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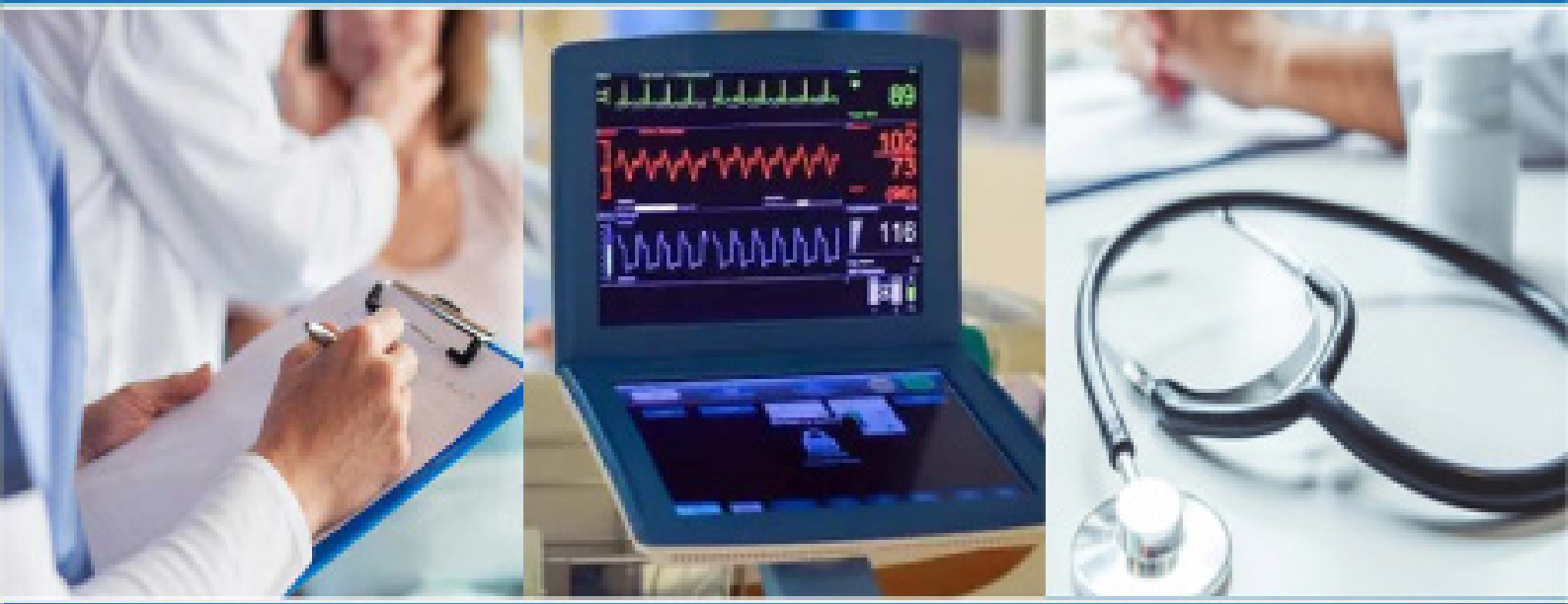

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Original Article

Analysis of the correlation between COVID-19 infection frequency and disease severity and mortality in relation to ABO and RH blood groups

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ABSTRACT

Aims: The etiology of the COVID-19 pandemic and the factors that predispose individuals to the disease remain little comprehended. Research indicates significant variability in outcomes related to blood types and COVID-19. These researches have examined ABO and Rhesus (Rh) blood types as different datasets. Our research is an unprecedented study that investigates the correlation between developing COVID-19 and/or disease severity/death by analyzing ABO and Rh blood groups concurrently.

Methods: This study retrospectively included 461 RT-PCR-diagnosed COVID-19 patients and 46 healthy volunteers aged 18 or older with known blood types from April 2020 to December 2020. All demographic and medical data came from electronic medical records (EMR). Rh and ABO blood types were established via card tests with microplates (forward and reverse grouping). Patients were grouped by clinical outcome and COVID-19 positivity. In SPSS 26, descriptive statistics, one-way ANOVA, Kruskal-Wallis, student's T test, Mann-Whitney U test, and Chi-square test assessed regularly distributed and non-normally distributed characteristics.

Results: The age distribution of the patients (62±13) was comparable to that of the control group (64±14) (p=0.295). No significant differences were seen between the groups regarding sex and blood group distribution (p=0.204 and p=0.087, respectively). Analysis of individuals by blood types revealed no significant differences in the incidence of COVID-19, age, sex, and clinical course (p=0.603, p=0.244, p=0.272, and p=0.810, respectively).

Conclusion: Our investigation demonstrated that, contrary to the current literature, there is no correlation between developing COVID-19 and/or the severity of the disease or mortality across the eight blood groups classified by ABO and Rh combinations. This may signify a realistic consequence or could be linked to genetic profiles. We contend that, contrary to assertions in the literature, there is no link between ABO and Rh blood types and the incidence, severity, or mortality of COVID-19.

Keywords: COVID-19, blood group antigens, SARS-CoV-2, Rh-Hr blood-group system, ABO blood-group system

INTRODUCTION

Following the initial identification of COVID-19 in Wuhan, China, the advent of the novel SARS-CoV-2 coronavirus precipitated a global public health catastrophe characterized by significant morbidity and mortality that swiftly overwhelmed healthcare systems worldwide. Nonetheless, the disease's impact exhibits significant diversity across countries and geographic regions for reasons that remain inadequately comprehended. In addition to variations in economic, sociological, behavioral, and political responses to the pandemic, genetic variables may potentially independently influence outcomes. Consequently, shortly after the onset of the pandemic, a publication from Wuhan, China, indicated an elevated risk of infection for those with blood group A, whereas conversely, individuals with blood group O exhibited a reduced risk.[1] Subsequently, connections with ABO and Rhesus (Rh) blood groups have been documented in numerous papers globally.[2-7] The influence of ABO and Rh blood types on SARS-CoV-2 infection and COVID-19 outcomes, as well as its implications for the pandemic's progression in various global locations and its potential significance for patient care, require more evaluation.

The findings concerning the relationship between ABO and Rh blood groups are inconsistent. Several studies have not established a definitive correlation between blood type and susceptibility to COVID-19, or have reported varying results. This study will examine the relationship between blood groups and COVID-19, drawing on existing literature to elucidate the potential effects of various blood groups on susceptibility to the virus and the progression of the disease. Also, the literature has analyzed COVID-19 in relation to ABO and Rh groups independently. Conversely, our study was conducted

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utilizing both ABO and Rh systems, encompassing 8 blood types. We assert that we will enhance the literature in this context.

METHODS

Study Population

This study retrospectively included 461 COVID-19 patients diagnosed with RT-PCR and 46 healthy participants between April 2020 and December 2020, all of whom were over 18 years old and had known blood types. Healthy people were chosen to match the patients in terms of sex and age distribution. Individuals lacking a documented blood type in their medical records were excluded from the study. There was no individual with COVID-19 vaccine history. The patients were further categorized into subgroups: outpatients, hospitalized individuals, and died patients. All clinical information were obtained from medical records. After obtaining a COVID-19 work permit and IRB confirmation from the Ministry of Health of Turkiye, the study was initiated after receiving approval from the Amasya University Non-interventional Clinical Researches Ethics Committee (Date: 11.06.2020, Decision No: 7/55). The Helsinki Declaration of Human Rights was followed.

Study Design

All demographic and medical data was extracted from electronic medical records (EMR). The Rh and ABO blood types were determined using card tests with microplate method (forward and reverse grouping techniques). Patients were categorized based on their clinical course and COVID-19 positivity. First, individuals were divided as COVID-19 PCR positives and negatives. Then, outpatients, inpatients, and deceased individuals were classified into primary categories. Comparisons were conducted between the control group and the patient groups based on all blood types. The relationship between blood groups and the frequency of disease occurrence and clinical progression was investigated.

Statistics Analysis

The study used SPSS version 26.0 for analyses, assessing parameters with normal distribution using Shapiro-Wilk's test. Descriptive statistics, one-way ANOVA, Kruskal-Wallis, student's T test, Mann-Whitney U test, and Chi-square test were used to compare normally distributed and non-normally distributed parameters. A p-value below 0.05 was considered significant.

RESULTS

The age distribution of the patients (62±13) did not differ from the control group (64±14) (p=0.295). Additionally, no differences were found between the groups in terms of sex and blood group distribution (p=0.204, and p=0.087, respectively). Upon analyzing individuals by blood types, we observed no significant differences in the incidence of COVID-19, age, sex, and clinical course (p=0.603, p=0.244, p=0.272, and p=0.810, respectively). Among all categories, the A Rh positive blood group was the most prevalent, whereas the A Rh negative was the least prevalent. The second most prevalent blood type is O Rh positive (**Table**). No correlation was identified between blood types and the severity or incidence of disease.

DISCUSSION

Blood groups and COVID-19 positivity

Researchers indicated that blood type A is correlated with the greatest likelihood of SARS-CoV-2 infection.[8-10] A preliminary study conducted in Wuhan, China, indicated a correlation between blood type A and COVID-19, highlighting that females with blood type A exhibited increased susceptibility to infection.[8] Subsequent research indicated that people with blood type A exhibited markedly increased odds of contracting SARS-CoV-2 infection in comparison to individuals with non-A blood types.[1,8,9] Numerous studies indicate that individuals with blood type O exhibit markedly reduced probabilities of infection, implying that blood type O may serve as a preventive factor against infections.[11,12] One multivariate analysis of 14,112 COVID-19-positive individuals found that blood types A, AB, and B were more common than O after correcting for race and ethnicity.[13] A study in China found that blood type increases COVID-19 risk in retrospective research. Infection risk was lower for blood type O patients than non-O patients and greater for blood type A patients than all other groups.[6] Although most studies have found that having blood type O protects against COVID-19,[11] researchers still can't agree on which blood types are more vulnerable. Furthermore, several studies have suggested that blood types B and AB are at a high risk, in contrast to those that identify blood type A as the most at-risk group.[12] A study indicated that blood types B and AB were correlated with increased odds of testing positive for SARS-CoV-2 infection, while blood type O was linked to decreased odds of testing positive. Nevertheless, the authors identified no association between blood type A and positive testing rates.[14] According to the findings of our research, we did not discover a correlation between blood types and the probability of getting COVID-19. This is with all due respect to the research that was already conducted. Several distinct conclusions were already being indicated by the literature data in an inconsistent manner. After taking into consideration all of this evidence, we have arrived at the conclusion that there is no correlation between blood types and COVID-19 infections.

