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Table of Contents

Letter to the editor

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Approach To the Metastatic Bone Lesions; Tumor Investigation in A Patient Without Cancer

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ABSTRACT

With the increase in the use of radiological imaging methods, the number of patients with a bone lesion (mostly in the form of a lytic lesion) or metastasis suspicion is also increasing. Patients with such a suspicious bone lesion are referred to internal medicine outpatient clinics for further investigation. However, there is no a standard approach for tumor investigation in incidental bone lesions in the literature. In this article, we mentioned about definition, clinical findings and diagnostic approach to these lesions.

Keywords: cancer, metastasis, bones

With the increase in the use of radiological imaging methods, the number of patients with a bone lesion (mostly in the form of a lytic lesion) or metastasis suspicion is also increasing. Patients with such a suspicious bone lesion are referred to internal medicine outpatient clinics for further investigation. However, there is no a standard approach for tumor investigation in incidental bone lesions in the literature. In this article, we mentioned about definition, clinical findings and diagnostic approach to these lesions.

Lung, breast, prostate, kidney, bladder, thyroid cancers, lymphomas and sarcomas are the main malignancies that metastasize to the bones. Bone metastases have been reported in 30-40% of thyroid, kidney and bronchial cancers in autopsy series and 50-70% of advanced breast and prostate cancers. Osteolytic bone lesions are present in 60% of myeloma patients at the time of diagnosis. Rarely, myeloma may also have osteosclerotic lesions and they are mostly associated with POEMS (polyneuropathy, organomegaly, endocrinopathy, monoclonal spike, skin changes) syndrome. Metastases are more common in areas such as the skull, vertebrae (more often in the lumbar region), proximal femur, pelvis and sacrum. [1, 2] Bone metastasis are classified as osteolytic or osteoblastic according to their radiological appearance. However, this distinction is not clear and many patients may have both osteolytic and osteoblastic metastasis (Table 1). [1]

Pathophysiology

Bone is the third most metastasized organ (after liver and lung) and metastases of bone are more common than primary bone tumors. Tumors spread to the bone by hematogenous route (venous) or local invasion. The mechanism of bone metastases is not fully understood. Through remodeling, bones try to maintain its strength by dynamic balance between osteoclastic and osteoblastic activity. Once a metastatic focus is located in the bone, tumor cells interact with osteoclastic and osteoblastic cells to increase bone turnover. It is assumed that tumoral cells stimulate osteoclasts via RANKL (receptor activator nuclear

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Table 1. Radiologic presentation of bone metastases

Mostly osteolytic:	Mostly osteosclerotic:	Mix:
- Multiple myeloma	**- Prostate cancer**	**- Breast cancer**
- Renal cell cancer	- Small cell lung cancer	- Gastrointestinal cancers
- Non-small cell lung cancer	- Hodgkin lymphoma	- Squamous cell cancers
- Thyroid cancer	- Carcinoid tumors	
- Non-Hodgkin lymphoma	- Medulloblastoma	
- Melanoma		

*The ones in bold are the tumors that metastasize most frequently to the bones and should be considered initially

factor kappa B ligand). In addition, many cytokines, chemokines and hormones secreted by tumor cells also stimulate osteoblasts and osteoclasts (such as; jagged-1, metalloproteinase-7, parathyroid hormone-related peptide, endothelin-1, bone morphogenic proteins, insulin-like growth factors, platelet-derived growth factors and fibroblast growth factors).[2]

Clinical and laboratory findings

Bone metastases are usually asymptomatic and diagnosed at the staging after a tumoral diagnosis. Pain is the most common symptom. Symptoms such as motor deficit, paralysis, loss of sensation, stool and urinary incontinence due to spinal cord compression can be seen in vertebral metastases. [2]

There is no a specific blood test in the diagnosis of bone metastases. However, elevated alkaline phosphatase (ALP) or calcium may be a finding of bone metastases. Osteolytic lesions can often cause hypercalcemia. On the contrary, in osteoblastic metastases, hypocalcemia may be seen with an increase in ALP. It increases significantly in bone metastases of lung, prostate, breast cancers and osteosarcoma. Acid phosphatase, on the other hand, may be increased with ALP by osteoclastic activity. There may be an increase in acid phosphatase especially in prostate cancer. [2]

Since bone metastases can be confused with osteoporosis in elderly women, care should be taken in these people. While the cortical bone is preserved in osteoporosis, it is generally destroyed in metastatic bone lesions.

Diagnosis

a) Screening for bone metastasis in a patient with known cancer

There is no a consensus in the screening and diagnosis of bone metastases in patients with cancer. Firstly, bone metastasis can be screened by direct radiological imaging. If lytic lesions are larger than 1 cm, they may be seen better than lesions smaller than 1 cm on direct radiological imaging. If there is no finding on direct radiography imaging, non-contrast computed tomography (CT) and magnetic resonance imaging (MRI) should be used. MRI is more sensitive than CT in detecting bone metastases, therefore it should be performed when MRI is contraindicated. The advantage of MRI is that bone marrow infiltrates can be evaluated. Bone scintigraphy (Technetium-99m) and positron emission tomography (PET) can be used as secondary imaging techniques. Bone scintigraphy is reliable for detecting metastases in tumors with increased osteoblastic activity, such as prostate and breast cancer. However, it is less sensitive to detect tumors with little or no osteoblastic activity (such as multiple myeloma). PET has high sensitivity and specificity for detection of distant metastases, also bone metastases. PET is superior to bone scintigraphy due to the advantages of detection all distant metastases and clinical staging of cancer. [2-4] Sensitivity and specificity of imaging techniques to detect bone metastasis are shown on Table 2. [3]

Table 2. Sensitivity and specificity of imaging techniques to detect bone metastasis

Imaging technique:	Sensitivity (%)	Specificity (%)
- Computed tomography	77.1	83.2
- Bone scintigraphy	75.1	93
- Magnetic resonance imaging	90.4	96.0
- Positron emission tomography	94.2	97.2

b) Detection of primary tumor without a diagnosis of cancer

First of all, it should be directed to the organ system where the patient has complaints and/or physical examination findings, if any. If there are no complaints and/or physical examination findings, a search for cancer, which is common according to gender and age, should be performed. For this purpose, first of all, solid internal organ cancers should be screened by using contrast-enhanced CT of the lung, abdomen and pelvis, and breast screening should be performed if female. Evaluation for multiple myeloma should also be done simultaneously. If the results of these techniques are negative, bone biopsy should be planned.[2, 3]

Authors' Contribution

Study Conception: SU,; Study Design: SU,; Supervision: SU, FB,; Literature Review: SU, FB,; Manuscript Preparation: SU,FB,; and Critical Review: SU.

REFERENCES

1. UpToDate. Mechanisms of bone metastases. Available at: https://www.uptodate.com/contents/mechanisms-of-bone-metastases?sectionName=Osteoblasts&search=bone%20metastasis&topicRef=91912&anchor=H2047254803&source=see_link#H2047254803. Accessed March 29, 2022.
2. UpToDate. Epidemiology, clinical presentation, and diagnosis of bone metastasis in adults. Available at: https://www.uptodate.com/contents/epidemiology-clinical-presentation-and-diagnosis-of-bone-metastasis-in-adults?search=-bone%20metastasiz&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1. Accessed March 29, 2022.
3. Maillefert JF, Tavernier C, Tebib J. Determining the site of the primary cancer in patients with skeletal metastasis of unknown origin: A retrospective study. Cancer. 2000 Apr;88(7):1759-61.
4. Özer H, Durmaz MS. Kemik Metastazları. Trd Sem 2021; 9: 137-155. (in Turkish)

Original Article

Internal Medicine

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Comprehensibility Levels of Informed Consent Forms in a State Hospital Internal Medicine Clinic: A Descriptive Study

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ABSTRACT

Objectives: Herein, we aimed to determine the comprehensibility levels of written informed consent forms in a state hospital internal medicine clinic.

Methods: Twenty-eight informed consent forms fordiagnostic interventions, treatment applications, and hospitalization processes in a state hospital internal medicine clinic were evaluated with the comprehensibility indexes developed by Ateşman and Bezirci-Yılmaz. We evaluated comprehensibility in four main groups: primary (1st-8th grade), high school (9th-12th grade), undergraduate (13th-16th grade), and graduate education (over 16th grade).

Results: According to both comprehensibility indexes, all forms required at least a high school education. According to Ateşman, median comprehensibility was at the 13th-14th grade; according to Bezirci-Yılmaz, a median of 14.6 years of education was required for comprehensibility.

Conclusion: For comprehensibility of the informed consent forms used in the internal medicine clinic, at least high school and median university-level education were required. Considering the rate of population with a high school or higher education degree in Turkey was 43% in 2020, it is predicted that the patients' comprehensibility of the written informed consent would be seriously low. Immediate regulations are required ethically and legally to increase the comprehensibility of existing written informed consent forms throughout society.

Keywords: comprehensibility, consent forms, informed consent, internal medicine

In daily clinical practice, informing patients before procedures and ensuring that patients participate in the process is a patient's right, an ethical rule, and a legal obligation.[1] This information is provided verbally and in writing within the "informed consent" between the physician and the patient.Informed consent is formed by explaining in a detailed, understandable, and structured way why the intervention is needed, how the intervention will be done, the benefits that the person will receive from this intervention, and the possible harm that may occur due to the procedure, the process they will experience if they are not treated, and the alternative options in the treatment.The informed consent process is concluded by the patient's verbal and written notification of the decision (either approval or refusal) about the procedure, where the patient has read and understood the information presented in writing.[2]

In addition to fulfilling ethical and legal requirements, the patient must understand the written informed consent forms to protect physicians from medical malpractice. One of the definitions used to describe the readability of written texts is comprehensibility.The comprehensibility level can be measured

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objectively using various mathematical formulas, and the measured values are defined by education level equivalencies (i.e., primary school, high school, undergraduate, or graduate level).[3] Various scoring systems use parameters such as the number of sentences in the text, the number of words in the sentences, and the number of syllables in words to calculate comprehensibility.[4-6] For Turkish texts, criteria developed by Ateşman and Bezirci and Yılmazevaluate comprehensibility.[7, 8]

According to their preference, each hospital or physician may have informed consent forms specific to the diagnostic procedures, treatment applications, or hospitalization processes that they use in daily clinical practice. In this study, we aimed to determine the comprehensibility levels of written informed consent forms used daily in a state hospital internal medicine clinic, define the comprehensibility of these texts, and determine which texts could be read according to education level.

METHODS

Herein, we evaluated twenty-eight different standardized informed consent forms developed by a state hospital for daily clinical use in the internal medicine clinic. Written permission was obtained from the state hospital administration to use informed consent forms.

Various methods have been developed to evaluate comprehensibility, using parameters such as the number of sentences in the text, how many words these sentences consist of, how many syllables each word has, and the rate of professional terminology use. The result obtained with these calculations expresses the text's comprehensibility according to the people's education level. Although there are more than forty formulas accepted as comprehensibility criteria , in this study, two separate comprehensibility criteria, developed by Ateşman in 1997 and Bezirci and Yılmaz in 2010 were used to evaluate Turkish informed consent texts.[2, 7, 8]

Ateşman Comprehensibility Index

Ateşman Comprehensibility Indexis a mathematical method to calculate comprehensibility that considers the length of words and sentences. According to Ateşman's formula, the average sentence length in Turkish is 9-10 words, and the average length of words is 2.6 syllables. The results obtained with the Ateşman Readability Criterion formula are determined as a readability value between 0-100; higher values indicate easier-to-read texts.[7] Ateşman Comprehensibility Indexwas applied as:198.825 - 40.175 x word length (total syllables / total words) - 2.610 x sentence length (total words/ total sentences). The numerical value obtained determined the text's comprehensibility according to the reader's education level (Table 1).

