibromin isimli tümör supresör proteini kodlar (3). Günümüzde NF-1 geni ile ilgili 1500'den fazla mutasyon belirlenmiştir (4). NF-1 tanısı National Institute of Health (NIH) tarafınca belirlenen tanı kriterlerinden en az ikisinin bulunması ile konur (Tablo 1) (5). NF1 de en sık gözlenen ortak bulgular; sütlükahve lekeler, Lisch nodülleri, nörofibromlar, aksiller ve inguinal çillenme olması ve beyinde hamartamatöz değişiklikler olmasıdır. Bunlara ek olarak öğrenme güçlükleri, endokrin patolojiler, hipertansiyon gibi sistemik durumlara da rastlanabilir. Bizim vakamızda aksiller çillenme, kahverengi yamalar, nörofibromlar, öğrenme güçlüğü bulunmaktaydı. Nörofibromatoziste beyin MR incelemelerinde en çok görülen patoloji, T2A serilerde farklı lokalizasyonlarda rastlanan hiperintens lezyonlardır. Hamartom isimli bu lezyonlar benigndir ve bunlara eşlik eden nörolojik problem yoktur (2). NF-1'li olgularda en sık görülen beyin tümörü optik gliomlardır. Çoğu asemptomatiktir (6). Duffner ve ark. (7) NF olgularda hamartomu %62, hamartom dışı anormal bulguları %12 bulmuşlardır. Bizim olgumuzda sık görülmeyen bir durum olarak Korpus kallozum agenezisi ve kolposefali buna bağlı mental retardasyon mevcuttu. Nörofibromatozis hastalarında nöbet sıklığı %3.8-6 olarak bildirilmektedir. Yapılan bir araştırmada epilepsi prevalansının %7 olduğunu bildirilmiş ve nöbetlerin %85'inin parsiyel, %15'inin jeneralize olduğunu saptanmıştır(8).Bizim olgumuzda çocukluk döneminde bir kere jeneralize nöbet öyküsü mevcuttu ve izlem amacıyla Nöroloji takibi önerildi. NF-1, malign tümör gelişim riski ve fonksiyon kayıpları ile önemli bir morbidite ve mortalite nedeni olabilir. Bu nedenle bu hastaların doğru tanınması, kalıtım riski dolayısıyla aile eğitimi, mortalite ve morbiditenin en aza indirilmesi için multidisipliner bir yaklaşımla takip edilmeleri gerekmektedir.

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Tablo 1. NF 1 Tanı Kriterleri

Sütlü kahve lekeleri (prepubertal >5 tane, >0,5 cm ya da postpubertal >1,5 cm),
>1 kutanöz ya da subkutanöz nörofibrom veya 1 pleksiform nörofibrom,
Aksiler çillenme,
Optik gliom,
Lisch nodülü,
İskelet displazisi,
Birinci derecede akrabada NF-1 tanısı olması

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