

Extremely elevated erythrocyte sedimentation rates: Associations with patients' diagnoses and clinical characteristics

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Abstract

Introduction: The aim of the study was to assess the etiological distribution of patients with an erythrocyte sedimentation rate (ESR) over 100 mm/hour and to evaluate differences in demographic, comorbidity, laboratory characteristics, and clinical outcomes.

Methods: This retrospective observational clinical study included patients aged 18 years and older who were admitted to the internal medicine inpatient clinic between May 1, 2015 and June 1, 2021 and had ESR values above 100 mm/h. Demographic data, comorbidities, laboratory parameters, imaging studies, histopathological findings, microbiological and serological data, along with in-hospital and post-discharge mortality, were collected from the hospital's electronic database. Two independent clinicians evaluated the data to identify diagnoses associated with elevated ESR. Patients were divided into six categories based on the most likely diagnosis.

Results: The study included 441 patients, 52.6% of whom were female, and the mean age was 72.6 years. The etiological distribution was as follows: infectious diseases (34%), malignancies (31.5%), undiagnosed cases (15.9%), renal diseases (9.8%), other causes (5%), and rheumatologic diseases (3.8%). Etiological distributions did not differ by gender, age, or ESR ranges. The in-hospital mortality rate was 3.6%, and the overall mortality rate from hospitalization to the data collection date was 64.4%. Mortality was higher in patients with malignancies (81.3%) compared to other etiologies ($p < 0.001$). Patients who died had higher mean age, ferritin levels, having diabetes mellitus, heart failure, or malignancy, and lower hemoglobin and lymphocyte levels compared to survivors ($p < 0.05$ for all).

Conclusion: Most patients with an ESR over 100 mm/hour had significant underlying medical conditions, with infectious diseases and malignancies comprising two-thirds of the cases.

Keywords: erythrocyte sedimentation rate; infectious diseases; malignancies; mortality; acute phase reactants.

What is new? What is important?

This study provides detailed information on the etiology and clinical characteristics of patients with extremely elevated ESR admitted to the internal medicine department of a tertiary hospital. It emphasizes that most of these patients had serious medical conditions, while highlighting that benign causes were more frequent than malignant ones. The findings underscore the importance of considering benign etiologies first in such cases.

INTRODUCTION

The erythrocyte sedimentation rate (ESR) is a standardized, accurate, widely available, and cost-effective method for measuring inflammation. When venous blood is placed in an upright tube, erythrocytes, being heavier than plasma, settle to the bottom under the influence of gravity. ESR is defined as the distance erythrocytes fall in one hour [1]. In the presence of elevated proteins such as fibrinogen or globulins, erythrocytes clump together more easily, forming rouleaux that settle at the bottom. Acute phase reactants (APR) refer

to molecules in the blood whose levels rise or fall in response to infection, inflammatory rheumatic diseases, allergic drug reactions, surgical interventions, or trauma [2]. ESR reflects the concentration of APRs and serves as an overall measure of inflammation. However, its sensitivity and specificity are low [3].

Studies in adults have shown that while moderate ESR elevations can occur without a known cause, ESR levels exceeding 100 mm/hour are associated with serious conditions and have a low rate of false positives [4]. The differential diagnosis of markedly elevated ESR has been

extensively studied since Zacharski *et al.*'s work in 1967, with infections, hematologic or oncologic diseases, and rheumatologic diseases consistently emerging as primary considerations [5,6]. However, variables such as the clinical setting and patient population can influence the frequency of these diagnoses and lead to differences in clinical outcomes [7].

This study aims to investigate the etiological distribution, comorbidities, and clinical outcomes of patients admitted to a tertiary hospital's internal medicine clinic with excessive ESR values, and to explore the associations among these factors.

MATERIALS AND METHODS

This retrospective, observational clinical study included patients aged 18 and older with ESR values over 100 mm/hour, admitted to the internal medicine inpatient clinic of Istanbul Medeniyet University Göztepe Training and Research Hospital between May 1, 2015, and June 1, 2021. Patients without discharge summaries or those with missing clinical, laboratory, or imaging data were excluded. The study was approved by the Ethics Committee of Istanbul Medeniyet University Göztepe Training and Research Hospital on December 8, 2021 (decision no: 2021/0620) and followed the principles of the Declaration of Helsinki. Patients' informed

consent was waived due to the retrospective study design.