Bezirci-YılmazComprehensibility Index

The comprehensibility index developed by Bezirci and Yılmaz takes into account the number of words in sentences, the number of syllables in words, and the distribution of words according to the syllable counts (Table 2). The result obtained with the Bezirci-YılmazComprehensibility Indexreveals the comprehensibility level as the number of years the person has been educated. When this level is evaluated considering the current education system in Turkey, it provides a grouping of readability according to education levels (Table 3).[8]

Table 1. The relationship between the Ateşman comprehensibility index and the comprehensibility level

Index	Comprehensibility Level
90 - 100	Can be easily understood by students in 4th grade and below
80 – 89	Can be easily understood by students in 5 th and 6 th grade
70 – 79	Can be easily understood by students in 7 th and 8 th grade
60 – 69	Can be easily understood by students in 9 th and 10 th grade
50 – 59	Can be easily understood by students in 11 th and 12 th grade
40 – 49	Can be easily understood by undergraduates
30 – 39	Can be easily understood by university graduates
< 29	Can be easily understood by university postgraduates

Table 2. Bezirci-Yilmaz comprehensibility index formula

Bezirci-Yilmaz comprehensibility index = $\sqrt{MWC[(S3 \times 0.84) + (S4 \times 1.5) + (S5 \times 3.5) + (S6 \times 26.25)]}$

MWC: mean word count; S3: mean number of words with three syllables; S4: mean number of words with four syllables; S5: mean number of words with five syllables; S6: mean number of words with ≥ six syllables

Table 3. The relationship between the Bezirci-Yilmaz comprehensibility index and the comprehensibility level

Comprehensibility level (years)	Education level
1–8	Primary school
9–12	High school
13–16	Undergraduate
> 16	Postgraduate

Data acquisition and evaluation

Each of the twenty-eight informed consent forms was transferred to the Microsoft Word program. Before evaluating comprehensibility, the titles of the informed consent forms were removed to prevent any incorrect effect on the comprehensibility level. Then, the forms were evaluated in the context of the comprehensibility formulas developed for the Turkish language by Ateşman, and Bezirci-Yilmaz.[7, 8] When performing these procedures, the computer software developed by Bezirci-Yilmaz was used. The purpose of informed consent forms was categorized into three main groups: diagnostic interventions, treatment applications, and hospitalization processes. In addition, the ratio of medical terms to the total number of words was determined by counting the medical terms used in the informed consent forms, and this ratio was expressed as a percentage. The minimum level of education required for the comprehensibility of the informed consent forms was evaluated in 4 main groups: primary (1st-8th grade), high school (9th-12thgrade), undergraduate (13th-16th grade), and graduate education (over 16th grade).

Statistical analysis

Data were analyzed using SPSS for Windows version 23.0 (SPSS, Chicago, Illinois, USA). Continuous variables were expressed as median (minimum-maximum) and categorical data as numbers and percentages. Chi-square tests were used to compare categorical data and Mann-Whitney U test for continuous variables. $P < 0.05$ was accepted as the statistical significance limit for all statistical tests.

RESULTS

The study evaluated twenty-eight informed consent forms in routine clinical use in a state hospital internal medicine clinic. Of these informed consent forms, 7 (25%) were related to the diagnostic interventions, 15 (53.6%) informed consent forms were for treatment applications, and 6 (21.4%) were for hospitalization processes. Informed consent forms had a median length of 607 words (260-2349 words). The median number of medical terms in the informed consent texts included 13 words (3-77 words), and the median percentage of medical terms was 1.96% (0.006%-12.2%).

The comprehensibility levels of all informed consent forms were evaluated with Ateşman and Bezirci-Yılmaz's comprehensibility indexes. According to the Ateşman comprehensibility index, the median comprehensibility level was 44.8 points (22.9-58.1), which can be interpreted as comprehensible by 13th and 14th -grade students. When evaluated with the

Table 4. Comprehensibility levels of the consent forms according to the Ateşman and the Bezirci-Yılmaz comprehensibility indexes

	Ateşman	Bezirci-Yılmaz
Primary school (1st-8th years)	0 (0%)	0 (0%)
High school (9th-12th years)	10 (35.7%)	13 (46.5%)
Undergraduate (13th-16th years)	17 (60.7%)	9 (32.1%)
Postgraduate (> 16 years)	1 (3.6%)	6 (21.4%)

Bezirci-Yılmaz comprehensibility index, the median comprehensibility level was 14.6 years (8.6-19.2 years), which can be interpreted as comprehensible at the undergraduate level. The distribution of comprehensibility levels of informed consent forms according to both comprehensibility indexes is presented in Table 4. None of the informed consent forms were readable at a primary school education level. 35.7% of the informed consent forms according to the Ateşman comprehensibility index and 46.5% according to the Bezirci-Yılmaz comprehensibility index were readable at the high school education level.

Informed consent forms were also divided into two groups by dividing from the median value of each variable: word count, medical term count, and medical term percentage. However, no significant difference was observed between these groups regarding comprehensibility. When the consent forms were analyzed according to their intended use, the comprehensibility of the informed consent forms related to the diagnostic interventions had higher comprehensibility according to the Ateşman ($p = 0.006$, chi-square test), and to the Bezirci-Yılmaz comprehensibility indexes ($p = 0.038$, chi-square test) (Table 5).

DISCUSSION

It is of ethical and legal importance that the written informed consent forms are comprehensible. This study aimed to determine the comprehensibility levels of informed consent forms used in daily clinical practice in a state hospital internal medicine clinic objectively, with the comprehensibility indexes developed by Ateşman and Bezirci-Yılmaz, and to define the corresponding level of education required for these texts. We determined that at least high school students can read informed consent forms according to both comprehensibility indexes. We observed that none of the included informed consent forms were readable at a primary school education level, and 35.7% according to the Ateşman comprehensibility index and 46.5% according to the Bezirci-Yılmaz comprehensibility index were comprehensible at a high school education level. In both indexes, we observed that the comprehensibility of the consent forms related to the diagnostic procedures are easier to comprehend, while the consent forms related to the hospitalization procedures are more challenging to comprehend. According to the Turkish Statistical Institute National Education Statistics Database, the rate of population with a high school or higher education degree in Turkey was 24.5% in 2008, and this percentage increased every year and reached 43% in 2020. The proportion of the population with at least an associate university degree has increased from 9.1% to 21.6%.9 According to the United Nations Educational Scientific and Cultural Organization (UNESCO) 2017 data, the average education level of Turkey was 8.27 years.10 When the comprehensibility of the informed consent forms is evaluated in the light of these statistical data, we believe that the comprehensibility of the informed consent forms used in daily clinical practice is seriously low.

Table 5. A comparison of comprehensibility levels of the consent forms according to their purpose

		Diagnostic interventions (n = 7)	Treatment applications (n = 15)	Hospitalization processes (n = 6)
Ateşman	High school (9^{th} - 12^{th} years)	6 (85.7%)	4 (26.7%)	0 (0%)
	Undergraduate (13^{th} - 16^{th} years)	1 (14.3%)	11 (73.3%)	5 (83.3%)
	Postgraduate (> 16 years)	0 (0%)	0 (0%)	1 (16.7%)
Bezirci-Yılmaz	High school (9^{th} - 12^{th} years)	6 (85.7%)	7 (46.7%)	0 (0%)
	Undergraduate (13^{th} - 16th years)	0 (0%)	5 (33.3%)	4 (66.7%)
	Postgraduate (> 16 years)	1 (14.3%)	3 (20%)	2 (33.3%)

The average education level of adults in the USA was determined to be at the 8th-grade level, and the American Medical Association and the National Institutes of Health recommended that the informed consent forms used for invasive procedures in the USA should be comprehensible at an education level corresponding to 6th grade.[11]However, Eltorai *et al*. evaluated the comprehensibility of the informed consent forms using seven different formulas, mainly Flesch-Kincaid; and they determined that the informed consent forms used for invasive procedures had a readability level corresponding to an average of 15 years of education, similar to our study.[12]

Although there is no clear recommendation about the comprehensibility of informed consent forms in Turkey, there are studies on the comprehensibility of Turkish informed consent forms used for various purposes. Ebem *et al*. analyzed 90 separate intramuscular and intravenous informed consent and determined the average comprehensibility was at 11th and 12th-grade education levels.[13] Ay *et al*. evaluated the informed consent forms used before ophthalmological surgical procedures, and Boztaş *et al*.evaluated the informed consent forms used before anesthesia, which both reported similar comprehensibility levels.[14, 15] The median comprehensibility in our study was at a 13th and 14th-grade education level according to the Ateşman comprehensibility index, and when evaluated with the Bezirci-Yılmaz comprehensibility index, the median comprehensibility was at 14.6 years. Compared to similar studies in the literature, informed consent forms used in internal medicine clinics require a higher level of education, and urgent correction and improvement are required to increase comprehensibility.

The percentage of medical terms in the informed consent forms is another factor that can affect the comprehensibility of the text. Ebem *et al*. reported that the use of medical term percentage in intramuscular and intravenous informed consent forms was 2.6%.[13] Ay *et al*.reporteda 3.7% medical term percentage in informed consent forms used for ophthalmological surgical procedures, and Boztaş *et al*. reported the average percentage of medical terms as 4% in pre-anesthesia consent forms.[14, 15] Although the median ratio of medical term percentage in our study was 1.96%, which is lower than the ratios reported in the literature, this difference may have arisen due to the differences in the procedures defined in the informed consent texts.

There are several limitations to our study. We considered the sentence length, word count, and the number of syllables in words. However, before a possible diagnostic procedure or treatment application, a patient's anxiety level may be higher than normal, which can affect the comprehensibility of the informed consent form. In addition, the font choice and the font size of the informed consent texts included in this study were not taken into account, which also may affect the comprehensibility of the text. Further studies of the comprehensibility levels of informed consent forms, focusing on new models, including characteristics such as education level, age, mental state, and patients' visual acuity, are necessary.

Our study demonstrated that the written informed consent forms used in daily clinical practice in a state hospital internal medicine clinic required at least a high school education level to be comprehensible. The median comprehensibility was at university-level education. Considering the statistics of the population with a high school or higher education level in Turkey, it is predicted that the patients' comprehensibility of the written informed consent forms is seriously low. Although further studies are required that consider other factors of comprehensibility of a text on this subject; urgent regulations are needed, ethically and legally, to increase the comprehensibility of existing written informed consent forms throughout society.

CONCLUSION

Ethical considerations:Ethics committee approval is not required as the author did not use human or experimental animal data in this study. The permission to use consent forms was obtained from the hospital administration and presented with the manuscript.

Conflicts of interest: The author declares none

Author Contributions: Study Conception: GT; Study Design: GT; Supervision: GT; Funding: GT; Materials: GT; Data Collection and/or Processing: GT; Statistical Analysis and/or Data Interpretation: GT; Literature Review: GT; Writer: GT; Critical Review: GT.

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REFERENCES

1. Ersoy N. Klinik Etiğin Önemli Bir Sorunu: Aydınlatılmış Onam. Turkiye Klinikleri J Med Ethics. 1994;2:131-6.
2. World Medical Association. World Medical Association Declaration of Helsinki. Ethical principles for medical research involving human subjects. Bull World Health Organ. 2001;79:373-4.
3. Goldbort R. Readable writing by scientists and researchers. J Environ Health. 2001;63:40-1.
4. Flesch R. A new readability yardstick. J Appl Psychol. 1948;32:221-33.
5. Walsh TM, Volsko TA. Readability assessment of internet-based consumer health information. Respir Care. 2008;53:1310-5.
6. Al-Khalifa H, Al-Ajlan A. Automatic readability measurements of the Arabic text: An exploratory study. Arab J Sci Eng. 2010;35:103-124.
7. Ateşman E. Measuring readability in Turkish. AU Tömer Lang J. 1997;58:171–4.
8. Bezirci B, Yılmaz AE. A software library for measurement of readability of texts and a new readability metric for Turkish. DEÜ FMD. 2010;12:49–62.
9. Türkiye İstatistik Kurumu. Bitirilen eğitim düzeyine göre nüfusun dağılımı (25+yaş). http://data.tuik.gov.tr/Kategori/GetKategori?p=egitim-kultur-spor-ve-turizm-105&dil=1. Erişim tarihi 17 Temmuz 2021.
10. UNESCO Institute for Statistics. Mean years of schooling-Turkey. http://data.uis.unesco.org/. Erişim tarihi 17 Temmuz 2021.
11. Weiss BD. Health literacy and patient safety: help patients understand. 2nd ed. Chicago, Ill: American Medical Association Foundation and American Medical Association; 2007.
12. Eltorai AE, Naqvi SS, Ghanian S, Eberson CP, Weiss AP, Born CT, Daniels AH. Readability of Invasive Procedure Consent Forms. Clin Transl Sci. 2015 Dec;8(6):830-3. doi: 10.1111/cts.12364.
13. Ebem E , Tutar M , Yıldız M , Canıtez A , Kara Ö , Kozanhan B. İntravenöz ve İntramüsküler Enjeksiyon Bilgilendirilmiş Onam Formlarının Okunabilirlik Açısından Değerlendirilmesi. Anadolu Klin. 2019;24:132-136. doi: 10.21673/anadoluklin.484708
14. Ay IE, Doğan M. An Evaluation of the Comprehensibility Levels of Ophthalmology Surgical Consent Forms. Cureus. 2021 Jul 26;13(7):e16639. doi: 10.7759/cureus.16639.
15. Boztaş N, Özbilgin Ş, Öçmen E, Altuntaş G, Özkardeşler S, Hancı V, Günerli A. Evaluating the Readibility of Informed Consent Forms Available Before Anaesthesia: A Comparative Study. Turk J Anaesthesiol Reanim. 2014 Jun;42(3):140-4. doi: 10.5152/TJAR.2014.94547

Original Article

Internal Medicine

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Investigation of acute kidney injury and related factors in hospital patients; single center experience

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ABSTRACT

Objectives: Acute Kidney Injury (AKI) is a very common clinical problem. This picture is seen in 5-7% of hospitalized patients and in 25-30% of patients hospitalized in intensive care units. The aim of this study was to determine the incidence, etiology, clinical features, prognosis and complications in adult patients hospitalized with of AKI.