Blood Groups and Clinical Outcome

A study indicated that patients with blood type A exhibited a reduced risk of intubation and mortality compared to those with blood type O, while those with blood type AB demonstrated an increased risk of intubation and death. Furthermore, those with blood type B had elevated intubation rates, although experienced reduced mortality in comparison to those with blood type O.[13] In contrast, population-based cohort research indicated that individuals with blood type O have a reduced chance of acquiring severe illnesses or mortality compared to all other blood types.[12] In a study employing Spearman's rank coefficient analysis on COVID-19 patients, researchers discovered that blood type O conferred protection against COVID-19 mortality, while blood type B exhibited a stronger correlation with infection and mortality rates.[14] A multicenter retrospective analysis indicated that individuals with blood type A or AB faced an increased risk of needing mechanical ventilation compared to those with blood type O or B, even after controlling for sex, age, and other variables. Following the adjustments, there were no observed differences in the median duration of ICU stay or the likelihood of ICU discharge or extubation. No correlation was found between

Table. The prevalence and intensity of diseases among persons categorized by blood groups, including numerical and percentage ranges

						Count n	Group n%	Total n%
RT-PCR	Non-COVID-19	Post-treatment course	Death	Blood group	0 Rh (-)	0	0.0%	0.0%
					0 Rh (+)	1	0.2%	12.5%
					A Rh (-)	0	0.0%	0.0%
					A Rh (+)	3	0.6%	37.5%
					B Rh (-)	1	0.2%	12.5%
					B Rh (+)	2	0.4%	25.0%
					AB Rh (-)	0	0.0%	0.0%
					AB Rh (+)	1	0.2%	12.5%
			Discharged	Blood group	0 Rh (-)	0	0.0%	0.0%
					0 Rh (+)	3	0.6%	13.6%
					A Rh (-)	1	0.2%	4.5%
					A Rh (+)	12	2.5%	54.5%
					B Rh (-)	0	0.0%	0.0%
					B Rh (+)	3	0.6%	13.6%
					AB Rh (-)	0	0.0%	0.0%
					AB Rh (+)	3	0.6%	13.6%
			No hospitalization	Blood group	0 Rh (-)	0	0.0%	0.0%
					0 Rh (+)	2	0.4%	15.4%
					A Rh (-)	0	0.0%	0.0%
					A Rh (+)	10	2.1%	76.9%
					B Rh (-)	0	0.0%	0.0%
					B Rh (+)	1	0.2%	7.7%
					AB Rh (-)	0	0.0%	0.0%
					AB Rh (+)	0	0.0%	0.0%
	COVID-19	Post-treatment course	Death	Blood group	0 Rh (-)	3	0.6%	2.2%
					0 Rh (+)	27	5.7%	19.7%
					A Rh (-)	8	1.7%	5.8%
					A Rh (+)	77	16.2%	56.2%
					B Rh (-)	3	0.6%	2.2%
					B Rh (+)	9	1.9%	6.6%
					AB Rh (-)	1	0.2%	0.7%
					AB Rh (+)	9	1.9%	6.6%
			Discharged	Blood group	0 Rh (-)	4	0.8%	1.5%
					0 Rh (+)	61	12.8%	22.2%
					A Rh (-)	17	3.6%	6.2%
					A Rh (+)	128	26.9%	46.5%
					B Rh (-)	4	0.8%	1.5%
					B Rh (+)	37	7.8%	13.5%
					AB Rh (-)	4	0.8%	1.5%
					AB Rh (+)	20	4.2%	7.3%
			No hospitalization	Blood group	0 Rh (-)	0	0.0%	0.0%
					0 Rh (+)	7	1.5%	35.0%
					A Rh (-)	2	0.4%	10.0%
					A Rh (+)	7	1.5%	35.0%
					B Rh (-)	1	0.2%	5.0%
					B Rh (+)	1	0.2%	5.0%
					AB Rh (-)	0	0.0%	0.0%
					AB Rh (+)	2	0.4%	10.0%

RT-PCR: Reverse-transcriptase polymerase chain reaction, Rh: Rhesus

blood type and mortality.[15] Our findings indicate that there is no correlation between outpatient treatment of patients, the clinical conditions necessitating hospitalization, the requirement for intensive care, or mortality rates and blood groups. While there are considerable investigations in the literature regarding various blood groups and their associated clinical outcomes, these studies seem to lack consistency in both hypothesis formulation and scientific reasoning. Our findings indicate that there is no correlation between blood groups and the clinical outcomes of COVID-19.

Rh Factor and COVID-19

Given that blood types are categorized as positive or negative based on the presence of the Rh factor protein, it is important to

explore the relationship between Rh and COVID-19 infection. A study indicated that Rh (+) correlated with increased odds of testing positive, as well as elevated risks of intubation and mortality.[12] A separate investigation by revealed that Rh (–) patients exhibited a 2.7% reduced risk of initial infection, intubation, and mortality after controlling for sex, age, and other demographic factors.[13] A research study conducted by Ray et al.[16] also suggested that those with Rh (–) blood type exhibited reduced susceptibility to SARS-CoV-2 infection, particularly among individuals with O-negative blood type. Nonetheless, a separate hematological investigation carried out in Sudan suggested that individuals with the O-positive blood group exhibit the least likelihood of experiencing severe symptoms, whereas the authors concurred that those with A-positive blood type are the most susceptible upon exposure to the virus.[17] Our data analysis revealed, in contrast to existing literature, that there is no correlation between Rh status and the incidence and/or severity of clinical outcomes related to COVID-19. The absence of statistical significance in our study data could be associated with the characteristics of our patient population, or it is possible that the disease does not genuinely correlate with the Rh factor.

Limitations

The main drawback of our study was that it was conducted as a single-centered investigation within a single region. It is our conviction that studies carried out across multiple centers, encompassing various ethnic regions and diverse patient populations, will yield greater benefits.

CONCLUSION

Our study revealed that, contrary to existing literature, there is no association between contracting COVID-19 and/or the severity of the disease or death across the 8 blood groups defined by the ABO and Rh combinations. This may represent a plausible outcome or could potentially be associated with genetic profiles. We assert that, contrary to claims in the literature, there is no correlation between ABO and Rh blood classes and the incidence, severity, or mortality of COVID-19.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Amasya University Non-interventional Clinical Researches Ethics Committee (Date: 11.06.2020, Decision No: 7/55).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

Carbapenem resistance profile of *Escherichia coli* and *Klebsiella pneumoniae* in our hospital

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ABSTRACT

Aims: This study aimed to evaluate the resistance rates of *Escherichia coli (E. coli)* and *Klebsiella pneumoniae (K. pneumoniae)* strains isolated from hospitalized patients in our hospital between 2011 and 2014 against carbapenem antibiotics.
Methods: A total of 5266 *E. coli* and 1360 *K. pneumoniae* strains isolated from different clinical samples were included in the study. Identification and antibiotic susceptibility tests were performed using the BD Phoenix 100 (Becton Dickinson, USA) automated system. Carbapenem resistance rates were evaluated according to imipenem, meropenem and ertapenem resistance.
Results: Carbapenem resistance was detected at a higher rate in *K. pneumoniae* strains compared to *E. coli* both bacteria were most frequently isolated from internal medicine ward and urine samples. Ertapenem stood out as the most resistant antibiotic. An increasing trend in carbapenem resistance was noted throughout the study.
Conclusion: The increasing carbapenem resistance observed in *K. pneumoniae* strains necessitates the development of more careful and effective strategies regarding antibiotic use in the management of nosocomial infections.
Keywords: Antibiotic resistance, *Enterobacteriaceae*, Carbapenem

INTRODUCTION

Escherichia coli (E. coli) and *Klebsiella pneumoniae (K. pneumoniae)* are the most common causative agents of urinary tract, respiratory tract and bloodstream infections worldwide. They can spread rapidly among patients in hospital settings and cause hospital outbreaks if appropriate prevention and control measures are not taken.[1] Increasing resistance mechanisms in *Enterobacteriaceae* members and rapid spread of resistant strains pose a problem for clinicians in the treatment of infections caused by these species. Carbapenem group antibiotics are one of the most preferred antibiotic groups in the treatment of these infections.[2] However, today, bacteria have acquired resistance to carbapenems thanks to the carbapenemase enzymes they synthesize, and as a result, this leads to treatment difficulties in infections caused by *Enterobacteriaceae*.[3]

The most important mechanism for gram-negative bacteria to develop resistance to beta-lactam antibiotics is beta-lactamase production.[4] The production of extended-spectrum beta-lactamases (ESBL) in the *Enterobacteriaceae* family, especially in *E. coli* and *K. pneumoniae*, is of great clinical and microbiological importance because they hydrolyze penicillins and broad-spectrum cephalosporins.[5] Globally, nosocomial infections caused by multidrug-resistant *E. coli* and *K. pneumoniae* pathogens are associated with the highest risk of mortality and cause high treatment costs.[6]

The aim of this study was to determine the frequency and antibiotic resistance rates of *E. coli* and *K. pneumoniae* strains isolated from various clinical samples from inpatients in our hospital and to contribute to the correct use of antibiotics by monitoring antibiotic resistance.