STUDY DESIGN

From 8,082 patients admitted to the internal medicine inpatient clinic and who had ESR measurements during the study period, the discharge summaries of patients with ESR values over 100 mm/hour were reviewed using the hospital's electronic database (n = 481). After excluding cases where the elevated ESR etiology was not investigated (n = 13), cases with insufficient discharge summary data (n = 16), and cases where patients or their relatives declined further investigation into the cause of ESR elevation (n = 11), 441 patients were included in the analysis. The study flow diagram is presented as Figure 1. For patients with multiple admissions, data from the admission in which the diagnosis related to the elevated ESR was made were used. Demographic data, comorbidities, laboratory parameters (C-reactive protein, ferritin, hemoglobin, leukocytes, platelets, neutrophils, lymphocytes, neutrophil/lymphocyte ratio), imaging results, and histopathological findings were recorded. Mortality data, including in-hospital and post-discharge deaths, were obtained from the hospital's electronic system and the national health system (e-Nabız) on February 1, 2022, which served as the index date for data collection.

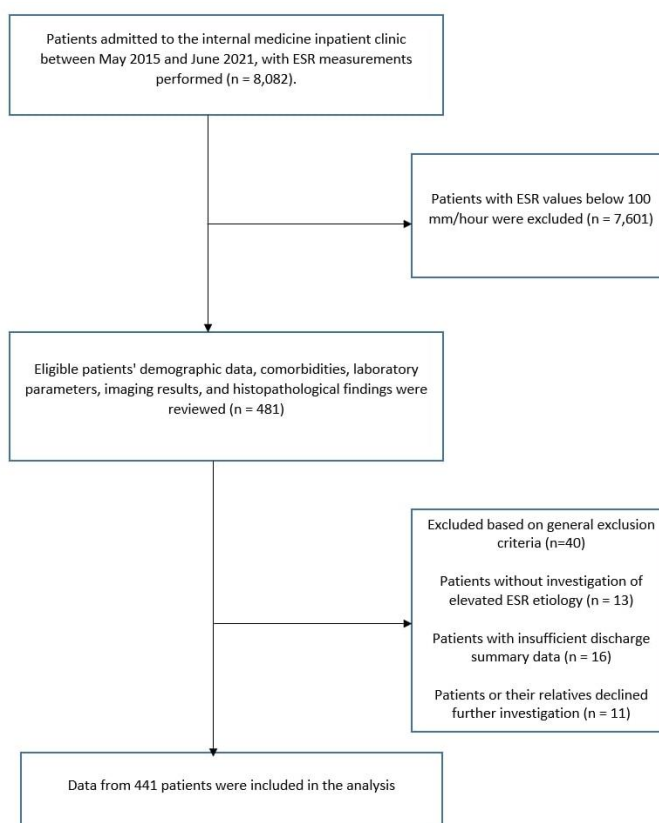


Figure 1. Flow diagram for inclusion and exclusion.

DIAGNOSTIC CATEGORIES

Diagnostic categories were determined by reviewing hospital records, including complete blood counts, biochemistry, urinalysis, histopathology, microbiology, serology, protein electrophoresis, special staining or flow cytometry, X-rays, endoscopic studies, computed tomography (CT), and magnetic resonance imaging (MRI). Two independent reviewers evaluated the data to identify diagnoses associated with elevated ESR. Based on the most likely diagnosis, patients were categorized into six groups: infectious diseases, malignancies, renal diseases, rheumatologic diseases, other causes, and undiagnosed cases. If more than one diagnosis was present, the condition most likely causing the elevated ESR was considered.

COMPARISONS

Diagnostic categories were compared by gender, age groups (<65 and ≥65 years), clinical outcomes (alive vs. exitus), ESR levels (100–120 mm/h and >120 mm/h), and laboratory findings. Additionally, demographic, comorbidity, and laboratory characteristics were compared between survivors and non-survivors.

LABORATORY MEASUREMENTS

C-reactive protein (CRP) was measured using the immunoturbidimetric method on the Roche Cobas c 501 analyzer, and ferritin was measured using the chemiluminescent method on the Roche Cobas e 601 analyzer. Complete blood count parameters (hemoglobin, leukocytes, platelets, neutrophils, and lymphocytes) were analyzed using the Mindray BC 6200 analyzer. ESR was measured using the ALIFAX Test 1 analyzer, based on the photometric capillary flow kinetic analysis principle, which calculates ESR kinetics by measuring erythrocyte aggregation capacity.