Methods: This study was organized as an observation study in which the files of the patients admitted to internal medicine and nephrology clinics between September 2012 and September 2017 were examined. All patients admitted to the internal medicine and nephrology clinics with the diagnosis of AKI were included in the study. But those under the age of 18, patients with chronic kidney damage, ex-patients after hospitalization, patients who were sent to the intensive care unit after hospitalization, patients who voluntarily refused treatment or left the service and who were hospitalized for more than 48 hours, but those who did not have biochemical analysis during their stay were excluded. RIFLE creatinine criteria were used for AKI identification.

Results: The study included 354 patients. 177 (50%) patients were male and 177 (50%) patients were female. The incidence of prerenal AKI in the internal medicine and nephrology clinics was 53.39%, renal AKI was 36.44% and postrenal AKI was 10.17%. When the causes of AKI were examined, 33.9% hypovolemia, 15.5% UTI and 13.5% gastroenteritis were detected. The dialysis rate was 23.7%.

Conclusion: Inconclusion, although the incidence of AKI is acceptable in our hospital. It is found to be compatible with the literature and it is possible to catch the early stage of injury by decreasing the frequency especially with better management of elderly patients and more closely monitoring renal functions in this group of patients

Key words: acute renal failure, hemodialysis, nephrology

Acute loss of kidney function with an increase in serum creatinine and/or a decrease in urine output was previously known as acute renal failure (ARF).[5-8] This clinical condition, which is now defined as acute kidney injury (AKI), has high morbidity and mortality and is a common condition in critically ill patients. Although there is significant progress in the diagnosis and treatment of AKI, the mortality rate increases considerably when AKI is sufficient to require renal replacement therapy in clinics and intensive care units.[16] Although RIFLE and AKIN have been proposed and approved definitions in AKI classification, in 2012 KDIGO needed a single definition both for its use in practice and research and for public health.[14, 19] Aim of this study, the etiology, clinical features, prognosis of hospitalized adult pa-

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tients with the diagnosis of AKI in Internal Medicine and Nephrology clinics between September 1, 2012 and September 1, 2017. AKI is a disease that is very common in the community and has multiple causes. We wanted to point this out in our study. AKI can be followed by both internal medicine and nephrology clinics. We wanted to investigate whether there is a different situation from the literature in terms of incidence among these clinics. AKI is a disease that can go as far as dialysis when it cannot be intervened in place and on time. We wanted to indicate how many people received dialysis treatment in our study.

METHODS

This study was retrospectively organized by scanning the files of patients hospitalized with the diagnosis of AKI in the internal medicine and nephrology clinics between September 1, 2012 and September 1, 2017. Hemogram, blood biochemistry, blood gas values of 354 patients included in our study, clinic in which they were hospitalized, duration of hospitalization, whether they were on dialysis, comorbidities and conditions leading to AKI were examined electronically from hospital records by scanning epicrisis.

Statistical Analysis

354 patients were included in the study. Whether the numerical variables obtained from these patients were compatible with the normal distribution were checked with Kolmogrov Smirnov and Shapiro Wilk normality tests. Summary statistics (mean ± standard deviation) and minimum-maximum values of the variables consistent with the normal distribution are given. Numerical variables that are not compatible with the normal distribution are summarized with median-percentages and minimum-maximum. Descriptive statistics for categorical variables are given in numbers and percentages. While the comparisons of two independent groups were evaluated in terms of numerical variables, two independent groups t-test was used since the condition of normal distribution and homogeneity of variance was met. The homogeneity of variance was checked with Levene's test. The study protocol was approved by the institutional ethics committee (date/number:17.08.2018-016) and conducted in accordance with the principles of the Declaration of Helsinki and the Good Clinical Practice guidelines of the International Conference on Harmonization. There was no sponsor for the study. SPSS 22.0 (Statistical Package for the Social Sciences) IBM Software program was used for statistical analysis.

Exclusion Criteria

1. Those under 18 years old
2. Those with a history of chronic kidney damage
3. Those who exited before the end of their treatment after hospitalization
4. Patients sent to the intensive care unit after hospitalization
5. Patients who refuse treatment or leave the service voluntarily
6. Those who did not undergo biochemical analysis during the hospitalization period, even if they were hospitalized for more than 48 hours

RESULTS

The patients whichs included in the study, 177 (50%) were male and 177 (50%) were female and of the 354 patients included in the study, 150 (42.4%) were hospitalized in the internal medicine service and 204 (57.6%) were hospitalized in the nephrology service (Table 1). The mean age of the 354 patients included in the study was 67.24 ± 17.10 years (18-104). The mean age of the patients who were divided into 3 groups for prerenal, renal and postrenal reasons are given in (Table 2). There was a statistically significant difference between the groups in terms of age ($p < 0.001$). The difference is seen between those hospitalized for renal (61.74 ± 18.46) and prerenal (70.83 ± 15.47) causes. (Table 2). According to their diagnosis, 189 (53.39%) patients were hospitalized for prerenal reasons, 129 (36.44%) for renal reasons, and 36 (10.17%) for postrenal reasons. (Table 3). The hospitalization period of the patients was 8.29 ± 6.088 days (2-53 days) in the prerenal group, 10.13 ± 7.394 days

Table 1. Number and Percentage Distribution of Patients by Service and Gender

Clinic	n (%)
Internal Medicine	150 (42.37)
Nefrology	204 (57.63)
Gender	
Female	177 (50)
Male	177 (50)
Total	**354 (100)**

Table 2. Average Age Values in Diagnostic Groups

Variable	Diagnosis	N	Mean ± Std. Deviation	Min-Max	*P*
Age	Prerenal	189	70.83 ± 15.47	18-104	< 0.001
	Renal	129	61.74 ± 18.46	19-89	
	Postrenal	36	68.11 ± 15.29	33-89	
	Total	354	67.24 ± 17.10	18-104	

(2-51 days) in the renal group, and 11.53 ± 6.926 days (2-37 days) in the postrenal group. (Table 4). During the follow-up, 84 (23.7%) of the patients received renal replacement therapy in the form of hemodialysis (Table 5). When we look at the most common causes of AKI in our study; we see that 33.9% of the patients have hypovolemia, 15.5% have urinary tract infection (UTI) and 13.6% have gastroenteritis. Apart from this, respectively; We can see NSAID use, acute tubular necrosis, contrast nephropathy, malignancy, benign prostatic hypertrophy, multiple myeloma, rhabdomyolysis, glomerulonephritis and kidney stones (Table 6).

Table 3. Distribution of the patients according to their diagnoses

Diagnosis	n (%)
Prerenal	189 (53.39)
Renal	129 (36.44)
Postrenal	36 (10.17)
Total	354 (100)

DISCUSSION

AKI is a clinical picture that progresses with deterioration of kidney functions and decrease in glomerular filtration rate within days or even hours.[10-13] According to the RIFLE and AKIN criteria recently used in the diagnosis of AKI, an increase of 0.3 mg/dl in creatinine, a 1.5-fold increase in basal creatinine, or a urine output of less than 0.5 ml/kg/hour in the last 6 hours makes the diagnosis of AKI.[1-4] Oliguria and creatinine values above 3 mg/dL at the time of diagnosis have been reported as poor prognostic indicators.[9] Mortality is high in elderly patients with multiorgan failure and accompanying sepsis. It is known that mortality is over 50% in patients who are followed in the intensive care unit and need mechanical ventilation.[3] Rabbani *et al*.[19] examined 898 patients diagnosed with AKI between 1991 and 2000 and reported that 551 (61%) patients were male and the mean patient age was 53 ± 17.6 (15-91). Wang *et al*.[20] examined 209 patients who were treated with the diagnosis of AKI in Beijing University Hospital between 1994-2003 and reported that the patient's age peaked in two periods (34-45 and 60-80 years). Selcuk *et al*.[22] examined 339 patients with AKI and found two or more etiological factors causing AKI in 46 (13.5%) of the patients. Prerenal and renal causes together in 26 (56%) of these patients, prerenal, renal and postrenal causes together in 12 patients (26%), renal and postrenal causes together in 4 (9%) patients, and prerenal and postrenal causes in 4 (9%) patients. Postrenal causes were identified together. Diarrhea and vomiting are the most common prerenal causes, gentamicin is the most common renal cause and prostatic hypertrophy is the most common postrenal cause. It was determined that 32 (70%) of the patients with more than one etiological factor were oliguric, 8 patients (17%) were anuric, and 6 (13%) were nonoli

Table 4. Length of stay of the patients according to the etiology of AKI

Diagnosis		N	Minimum	Maximum	Mean	Std. Deviation
Prerenal	Length of stay	189	2	53	8.29	6.088
Renal		129	2	51	10.13	7.394
Postrenal		36	2	37	11.53	6.926

Table 5. Renal replacement therapy (hemodialysis) status of the patients

Dialysis	n (%)
Yes	84 (23.7)
No	270 (76.3)
Total	354 (100)

guric. It was stated that 19 (41%) patients were given medical therapy alone, and 27 (59%) patients were given dialysis together with medical treatment. It was reported that 5 (10.8%) patients died. El- Reshaid *et al*.[17] reported the most common causes of AKI etiology as drugs, sepsis and hypovolemia. In our study, of 354 patients followed up with AKI, 177 (50%) were male and 177 (50%) were female (Table 2). The mean age of the patients was 67.24 ± 17.10 (18-104) years. Considering the age distribution according to the etiology of AKI, the mean age of the prerenal group was 70.83 ± 15.47 (18-104), the mean age of the renal group was 61.74 ± 18.46 (19-89), and the mean age of the postrenal group was 68.11 ± 15 years (33-89) years (Table 2). There is a statistically significant difference in age among patients according to the cause of renal failure. The difference is seen between patients who came to the hospital for renal (61.74 ± 18.46) and prerenal (70.83 ± 15.47) reasons. ($p < 0.001$). Considering the clinics in which the patients were admitted in our study, 150 (42.37%) were hospitalized in internal medicine and 204 (57.63%) were hospitalized in nephrology (Table 1). Considering the etiology of AKI, 189 (53.39%) patients were in the prerenal group, 129 (36.44%) were in the renal group, and 36 (10.17%) were in the postrenal group (Table 3). When the causes of AKI are examined according to etiology; Out of 354 causes of renal AKI, 120 (33.9%) of AKI's were due to dehydration (hypovolemia), 55 (15.5%) were due to urinary tract infection, 48 (13.5%) were due to gastroenteritis, and 10 (2.8 %) was due to benign prostatic hyperplasia (BPH) (Table 6). Considering the causes of AKI due to toxic nephropathy, 16 patients were followed up as AKI due to NSAID use, 7 patients as AKI due to glomerulonephritis, 9 patients as AKI due to contrast nephropathy, 9 patients as AKI due to multiple myeloma, and 8 patients as AKI due to rhabdomyolysis (Table 6). Considering the causes of postrenal renal failure, there were BPH in 10 patients, mass compression due to malignancy in 11 patients, prostate ca in 2 patients, bladder ca in 2 patients, kidney stone disease in 5 patients, and idiopathic hydronephrosis in one patient. Hemodialysis is not routinely applied in AKI, but is performed in the presence of emergency dialysis indications such as uremic encephalopathy, pericarditis, oliguria-anuria. Selcuk *et al*.[15, 22] examined a total of 339 patients with AKI and reported that 59% of the patients needed dialysis. Zhang *et al*.[23] reported that 39 (37.5%) of the 104 patients they followed up with the diagnosis of AKI required dialysis. Mahajan *et al*.[24] found the