METHODS

This study was produced from a master's thesis titled "Carbapenem resistance status in *Escherichia coli* and *Klebsiella pneumoniae* bacteria in our hospital" conducted at Sivas Cumhuriyet University, Institute of Health Sciences. Before starting the study, written permission was obtained from the Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 19.02.2016, Decision No: 2016-02/10). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

In our study, *E. coli* and *K. pneumoniae* isolates from the cultures of various clinical samples sent to the Microbiology Laboratory of Sivas Cumhuriyet University Medical Faculty Application and Research Hospital during the four-year period between 2011-2014 were retrospectively analyzed. BACTEC (Becton Dickinson, USA) fully automated blood culture systems were used for the study of blood culture samples. For the cultivation of all samples, 5% sheep blood agar and eosin methylene blue (EMB) agar media were used and petri dishes were incubated at 36+1°C for 24-48 hours. Phoenix™100 automated identification system (BD Phoenix System, Beckton Dickinson, USA) was used for species level

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identification of *Enterobacteriaceae* isolates determined by conventional methods such as colony morphology, gram staining, carbohydrate and citrate utilization, urease test. In-vitro antibiotic susceptibilities of bacteria were studied with the Phoenix™100 automated identification system (BD Phoenix System, Beckton Dickinson, USA) used for identification according to Clinical and Laboratory Standards Institute (CLSI) criteria. The first isolate identified from each patient was evaluated.

Statistical Analysis

The data of the study were transferred to the SPSS 22.0 package program in computer environment and data control and analysis were performed in this program. In statistical evaluation, descriptive values were given as mean and (%) percentages.

RESULTS

In our study, 174707 various clinical samples sent to the laboratory from outpatient clinics and clinics of Sivas Cumhuriyet University Hospital between 2011-2014 were cultured.

Antimicrobial resistance tests were performed on 29355 (16.80%) bacteria isolated from these cultures and thought to be possible infection agents.

When the distribution of *E. coli* and *K. pneumoniae* bacteria isolated from the samples delivered from outpatient clinics/clinics was analyzed according to clinical samples, it was observed that the most common bacterial isolation was in urine, followed by wound swab, blood, respiratory secretions, vaginal swabs, abdominal specimens, sterile fluids (pleural, thoracentesis and paracentesis), abscess swabs and other specimens (Table 1).

Table 1. Distribution of *E. coli* and *K. pneumoniae* bacteria isolated from various clinical samples between 2011 and 2014

	Bacteria type		
Sample type	***E. coli* n (%)**	***K. pneumoniae* n (%)**	**Total n (%)**
Urine	3648 (82.6)	766 (18.4)	4414 (66.6)
Wound swab	387 (81.1)	90 (18.9)	477 (7.20)
Blood	326 (69.8)	141 (30.2)	467 (7.1)
Respiratory secretion	200 (52.1)	184 (47.9)	384 (5.8)
Vaginal swab	230 (83.9)	44 (16.1)	274 (4.1)
Abdominal region	89 (92.7)	7 (7.3)	96 (1.5)
Sterile liquids	48 (78.7)	13 (21.3)	61 (0.9)
Abscess swab	44 (91.7)	4 (8.3)	48 (0.7)
Other	294 (72.6)	111 (27.4)	405 (6.1)
Total	5266 (79.5)	1360 (20.5)	6626

E. coli: Escherichia coli, K. pneumoniae: Klebsiella pneumoniae

When the distribution of isolated *E. coli* and *K. pneumoniae* bacteria according to the services was examined, it was seen that the most frequently isolated service was internal medicine service, followed by pediatrics+newborn service, urology, obstetrics and gynecology, ICU, general surgery, neurology, infection, emergency department, other (Table 2).

When the resistance and susceptibility of *E. coli* isolates to ertapenem, imipenem and meropenem between 2011-2014 were analyzed, the changes in resistance rates against these antibiotics were found to be significant (Table 3).

Table 2. Distribution of isolated *E. coli* and *K. pneumoniae* bacteria according to wards between 2011-2014

	Bacteria type		
Wards	***E. coli* n (%)**	***K. pneumoniae* n (%)**	**Total n (%)**
Internal medicine	1147 (81.6)	259 (18.4)	1406 (21.2)
Pediatrics+newborn	1002 (76.7)	305 (23.3)	1307 (19.7)
Urology	798 (86.7)	122 (13.3)	920 (13.9)
Obstetrics and gynecology	411 (86.9)	68 (13.1)	479 (7.2)
ICU	283 (66.4)	143 (33.6)	426 (6.4)
General surgery	358 (85.6)	60 (14.4)	418 (6.3)
Neurology	179 (68.6)	82 (31.4)	261 (3.9)
Infection	164 (87.7)	23 (12.3)	187 (2.8)
Emergency department	157 (84.4)	29 (15.6)	186 (2.8)
Other	767 (74.0)	269 (26.0)	1036 (15.6)
Total	5266 (79.5)	1360 (20.5)	6626

E. coli: Escherichia coli, K. pneumoniae: Klebsiella pneumoniae, ICU: Intensive care unit

Table 3. Carbapenem resistance status of *E. coli* isolates between 2011-2014

	Years					
Antibiotics	**2011**	**2012**	**2013**	**2014**	**Total**	**p**
Ertapenem	45/1393 (3.23%)	31/1288 (2.40%)	65/1161 (5.59%)	59/1403 (4.20%)	200/5245 (3.81%)	p=0.003*
Imipenem	0/1393 (0.0%)	1/1288 (0.07%)	39/1161 (3.35%)	47/1403 (3.34%)	87/5245 (1.65%)	p=0.001*
Meropenem	0/1393 (0.0%)	0/1288 (0.0%)	4/1161 (0.34%)	32/1403 (2.28%)	36/5245 (0.68%)	p=0.001*

E. coli: Escherichia coli, *p<0.05 important

The changes in resistance against *K. pneumoniae* isolates between 2011 and 2014 were significant for ertapenem and imipenem, whereas the difference for meropenem was not statistically significant (Table 4).

Table 4. Carbapenem resistance status of K. pneumoniae isolates between 2011-2014

	Yıllar					
Antibiyotik	**2011**	**2012**	**2013**	**2014**	**Toplam***	**p**
Ertapenem	60/379 (15.83%)	13/339 (3.83%)	40/291 (13.74%)	32/349 (9.16%)	145/1358 (10.67%)	p=0.001*
Imipenem	16/379 (4.22%)	3/339 (0.88%)	18/291 (6.18%)	26/349 (7.44%)	63/1358 (4.63%)	p=0.001*
Meropenem	17/379 (4.48%)	0/339 (0.0%)	10/291 (3.43%)	19/349 (5.44%)	46/1358 (3.38%)	p=0.233

*p<0.05 important

DISCUSSION

Antimicrobial resistance (AMR) has been reported by the World Health Organization as one of the top 10 global public health threats facing humanity.[7] Antibacterial resistance may develop through different mechanisms. Some microorganisms have the potential to be resistant to multiple drugs by harboring several mechanisms. The emergence of multidrug-resistant gram-negative enteric bacteria poses a major problem in the management of both nosocomial and community-acquired infections.[8] Like *E. coli*, *K. pneumoniae* is a common cause of urinary, respiratory tract and bloodstream infections and can be easily transmitted, leading to the risk of nosocomial outbreaks.[9]

In a study covering four years in Turkiye, it was reported that carbapenem-resistant *K. pneumoniae* isolates were mostly isolated from urine (45.1%), blood (25.8%) and respiratory tract samples (18.5%), while carbapenem-resistant *E. coli* isolates were isolated from urine (71.0%), blood (15.0%) and wound (7.0%) samples.[10] Duran et al.[11] also reported that 56.8% of *E. coli* strains were isolated from urine, 16.7% from endotracheal aspirate (ETA), 16.5% from blood and 6.8% from wound specimens; 37.1% of *K. pneumoniae* strains were isolated from urine, 32.7% from ETA, 19.3% from blood and 5.4% from wound specimens. In accordance with these studies, the most common isolations of both bacteria were isolated from urine, blood, wound site and respiratory specimens.

In a study conducted in our country, the distribution of carbapenem-resistant *K. pneumoniae* strains according to clinics was determined as internal medicine wards (40%), intensive care units (36.0%), surgical wards (15.0%), and pediatric wards (9.0%). In the same study, it was emphasized that there was an increasing resistance (from 0.6% to 14.2%) in *K.pneumoniae* bacteria between years (2012-2020). In the study conducted by Telli,[12] similar results to our study were found and it was observed that the most frequently isolated wards of both bacteria were internal medicine wards and there was an increasing resistance in *K. pneumoniae* bacteria.

Between 2019 and 2023, carbapenem-resistant *K. pneumoniae* showed the largest increase (+2.9%) in the European Union/European Economic Area (EU/EEA) population-weighted average AMR percentage of all bacterial-antibiotic combinations under EARS-Net surveillance.[13]

Referring to isolates obtained in 2021, it was emphasized that resistance to carbapenems reported to AMR surveillance networks was higher in *K. pneumoniae* than in *E. coli*. For *K. pneumoniae*, out of 45 countries in the WHO European region, 14 (31%) reported AMR percentages below 1%, 15 (33%) equal to or above 25% and eight (18%) equal to or above 50% (Belarus, Georgia, Greece, Moldova, Romania, Russia, Serbia and Ukraine). For *E. coli*, percentages were also reported to be generally low in the northern and western parts of the WHO European Region. Eight out of 44 countries (18%) (Belarus, Cyprus, Georgia, Greece, Russia, Serbia, Turkey and Ukraine) reported percentages of 1% or higher in 2021, with the remaining countries reporting <1% (9).

In a multicenter study conducted by Süzük et al.[14] in our country, *K. pneumoniae* resistance rates were reported to be higher than *E. coli*. For *E. coli*, ertapenem, imipenem and meropenem resistance rates were 25.2%, 17.3% and 17.3%, respectively. In the same study, it was reported that ertapenem, imipenem and meropenem resistance rates for *K. pneumoniae* were 58.2%, 48.6% and 51.9%, respectively. In the study by Tümtürk et al.[15] the carbapenem resistance rate among *E. coli* strains was found to be 7.5% in 2017, compared to 4.1% in 2014. While the carbapenem resistance rate among *K. pneumoniae* strains was 32.2% in 2014, this rate increased to 48.9% in 2017. In 2017, it was determined that the resistance rate continued to increase. In a 2021 meta-analysis, it was reported that the carbapenem resistance rate was 16.6% for *E. coli* and 34.9% for *K. pneumoniae*.[16] Consistent with our study, higher resistance rates to carbapenem antibiotics were found in *K. pneumoniae* compared to *E. coli*. At the same time, it is noteworthy that the resistance rates increased as the years progressed.