STATISTICAL ANALYSIS

Data were analyzed using SPSS 25. Frequency and percentage values were presented for categorical variables. The normality of data distribution was tested using the Shapiro-Wilk test. For normally distributed variables, arithmetic means and standard deviations were reported; for non-normally distributed variables, medians, minimums, and maximums were presented. Comparisons between two categorical variables were made using the Chi-square. For comparisons between two categorical and one continuous

variable, the independent samples t-test was used for normally distributed data, and the Mann-Whitney U test for non-normally distributed data. For comparisons involving more than two groups, the Kruskal-Wallis H test was used, and significant differences were further examined using the Mann-Whitney U test with Bonferroni correction. Effect sizes were calculated to complement p-values: Cohen's d was used for independent samples t-test, eta squared (η^2) was used for Kruskal-Wallis H test, and the Mann-Whitney U test's effect size was expressed as r. For categorical variables, Cramér's V was used with Chi-square tests. All effect sizes were presented with their 95% confidence intervals. A type I error rate of 0.05 was used throughout the study.

RESULTS

A total of 441 patients, aged between 20–100 years, were included in the study. The mean age was 72.6 years and 52.6% of the patients were female. Most of the cases (72.5%) were aged 65 and older.

The most common etiological causes of extremely elevated ESR were infectious diseases (34%), malignancies (31.5%), undiagnosed cases (15.9%), renal diseases (9.8%), other causes (5%), and rheumatologic diseases (3.8%). When examining sub-diagnoses within each group, pneumonia accounted for 40% of the infectious diseases, multiple myeloma for 13.7% of the malignancies, chronic kidney injury for 51.2% of the renal diseases, and rheumatoid arthritis for 64.7% of the rheumatologic diseases (Table 1).

When comparing the six etiological categories, there were no significant differences in terms of gender ($p=0.261$), age groups ($p=0.198$), or ESR levels ($p=0.507$). The malignancy group had a significantly higher mortality rate compared to the other groups ($p<0.001$). Ferritin levels were also notably higher in the malignancy group ($p<0.001$). Hemoglobin levels were significantly lower in the undiagnosed group compared to the other groups ($p<0.001$). In the infectious disease group, leukocyte counts ($p=0.001$), neutrophil levels ($p<0.001$), neutrophil-to-lymphocyte ratio (NLR) ($p<0.001$), and CRP levels ($p<0.001$) were significantly higher than those in the malignancy and undiagnosed groups (Table 2).

Patients with ESR >120 mm/hour had significantly lower hemoglobin levels (8.33 ± 1.84 g/dL) compared to those with ESR between 100–120 mm/hour (9.31 ± 2.11 g/dL) ($p<0.001$).

When evaluating comorbidities independent of their relationship with elevated ESR, the most frequent comorbid conditions were hypertension (51%), diabetes mellitus (40.1%), coronary artery disease (22.4%), chronic kidney disease (20.9%), malignancies (19.5%), congestive heart failure (11.8%), cerebrovascular disease (10.7%), and chronic obstructive pulmonary disease (9.3%) (Table 3).

It was observed that 16 patients (3.6%) died during hospitalization, 56 (12.7%) were transferred to the intensive care unit (ICU), and 369 (83.7%) were discharged. Up to the data collection date of the study, 54 (96.4%) of those initially transferred

to the ICU and 214 (58%) of those discharged were found to have died. In total, 284 patients (64.4%) had died.

Patients who died had a higher mean age ($p<0.001$), a greater proportion of those aged 65 and above ($p<0.001$), and higher rates of diabetes mellitus ($p=0.043$), congestive heart failure ($p=0.021$), and malignancies ($p<0.001$). Additionally, ferritin levels were higher ($p=0.002$), while hemoglobin ($p<0.001$) and lymphocyte levels ($p=0.021$) were lower in the deceased group compared to survivors (Table 3).