Table 6 Table of Causes of AKI

Causes of AKI	N	%
Hypovolemia	120	33.9
Uriner Tract Infection	55	15.5
Gastroenteritis	48	13.6
Use of NSAİD	16	4.5
Acute tubuler necrosis	13	3.7
Contrast Nefropaty	11	3.1
Malignancy	11	3.1
BPH	10	2.8
Multiple Myeloma	9	2.6
Rhabdomyolysis	8	2.3
Upper GI Bleeding	8	2.3
Glomerulonephritis	7	2.0
Kidney Stone	5	1.7
Others	33	9.3
Total	**354**	**100**

rate of need for renal replacement therapy (RRT) to be 33.5%. In the study of Uyanik *et al*.[25] reported that 74 (29%) of 256 AKI patients needed hemodialysis. In our study, the rate of patients in need of dialysis was found to be 23.7% with 84 patients. It was remarkable that the rate of patients requiring dialysis was similar to other studies. The dialysis indications of our patients were anuria, hypervolemia, uremic encephalopathy, uremic hiccups, preoperative dialysis in terms of uremic bleeding, tumor lysis syndrome and hyperuricemia. While 33 (17.5%) of the prerenal patients were taken to hemodialysis, 37 (28.7%) of the renal AKI's and 14 (38.9%) of the postrenal AKI's were taken to hemodialysis (Table 5).

CONCLUSION

As a result, although the etiology of AKI includes a wide variety of factors that was grouped according to prerenal, renal and postrenal causes as main groups and both the etiologies of patients hospitalized with AKI and the symptoms of AKI in our hospital, internal medicine and nephrology clinics, show a great similarity in the literature. Although AKI patients receive more effective treatment with the widespread use of dialysis today. It is still an important cause of morbidity and mortality in hospitalized patients.[26] Likewise, the rates of patients undergoing hemodialysis or peritoneal dialysis are similar. This shows that the patients hospitalized in the internal medicine and nephrology clinic of our hospital are correctly diagnosed and treated appropriately.

Authors' Contribution

Study Conception: MB,; Study Design: MB,; Supervision: FB,; Materials: MB,; Data Collection and/or Processing: FB,; Statistical Analysis and/or Data Interpretation: FB,; Literature Review: MB,; Manuscript Preparation: MB and Critical Review: FB.

REFERENCES

1. Lameire N, Van Biesen W, Vanholder R. Acute renal failure. Lancet 365; 2005:417-430.
2. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P; Acute Dialysis Quality Initiative workgroup. Acute renal failure—definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. Crit Care 2004; 8:204-12.
3. Kellum JA, Bellomo R, Ronco C. Classification of acute kidney injury using RIFLE: What's the purpose? Crit Care Med 2007; 35:1983-4.
4. Akcan-Arikan A, Zappitelli M, Loftis LL, Washburn KK, Jefferson LS, Goldstein SL. Modified RIFLE criteria in critically ill children with acute kidney injury. Kidney Int 2007; 71:1028-35.
5. Hoste EA, Clermont G, Kersten A, Venkataraman R, Angus DC, De Bacquer D, Kellum JA. RIFLE criteria for acute kidney injury are associated with hospital mortality in critically ill aptients: A cohort analysis. Crit Care 2006; 10:R73
6. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, Levin A. Acute Kidney Injury Network Acute Kidney Injury Network.: report of an initiative to improve outcomes in acute kidney injury. Crit Care 2007; 11:R31
7. Lopes JA, Fernandes P, Jorge S, Gonçalves S, Alvarez A, Costa e Silva Z, França C, Prata MM. Acute kidney injury in intensive care unit patients: a comparison between the RIFLE and the Acute Kidney Injury Network classifications. Crit Care 2008; 12(4): R110
8. Mehta RL, Pascual MT, Soroko S, Savage BR, Himmelfarb J, Ikizler TA, Paganini EP, Chertow GM. Spectrum of acute renal failure in the intensive care unit: the PICARD experience. Kidney Int. 2004; 66:1613-21
9. Lamiere N, Biesen WV, Vanholder R: Acute renal failure. Lancet 2005; 365:417- 30.
10. Gill N, Nally Jr JV, Fatica RA. Renal failure secondary to acute tubuler necrosis: epidemiology, diagnosis, and management. Chest 2005; 128:2847-63.
11. Ympa YP, Sakr Y, Reinhart K, Vincent JL. Has mortality from acute renal failure decreased? Asystematic review of the literature. Am J Med 2005; 118:827-32.
12. Liu KD, Chertow GM. Acute Renal Failure In: Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, Loscalzo J (eds). Harrıson's Principles of Internal Medicine.. USA. Mc Graw Hill Medical 2008:1752-61.
13. Jafferson JA, Thurman JM, Schrier RW. Pathophysiology and etiology of acute kidney injury. In: Floege J, Jonhson RJ, Feehally J (eds). Comprehensive Clinical Nephrology.. St. Louis, Misouri, USA. Elsevier 2010: 797-813
14. Singri N, Ahja SN, Levin ML. Acute renal failure. JAMA 2003; 289:747-51.
15. Selcuk NY, Odabaş AR, Cetinkaya R ,Tonbul HZ, San A. Frequency and outcome of patients with acute renal failure have more causes than one in etiology. Ren Fail 2000; 22:459-64.
16. Macedo E, Bouchard J, Mehta RL. Prevention and nondialytic management of acute kidney injury. In: Floege J, Jonhson RJ, Feehally J (eds). Comprehensive Clinical Nephrology.. St. Louis, Misouri, USA. Elsevier 2010: 830-43.
17. El-Reshaid K, Kapoor M, Johny KV, Sugathan TN. Acute renal failure in Kuwait- aprospective study. J Trop Med Hyg. 1993; 96:323-9.
18. Kohli HS, Bhaskaran MC, Muthukumar T, Thennarasu K, Sud K, Jha V, Gupta KL,Sakhuja V. Treatment-related acute renal failure in the elderly: a hospital-based prospective study. Nephrol Dial Transplant. 2000 ;15:212-7.
19. Rabbani MA, Habib HB, Siddiqui BK, Tahir MH, Ahmad B, Murtaza G, Maria Q,Ahmad A. Etiology of acute renal failure in a tertiary center. Saudi J Kidney DisTranspl. 2008 ;19:1009-14.
20. Wang Y, Cui Z, Fan M. Retrospective analysis on Chinese patients diagnosed with acute renal failure hospitalized during the last decade (1994-2003). Am J Nephrol. 2005 ;25:514-9.

21. Biesenbach G, Janko O, Schmekal B. Etiology and prognosis of "internal medicine" acute renal failure in 1981-1990 and 1991-2000-an analysis of 510 cases in a single centerWien Med Wochenschr. 2003; 15
22. Selçuk NY, Odabas AR, Cetinkaya R, Tonbul HZ, San A. Frequency and outcome of patients with acute renal failure have more causes than one in etiology. Ren Fail. 2000; 22:459-64.
23. Zhang L, Wang M, Wang H. Acute renal failure in chronic kidney disease-clinical and pathological analysis of 104 cases. Clin Nephrol. 2005; 63:346-50.
24. Mahajan S, Tiwari S, Bhowmik D, Agarwal SK, Tiwari SC, Dash SC. Factors affecting the outcome of acute renal failure among the elderly population in India: a hospital based study. Int Urol Nephrol. 2006; 38:391-6.
25. Uyanık A. Akut Böbrek Yetmezliğinde Prognoza Etki Eden Faktörlerin Araştırılması. Uzmanlık Tezi. Atatürk Üniversitesi Tıp Fakültesi, Ġç Hastalıkları Anabilim Dalı, Nefroloji Bilim Dalı, 2010.

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Relationship between platelet parameters and disease severity and coagulpathy in COVID 19

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ABSTRACT

Objectives: Coagulopathy plays an important role in the clinical course of Covid-19 disease. The aim of our study is to examine the factors affecting the severity of this disease and to examine whether there is a relationship between platelet parameters and disease severity and coagulopathy markers.

Methods: The study was planned single-center, retrospective, and cross-sectional. 189 patients diagnosed with Covid-19 were admitted to the Internal Medicine Department. Patients were divided into 3 clinical categories according to the severity of the disease. The relationship between mean platelet volume and other platelet parameters, and disease severity and coagulopathy parameters were statistically analyzed.

Results: The study included 189 patients.182 of whom were discharged and 7 of whom died. The average age of the patients was 54.13 ± 14.21. D-Dimer levels were compared between the groups and were found to be significantly higher in cases of severe pneumonia. The group with severe pneumonia group had a higher PDW level than other groups. MPV was detected over 10 fl in the severe pneumonia group, but no statistically significant difference was found with the other groups. PT and INR levels are higher in patients with upper respiratory tract infection (URTI) compared to patients with mild to moderate pneumonia. APTT levels were found to be higher in patients with URTI than in patients with severe pneumonia.

Conclusion: In our study, PDW height and MPV height were determined from the findings showing platelet activation in patients with severe pneumonia. If an increase in these parameters is detected in patients diagnosed with the Covid 19 disease, close follow-up should be performed in terms of the development of complications.
Keywords: Coronavirus, Covid-19, platelet parameters, prognostic markers.

The Coronavirus disease (Covid-19) was first detected in Wuhan, China in December 2019. The Covid-19 disease is a disease in which the new type of beta coronavirus (SARS-CoV2) from the coronavirus family is the causative pathogen. İt can cause respiratory tract infection, and can develop in acute respiratory distress syndrome (ARDS) in severe cases.[1] This disease, which has spread around the world in a short period of time, was declared a pandemic by the World Health Organization on March 11, 2020.[2] Asymptomatic, mild viral infection, pneumonia and ARDS are observed in the clinic. Cases that develop Pneumonia are divided into two groups: mild-moderate pneumonia and severe pneumonia.[3] As the pandemic process progresseds, it has been determined that the disease is not limited to the respiratory tract, but it

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affects other systems, and various complications may develop. SARS-CoV2 enters the cell by binding to the angiotensin-converting enzyme 2(ACE2) receptor. These receptors are known to exist in many tissues in the body(alveoli, vascular endothelium, cardiac myocytes, endocrine cells, etc.).[4] In clinical studies, Covid-19 has been shown to display a predisposition to thrombosis and thromboembolic complications during the course of the disease.[5] Especially in severe cases, findings such as thrombocytopenia, increased fibrin destruction products, lactate dehydrogenase height, fibrinogen height and prothrombin time prolongation were found.[6]

Platelets are the cells responsible for primary hemostasis and thrombosis in the peripheral circulation. They also contain granules with many immune receptors on the cell surface and various immune mediators in the cytoplasm. For this reason, it is believed that platelets are part of the immune system and have a regulatory and activating role in the immune response. [7] It is likely that the immune response caused by uncontrolled platelet activation can cause uncontrolled thrombosis and other complications(microvascular angiopathy, embolism, disseminated intravascular coagulation). Mean platelet volume(MPV) can increase due to increased platelet production, and MPV high platelets are more reactive.[8] The Platelet distribution rate(PDW) is a quantitative indicator of platelet size and volume and increases in the presence of platelet anisocytosis.[9] Plateletcrit (PCT) refers to platelet percentage and platelet large cell ratio (P-LCR) refers to the ratio of circulating large-sized platelets to other platelets.

In this study, we aimed to investigate whether there is a relationship between platelet parameters and coagulopathy, differences in prognostic factors in Covid-19 disease and differences in development laboratory levels according to clinical categories.