Carbapenem resistance is usually caused by carbapenemase production and mechanisms such as efflux pump, impermeability, AmpC or ESBL production are reported to be involved in resistance development.[17] ESBL were first reported in Germany in 1983, just after the introduction of broad-spectrum beta-lactam antibiotics against *K. pneumoniae* species.[18] *K. pneumoniae* and *E. coli*, members of *Enterobacterieceae*, have been reported to possess genes encoding the enzyme extended-spectrum beta-lactamase (ESBL).[19] In a study conducted by Orak et al.[20] in 2023, 40.7% OXA-48, 31.5% MBL and 22.3% ESBL were detected in carbapenem resistant *E.coli* and *Klebsiella* spp. isolates. In a study conducted in Turkiye in 2025, it was reported that *E. coli* isolates were resistant to ertapenem, imipenem and meropenem by 1.0%, 1.0% and 10.0%, respectively, and 48% (n=28) of the isolates had ESBL. In the same study, it was reported that 49.0%, 49.0% and 54.0% of *K. pneumoniae* isolates were resistant to ertapenem, imipenem and meropenem, respectively, and ESBL was detected in 80.0% (n=37) of the isolates.[21]

Limitations

This study has several limitations. Firstly, as it is a retrospective design, it is based on tests performed in a specific time interval for complete and accurate data collection. Furthermore, only carbapenem group antibiotics were analyzed and clinical findings and other antibiotic groups were not evaluated. In addition, the data obtained from a specific geographical region in our study may be insufficient to reflect the overall carbapenem resistance.

CONCLUSION

In conclusion, we retrospectively analyzed the resistance data of *E. coli* and *K. pneumoniae* bacteria against carbapenem group antibiotics. These resistance data are regionally important in terms of the start of correct empirical treatment and effective treatment results. In our hospital and current studies, an increasing resistance is observed especially in *K. pneumoniae* bacteria. We believe that determination of beta-lactamase enzymes both retrospectively and by molecular and genotypic methods is extremely important for more accurate antibiotic selection and monitoring of effective treatment methods.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 19.02.2016, Decision No: 2016-02/10).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

Evaluation of the impact of nutritional parameters on mortality in patients with multiple myeloma

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ABSTRACT

Aims: Multiple myeloma (MM) is a type of cancer originating in plasma cells. While it can be managed with treatment, it is typically not curable. Recent research has underscored the significance of nutritional factors in forecasting the prognosis of patients with MM. This study aims to investigate the impact of nutritional indicators on mortality among patients diagnosed with multiple myeloma.

Methods: We performed a retrospective study to analyze overall survival (OS) in 225 patients with MM, focusing on the association between the controlling nutritional status (CONUT) score, the Geriatric Nutritional Risk Index (GNRI), and patient outcomes.

Results: Of the patients, 69 (30.7%) were younger than 65, while 156 (69.3%) were aged 65 years or older. The impact of CONUT scores on OS was statistically significant, particularly in patients aged 65 years and older (p=0.042). Among patients who had undergone autologous peripheral blood stem cell transplantation (Auto-PBSCT), a statistically significant correlation was observed between GNRI scores and survival times (p=0.002). Our results suggest improving patients' nutritional status positively influences treatment outcomes and survival rates.

Conclusion: The efficacy of nutritional scores on survival in MM has been demonstrated. We recommend clinicians assess patients' nutritional status when developing treatment plans and consider implementing appropriate nutritional interventions.

Keywords: CONUT, GNRI, multiple myeloma, nutritional, overall survival

INTRODUCTION

Multiple myeloma (MM) is a blood malignancy characterized by the excessive proliferation of atypical plasma cells in the bone marrow. It stands as the second most prevalent hematologic cancer after lymphoma, representing roughly 1% of all cancers and approximately 10% of hematologic malignancies.[1] The median age at diagnosis is 65 years, with less than 3% of patients being younger than 40 years old.[2] The disease progression, treatment processes, and patients' quality of life are significantly influenced by nutritional factors. In this article, we aim to evaluate the impact of nutritional parameters, particularly on mortality, in patients with MM. In patients with MM, advanced age at diagnosis and treatment-related complications variably affect OS. Inadequate nutritional status has been linked to reduced response to chemotherapy and a higher risk of treatment-related complications, both of which can negatively affect the overall prognosis in individuals with cancer.[3] When assessing performance status and frailty in patients with various cancer types, nutritional status indicators such as CONUT, Prognostic Nutritional Index (PNI), and the Geriatric Nutritional Risk Index (GNRI) provide valuable insights. Studies have demonstrated the importance of evaluating these measurements to manage chemotherapy response and toxicities.[4-9]

The CONUT score is calculated using total cholesterol, serum albumin, and lymphocyte count. This scoring system reflects patients' immune and nutritional statuses. Due to the simplicity of obtaining and calculating the parameters used in the CONUT score, it has been widely employed in recent studies for evaluating patients' nutritional statuses. Patients receive scores based on specified laboratory parameters in the CONUT scoring system, with the total score indicating the patient's CONUT score. CONUT score primarily assesses patients' nutritional status and has gained prominence recently. It was initially introduced to predict prognosis by evaluating postoperative complications and mortality among hospitalized patients, particularly those undergoing gastrointestinal surgery.[10] Recent studies have shown that the CONUT scoring system effectively predicts prognosis in certain malignancies and chronic diseases.[11,12] In this scoring system, albumin, a crucial parameter for evaluating nutritional status and inflammation, has the most significant

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impact. Additionally, lymphocyte count is considered an indicator of immune system function, and low levels of cholesterol have been noted to correlate with poor prognosis in malignant diseases.[11] Accordingly, these findings suggest that the CONUT score can be utilized to monitor patients' nutritional status and predict prognosis and mortality in chronic and malignant diseases.

The GNRI is a tool commonly used to assess nutritional risk, particularly in older adults. Research has demonstrated that GNRI is associated with a range of clinical outcomes. Higher GNRI scores in elderly patients with acute respiratory failure have been linked to lower hospital mortality rates and shorter hospital stays.[13] The GNRI is an important screening tool that assesses nutritional risk calculated by serum albumin level and ideal body weight.[14]

The GNRI was initially employed in 2005 to assess the relationship between malnutrition and mortality among elderly patients hospitalized. This index also can predict potential complications caused by inadequate nutrition.[15] GNRI was developed to predict the risk of morbidity and mortality due to malnutrition in the elderly population and is associated with poor outcomes linked to various diseases, including cancer. The GNRI score requires evaluating serum albumin levels and calculating ideal body weight using the Lorentz formula. The score is computed using the following equation.[14-19]

The GNRI has become a valuable predictor of outcomes across various malignancies, including hematologic and gastrointestinal cancers. Meta-analyses indicate that a low GNRI is associated with unfavorable OS, progression-free survival, and disease-free survival in patients with hematologic malignancies.[20,21] In conditions such as myelodysplastic syndrome and acute myeloid leukemia with myelodysplasia-related changes, a low GNRI predicts early mortality and shorter OS among patients treated with azacitidine.[22] Similarly, in gastrointestinal cancers, a low GNRI is linked to increased postoperative complications and poorer long-term outcomes.[23] The prognostic value of GNRI appears consistent across different cancer types and treatment approaches, underscoring its potential as a straightforward yet effective tool for assessing nutritional risk and predicting adverse outcomes in cancer patients.[21] This study evaluated the effect of GNRI and CONUT scores on response to treatment and OS in patients with MM.

METHODS

Patients and Treatments

Between 2013 and 2023, a total of 225 individuals diagnosed with symptomatic multiple myeloma (MM) at Sivas Cumhuriyet University Faculty of Medicine (Sivas, Turkiye) were retrospectively evaluated in this study. The final follow-up was conducted in May 2024. Information regarding patient demographics and clinical features was collected from institutional medical records and the hospital database. Approval was received for this retrospective study from the Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 18.01.2024, Decision No: 2024-01/08). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

CONUT Score

The CONUT score, which is calculated using serum albumin, total lymphocyte count, and total cholesterol levels, is an effective method for the early assessment of nutritional deficiencies. Based on the score, patients are classified into four nutritional status groups: normal (0-1), mild malnutrition (2-4), moderate malnutrition (5-8), and severe malnutrition (9-12).[25]

GNRI Score

The GNRI, introduced by Bouillanne et al.[14] in 2005, is a straightforward and reliable tool for assessing nutritional status. It evaluates nutritional risk by considering serum albumin levels and the ratio of current body weight to ideal body weight. The GNRI calculation formula is as follows:

GNRI=1.489×albumin (g/L)+41.7×ideal weight current weight

Ideal weight is calculated using the Lorentz formula:

- For males: Height (cm)-100-[(Height (cm)-150)/4]
- For females: Height (cm)-100-[(Height (cm)-150)/2.5]

The GNRI value serves as a tool used by healthcare professionals, typically in geriatric populations, to evaluate the nutritional status of patients.[14] According to GNRI scores, the GNRI is categorized into four layers based on nutritional risk (Q1-Q4): Q1 represents a major-risk layer with GNRI<82; Q2 signifies a moderate-risk layer with 82≤GNRI<92; Q3 indicates a low-risk layer with 92≤GNRI≤98; and Q4 denotes a no-risk layer with GNRI>98.[26]

Statistical Analysis

The data collected during the study were analyzed using the IBM SPSS software, version 26.0. The normality of the measurements was assessed using the Kolmogorov-Smirnov test, and descriptive statistics, including minimum, maximum, mean, standard deviation, median, and 25^{th}-75^{th} percentile values, were presented. For variables meeting the assumptions of parametric tests, one-way ANOVA was used for comparisons involving more than two groups. The Kruskal-Wallis H test was preferred for continuous variables with unmet parametric test assumptions. In cases where measurements followed a normal distribution, if the statistical difference between group means was significant in comparisons involving more than two groups, the LSD test was used to determine the differentiation between group means for homogeneous data, and Tamhane's T2 test was applied for non-homogeneous data. The Mann-Whitney U test compared two groups with non-normally distributed data. Survival rates in the disease were calculated using the Kaplan-Meier method and compared using the log-rank test. A significance level of $p<0.05$ was accepted; however, Bonferroni correction was applied for multiple comparisons to control the type I error.