Table 1

Detailed distribution of diagnostic subcategories by disease type

Etiology of elevated ESR	n, %
Malignancies	139 (31.5)
Gastrointestinal cancers	27 (6.1)
Colon	15 (3.4)
Gastric	9 (2.0)
Pancreas	3 (0.7)
Hematologic cancers	50 (11.3)
Multiple myeloma	19 (4.3)
Leukemias	14 (3.2)
Myelodysplastic syndrome	12 (2.7)
Lymphomas	5 (1.1)
Urologic cancers	18 (4.1)
Bladder	7 (1.6)
Prostate	6 (1.4)
Renal cell carcinoma	5 (1.1)
Gynecologic cancers	15 (3.4)
Breast	6 (1.4)
Cervix	5 (1.1)
Ovary	4 (0.9)
Respiratory cancers	16 (3.7)
Lung	13 (3)
Larynx	3 (0.7)
Other cancer types	13 (3)
Infectious diseases	150 (34)
Pneumonia	60 (13.6)
Urinary tract infection	35 (7.9)
Diabetic foot infection	12 (2.7)
Sepsis	10 (2.3)
Osteomyelitis	5 (1.1)
Other infections	28 (6.4)
Rheumatologic diseases	17 (3.9)
Rheumatoid arthritis	11 (2.5)
Polymyalgia rheumatica	3 (0.7)
Adult-onset Still's disease	2 (0.5)
Systemic lupus erythematosus	1 (0.2)
Renal diseases	43 (9.8)
Chronic kidney disease	22 (5)
Acute kidney injury	12 (2.7)
Glomerulonephritis	6 (1.4)
Nephrotic syndrome	3 (0.7)
Other causes	22 (5)
Heart failure	13 (3)
Liver cirrhosis	4 (0.9)
Autoimmune thyroiditis	3 (0.7)
Crohn disease	2 (0.4)
Undiagnosed	70 (15.9)

ESR: erythrocyte sedimentation rate

Table 2

Etiology-based comparison of demographic, laboratory, and clinical characteristics

Variable	Infectious diseases (n=150)	Malignancies (n=139)	Other causes (n=22)	Renal diseases (n=43)	Undiagnosed (n=70)	Rheumatologic (n=17)	Effect size (95% CI)	p value
Male (n=209)	67 (32.1)	78 (37.3)	9 (4.3)	19 (9.1)	29 (13.9)	7 (3.3)	0.121 [0.079-0.243]	0.261
Female (n=232)	83 (35.8)	61 (26.3)	13 (5.6)	24 (10.3)	41 (17.7)	10 (4.3)		
Age <65 (n=121)	34 (28.1)	41 (33.9)	8 (6.6)	9 (7.4)	21 (17.4)	8 (6.6)	0.129 [0.078-0.252]	0.198
≥65 (n=320)	116 (36.3)	98 (30.6)	14 (4.4)	34 (10.6)	49 (15.3)	9 (2.8)		
ESR 100-120 (n=365)	130 (35.6)	109 (29.9)	18 (4.9)	34 (9.3)	60 (16.4)	14 (3.8)	0.099 [0.073-0.227]	0.507
ESR>120 (n=76)	20 (26.3)	30 (39.5)	4 (5.3)	9 (11.8)	10 (13.2)	3 (3.9)		
Exitus (n=284)	91 (60.7)	113 (81.3)	13 (59.1)	27 (62.8)	33 (47.1)	7 (41.2)	0.268 [0.201-0.375]	<0.001
Alive (n=157)	59 (39.3)	26 (18.7)	9 (40.9)	16 (37.2)	37 (52.9)	10 (58.8)		
Ferritin (ng/mL)	398.5 (32-40000)	611 (4.8-9155)	201 (7.8-40000)	352 (45-3595)	184.5 (2-11835)	422 (99-13980)	0.020 [0.001-0.038]	<0.001
Hemoglobin (mg/dL)	9.8 (5.2-15.5)	8.6 (4.3-15.8)	9.9 (7.4-13)	9.2 (5-13.5)	7.25 (3.7-13.2)	9.9 (6-12.1)	0.184 [0.133-0.235]	<0.001
MCV (fL)	86 (62-112)	86 (19-106)	89 (58-96)	87 (72-109)	81.5 (61-124)	85 (76-102)	0.012 [0-0.026]	0.037
Leukocytes (/mm ⁶)	11.5 (0.4-93.6)	9.2 (0.2-102)	10.1 (4.4-31.9)	10.9 (3.8-28.1)	9 (0.3-20.5)	7.8 (0.3-26)	0.018 [0.001-0.035]	0.001
Neutrophils (/mm ⁶)	9.3 (0.01-32.7)	6.2 (0-37)	8.4 (2-25)	8.7 (2.8-23.4)	6.5 (0.1-19.4)	6.1 (0.2-24)	0.054 [0.024-0.084]	<0.001
Lymphocytes (/mm ⁶)	1.2 (0.2-87.3)	1.1 (0-74.7)	1.3 (0.4-4.9)	1.2 (0.5-4.2)	1.6 (0.1-4)	1.2 (0.2-2.6)	0.003 [0.001-0.011]	0.146
NLR	7.5 (0.03-90)	4.5 (0.01-116)	5.9 (1-39)	6.2 (1.4-39.8)	3.7 (0.03-48.5)	5.1 (0.9-23)	0.024 [0.004-0.045]	<0.001
Thrombocytes (/mm ⁶)	260 (20.4-818)	231 (2.2-100.4)	252 (81.5-764)	286 (45-635)	319 (3.2-880)	269 (9-548)	0.025 [0.004-0.046]	0.038
CRP (mg/dL)	14 (0.3-45)	10.7 (0.1-42)	9.2 (0-35)	8.6 (0.2-96)	6 (0-32)	13 (4.7-38)	0.057 [0.026-0.087]	<0.001