METHODS

PatientReception

This cross-sectional study included 189 patients between the ages of 26 and 87 who were hospitalized with the diagnosis of Covid-19 between the periods of April 2020 June 2020, a single-center. Covid-19 was diagnosed by polymerase chain reaction (PCR) test (Rotor-Gene Q, Qiagen, Hilden, Germany).

The fallowing groups were excluded from this study; under the age of eighteen, patients whom could not use drugs that affect platelet function, patients with hematologic and oncologic malignancies, patients with immune thrombocytopenia, patients with the diagnosis of coagulopathy, severe vitamin B12 deficiency, bone marrow and other related pathologies(essential thrombocytosis, myelodysplastic syndrome, aplastic anemia, etc.), patients with other diseases of platelet number and function that are affected bye use of drugs; patients with the presence of liver cirrhosis, splenomegaly, renal disease, collagen, connective tissue disorders, immunosuppressive, rheumatologic diseases and lastly patients with immunomodulatory.

This study was evaluated and accepted by the Ethics Committee of the Faculty of Medicine of Kütahya University of Health Sciences (Approval number is 2020/13-19. Date: 19.08.2020).

Data Collection

Demographic data (age, gender), comorbidities (chronic obstructive pulmonary disease, diabetes mellitus, hypertension, cardiovascular disease), clinical findings and hospitalization laboratory levels of the patients hospitalized with the diagnosis of Covid-19 were recorded through the system. Among the hemogram parameters white blood cell count (WBC), lymphocyte count(LYM), hemoglobin(Hgb), red blood cell count(RBC), erythrocyte distribution width (RDW), mean erythrocyte volume (MCV), platelet count (PLT) percentage of platelets (PCT, %), mean platelet volume (MPV, fl), platelet distribution ratio (PDW%) and platelet-large cell ratio (P-LCR%) were recorded.

Biochemical parameters urea, creatinine,aspartate transaminase (AST), alanine transaminase (ALT), lactate dehydrogenase (LDH) and D-Dimer levels were noted. Fibrinogen levels, prothrombin time (PT), INR and activated partial thromboplastin time (aPTT) were recorded as markers of coagulopathy.

Statistical Analysis

SPSS (Statistical Package for Social Science) version 22 program was used for the analysis of the data. The compliance of continuous variables to normal distribution was examined by Kolmogorov-Smirnov and Shapiro-Wilk tests. Normally distributed data was expressed as mean ± standard deviation, non-normally distributed data was expressed as median and interquartile range (25-75 percent), and categorical variables as percentages. Differences between independent groups were compared using Student's t test for normally distributed data and

Mann-Whitney U test for data not showing normal distribution. Categorical parameters were analyzed using the Chi-Square test. In correlation analysis, Pearson correlation test was used for variables with normal distribution, and Spearman correlation test was used for variables with abnormal distribution. *P* value of < 0.05 was considered statistically significant for all tests.

RESULTS

A total of 189 patients, 96 females and 93 males, participated in the study. 7 of the 19 patients with Covid-19 who were followed-up with inpatient treatment died. Sociodemographic characteristics and chronic diseases of our patients taken into the study are shown in Table 1. Mean age of the patients was 54.13 ± 14.21. The average day of hospitalization was 10.45 ± 5.99. Smoking rates, DM and HT incidence and mortality rates were significantly higher in patients with severe pneumonia than in other groups ($p < 0.005$).

Evaluation of laboratory parameters in clinical categories is shown in Table 2. Glucose levels in patients with upper respiratory tract infection (URTI) were lower than in patients with mild to moderate pneumonia and severe pneumonia ($p < 0.001$). Urea levels in patients with severe pneumonia were higher than in patients with URTI and mild to moderate pneumonia ($p < 0.05$). AST levels were higher in patients with severe pneumonia and in patients with mild to moderate pneumonia ($p < 0.001$). In patients with severe pneumonia, the PDW level is higher than in patients with URTI and mild to moderate pneumonia ($p < 0.05$). MPV was detected over 10 fl in the severe pneumonia group, but no statistically significant difference was found with the other groups ($p > 0.05$). PT (p: 0.024) and INR (p: 0.003) levels were higher in patients with URTI than patients with mild to moderate pneumonia. aPTT level was higher in patients with URTI than in patients with severe pneumonia (p: 0.033).

In severe pneumonia, the CRP level increases until the 3rd day, and a decrease began after the 3rd day. The CRP level of those with URTI decreased after the first day.CRP levels increased for up to 5 days in patients with mild to moderate pneumonia and. it decreased after the 5th day (Figures 1 and 2). Although there was a significant relationship between the groups in

Table 1. Sociodemographic characteristics and chronic diseases of the patients*

		URTI		Mild-Moderate Pneumonia		Severe Pneumonia		P
		n	%	n	%	n	%	
Gender	Male	19	(51.35)	49	(45.79)	25	(55.56)	0.524
	Female	18	(48.65)	58	(54.21)	20	(44.44)	
Cigarette	No	26	(70.27)	56	(52.34)	16	(35.56)	**0.038**
	Yes	9	(24.32)	37	(34.58)	22	(48.89)	
	Former	2	(5.41)	14	(13.08)	7	(15.56)	
DM	No	31	(83.78)	68	(63.55)	12	(26.67)	**< 0.001**
	Yes	6	(16.22)	39	(36.45)	33	(73.33)	
HT	No	29	(78.38)	73	(68.22)	23	(51.11)	**0.027**
	Yes	8	(21.62)	34	(31.78)	22	(48.89)	
HL	No	35	(94.59)	90	(84.11)	36	(80.00)	0.161
	Yes	2	(5.41)	17	(15.89)	9	(20.00)	
COPD	No	32	(86.49)	91	(85.05)	34	(75.56)	0.300
	Yes	5	(13.51)	16	(14.95)	11	(24.44)	
Chronic Heart Disease	No	34	(91.89)	99	(92.52)	42	(93.33)	0.969
	Yes	3	(8.11)	8	(7.48)	3	(6.67)	
Result	Discharge	37	(100.00)	107	(100.00)	38	(84.44)	**< 0.001**
	Exitus	0	(.00)	0	(.00)	7	(15.56)	

*Chi-Square Test

Table 2. Comparison of Laboratory Parameters in Clinical Groups*

	URTI			Mild-Moderate Pneumonia			Severe Pneumonia			*P*
	Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	
Glucose	114.30	± 36.68	100.00	135.58	± 54.66	119.00	154.36	± 71.01	138.00	**< 0.001**
Urea	35.55	± 28.03	26.00	34.50	± 23.36	31.00	43.91	± 29.98	36.00	**0.008**
Creatinine	1.12	± 1.31	.86	1.05	± .89	.91	1.16	± .88	.99	**0.059**
AST	24.81	± 18.91	22.00	29.18	± 17.94	24.00	36.31	± 16.73	34.00	**< 0.001**
ALT	23.08	± 19.13	20.00	24.34	± 18.46	18.00	26.71	± 14.19	23.00	0.235
WBC	5.61	± 2.08	5.18	5.29	± 1.94	4.76	6.03	± 2.66	5.35	0.242
Hgb	13.72	± 2.13	14.00	13.11	± 1.62	13.20	12.90	± 1.77	12.80	0.073
RBC	4.70	± .55	4.69	4.59	± .53	4.60	4.43	± .55	4.33	0.063
PLT	208.97	± 59.00	198.00	205.79	± 61.60	198.00	193.36	± 78.18	173.00	0.221
MPV	9.82	± 1.25	9.60	9.75	± 1.14	9.60	10.02	± 1.21	10.30	0.313
PDW	16.06	± .35	16.10	16.07	± .46	16.10	16.28	± .39	16.30	**0.013**
PCT	.20	± .05	.19	.20	± .06	.19	.19	± .06	.17	0.323
P-LCR	25.66	± 8.46	24.10	25.34	± 7.80	24.60	27.22	± 8.33	28.20	0.303
PT	11.65	± .83	11.50	11.23	± .70	11.20	11.54	± .98	11.40	**0.024**
INR	1.02	± .08	1.00	.97	± .07	1.00	1.01	± .10	1.00	**0.003**
APTT	24.74	± 3.23	24.55	23.42	± 2.23	23.50	23.92	± 4.64	23.00	**0.033**