RESULTS

A total of 225 newly diagnosed multiple myeloma (MM) patients were enrolled in the study, including 87 females (38.7%) and 138 males (61.3%). The age distribution of the patients was as follows: 69 patients (30.7%) were younger than 65 years old, and 156 patients (69.3%) were 65 years or older.

In the first-line treatment, patients received Bortezomib + Cyclophosphamide + Dexamethasone (68.4%), Vincristine + Adriamycin + Dexamethasone (14.2%), Melphalan + Prednisolone (5.3%), Bortezomib + Dexamethasone (4.4%), Bortezomib + Dexamethasone (1.8%), and lenalidomide + Dexamethasone (0.4%). Twelve patients (5.3%) were managed with observation without treatment. The response rate to first-line treatment was 40.9%, and the non-response rate was 53.8%. 60 patients (26.7%) underwent autologous stem cell transplantation (ASCT) following first-line treatment.

In the second-line treatment, lenalidomide + Dexamethasone (30.2%), Bortezomib + Cyclophosphamide + Dexamethasone (15.6%), Bortezomib (1.8%), Bortezomib + Dexamethasone (1.3%), and Bortezomib + Lenalidomide + Dexamethasone (0.4%) protocols were administered to a total of 111 patients. Forty-eight patients (21.3%) achieved a response, and 21 patients (9.3%) underwent ASCT following second-line treatment.

Third-line treatment included lenalidomide + Dexamethasone (11.1%), Bortezomib + Cyclophosphamide + Dexamethasone (6.2%), Daratumumab + lenalidomide + Dexamethasone (1.3%), Bortezomib (0.9%), Melphalan + Prednisolone (0.4%), Pomalidomide + Dexamethasone (0.4%), and VTD-PACE (0.4%) protocols administered to 47 patients. Nineteen patients (8.4%) achieved a response, and 7 patients (3.1%) underwent ASCT, while 2 patients (0.9%) received allogeneic stem cell transplantation (allo-SCT) following third-line treatment.

In the fourth-line treatment, lenalidomide + Dexamethasone (8.0%), Bortezomib + Cyclophosphamide + Dexamethasone (0.4%), and Bortezomib (0.4%) protocols were administered to 20 patients. Eight patients (3.6%) achieved a response, although none underwent stem cell transplantation. Table 1 presents the patients' anthropometric distributions. Table 2 and 3 present the distribution of patients' laboratory findings at the time of diagnosis according to CONUT and GNRI scores, respectively. A reduced response to first-line therapy was noted in individuals with moderate to high CONUT scores. As shown in Table 4, there was no statistically significant relationship between the CONUT score and the response to second- and third-line treatments. A lower response to first-line treatment has been observed in patients categorized as moderate/severe risk based on GNRI score. Table 5 shows that no statistically significant relationship was observed between GNRI scores and the response to second- and third-line treatments.

Table 1. Anthropometric distributions of patients

Height X±SD	163.40±10.14	
Weight X±SD	73.03±13.02	
Age	**Number (n)**	**Percent (%)**
<65	69	30.7
≥65	156	69.3
CONUT	**Number (n)**	**Percent (%)**
Normal	51	22.7
Mild	97	43.1
Moderate	66	29.3
Severe	11	4.9
GNRI	**Number (n)**	**Percent (%)**
Severe risk	32	14.2
Moderate risk	30	13.3
Low risk	31	13.8
No risk	132	58.7

SD: Standard deviation, CONUT: Controlling nutritional status, GNRI: Geriatric Nutritional Risk Index

Table 2. Distribution of laboratory measurements of patients according to CONUT scores

	CONUT				
	Normal	**Mild**	**Moderate**	**Severe**	**p**
Chol (mg/dl)	199.13±43.73	148.87±45.97	133.19±47.28	101.18±31.60	.000*
Cre (mg/dl)	.99(.74-1.3)	.95(.75-1.51)	1.15(.84-1.84)	1.08(.80-2.1)	.181
Albumin (g/L)	4.1(3.74-4.51)	3.53(3.25-4.16)	2.93(2.6-3.1)	2.39(2.3-2.84)	.000*
WBC (10^9/L)	6.87(5.52-8.17)	6.07(4.68-8.04)	5.34(4.097-7.425)	5.1(3.91-7.02)	.040*
Neu (10^9/L)	3.73(3.08-5.28)	3.54(2.78-5.13)	3.06(2.38-4.75)	3.50(2.00-4.70)	.274
Lymp (10^9/L)	2.00(1.66-2.43)	1.66(1.28-2.30)	1.235(0.95-2.298)	0.8(0.32-0.98)	.000*
Hgb (g/dl)	11.7(10-13.1)	10.5(9.5-11.85)	10.05(8.7-11.27)	10.3(8.1-11.1)	.001*
Plt (10^9/L)	221.60±105.10	203.49±99.92	204.98±109.91	133.54±62.42	.087

*p<0.05, CONUT: Controlling nutritional status, Chol: Cholesterol, Cre: Creatine, WBC: White Blood Cell, Neu: Neutrophil, Lmph: Lymphocyte, Hgb: Hemoglobin, Plt: Platelet

Table 3. Distribution of basic patient characteristics according to GNRI scores

	GNRI				
	Severe	**Moderate**	**Low risk**	**No risk**	**p**
Chol (mg/dl)	118±35.95	146.6±52.03	166.00±57.42	160.46±51.61	.000*
Cre (mg/dl)	.95 (.79-1.55)	1.36 (.98-2.38)	1.10(.83-1.56)	.97(.74-1.43)	.034*
Albumin (g/L)	3 (2.39-3.3)	2.87 (2.6-3.23)	3.20(2.89-3.51)	3.90(3.4-4.3)	.000*
WBC (10^9/L)	6.82 (4.48-8.65)	5.68 (4.10-8.94)	5.50(4.16-7.81)	6.16(4.77-7.77)	.786
Neu (10^9/L)	4.66 (2.80-5.66)	3.35 (2.29-6.03)	3.28(2.72-4.28)	3.50(2.61-5.01)	.420
Lymp(10^9/L)	1.17(0.97-1.64)	1.54 (1.11-2.22)	1.68(0.96-2.53)	1.77(1.25-2.40)	.018*
Hgb (g/dl)	10.2 (9.25-1.65)	9.65 (9.2-11.1)	10.8(9.1-12)	10.55(9.6-12.4)	.195
Plt (10^9/L)	241.97±131.59	168.76±68.35	153.33±82.459	215.76±101.44	.001*

*p<0.05, GNRI: Geriatric Nutritional Risk Index, Chol: Cholesterol, Cre: Creatine, WBC: White Blood Cell, Neu: Neutrophil, Lmph: Lymphocyte Hgb: Hemoglobin, Plt: Platelet,

Table 4. Relationship between patients' response to treatment and CONUT score

		CONUT				
		Normal n (%)	Mild n (%)	Moderate n (%)	Severe n (%)	Test/p
First-line treatment	No response	21(42.9)	44(47.8)	49 (80.3)	7 (63.6)	X^2=20.873/.000*
	Response	28 (57.1)	48 (52.2)	12 (19.7)	4 (36.4)	
Second-line treatment	No response	17 (60.7)	24 (50.0)	18 (62.1)	4 (66.7)	X^2=1.645/.649
	Response	11 (39.3)	24 (50.0)	11 (37.9)	2 (33.3)	
Third-line treatment	No response	8 (28.6)	10 (35.7)	7 (25.0)	3 (10.7)	LR=.892/.832
	Response	5 (26.3)	9 (47.4)	4 (21.1)	1 (5.3)	

CONUT: Controlling nutritional status

Table 5. Relationship between patients' response to treatment and GNRI score

		GNRI				
		Severe risk n (%)	Moderate risk n (%)	Low risk n (%)	No risk n (%)	Test/p
First-line treatment	No response	25 (78.1)	20 (71.4)	16 (51.6)	60 (49.2)	X^2=11.600/.009*
	Response	7 (21.9)	8 (28.6)	15 (48.4)	62 (50.8)	
Second-line treatment	No response	11 (50.0)	7 (63.6)	8 (80.0)	37 (54.4)	X^2=2.975/.396
	Response	11 (50.0)	4 (36.4)	2 (20.0)	31 (45.6)	
Third-line treatment	No response	5 (55.6)	2 (50.0)	2 (66.7)	19 (61.3)	LR=.311/.958
	Response	4 (44.4)	2 (50.0)	1 (33.3)	12 (38.7)	

GNRI: Geriatric Nutritional Risk Index

Significant effects of CONUT scores on OS in patients aged 65 years and older were found. No statistically significant relationship was observed between CONUT score and survival durations in patients under 65 (**Figure A**). Elderly patients with severe CONUT levels had shorter survival than those with normal, mild, and moderate levels (**Figure B**). Across all age groups, there was no statistically significant association between GNRI scores and survival durations (**Figure C and D**). Among patients without a history of Auto-PBSCT, a statistically significant relationship was found between CONUT scores and survival durations. Patients with severe CONUT scores had shorter survival durations than those with moderate, mild, and normal scores (**Figure F**). However, no statistically significant association was observed among patients with a history of Auto-PBSCT between CONUT scores and survival durations (**Figure E**). Patients with a history of Auto-PBSCT exhibited a statistically significant relationship between GNRI scores and survival durations. Patients in the low-risk group had shorter survival durations than those in the no risk and severe/moderate-risk groups. No statistically significant association was found between survival durations and GNRI scores among patients without a history of Auto-PBSCT (**Figure G and H**).