ESR: erythrocyte sedimentation rate; MCV: Mean corpuscular volume; NLR: Neutrophil-to-lymphocyte ratio CRP: C-reactive protein.

Data were given as noun (%) or median (minimum-maximum).

Chi-square tests with Cramér's V and Kruskal-Wallis tests with eta-squared were used to calculate effect sizes for categorical and continuous variables, respectively.

Table 3

Demographic, comorbidity, and laboratory characteristics of patients based on mortality and survival status

Variables		Exitus (n=284)	Survivor (n=157)	Total (N=441)	Effect size (95% CI)	p value
Age		78 (27-100)	68 (20-92)	75 (20-100)	0.274 [0.860-0.359]	<0.001
Age	≥65	227 (70.9)	93 (29.1)	320 (100)	0.222 [0.117-0.319]	<0.001
Gender	Male	141 (67.5)	68 (32.5)	209 (100)	0.061 [0.003-0.151]	0.232
Comorbidities						
Diabetes mellitus		104 (58.8)	73 (41.2)	177 (100)	0.096 [0.011-0.191]	0.043
Hypertension		141 (62.7)	84 (37.3)	225 (100)	0.037 [0.002-0.132]	0.438
CKD		63 (68.5)	29 (31.5)	92 (100)	0.044 [0.003-0.130]	0.358
HF		41 (78.8)	11 (21.2)	52 (100)	0.110 [0.026-0.190]	0.021

Table 3 (continued)

Variables	Exitus (n=284)	Survivor (n=157)	Total (N=441)	Effect size (95% CI)	p value
CAD	70 (70.7)	29 (29.3)	99 (100)	0.071 [0.005-0.155]	0.155
COPD	30 (73.2)	11 (26.8)	41 (100)	0.059 [0.003-0.145]	0.218
Malignancy	76 (88.4)	10 (11.6)	86 (100)	0.246 [0.176-0.319]	<0.001
Cerebrovascular	34 (72.3)	13 (27.7)	47 (100)	0.057 [0.002-0.143]	0.229
Laboratory results					
Hemoglobin (g/dL)	8.86±1.97	9.68±2.23	9.14±2.1	0.390 [0.190-0.590]	<0.001
MCV (fL)	85.35±9.43	85.8±9.97	85.49±9.59	0.046 [-0.102-0.194]	0.638
CRP (mg/dL)	12.54±9.09	13.91±12.76	13.08±10.55	0.142 [-0.006-0.290]	0.242
Ferritin (ng/ml)	447.5 (4.8-4000)	283 (2-13980)	402 (2-40)	0.145 [0.048-0.238]	0.002
Leucocytes (/mm ⁶)	10 (0.2-102)	10.6 (0.5-80.2)	10.3 (0.2-102)	0.091 [-0.003-0.183]	0.056
Neutrophils (/mm ⁶)	7.3 (0-37)	7.9 (0-35)	7.5 (0-37)	0.093 [-0.001-0.185]	0.053
LYM (/mm ⁶)	1.2 (0-87)	1.4 (0-74.7)	1.2 (0-87.3)	0.110 [0.017-0.202]	0.021
NLR	5.5 (0.02-90)	5.83(0.01-116)	5.7 (0.01-116)	0.018 [-0.076-0.112]	0.707
PLT (/mm ⁶)	253 (2.2-1004)	283 (16.8-764)	263 (2.2-1004)	0.086 [-0.008-0.178]	0.093