*Kruskal-Wallis Test

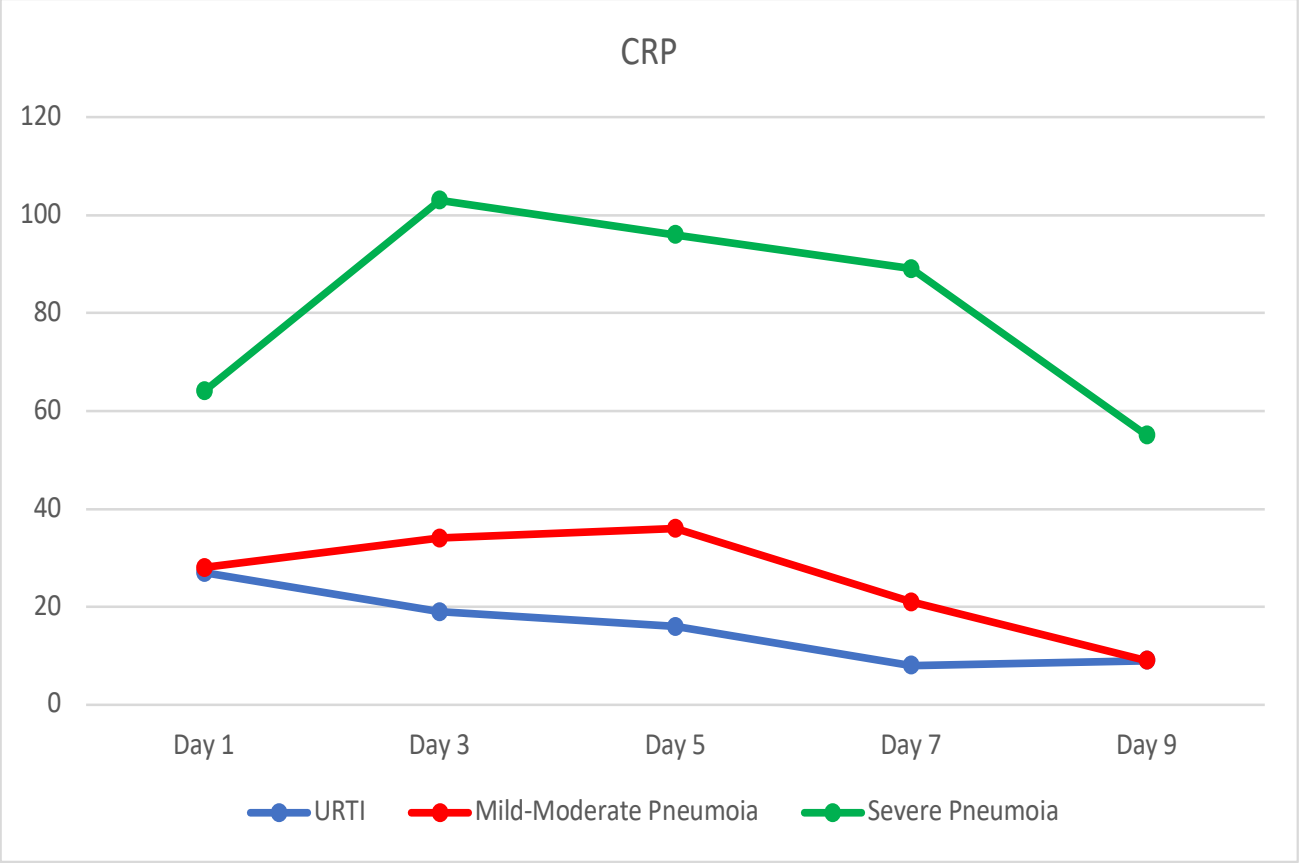

Figure 1. Change of CRP In Follow Up

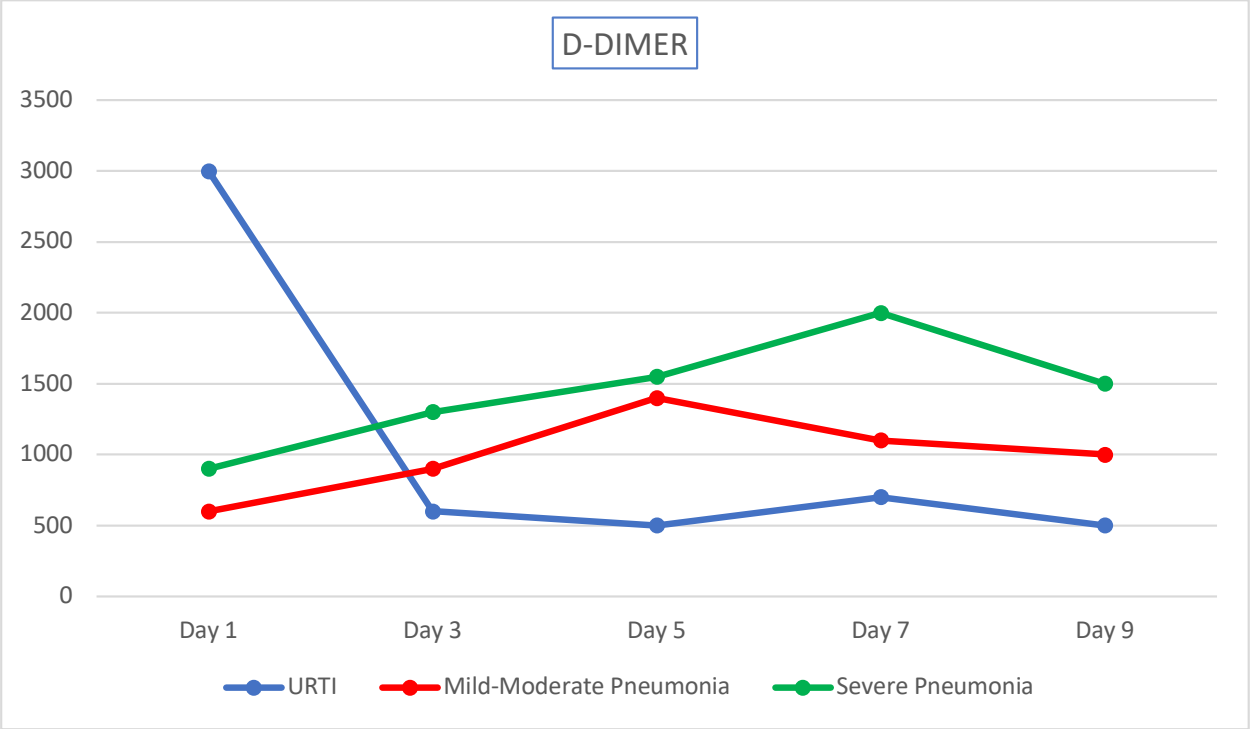

Figure 2. Change of D-DIMER In Follow Up

terms of the change in D-Dimer levels, no significant relationship was found in the post hoc analysis (Table 3). Figure 1 and Figure 2 demonsrate daily changes in CRP and D-Dimerlevels between groups. According to the results of PLT, patients were grouped and the groups and changes in CRP, ferritin, D-Dimer, lymphocyte, lactate, LDH, fibrinogen and troponin levels were examined and it was determined that no significant differences were found (Table 4). When the platelet parameters and coagulopathy markers and coagulation parameters were compared, the same direct correlation was found between aPTT and MPV and P-LCR, and an inverse correlation with PLT was found (Table 5)

DISCUSSION

With the Covid-19 disease, advanced age, smoking and the presence of additional comorbid diseases have been shown to cause an increase in the severity of the disease and a poorer prognosis.

In our study, we aimed to compare the chronic diseases, prognostic factors and platelet parameters in hospitalized patients with Covid-19. As a result of the study, we found that the RDW and MPV values of the platelet parameters in Covid 19 patients were high in cases of severe disease.

Platelet parameters vary according to the activation state of platelets and turnover rate. Young platelets are larger and more active.[8] MPV increase may happen due to cell activation or increase in production.[10] MPV has been shown to be significant as a prognostic marker in cardiovascular diseases and atherosclerosis. Chu *et al*. demonsrated in their study that MPV could be used as a cardiovascular disease risk marker.[11] In the study conducted by Zhang Y *et al*, it was found that in critical patients in intensive care, the RDW level of platelet parameters may again increase depending on the activation state (number of PLT, MPV, PCT, PDW). They found that there are independent risk factors for mortality.[12] The result of the study conducted by Zhang *et al*, revealed that PLT indices are an important marker in evaluating clinical indicators and assessing disease severity. Abnormally low PLT, high MPV levels and high PDW levels were found to be associated with more severe diseases. Again, high PDW has been shown in various studies to be a poor prognostic criterion in sleep apnea syndrome, chronic obstructive pulmonary disease and myocardial infarction.[13, 14] In this study that we conducted with Covid-19 patients, we revealed that PDW, one of the PLT indices, increased in a statistically significant way in severe disease with severe pneumonia ($p < 0.005$). MPV value was found over 10 fl in severe pneumonia and below 10 fl in other groups. However, no statistically significant difference was found with the other groups. No statistically significant relationship

Table 3. Relationship between clinical groups and bad prognostic factors*

	URTI			Mild-Moderate Pneumonia			Severe Pneumonia			*P*
	Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	
CRP (1st day)	15.65	± 45.44	3.77	21.33	± 31.29	11.54	64.08	± 57.79	46.50	**0.034**
CRP (3rd day)	12.84	± 41.96	2.97	27.93	± 37.78	10.82	102.89	± 91.70	72.04	
CRP (5th day)	10.65	± 21.33	2.65	27.47	± 37.13	10.62	93.56	± 76.92	83.34	
CRP (7th day)	9.19	± 21.78	1.00	21.20	± 29.36	9.85	88.86	± 116.23	35.73	
CRP (9th day)	8.00	± 19.93	1.42	8.61	± 14.58	3.48	50.21	± 86.12	8.56	
Ferritin (1st day)	120.83	± 250.21	73.00	134.70	± 177.03	95.00	271.52	± 305.59	188.50	0.133
Ferritin (3rd day)	146.88	± 290.34	72.50	148.76	± 184.81	108.00	343.79	± 362.49	225.50	
Ferritin (5th day)	133.26	± 177.86	67.00	163.91	± 189.21	110.00	370.77	± 357.46	291.00	
Ferritin (7th day)	161.50	± 144.33	97.00	163.10	± 205.88	114.00	390.10	± 391.35	243.00	
Ferritin (9th day)	103.36	± 90.90	91.50	136.14	± 192.75	91.00	287.64	± 274.62	206.00	
D-Dimer (1st day)	1678.03	± 5849.97	378.00	568.68	± 506.45	458.00	870.47	± 757.53	687.00	**0.008**
D-Dimer (3rd day)	542.50	± 431.65	352.50	904.69	± 1239.74	517.50	1204.00	± 929.95	935.50	
D-Dimer (5th day)	620.53	± 1051.49	390.50	1095.99	± 1774.76	546.00	1471.95	± 1396.94	769.00	
D-Dimer (7th day)	636.65	± 696.54	402.00	977.05	± 1560.84	507.00	1997.90	± 2797.49	1011.00	
D-Dimer (9th day)	481.21	± 329.82	369.50	875.16	± 1439.28	470.00	1386.27	± 1312.17	848.00	
LYM (1st day)	1.77	± .64	1.70	1.51	± .61	1.43	1.19	± .50	1.13	0.065
LYM (3rd day)	1.96	± .69	1.86	1.56	± .61	1.45	1.16	± .57	1.03	
LYM (5th day)	2.06	± .83	1.85	1.74	± .68	1.67	1.19	± .69	1.05	
LYM (7th day)	2.10	± .63	2.11	1.86	± .78	1.70	1.36	± .73	1.19	
LYM (9th day)	2.21	± .67	2.20	1.94	± .71	1.81	1.72	± 1.19	1.48	
Lactate (1st day)	2.37	± 1.13	2.20	1.99	± .89	1.80	1.87	± .77	1.70	0.476
Lactate (3rd day)	1.59	± .65	1.60	1.92	± .70	1.90	1.98	± 1.04	1.60	
Lactate (5th day)	1.93	± .66	2.00	2.08	± .73	2.10	2.44	± 1.00	2.10	
Lactate (7th day)	2.11	± .52	1.90	2.31	± 1.56	2.00	2.26	± .87	2.00	
Lactate (9th day)	2.09	± .73	1.95	2.43	± .83	2.30	2.38	± 1.40	2.10	
LDH (1st day)	224.40	± 84.28	198.00	260.02	± 96.04	236.00	300.87	± 106.80	290.00	0.747
LDH (3rd day)	235.27	± 138.60	178.50	256.45	± 77.77	241.00	322.49	± 114.56	314.00	
LDH (5th day)	240.78	± 110.05	215.00	264.99	± 84.29	241.00	354.98	± 104.15	356.50	
LDH (7th day)	269.00	± 118.69	233.00	293.21	± 104.22	263.50	366.33	± 139.95	326.00	
LDH (9th day)	233.52	± 63.52	225.00	273.77	± 187.27	236.00	303.83	± 136.52	273.50	
Fibrinogen (1st day)	356.29	± 113.11	334.50	425.73	± 110.60	414.50	516.02	± 110.06	514.00	0.797
Fibrinogen (3rd day)	383.78	± 118.93	362.50	445.84	± 113.45	449.20	540.40	± 155.74	510.40	
Fibrinogen (5th day)	379.15	± 142.68	316.30	442.95	± 116.53	434.10	550.17	± 123.19	568.10	
Fibrinogen (7th day)	398.55	± 164.11	426.00	431.89	± 123.90	412.00	520.28	± 155.09	537.00	
Fibrinogen (9th day)	339.09	± 100.45	333.50	368.47	± 123.43	341.00	471.47	± 165.23	439.00	
TROP (1st day)	4.78	± 6.33	3.00	4.98	± 7.46	3.20	13.26	± 23.35	5.70	0.706
TROP (3rd day)	5.24	± 6.12	3.30	5.45	± 8.24	3.20	12.86	± 21.81	4.70	
TROP (5th day)	3.85	± 3.75	2.55	4.86	± 6.76	3.20	66.58	± 315.64	4.70	
TROP (7th day)	5.52	± 4.95	3.90	825.12	± 6401.14	3.10	70.22	± 320.90	3.60	
TROP (9th day)	3.88	± 4.65	2.30	429.02	± 3425.20	2.90	10.86	± 17.57	3.40	

*Analysis Of Repetitive Measurements

was found between other platelet parameters (PCT, P-LCR) and disease severity.

Uncontrolled activation of thrombocytes may play a role in the pathogenesis of coagulopathy and thromboembolic complications in Covid-19. These findings showing thrombocyte activation in patients with severe pneumonia (PDW elevation, MPV above 10 fl) may have developed secondary to severe inflammationand may also have caused the development of severe pneumonia as the platelet activation exacerbates the inflammation. When the relationship between platelet parameters and coagulation tests and coagulopathy markers was examined, a positive significant relationship was found between aPTT and MPV and P-LCR, and a negative relationship was found with PLT.