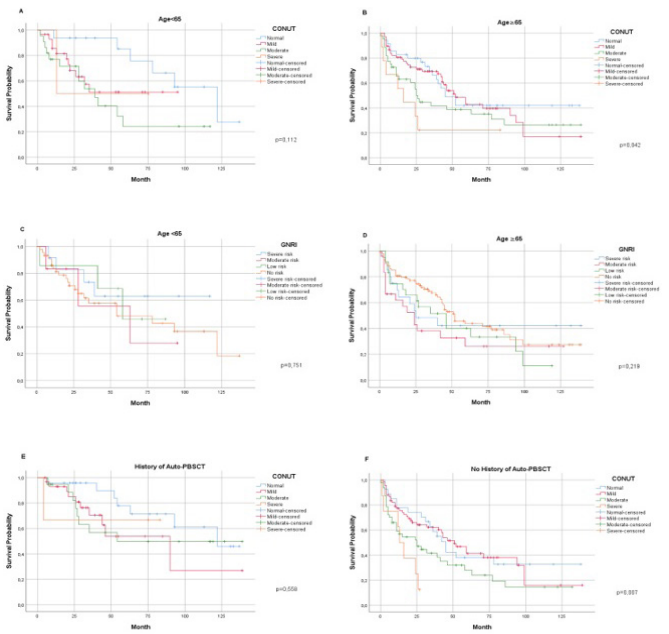

Figure. (A)The Kaplan-Meier curve estimates for overall survival (OS) among patients younger than 65 years indicate that the median OS for those with a normal CONUT score was 122 months. In contrast, patients with moderate and severe CONUT scores had a median OS of 39 and 13 months, respectively. (B) For patients aged 65 and older, the median OS was 45 months for those with a normal CONUT score, 52 months for those with a mild CONUT score, 25 months for those with a moderate CONUT score, and 16 months for those with a severe CONUT score. (C) In the cohort under 65, the median OS was 63 months in moderate GNRI score patients; individuals with a low-risk GNRI score had a median OS of 58 months, while those with no risk had a median OS of 54 months. (D) Among patients aged 65 and older, the median OS was 24 months for those with severe GNRI risk, 24 months for those with moderate GNRI risk, 46 months for low GNRI risk, and 52 months for no risk GNRI. (E) For patients with a history of Auto-PBSCT, the median OS was 122 months for those with a normal CONUT score, 90 months for those with a mild CONUT score, and 54 months for those with a moderate CONUT score. (F) In contrast, for patients with no history of Auto-PBSCT, the median OS was 45 months for those with a normal CONUT score, 51 months for those with a mild CONUT score, 25 months for those with a moderate CONUT score, and 13 months for those with a severe CONUT score. (G) Among patients with a history of Auto-PBSCT, the median OS was 63 months for those with moderate GNRI scores, 35 months for low-risk GNRI scores, and 122 months for those with no risk. (H) Additionally, in patients with no history of Auto-PBSCT, the median OS was 25 months for those with severe GNRI scores, 19 months for those with moderate GNRI scores, 58 months for those with low-risk GNRI scores, and 43 months for those with no risk

DISCUSSION

Malnutrition is a clinical condition that often goes unnoticed in clinics but, if left untreated, significantly increases morbidity and mortality risks, especially in the elderly population.[27] Those with chronic illnesses, organ transplant recipients, oncology patients, individuals requiring palliative care, the elderly, individuals in intensive care, and those who have undergone major surgery are recognized as high-risk groups for malnutrition.[28] Malnutrition is more commonly observed in elderly cancer patients undergoing chemotherapy and radiotherapy. Numerous studies have demonstrated that scoring systems such as CONUT and GNRI can monitor nutritional status and predict prognosis and mortality in chronic and malignant diseases.[29-31]

Multiple myeloma can occur in adults across a wide age range; however, it is most commonly seen in older individuals. Deaths associated with MM are most frequently observed in patients aged 65 and older.[32] This highlights the increasing risk of the disease with age and underscores the importance of managing and treating this elderly population effectively.[33] In recent years, the introduction of novel anti-myeloma agents has notably extended overall survival in patients with multiple myeloma. Despite these advancements, factors such as biological and genetic characteristics, along with complications arising from treatment, may affect individual responses to therapy. Therefore, improving treatment outcomes in MM patients necessitates a focus on minimizing therapy-related adverse effects.[34]

In this context, regular evaluation of patients' nutritional status and provision of nutritional support as needed are critical for optimizing management outcomes in these patients. The CONUT score has emerged as a significant prognostic indicator for patients with MM. Numerous studies have demonstrated that a higher CONUT score is associated with poorer OS in MM patients.[35-37] The CONUT score, which incorporates serum albumin, total cholesterol, and absolute lymphocyte count, reflects both nutritional and inflammatory status in hematological malignancies.[38] As an immune-nutritional index, the CONUT score offers a convenient and accessible method for predicting MM patient outcomes, potentially guiding treatment strategies, and improving clinical management.[37,38]

Lu and Li;[39] conducted a meta-analysis investigating the role of the CONUT score in hematologic malignancies. The study reviewed 23 articles and found that the CONUT score independently predicts poor OS in patients with hematologic malignancies. Additionally, they found that a high CONUT score is linked to a lower progression-free survival (PFS). These results indicate that nutritional status plays a crucial role in the prognosis of hematologic malignancies, underscoring the importance of the CONUT score in the management of these patients.

The GNRI has emerged as a valuable prognostic tool in various hematologic malignancies. Studies have shown that a low GNRI score is associated with poorer OS and PFS in patients with hematologic malignancies.[20] In multiple myeloma, the International Myeloma Working Group score, which incorporates elements similar to GNRI, has demonstrated substantial prognostic value for functional decline and OS.[40] In patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia with myelodysplasia-related changes (AML-MRC) treated with azacitidine, a low GNRI was independently linked to increased early mortality and shorter overall survival (OS). While the GNRI was initially validated in cardiovascular patients, its relevance in hematologic malignancies emphasizes its potential as a straightforward and effective tool for evaluating nutritional risk and predicting outcomes in these patient groups.[41]

Academic studies on CONUT score in MM patients provide valuable insights into assessing patients' nutritional status and predicting prognosis. These studies typically focus on examining the impact of patients' nutritional status on the course of MM and their response to treatment. This study has demonstrated that CONUT and GNRI scores, indicators of nutritional status in patients with MM, may serve as independent prognostic factors for OS. The findings indicate that, especially in MM patients aged 65 years and older, the CONUT score is consistent with its role in other cancer types, showing malnutrition as a marker of poor prognosis. Additionally, in patients without a history of auto-PBSCT, the CONUT score was associated with OS. On the other hand, the GNRI score was correlated with response to first-line treatment and OS in patients with a history of Auto-PBSCT. These findings underscore the significant role nutritional status assessments can play in managing treatment and prognosis in MM patients.

CONCLUSION

This study has helped us understand the impact of nutritional parameters on mortality in MM patients. Our findings suggest improving patients' nutritional status can positively affect treatment outcomes and survival. Scoring systems such as CONUT and GNRI are essential tools for assessing nutritional status and plan treatments for MM patients. Academic research in this field enhances our understanding of the effectiveness and significance of these scores in clinical practice.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Sivas Cumhuriyet University Non-interventional Clinical Researches Ethics Committee (Date: 18.01.2024, Decision No: 2024-01/08).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Original Article

Prognostic role of hemoglobin, albumin, lymphocyte, platelet (HALP) and modified Glasgow prognostic score (mGPS) in predicting intensive care needs in cancer patients: a retrospective study

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ABSTRACT

Aims: Early identification of clinical deterioration and intensive care unit (ICU) needs in patients with solid tumors is crucial for improving outcomes. This study aimed to evaluate the predictive role of the HALP score and the modified Glasgow prognostic score (mGPS) in forecasting ICU admissions.

Methods: A retrospective analysis was conducted on 302 patients with solid tumors who were hospitalized between May and July 2024. HALP and mGPS scores were calculated using laboratory values obtained at admission. Patients were divided into two groups based on the median HALP score. ICU transfer status was compared between groups along with clinical and laboratory parameters.

Results: ICU transfer was required in 26.5% of the patients. ICU need was significantly more common in patients with low HALP scores and high mGPS values ($p=0.01$ and $p<0.01$, respectively). Metastatic patients had a significantly higher ICU transfer rate compared to non-metastatic patients ($p=0.01$). There was no significant association between ICU requirement and comorbidity status ($p=0.59$) or tumor type ($p=0.10$).

Conclusion: HALP and mGPS are simple, accessible prognostic tools reflecting systemic inflammation and nutritional status. These scores may contribute to the early identification of high-risk patients during hospitalization and support timely clinical decision-making regarding ICU admission in cancer patients.

Keywords: HALP score, mGPS, intensive care, cancer patients, prognostic marker, risk prediction

INTRODUCTION

Early prediction of clinical deterioration in oncology patients is crucial for improving patient management and ensuring the efficient use of intensive care unit (ICU) resources. Timely identification of ICU needs in hospitalized cancer patients may enhance patient survival and prevent unnecessary ICU utilization. However, there remains a need for simple, practical, and reliable biomarkers to predict ICU requirement and disease prognosis in this patient population.[1,2]

In this context, the HALP score (hemoglobin, albumin, lymphocyte, platelet) and the modified Glasgow prognostic score (mGPS) are two important laboratory-based, inexpensive, and easily calculable scoring systems that reflect systemic inflammation and nutritional status. The HALP score integrates the patient's hematologic and nutritional status with immune response capacity, allowing for meaningful clinical insights, while the mGPS reflects systemic inflammation based on C-reactive protein (CRP) and albumin levels.[3-5]

Previous studies have demonstrated that scoring systems used in various types of cancer have potential in predicting progression-free survival (PFS) and overall survival (OS).[3-5] In addition, these scoring systems have also been evaluated in predicting the prognosis of non-cancer-related diseases.[6-9] However, there is no existing study in the literature evaluating the ability of these two scoring systems to predict ICU requirement in oncology patients. In cancer patients, the need for intensive care is typically determined based on acute clinical parameters such as the number of organ dysfunctions, need for ventilatory support, hemodynamic instability, and sepsis. In this context, the aim of our study is to assess the predictive potential and reliability of the HALP score and mGPS in estimating ICU requirement among cancer patients.

METHODS

This retrospective observational study was conducted in accordance with the principles of the Declaration of Helsinki and received ethical approval from the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 12.02.2025, Decision No: AEŞH-BADEK-2025-0117).

The study included adult individuals who met the eligibility criteria among patients hospitalized in the Medical Oncology

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Department of Ankara Etlik City Hospital between May and July 2024.