CKD: Chronic kidney disease; HF: Heart failure; CAD: Coronary artery disease; COPD: Chronic obstructive pulmonary disease; MCV: Mean corpuscular volume; CRP: C-reactive protein; Lym: Lymphocyte; NLR: Neutrophil-to-lymphocyte ratio PLT: Platelet Data were given as n (%) or median (minimum-maximum), or mean ± SD.

Effect sizes were calculated using Cohen's d for independent samples t-tests, rank-biserial correlation for Mann-Whitney U tests, and Cramér's V for chi-square tests.

DISCUSSION

The findings of this study revealed that the average age of hospitalized patients with significantly elevated ESR was high, with nearly three-quarters being 65 years or older. The leading etiologic causes, in descending order, were infectious diseases, malignancies, undiagnosed conditions, renal diseases, other causes, and rheumatologic diseases. The most common comorbidities included hypertension, diabetes mellitus, and coronary artery disease. Although in-hospital mortality rates were low, a notably high mortality rate was observed from discharge to the data collection date. Mortality was most prevalent among patients aged 65 and older, with the highest rates occurring in those with malignancies.

ESR is a well-established laboratory test used in clinical diagnosis and monitoring. Although moderate elevations can occasionally occur without an obvious cause, our study confirmed that extreme ESR levels, particularly those exceeding 100 mm/hour, are mostly associated with an identifiable underlying disease, providing important clinical insights for physicians. A 1967 study by Zacharski and colleagues was one of the first to report that 58% of patients with elevated ESR had malignancies, which influenced clinicians to conduct extensive diagnostic investigations when faced with high ESR levels [5]. However, it is important

to consider that this study was conducted in a referral center, and subsequent studies have not consistently shown malignancies to be the most frequent cause [8]. In fact, in our study, only one in three patients had malignancies. These findings suggest that while extreme ESR elevations should be taken seriously, it is prudent to first screen for benign causes before pursuing more extensive diagnostic evaluations.

One of the most comprehensive studies on excessive ESR elevation, conducted by Daniels *et al.* with 4807 patients, found that the underlying cause was infectious diseases in 40%, inflammatory diseases in 38%, and malignancies in 36% of patients with ESR >100 mm/hour [6]. Similarly, in a study by Cengiz *et al.* of 110 geriatric patients with ESR ≥80 mm/hour, infectious diseases were the most common cause (48.2%), followed by oncological diseases (17.3%) [9]. Yousuf and colleagues, in a study of 508 patients with ESR ≥100 mm/hour, also found infectious diseases to be the most frequent cause (38.6%) [10]. Despite variations in results due to study design differences, the two most common causes across these studies align with our findings: infectious diseases and malignancies.

In our study, the most frequent infectious diseases were pneumonia (40%), and urinary tract infections (23.3%). Similarly, Daniels and colleagues identified pneumonia as the most common cause,

followed by cellulitis, bacteremia, abscesses, and osteomyelitis [6]. However, the etiology of elevated ESR, particularly for infectious causes, can vary significantly by geographic region. For example, Levay *et al.*, in a study conducted at a tertiary hospital in South Africa, identified *Mycobacterium tuberculosis* as the most common infective organism, influenced by the high prevalence of HIV-positive patients in their cohort [11]. This highlights the impact of regional factors on the distribution of ESR etiologies.

Malignancies ranked second in etiological distribution in our study. In a study by Uguz *et al.* involving 205 patients over 65 years of age, the malignancies most associated with marked ESR elevations were acute myeloid leukemia, multiple myeloma, and lung cancer [12]. Although the frequency of diseases causing extremely elevated ESR varies across the literature, multiple myeloma and acute leukemias are among the most common. However, our findings, along with similar studies, suggest that in cases of extreme ESR elevations, solid tumors should also be considered as potential underlying causes, alongside hematologic malignancies.