Table 4. Relationship between PLT levels and bad prognostic factors*

		PLT Group												
		< 100			100-149			150-199			> 200			*P*
		Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	Mean	Sd	Median	
CRP	1st day	24.84	± 32.97	6.52	27.05	± 35.30	16.48	28.92	± 51.23	7.60	32.97	± 46.04	12.95	0.485
	3rd day	28.58	± 37.81	10.39	45.79	± 59.91	16.34	49.88	± 72.31	9.61	40.28	± 66.25	13.66	
	5th day	60.56	± 77.99	60.56	49.82	± 59.12	20.28	47.65	± 66.97	9.64	32.97	± 48.74	12.57	
	7th day	37.39	± 47.72	37.39	41.45	± 65.00	12.15	57.97	± 110.63	14.17	28.57	± 49.25	8.36	
	9th day	6.28	± 5.88	6.28	27.11	± 51.76	3.48	24.22	± 63.56	2.72	15.90	± 42.65	5.11	
Ferritin	1st day	315.33	± 316.50	222.00	195.68	± 322.67	98.50	187.89	± 277.64	100.00	130.92	± 136.10	97.50	0.390
	3rd day	286.33	± 286.31	178.00	242.00	± 370.45	99.00	276.07	± 345.23	128.00	136.74	± 136.99	104.50	
	5th day	571.50	± 727.61	571.50	255.34	± 295.30	170.50	272.43	± 334.34	152.00	154.99	± 144.60	110.00	
	7th day	540.00	± 697.21	540.00	264.34	± 353.33	148.00	270.59	± 333.15	170.00	176.09	± 174.00	114.50	
	9th day	500.50	± 651.25	500.50	160.11	± 156.41	118.00	216.77	± 280.83	115.00	143.95	± 165.83	93.00	
D-Dimer	1st day	1092.67	± 890.65	660.00	1485.51	± 5847.01	454.00	750.21	± 1316.51	448.10	679.48	± 581.66	521.00	0.228
	3rd day	1510.33	± 1907.68	430.00	756.39	± 571.08	607.00	783.04	± 761.65	528.00	1061.30	± 1355.81	561.00	
	5th day	1156.00	± 551.54	1156.00	909.72	± 678.10	692.00	989.98	± 1319.65	499.00	1264.28	± 1972.89	540.00	
	7th day	1560.00	± 1343.50	1560.00	926.27	± 1006.15	629.50	1689.47	± 3090.07	658.50	1120.28	± 1513.99	574.00	
	9th day	1380.50	± 1137.73	1380.50	811.48	± 859.24	554.00	870.77	± 1087.74	500.00	1066.23	± 1601.52	553.00	
LYM	1st day	1.20	± .59	.94	1.36	± .65	1.11	1.49	± .57	1.41	1.54	± .65	1.52	0.504
	3rd day	1.20	± .59	1.43	1.34	± .64	1.31	1.46	± .64	1.36	1.69	± .67	1.61	
	5th day	.99	± .30	.91	1.36	± .67	1.30	1.59	± .73	1.50	1.85	± .79	1.72	
	7th day	.82	± .35	.82	1.55	± .79	1.34	1.68	± .68	1.58	1.91	± .82	1.81	
	9th day	1.17	± .36	1.17	1.59	± .71	1.42	1.85	± .60	1.67	2.15	± 1.06	1.99	
Lactate	1st day	1.85	± .07	1.85	1.74	± .74	1.60	2.07	± .79	2.10	2.09	± 1.02	1.80	0.820
	3rd day	1.85	± .64	1.85	1.96	± .97	1.80	1.79	± .60	1.80	1.95	± .97	1.80	
	5th day	1.95	± .21	1.95	2.17	± 1.08	1.80	2.12	± .69	2.00	2.26	± .86	2.20	
	7th day	2.30	± .42	2.30	2.08	± .63	1.90	2.33	± 1.18	2.00	2.28	± 1.34	1.90	
	9th day	2.55	± .78	2.55	2.25	± 1.31	2.00	2.41	± 1.45	2.20	2.35	± .79	2.20	
LDH	1st day	262.00	± 122.34	199.00	260.42	± 92.40	239.00	233.39	± 83.05	202.00	285.20	± 108.01	259.00	0.754
	3rd day	276.50	± 173.24	276.50	279.54	± 139.97	244.00	271.00	± 92.26	241.00	269.07	± 98.54	257.00	
	5th day	331.00	± .00	331.00	307.04	± 142.58	262.50	290.67	± 92.53	285.00	277.73	± 96.03	257.50	
	7th day	218.50	± 48.79	218.50	305.11	± 98.59	289.50	353.83	± 162.36	306.50	299.48	± 99.19	278.00	
	9th day	181.50	± 27.58	181.50	279.28	± 105.94	244.00	260.97	± 119.94	233.00	290.89	± 201.34	244.00	
Fibrinogen	1st day	324.90	± 66.37	353.70	419.87	± 95.86	424.00	425.71	± 138.94	381.00	458.25	± 118.86	456.50	0.335
	3rd day	356.65	± 58.90	356.65	458.26	± 114.24	439.25	487.80	± 178.33	458.00	453.70	± 117.99	452.00	
	5th day	361.15	± 14.35	361.15	454.83	± 125.57	439.00	482.07	± 164.11	520.00	459.02	± 122.94	460.00	
	7th day	368.85	± 28.07	368.85	413.52	± 118.46	393.45	498.61	± 178.84	491.90	454.57	± 128.19	456.50	
	9th day	190.25	± 133.29	190.25	374.21	± 118.95	331.60	405.28	± 186.91	366.00	418.24	± 112.94	408.35	
TROP	1st day	4.93	± .71	4.80	8.54	± 14.02	5.10	6.77	± 10.98	3.45	6.52	± 15.09	3.20	0.664
	3rd day	3.50	± .71	3.50	9.00	± 9.39	5.05	10.58	± 21.13	3.95	5.03	± 7.95	3.30	
	5th day	5.50	± 3.96	5.50	7.24	± 7.09	4.90	53.63	± 293.09	3.60	6.49	± 17.95	3.20	
	7th day	3.45	± 3.46	3.45	9.10	± 12.98	5.20	68.99	± 330.17	3.65	987.70	± 7000.37	3.00	
	9th day	3.50	± .42	3.50	4.34	± 4.22	3.15	7.10	± 12.68	2.80	606.22	± 4071.34	2.75	

*Analysis Of Repetitive Measurements

Thrombocytopenia may be an indicator of the poor prognosis in infectious diseases. Development of thrombocytopenia in community-acquired pneumonia is associated with poor clinical outcomes.[15] In Severe Acute Respiratory Syndrome (SARS), thrombocytopenia has been detected at a rate of 50% and it is known to be an important marker of poor prognosis.[16] Thrombocytopenia may develop in Covid-19, as in the SARS epidemic.[17] Liu Y *et al*., in his study found that, Covid-19 patients with thrombocytopenia had 3 times more mortality compared to patients without thrombocytopenia, and the platelet count was shown to be an independent risk factor for mortality.[18] In a meta-analysis, it was shown that severe Covid-19 infection is three times higher in the presence of thrombocytopenia.[19] Ourstudy was conducted in internal medicine clinic and no significant relationship was found between the platelet count and disease severity.Again,the patients were grouped according to the platelet count (< 100 thousand, 100-

Table 5. Relationship between PLT parameters and coagulopathy markers*

		PCT	MPV	PDW	P-LCR	PLT
D-Dimer mean	r	-0.011	-0.035	0.120	-0.036	0.016
	p	0.911	0.714	0.209	0.705	0.869
LDH mean	r	-0.033	0.046	0.115	0.016	-0.048
	p	0.776	0.690	0.321	0.890	0.675
Fibrinogen mean	r	0.095	-0.084	0.098	-0.059	0.158
	p	0.397	0.455	0.386	0.603	0.159
PT	r	-0.080	0.060	0.068	0.082	-0.104
	p	0.280	0.413	0.353	0.268	0.159
APTT	r	-0.076	**0.147**	0.141	**0.163**	**-0.151**
	p	0.306	**0.046**	0.055	**0.027**	**0.041**
INR	r	-0.024	0.056	0.039	0.072	-0.057
	p	0.749	0.450	0.600	0.326	0.442

*Spearman Correlation Test

150 thousand, 150-200 thousand, > 200 thousand) and their relationship with poor prognostic factors was evaluated using repetitive measurement analysis, and no significant difference was found in bad prognostic factor levels according to platelet count.

Covid-associated coagulopathy is related to the severity of the disease, and factors such as increased inflammation, immobility, platelet activation, and endothelial damage are thought to be effective in its pathogenesis.20D-Dimer is a fibrin degradation product and can be detected high in blood due to fibrinolysis.[21] LDH can be detected high due to cell damage (especially lung and endothelial cell damage) and fibrinogen can be detected high due to inflammation in Covid-19. These markers rise in relation to disease severity in the right direction.[22, 23]In a study, D-Dimer levels were found to be higher in Covid-19 patients who died compared to those who survived.[24] In another study, it was observed that the mortality rate was high in those with D-Dimer levels above 1 µg / dl.[25] In light of these studies, it is suggested that D-Dimer level can be used as a marker of poor prognosis in the early period.[26] In our study, the D-Dimer level was found to be high in all patient groups, and it was found to be higher in the group with severe pneumonia in clinical follow-ups compared to the other groups. İn addition, fibrinogen and LDH were found to be high compared to normal, and no significant differences were found between the study groups.

PT-INR, aPTT levels were found to be high in intensive care patients developing disseminated intravascular motility (DIC).[27] In our study, the PT-INR level was found to be significantly higher in the group with URTI compared to the group with mild-moderate pneumonia, and also significantly higher in the group with URTI than the group with severe pneumonia. As the severity of the disease increases, the severity of inflammation increases and consequently the increase in thrombosis susceptibility may explain this finding.

In individuals diagnosed with Covid-19, poor prognostic factors (ferritin, C-reactive protein (CRP), fibrinogen, D-Dimer, lactate dehydrogenase (LDH), lactate and troponin) are used in clinical follow-up to evaluate the severity of the disease and response to treatment. CRP, an acute phase reactant, has been shown to be associated with the severity of the disease. A study found that CRP levels were significantly higher in severe covid-19 patients than in non-severe ones.[28] In another study, CRP level was determined above 41.8 mg/dl in severe patients.[29] In our study, CRP level was significantly higher in the group with severe pneumonia than in other groups. It was also observed that the CRP response to treatment varies according to the disease severity.

Our study has some limitations. The first is that coagulopathy was defined by laboratory findings and radiological scanning was not performed. Second, the intensive care patient group who developed ARDS was not included in the study

CONCLUSION

In our study, high PDW and high MPV were

detected among these findings indicating thrombocyte activation in patients with severe pneumonia. This situation supports the role of uncontrolled activation of platelets in the pathogenesis of coagulopathy and thromboembolic complications in Covid-19. PLT indices can be measured simply and quickly. There may be a relationship between the severity of inflammation and platelet activation in the disease. High detection of these parameters, which are platelet activation markers, may predict the risk of severe disease and coagulopathy, and these patients may need to be followed up more closely.

More comprehensive studies are needed to fully demonstrate the role platelet activation plays in the pathogenesis of Covid-19.

Authors' Contribution

Study Conception: SE, TPK, SAÇ, HHG, MA, AG,; Study Design: SE, TPK, SAÇ, HHG, MA, AG,; Supervision: SE, TPK, SAÇ, HHG, MA, AG,; Materials: SE, TPK, SAÇ, HHG, MA, AG,; Data Collection and/or Processing: SE, TPK, SAÇ, HHG, MA, AG,; Statistical Analysis and/or Data Interpretation: SE, TPK, SAÇ, HHG, MA, AG,; Manuscript Preparation: SE, TPK, SAÇ, HHG, MA, AG