Inclusion criteria;

- Aged 18 years or older
- Diagnosed with a solid tumor
- Hospitalized in the medical oncology department during the specified period
- Complete availability of clinical and laboratory data

Exclusion criteria;

- Repeated hospitalizations of the same patient (only the first admission was included)
- Hospitalizations solely for the administration of active systemic anticancer therapy (e.g., chemotherapy, radiotherapy, immunotherapy, targeted therapy, etc.)
- Patients with missing clinical or laboratory data

Following the application of these criteria, 455 patients were evaluated, of whom 153 were excluded (due to repeated hospitalizations and missing laboratory data). The remaining 302 patients were included in the study. Demographic characteristics of the patients, including age, sex, primary tumor type, disease stage (metastatic or non-metastatic), presence of comorbidities, type of admission (emergency, outpatient clinic, transfer from ICU, etc.), length of hospital stay, reasons for hospitalization, discharge status, and ICU transfer status, were obtained from electronic medical records. Biomarker-based scores were calculated based on laboratory findings obtained at the time of hospital admission, including the HALP score, and mGPS.

Scoring Systems Used in the Study

HALP score was calculated using the following formula:

(Hemoglobin [g/dl]×albumin [g/dl]×lymphocyte count [/mm^3]) /platelet count [/mm^3]

mGPS was defined as:

- mGPS 0: CRP <10 mg/L and Albumin ≥3.5 g/dl
- mGPS 1: CRP ≥10 mg/L and Albumin ≥3.5 g/dl
- mGPS 2: CRP ≥10 mg/L and Albumin <3.5 g/dl

Patients who were transferred to the ICU were compared with those who were not. Clinical and laboratory parameters potentially associated with ICU transfer-including disease stage, presence of comorbidities, primary tumor type, reason for hospitalization, HALP score, and mGPS, were analyzed to evaluate their predictive potential.

Statistical Analysis

Statistical analyses were performed using SPSS (Statistical Package for the Social Sciences). Continuous variables were presented as median (minimum-maximum), while categorical variables were expressed as counts and percentages. The Chi-square test and Mann-Whitney U test were used for comparisons between groups.

The predictive potential of the HALP score for ICU requirement was evaluated by stratifying patients into low- and high-risk groups based on the median value. The mGPS was analyzed according to its predefined categorical levels. A p-value of <0.05 was considered statistically significant for all tests.

RESULTS

A total of 302 patients admitted to the oncology ward were included in this study. The median age was 63 years (range: 20-90), and 57.9% of the patients were male. The most common primary tumor types were lung cancer (23.2%), gastric cancer (16.6%), and colorectal cancer (12.6%). Metastatic disease was present in 73.5% of the patients, and 51.3% had at least one comorbid condition. The most frequently observed comorbidities were hypertension (33.1%), diabetes mellitus (20.5%), and coronary artery disease (9.3%). The clinical and sociodemographic characteristics of the patients are summarized in **Table 1**.

Table 1. Sociodemographic and clinical characteristics

Age median (range) year	63.0 (20.0-90.0)
Sex no (%)	
Male	175 (57.9)
Female	127 (42.1)
Primary no (%)	
Lung	70 (23.2)
Breast	33 (10.9)
Pancreas	19 (6.3)
Gastric	50 (16.6)
Colorectal	38 (12.6)
Cholangiocarcinoma	10 (3.3)
Gynecological	23 (7.6)
Head&neck	21 (7.0)
Other	38 (12.5)
Stage no (%)	
Metastatic	222 (73.5)
Non-metastatic	80 (26.5)
Comorbidity no (%)	
Yes	155 (51.3)
No	147 (48.7)
Comorbidity no (%)	
Hypertension	100 (33.1)
Diabetes mellitus	62 (20.5)
Coronary artery disease	28 (9.3)
Cerebrovascular disease	23 (7.6)
Asthma/COPD	28 (9.3)
Thyroid (hypo/hyper) disease	13 (4.3)
Other	36 (11.9)

COPD: Chronic obstructive pulmonary disease

The most common reasons for hospitalization were palliative care (29.8%) and infectious diseases (25.1%). Of the total cohort, 47.7% were admitted via outpatient services, while 37.4% were emergency admissions. The median length of hospital stay was 7 days (range: 1-43 days). Intensive care unit transfer occurred in 26.5% of patients, 4.6% were referred to palliative care, and 1% of patients died during hospitalization, as presented in **Table 2**.

There were significant associations between ICU transfer status and several clinical and laboratory parameters. ICU transfer was significantly more frequent among patients with a HALP score below the median value of 16.03 (p=0.01), and in those with metastatic disease compared to non-metastatic cases (29.2% vs. 16.3%, p=0.01). Conversely, no statistically significant associations were observed between ICU transfer

Table 2. Hospitalization and discharge features	
Referred department no (%)	
Oncology outpatient clinic	144 (47.7)
Emergency	113 (37.4)
Transfer from intensive care	22 (7.3)
Other	23 (7.6)
Cause for hospitalization no (%)	
Palliative care	90 (29.8)
Infection	76 (25.1)
Interventional procedures	66 (21.9)
Blood transfusion	33 (10.9)
Electrolyte imbalance	31 (10.3)
Other	6 (2.0)
Duration of hospitalisation median (range) days	7.0 (1.0-43.0)
Duration of hospitalisation no (%)	
1-7 days	121 (40.1)
8-21 days	116 (38.4)
>21 days	65 (21.5)
Discharge status no (%)	
Discharged	204 (67.5)
Transfer to intensive care ward	80 (26.5)
Transfer to palliative service	14 (4.6)
Transfer to other clinics	1 (0.4)
Deceased	3 (1.0)

and comorbidity status (p=0.59) or primary tumor type (p=0.10), although the ICU admission rate was relatively higher in patients with gastric cancer. These findings, including HALP score stratification, disease stage, and other clinical variables, are summarized in Table 3.

Table 3. Patient characteristics of patients transferred to intensive care unit and relationship with laboratory parameters			
Parameters	**Intensive care transfer**	**Intensive care non-transfer**	**p-value**
Cancer primary type			p=0.1
Lung	14	56	
Breast	4	29	
Pancreas	4	15	
Gastric	22	28	
Colorectal	9	29	
Cholangiocarcinoma	4	6	
Gynecological	8	15	
Head & neck	4	17	
Other	11	27	
Stage			p=0.01
Non-metastatic	13	67	
Metastatic	67	155	
Comorbidity			p=0.59
No	41	106	
Yes	39	116	
HALP score (median: 16.03)			p=0.01
Low	53	98	
High	27	124	
Modified Glasgow prognostic score			p<0.01
0	6	112	
1	12	54	
2	62	56	
Pearson's Chi-square test			

A strong statistical association was observed between the mGPS and ICU transfer status (p<0.01). Among patients with an mGPS score of 2, 52.5% required ICU admission, whereas only 5.1% of those with a score of 0 were transferred to the ICU. This distribution indicates that mGPS may serve as a useful determinant for clinical risk stratification, and this association is illustrated in Figure.

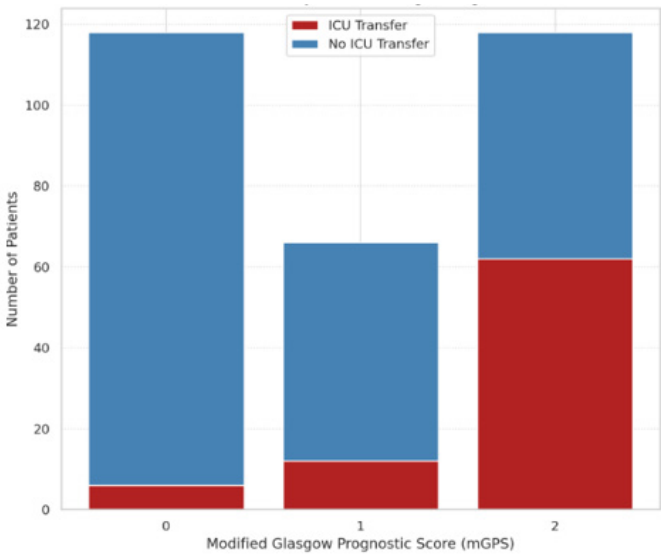

Figure. The association between modified Glasgow prognostic score and intensive care unit admission

DISCUSSION

This study demonstrated that the HALP score and mGPS have significant value in predicting ICU requirements in patients with solid tumors. Our findings revealed that patients who required ICU transfer had lower HALP scores and higher mGPS values. This suggests that inflammatory burden and malnutrition are associated with clinical deterioration in critically ill patients.

The results of our study are consistent with the existing literature regarding the prognostic significance of mGPS and HALP scores in oncology. Previous studies have repeatedly reported that deterioration in these scores is associated with poorer survival outcomes in cancer patients.[4,10-13] For instance, a comprehensive meta-analysis involving 13,110 patients demonstrated that a low HALP score is a reliable negative prognostic biomarker for survival outcomes in cancer patients.[3] Similarly, a recent review study demonstrated that high mGPS values are associated with poor overall and disease-specific survival across various malignancies.[5] These findings support the notion that worsening systemic inflammation and nutritional status, as reflected by both the HALP score and mGPS, have a significant impact on the course of malignancy. Moreover, both HALP and mGPS have emerged in the literature as prognostic markers in critical conditions outside of oncology. For example, a study conducted in patients presenting to the emergency department with acute heart failure reported that a low HALP score was associated with increased mortality.[7] Similarly, in patients with acute stroke, the HALP score has been shown to be associated with poor neurological outcomes and increased mortality.[8] These findings indicate that indices such as HALP and mGPS reflect not only cancer prognosis but also the overall burden of systemic disease and the clinical course of critically ill patients.

However, the role of HALP and mGPS in predicting progressive clinical deterioration among oncology inpatients has not been clearly established to date. To the best of our knowledge, there has been no prior study in the literature specifically evaluating these two scores in the context of predicting ICU transfer requirements. In this respect, our study provides a novel contribution to the literature. The results we obtained suggest that HALP and mGPS, as objective scores calculated from simple laboratory parameters, may aid in risk stratification of patients followed in oncology wards. In our study, the HALP score was analyzed by dividing patients into two groups based on the median value, and lower scores were significantly associated with ICU transfer. This indicates that such scoring systems may play a supportive role in clinical decision-making. In a study conducted among critically ill breast cancer patients admitted to the ICU, it was reported that those with an mGPS score of 2 had approximately 20 times higher mortality risk compared to those with a score of 0.[14] In this context, the association of HALP and mGPS with ICU requirement observed in our study further highlights the importance of these scores in clinical risk assessment. In particular, a high mGPS value in patients with advanced-stage cancer may warrant closer clinical monitoring and consideration for early ICU admission.