Studies examining mortality in patients with elevated ESR levels show that very high ESR is associated with increased mortality. In the prospective, population-based Rotterdam cohort study (1990–2014), which included 5,226 participants with a mean age of 70.3 years, a 14.9-year follow-up revealed that individuals with baseline ESR levels of 20–50 mm/hour had a 27% higher risk of mortality, while those with ESR levels exceeding 50 mm/hour faced an 89% increased risk. These findings suggest that even moderate ESR elevations serve as an independent prognostic factor for mortality [13]. In our study, although the in-hospital mortality rate was low (3.6%), we observed a high post-discharge mortality rate of 63.4%, consistent with existing literature. The highest mortality was observed in the malignancy group, as expected. Since only patients with ESR ≥ 100 mm/hour were included in this study and no control group was used, we cannot conclude that elevated ESR is an independent prognostic factor

for mortality. However, based on our findings and previous research, we believe that severe underlying diseases and comorbidities contribute to ESR values exceeding 100 mm/hour, which in turn is associated with high mortality.

Patients with ESR levels between 100–120 mm/hour were found to have higher hemoglobin levels compared to those with ESR >120 mm/hour, in line with the known inverse relationship between hemoglobin and ESR [14]. CRP and NLR levels were higher in the infectious diseases group, consistent with the literature [15,16].

The retrospective and single-center design, the inclusion of only patients with ESR ≥ 100 mm/hour, and the absence of a control group are the main limitations of this study. Accepting the most likely diagnosis that could cause elevated ESR as the final diagnosis is another limitation, which could introduce bias due to potential inaccuracies or misattributions in diagnosis. The retrospective nature of the study may also result in data completeness issues, as some clinical or laboratory data may be missing or inconsistently recorded. Furthermore, although most patients were observed to have died post-discharge, we were unable to access cause-of-death information from the National Database, and thus no causal relationship between elevated ESR and mortality can be inferred from this study. Finally, it is worth noting that the etiology of elevated ESR can vary significantly across geographic regions due to differences in the prevalence of infectious, inflammatory, or malignant diseases, which may limit the generalizability of our findings to other populations.

CONCLUSIONS

The results of this study suggest that the detection of extremely elevated ESR values in hospitalized patients, particularly the elderly, may indicate the presence of serious underlying conditions. Infectious diseases and malignancies should be considered as primary causes.

Introducere: Scopul studiului a fost de a evalua distribuția etiologică a pacienților cu o viteză de sedimentare eritrocitară (VSH) peste 100 mm/oră și de a evalua diferențele demografice, de comorbiditate, caracteristicile de laborator și aspectele clinice.

Metode: Acest studiu clinic observațional retrospectiv a inclus pacienți cu vârsta peste 18 ani care au fost internați în clinica de medicină internă între 1 mai 2015 și 1 iunie 2021 și au avut valori VSH peste 100 mm/h. Datele demografice, comorbiditățile, parametrii de laborator, studiile imagistice, constatările histopatologice, datele microbiologice și serologice,

împreună cu mortalitatea în spital și după externare, au fost colectate din baza de date electronică a spitalului. Doi clinicieni independenți au evaluat datele pentru a identifica diagnostichele asociate cu VSH crescut. Pacienții au fost împărțiți în șase categorii pe baza diagnosticului cel mai probabil.

Rezultate: Studiul a inclus 441 de pacienți, dintre care 52,6% erau femei, iar vârsta medie a fost de 72,6 ani. Distribuția etiologică a fost următoarea: boli infecțioase (34%), afecțiuni maligne (31,5%), cazuri nediagnosticate (15,9%), boli renale (9,8%), alte cauze (5%) și boli reumatologice (3,8%). Distribuțiile etiologice nu au fost diferite în funcție de sex, vârstă sau intervale de VSH. Rata mortalității în spital a fost de 3,6%, iar rata globală a mortalității de la spitalizare până la data colectării datelor a fost de 64,4%. Mortalitatea a fost mai mare la pacienții cu tumori maligne (81,3%) comparativ cu alte etiologii ($p < 0,001$). Pacienții care au decedat au avut o vârstă medie mai mare, niveluri de feritină, diabet zaharat, insuficiență cardiacă sau malignitate și niveluri mai scăzute de hemoglobină și limfocite în comparație cu supraviețuitorii ($p < 0,05$ pentru toți).