REFERENCES

1. Chan JF, Kok KH, Zhu Z, Chu H, To KK, Yuan S, et al. Genomic characterization of the 2019 novel human-pathogenic coronavirus isolated from a patient with atypical pneumonia after visiting Wuhan. Emerg Microbes Infect 2020;9: 221.36.
2. C. Calisher, D. Carroll, R. Colwell, R.B. Corley, P. Daszak, C. Drosten, L. Enjuanes, J. Farrar, H. Field, J. Golding. Statement in support of the scientists, public health professionals, and medical professionals of China combatting COVID-19, The Lancet, 395 (2020) e42-e43.
3. J. P. Metlay, G. W. Waterer, A. C. Long, et al. Diagnosis and treatment of adults with community-acquired pneumonia: An official clinical practice guideline of the American Thoracic Society and Infectious Disease Society of America, Am. J. Respir Crit Care Med 200(2019): e45–e67.
4. Zhang H, Penninger JM, Li Y, Zhong N, Slutsky AS. Angiotensin-converting enzyme 2(ACE2) as a SARS-CoV-2 receptor: molecular mechanisms and potential therapeutic target. Intensive Care Med 2020;46(4):586-590.
5. Han H, Yang L, Liu R, at al. Prominent changes in blood coagulation of patient with SARS-Cov-2 infection. Clin Chem Lab Med 2020.
6. Guan WJ, Ni ZY, Hu Y, et al. Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med. 2020;382(18):1708-1720.
7. Von Hundelshausen P, Weber C. Platelets as immune cells. Bridging inflammation and cardiovascular disaese. Circ Res 2007;100: 27-40.
8. Bath PM, Butterworth RJ. Platelet size: measurement, physiology and vascular disease. Blood Coagul Fibrinolysis 1996 Mar;7(2):157- 161.
9. Van der Lelie J, Von dem Borne AEG. Platelet volume analysis for differential diagnosis of thrombocytosis. J Clin Pathol 1986;39: 129.
10. Tavil Y, Sen N, Yazici H, et al. Coronary heart disease is associated with mean platelet volume in type 2 diabetic patients. Platelets 2010;21(5):368-372.
11. Chu SG, Becker RC, Berger PB, et al. Mean platelet volume as a predictor of cardiovascular risk: a systematic review and meta-analysis. J ThrombHaemost 2010 Jan;8(1):148-156.
12. Zhang S, Cui Y, et al. Use of Platelet Indices for Determining Illness Severity and Predicting Prognosis in Critically Ill Patients. Chin Med J (Engl). 2015 Aug 5; 128(15): 2012–2018.
13. Steiropoulos P, Papanas N, Nena E, et al. Mean platelet volume and platelet distribution with in patients with chronic obstructive pulmonary disease: The role of comorbidities. Angiology 2013; 64:535 9.
14. Kirbas Ö, Kurmus Ö, Köseoglu C, Duran Karaduman B, Saatçi Yasar A, Alemdar R, et al. Association between admission mean platelet volume and ST segment resolution after thrombolytic therapy for acute myocardial infarction. Anadolu KardiyolDerg 2014; 14:728 32.
15. Brogly N, Devos P, Boussekey N, Georges H, Chiche A, Leroy O. Impact of thrombocytopenia on outcome of patients admitted to ICU for severe community-acquired pneumonia. J Infect 2007; 55:136–140.
16. Wong RS, Wu A, To KF, et al. Hematological manifestations in patients with severe acute respiratory syndrome: retrospective analysis. BMJ 2003; 326:1358–1362.
17. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2020.
18. Liu Y, Sun W, et al. Association between platelet parameters and mortality in coronavirus disease 2019: Retrospective cohort study. Journal Platelets. 2020; 31(4): 490-6.
19. Lippi G, Plebani M, Michael Henry B. Thrombocytopenia is associated with severe coronavirus disease 2019 (COVID-19) infections: A meta-analysis. Clin Chim Acta 2020.
20. Cannegieter SC, Klok FA. COVID-19 associated coagulopathy and thromboembolic disease: Commentary on an interim expert guidance. Res PractThrombHaemost 2020 April 20.
21. Zhang L, Long Y, Xiao H, at al. Use of D -dimer in oral anticoagulation therapy. International Journal of Laboratory Hematology. 2018;40(5):503 –7.
22. Ferrari D, Motta A, Strollo M, Banfi G, Locatelli M. Routine blood tests as a potential diagnostic tool for COVID-19. Clin Chem Lab Med. 2020 Apr 16.
23. Li CX, Wu B, Luo F, Zhang N. Clinical Study and CT Findings of a Familial Cluster of Pneumonia with Coronavirus Disease 2019 (COVID-19). Sichuan Da XueXue Bao Yi Xue Ban. 2020;51(2):155-158.
24. Tang N, Li D, Wang X, Sun Z. Abnormal coagulation parameters are associated with poor prognosis in patients

with novel coronavirus pneumonia. J ThrombHaemost. 2020;18(4):844 –847.
25. Zhang L, Yan X, Fan Q, et al. D -dimer levels on admission to predict in -hospital mortality in patients with Covid -19. J ThrombHaemost. 2020 Apr 19. 18(6): 1324-29.
26. Muhammed Kermali, Raveena Kaur Khalsa, Kiran Pillai, at al. The role of biomarkers in diagnosis of COVID-19 – A systematic review. Life Sciences. 2020.
27. Han H, Yang L, et al. Prominent changes in blood coagulation of patients with Sars-CoV2 infection. Clin Chem Lab Med. 2020. Jun 25;58(7):1116-20.
28. Qin C, Zhou L, Hu Z, et al. Dysregulation of immune response in patients with COVID -19 in Wuhan, China. Clin Infect Dis. 2020 Mar 12; 9.
29. Liu F, Li L, Xu M, et al. Prognostic level of interleukin -6, C-reactive protein, and procalcitonin in patients with COVID-19. J Clin Virol. 2020 Apr 14;127: 104370.

Case Report

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Acute Pancreatitis Following Thiocolchicoside Use: A Case Report

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ABSTRACT

Acute pancreatitis (AP) is an inflammatory disease with high mortality and morbidity, characterized by elevated amylase and lipase, accompanied by typical abdominal pain. In this case, we present a case of acute pancreatitis developed after the use of thiocolchicoside in a 52-year-old patient with a history of cholecystectomy. There was no history of intrahepatic and choledochal stones or enlargement, hyperlipidemia, and alcohol use on magnetic resonance cholangiopancreatography (MRCP). After excluding the possible cause, a diagnosis of AP caused by thiocolchicoside, a rare side effect of this drug, was made. There are case reports about the development of AP secondary to drugs in the literature, but the development of AP after thiocolchicoside is extremely rare. It is important to determine the etiology in AP cases. It is aimed to raise awareness on this issue with this case, which shows that thiocolchicoside, which is frequently prescribed in primary and secondary health care institutions, may rarely cause AP.

Keywords: Acute pancreatitis, thiocolchicoside, cholecystectomy

Acute pancreatitis (AP) is an inflammatory disease with high mortality and morbidity, characterized by elevated amylase and lipase level, accompanied by typical abdominal pain. [1]

The incidence of AP ranges from 5 to 80 per 100,000 year. While the most common causes of AP are gallstones and alcohol, one of the rare causes is drugs.[2] In this case, we present a case of acute pancreatitis following the use of thiocolchicoside in a 52-year-old patient with a history of cholecystectomy.

CASE REPORT

A 52-year-old female patient was admitted to the emergency department with abdominal pain for 12 hours. In her history, she was admitted to the hospital 3 days ago with the complaint of low back pain and was prescribed thiocolchicoside 4mg intramuscular (IM) twice daily (BID) and etofenemate 1000 mg IM (1x1) with the diagnosis of lumbalgia. She used these drugs for two days and on the morning of the third day, she had severe abdominal pain radiating to the back accompanied by nausea and vomiting. She had a history of cholecystectomy three years ago. She was on metoprolol 50 mg tablet 1x1 with a diagnosis of arrhythmia and metformin 500 mg tab BID with a diagnosis of insulin resistance for three years. The patient had no alcohol consumption, no smoking, and no family history of pancreatitis. Physical examinations were such follows; fever: 36.7C, heart rate: 90/min, BP: 110/70 mmHg, saturation: 96%, respiratory rate: 16/min. In her abdominal examination, there was diffuse tenderness, no defense, and no rebound. Other system examinations were normal. Laboratory tests were follows; WBC:13.3 x103/uL (4.6-10.2 x10^3/uL),

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HCT: 38% (37.7-53.7%), PLT:356 x10^3/uL (142-424 x10^3/uL), AST:13 u/L (11-25 U /L), ALT:14 u/l (7.0-22 U/L), GGT:16 u/L (0-65 U/L), ALP:62 u/L (25-100 U/L), Total bilirubin:0.24 mg/dL (0.0 -1.2 mg/dL), Amylase: 1224 u/L (34-119 u/L) and Lipase: 1602 u/L (70 < u/L) other tests were within normal limits. Her electrocardiogram was in normal sinus rhythm and there was no ST-segment change.

In the whole abdominal ultrasonography: the gall bladder was not observed (operated), there was no pathology in the liver and spleen, and slight expansion of the pancreas is observed. The patient was admitted to the ward with the suspect of acute pancreatitis. The patient was NPO and parenteral hydration and nutritional support were administered. Oral intake was started after 48 hours. A diet low in cholesterol was given. Two days after hospitalization, MRCP was performed. The common bile duct diameter was measured as 6 mm and it was within the normal range. No dilatation was observed in the intrahepatic bile ducts. No obvious stone was observed in the common bile duct tracing. Laboratory results performed in the service were follows: calcium: 8.7 mg/dL (8.4-10.2 mg/dL), Triglyceride: 199 mg/dL (50-200 mg/dL), Total cholesterol: 244 mg/dL (110- 200 mg/dL), HBsAg (-), Anti-HBs (-), Anti-HCV (-), and Anti-HIV (-). Viral serologies (including Mycoplasma IgM, Mumps IgM, and Rubeola IgM) and autoimmune antibodies ANA, ASMA, IgG levels were found to be normal. After excluding hypercalcemia, hyperlipid, absence of stones in MRCP, and other etiological reasons, a diagnosis of AP was made after the use of thiocolchicoside. Blood amylase values returned to normal as 768 U/L, 363 U/L, and 166 U/L on days 2, 3, and 4, respectively. 48 hours after the patient's hospitalization, her general condition improved and her symptoms resolved. When the laboratory values and symptoms returned to normal levels on the 5th day of hospitalization, the patient was discharged with recommendations

DISCUSSION

Acute pancreatitis is an inflammatory condition of the pancreas characterized by nausea, vomiting, typical abdominal pain, and elevated levels of amylase and lipase in the blood.[1] As etiological factors, gallstones and alcohol occur in 80% of the cases in the literature.[3] While alcohol occupies the first place in the etiology of AP in Western societies, biliary causes are the first in Turkey.[4-7] Abdominal trauma, high triglyceride levels, ampulla of vater or pancreatic tumor, drugs, HIV, endoscopic retrograde cholangiopancreatography (ERCP), or surgical procedures can be among other possible causes.[8, 9] In our case, the patient had gallbladder surgery 3 years ago. There were no intrahepatic and common bile duct stones or enlargement in the MRCP, and there was no history of hyperlipidemia and alcohol use. Following exclusion of possible cause AP caused by thiocolchicoside, which is a rare side effect of this drug, was diagnosed. There are case reports about the development of AP secondary to drugs in the literature, but the development of AP after thiocolchicoside is extremely rare. It is important to determine the etiology in AP cases. Although the most common causes are gallstones and alcohol, it is important to know the rare causes and to examine and determine them in the patient's history. With this case, it has been aimed to raise awareness on this issue, which shows that thiocolchicoside, which is frequently prescribed in primary and secondary health care institutions, can cause AP, albeit rarely.

CONCLUSION

Authors' Contribution

Study Conception: İS,; Study Design: İS, SÖ,; Supervision: İS, MO,; Materials: İS, MO,; Data Collection and/or Processing: İS,; Statistical Analysis and/or Data Interpretation: MO,; Literature Review: MO; Manuscript Preparation: JK,; and Critical Review: İS, JK.

REFERENCES

1. Solmaz İ, Alakuş Ö, Ekin N, Araç S, Kalın BS. Akut Pankreatitte Prognoz Belirteci Olarak Prokalsitonin. Fırat Tıp Dergisi/Firat Med J 2021; 26(1): 23-27
2. Pekmezci S. Akut Pankreatitte Yaklaşım ve Tedavi. İ. Ü. Cerrahpasa Tıp Fakültesi Sürekli Tıp Egitimi Etkinlikleri HepatoBiliyer Sistem ve Pankreas Hastalıkları Sempozyum Dizisi No:28; Ocak 2002:239-62.
3. Solmaz İ, Araç S, Ekin N, Kalın BS. Akut pankreatitli olguların klinik ve laboratuar bulgularının prognoz üzerine etkisi: retrospektif değerlendirme. Ahi Evran Med J. 2021;5(2):85-89. DOI: 10.46332/aemj.790888
4. Sargent S. Pathophysiology, diagnosis, and management of acute pancreatitis. Br J Nurs. 2006; 15: 999-1005.
5. Tran DD, Cuesta MA. Evaluation of severity in patients with acute pancreatitis. Am J Gastroenterol 1992;87:604-608.

6. Ertekin C, Kemertaş K, Günay K. Akut Pankreatit Ulusal Travma Dergisi 1995; 1: 14-21.
7. DiMagno MJ, DiMagno EP. New advances in acute pancreatitis. Curr Opin Gastroenterol. 2007;23:494-501.
8. Vissers RJ, Abu-Laban RB. Acute and chronic pancreatitis. In: Tintinalli JE, Kelen GD, Stapczynski JS (eds.), Emergency medicine. A comprehensive study guide. 5th edition, New York: McGraw-Hill, 2000: pp.588-592.
9. Alhajeri A, Erwin S. Acute pancreatitis: value and impact of CT severity index. Abdom Imaging. 2008; 33: 18-20.