In our study, the rate of ICU transfer was significantly higher in patients with metastatic disease (29.2% versus 16.3% in non-metastatic patients; p=0.01). These findings suggest that patients with a higher tumor burden may be more prone to clinical deterioration requiring intensive care.

One of the most important clinical contributions of our study is the demonstration that HALP and mGPS scores can serve as early warning indicators that are easily calculable at the bedside using routine laboratory data. In current oncology practice, it is often challenging to predict early clinical deterioration in hospitalized patients under ward follow-up. Existing decision-making is largely based on vital signs, changes in laboratory parameters, and the overall clinical course; however, an objective and standardized risk scoring system is not widely used in routine practice.[15] In this context, easily accessible scores such as HALP and mGPS may serve as practical and reliable tools for the early identification of high-risk patients. Indeed, the literature has shown that early ICU transfer in cancer patients is associated with improved survival outcomes.[2] Therefore, early intervention, prophylactic strategies, or timely intensive care support in patients identified with high-risk scores may support prevent adverse outcomes. Similarly, the use of these scores may contribute to more efficient utilization of healthcare resources by reducing unnecessary ICU admissions.[16] In our study, only 5% of patients with an mGPS score of 0 required ICU care, whereas more than half of those with a score of 2 were transferred to the ICU. This finding suggests that the mGPS score may serve as a useful tool in guiding clinical decision-making.

Limitations

Our study has several limitations. First, it was conducted retrospectively at a single center. Therefore, the findings demonstrate associations rather than causal relationships. Additionally, multicenter and prospective studies are needed to determine whether these results are applicable to other patient populations. Second, although the HALP and mGPS scores reflect the overall condition of the patient, certain important factors that may influence ICU admission decisions such as performance status, changes in vital signs, and physicians' clinical evaluations were not included in our analysis. Furthermore, ICU transfer decisions may also be affected by institutional differences such as local protocols and ICU bed capacity. This study included only patients with solid tumors; patients with hematological malignancies were not analyzed. Since the ICU management of this subgroup may differ, this limitation should be taken into account when generalizing the results to the entire oncology population. Despite all these limitations, our study provides meaningful and guiding evidence that the HALP and mGPS scores may assist in identifying patients at risk of clinical deterioration in the oncology ward setting.

CONCLUSION

The HALP and mGPS scores may serve as valuable tools in predicting ICU transfer requirements in cancer patients. By reflecting systemic inflammation and nutritional status, these scores can serve as early indicators of clinical deterioration risk. Our study offers a novel perspective to the literature, suggesting that the use of these easily applicable scores in oncology practice may aid in the early identification and management of critically ill patients. Future large-scale prospective studies are needed to validate the predictive power of these scores and facilitate their integration into clinical protocols.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was carried out with the permission of the Ankara Etlik City Hospital Scientific Researches Evaluation and Ethics Committee (Date: 12.02.2025, Decision No: AEŞH-BADEK-2025-0117).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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Case Report

Retroperitoneal hematoma complicated with colocutaneous fistula in a case of severe hemophilia B*

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ABSTRACT

Retroperitoneal hematoma rarely occurs in hemophilia B cases caused by factor IX deficiency. It typically arises as a result of trauma or surgical procedures, though spontaneous cases are rare. We present our patient who developed spontaneous retroperitoneal hematoma and was subsequently complicated by abscess, coloenteric fistula, osteomyelitis and arteria lumbalis bleeding. Surgical intervention was avoided for a long time due to difficulty of hemophilia B management for surgery. Therefore, the complication became severe and life-threatening. The patient was treated with successful and long-lasting surgical interventions, intravenous antibiotics and factor IX replacements. To the best of our knowledge, the case we present is the first hemophilia patient in the literature complicated by colocutaneous fistula.

Keywords: Hemophilia-B, retroperitoneal hematoma, colocutaneous fistula

*Presented as an oral presentation at the 10th HEVES congress in Antalya on 22-24 March 2024.

INTRODUCTION

Hemophilia B is a rare bleeding disorder that is transmitted in an X-linked manner and occurs in approximately 1 in 25,000 male births.[1] The severity of bleeding in hemophilia B is inversely proportional to the factor level. The most common bleeding sites are intra-articular and intra-muscular. Retroperitoneal bleeding is extremely rare in hemophilia B, with its exact frequency remaining undetermined due to the limited data available from case reports.[2,3]

Although there have been significant advances in the treatment of hemophilia, most of the patients around the world still cannot access these treatments due to social and economic problems. For this reason, serious complications can still be seen in undeveloped and developing countries.

CASE

A 37-year-old male patient was diagnosed with hemophilia-B at the age of 13. He could not walk at the age of 12 because of arthropathy in both knees due to the delay in diagnosis. The patient had an operation at an external center 3 years ago due to retroperitoneal hematoma and then received intensive factor therapy due to recurrent bleedings, developed multiple skin fistulas and then colon fistulas at the operation site and around it. Radical procedures could not be performed because of the anatomical location of the bleeding and the complications with infection. Intensive antibiotic treatment had to be applied during this process. The patient was hospitalized with the existing retroperitoneal hematoma turning into a fistulizing abscess on the colon+lumbar region skin. The lesions at the time of admission and the healing findings are shared in **Figure 1** after the informed consent form was obtained.

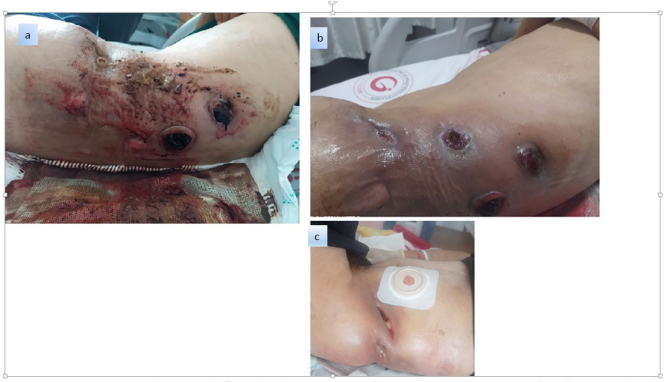

Figure 1. a) Discharged fistula lesions at first admission to the hospital, b) Clean skin fistulas after the surgery, c) Ileostomy

The patient had colonic contents leaking from the fistula mouths; there was a heavy anaerobic odor emanating from the wound areas and putting a strain on his social life. His laboratory findings at the time of admission were as follows: Hgb: 6.4 gr/dl, WBC: 6.3x10^9/L, Plt: 207x10^9/L, aPTT: 49.8 sn, INR: 1.2, CRP: 190 mg/L. Wound cultures yielded *E. coli*, *Morganella morganii*, *Proteus mirabilis*, and blood culture yielded *Psychrobacter*. was given Intravenous antibiotics was given. Abdominal tomography showed an image that started from the posterior neighborhood of the left kidney and spleen that extended to the pelvis, opened to the skin, contained air densities and contrast material extravasation suggesting active bleeding (originating from the left a. lumbalis and the

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aorta), could not be distinguished from the bowel loops, and eroded the left 12th rib, L4 and L5 vertebral processes, and left iliac bone. The radiological image is shown in **Figure 2**. The general surgery team performed extensive debridement of the complex hematoma and abscess, which extended into the abdominal and retroperitoneal regions. Ileostomy was performed, colon and skin fistulas were repaired. During the hospitalization, which lasted approximately 7 months, the patient underwent numerous surgeries for wound site revision. All skin fistulas closed; the source of infections was eliminated. With the use of effective factor IX replecaments both before and after the operation, the patient did not experience any bleeding and hemostatic problems.

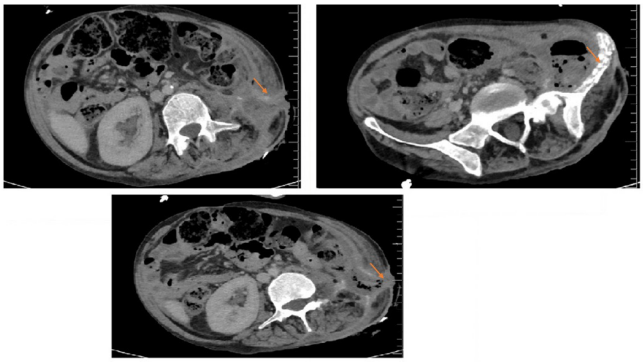

Figure 2. Computerized tomography images showing the patient's colocutaneous fistula and the deterioration of the structure of the iliac bone

DISCUSSION

Fistula is defined as an abnormal connection between two body structures that should not be connected.[5] Colocutaneous fistulas mostly develop as a complication of Crohn's disease, diverticulitis or surgical intervention.[5-7] Our patient also underwent an intervention for hematoma drainage 3 years ago.

It has been stated in the literature that it is important for enterocutaneous fistula treatment to be performed in a center with serious experience and to use a multidisciplinary approach.[9] Similarly, retroperitoneal hematoma is an important condition with high mortality, where early diagnosis and correct treatment are important.[8] Intervention in a patient with severe hemophilia who develops two serious complications, retroperitoneal hematoma and enterocutaneous fistula, can be frightening. However, these conditions with high morbidity and mortality risks can be managed by performing effective factor replacement at an early stage. In late cases, a long process requiring patience is required with the cooperation of hematology, general surgery and infectious diseases. The shared case has identified this situation.

Surgeons should be encouraged to intervene early in life-threatening and life-disrupting complications such as colocutaneous fistula in hemophilia patients. The most important task in this regard falls to internal medicine specialists and hematologists.

CONCLUSION

Despite the advances in hemophilia treatment in recent years, there may still be complicated cases. It is more common in undeveloped and developing countries where access to treatment is limited. Early intervention in complications that develop in hemophilia cases will increase the chance of success. When surgery is necessary in hemophilia patients, it is necessary not to hesitate to intervene. Good relationship and multidisciplinary approach that encourages courage should be established between the hematologist and the surgeon.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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