Concluzie: Majoritatea pacienților cu o VSH peste 100 mm/oră au avut afecțiuni medicale subiacente semnificative, bolile infecțioase și malignitățile cuprinzând două treimi din cazuri.

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REFERENCES

- PIVA E., SANZARI MC., SERVIDIO G., PLEBANI M. Length of sedimentation reaction in undiluted blood (erythrocyte sedimentation rate): variations with sex and age and reference limits. *Clin Chem Lab Med.* 2001;**39**(5):451–454.
- LAPIĆ I., PADOAN A., BOZZATO D., PLEBANI M. Erythrocyte Sedimentation Rate and C-Reactive Protein in Acute Inflammation. *Am J Clin Pathol.* 2020;**153**(1):14–29.
- GRZYBOWSKI A., SAK J. A short history of the discovery of the erythrocyte sedimentation rate. *International Journal of Laboratory Hematology.* 2012;**34**(4):442–444.
- FINCHER, RM E., Page MI. Clinical significance of extreme elevation of the erythrocyte sedimentation rate. *Arch Intern Med.* 1986. **146**(8): 1581–1583.
- ZACHARSKI LR., KYLE RA. Significance of extreme elevation of erythrocyte sedimentation rate. *JAMA.* 1967;**202**(4):264–6.
- DANIELS LM., TOSH PK., FIALA JA., SCHLECK CD., MANDREKAR JN., BECKMAN TJ. Extremely elevated erythrocyte sedimentation rates: associations with patients' diagnoses, demographic characteristics, and comorbidities. *Mayo Clin Proc.* 2017;**92**(11):1636–1643.
- BOCHEN K., KRASOWSKA A., MILANIUK S., KULCZYŃSKA M., PRYSTUPA A., DZIDA G. Erythrocyte sedimentation rate – an old marker with new applications. *J Pre Clin Clin Res.* 2011;**5**(2):50–55.
- WYLER DJ. Diagnostic implications of markedly elevated erythrocyte sedimentation rate: a reevaluation. *South Med J.* 1977;**70**(12):1428–30.
- CENGİZ OK., ESMEN SE., VARLI M., YALCIN, A., ARAS S., ATMIS V., et al. Markedly elevated erythrocyte sedimentation rate in older adults. How significant clinically? *Eur Geriatr Med.* 2013;**4**(1):28–31.
- YOUSUF M., AKHTER J., AL-KHAIRY K., AL-SAADAN MA., BIN-SALIH S. Extremely elevated erythrocyte sedimentation rate: etiology at a tertiary care center in Saudi Arabia. *Saudi Med J.* 2010;**31**(11):1227–31.
- Levay PF., Retief JH. Causes of high erythrocyte sedimentation rates in an inpatient population. *S Afr Med J.* 2005;**95**(1):45–6.
- UGUZ N., CELIK T., TORUN GUNGOR O., BAL C., BAKIR F., KAZANCI F., et al. Causes of high erythrocyte sedimentation rates in elderly patients. *Turk Bul Hyg Exp Biology,* 2013;**70**(3): 135–140.
- FEST J., RUITER R., MOOIJAAART SP., IKRAM MA., VAN EIJCK CHJ., STRICKER BH. Erythrocyte sedimentation rate as an independent prognostic marker for mortality: a prospective population-based cohort study. *J Intern Med.* 2019;**285**(3):341–348.

14. KANFER EJ., NICOL BA. *Haemoglobin concentration and erythrocyte sedimentation rate in primary care patients*. J R Soc Med. 1997;**90**(1):16–8.
15. HEIKKILÄ K., EBRAHIM S., LAWLOR DA. *A systematic review of the association between circulating concentrations of C reactive protein and cancer*. J Epidemiol Community Health. 2007;**61**(9):824–33.
16. HUANG Z., FU Z., HUANG W., HUANG K. *Prognostic value of neutrophil-to-lymphocyte ratio in sepsis: a meta-analysis*. Am J Emerg Med. 2020;**38**(3):641–7.

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