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Association between Hematology Indices as Early Markers and Urinary Tract Infection, Septicemia, Pneumonia, and Diabetic Foot Infection

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ABSTRACT

Backgrounds: Infectious diseases are one of the main leading causes of morbidity and mortality worldwide. Therefore, diagnosis and treatment of infectious diseases are very important. Infection affects some blood indices that could be used as diagnostic markers. Therefore, this study aimed to compare blood parameters in four important and prevalent infectious diseases.
Materials & Methods: In this study, 202 out of 892 patients with a final diagnosis of UTI (urinary tract infection), septicemia, pneumonia, or diabetic foot infection were evaluated; they were hospitalized in Rasoul Akram hospital in Iran from August 2017 to February 2018. Patients' demographic and laboratory data, such as RDW (red cell distribution width), PDW (platelet distribution width), RBC (red blood cell), CRP (C-reactive protein), ESR (erythrocyte sedimentation rate), and, WBC (white blood cells), were evaluated.
Findings: This study results showed that mortality rate in sepsis cases was higher than in other cases (42.1%). Changes in blood parameters such as RDW, PDW, and EDR levels as well as monocyte, basophil, and eosinophil counts were significant among patients with different infectious diseases, while there was no significant difference in terms of changes in some blood parameters, such as WBC, neutrophil, and lymphocyte counts and CRP level between patients with different infectious diseases. For statistical analysis, one-way ANOVA and LSD post hoc tests were used.
Conclusion: According to this study results, it was found that the range of blood parameters varies in different types of infectious diseases. Therefore, the physician could employ routine blood parameters along with other diagnostic factors to more accurately diagnose the type of infection and prescribe more appropriate antibiotics.

Keywords: RDW, PDW, UTI, Septicemia, Pneumonia, Diabetic foot infection.

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Introduction

Infectious diseases are one of the main leading causes of morbidity and mortality worldwide [1].

Diagnosis and treatment of infectious diseases are very important, especially their acute types [1, 2]. Also, accurate diagnosis is the first step in the treatment of infectious diseases. Therefore, prompt, easy, and inexpensive diagnosis is important for physicians and patients [3, 4]. Early diagnosis of infectious diseases is essential due to the possibility of rapid transmission, the development of nosocomial infections, and the high cost of antimicrobial therapies. Therefore, it is important to provide rapid and accurate diagnostic methods for infectious diseases [4-6]. Common infections in hospitals, requiring serious attention include urinary tract infection (UTI), septicemia, pneumonia, and diabetic foot infection, because serious illnesses are associated with severe complications and mortality [2]. Also, these four groups of infectious diseases are among the most common diseases in different societies [2, 7, 8]. One of the main concerns of infectious disease physicians is the early diagnosis of infectious diseases. Since microbiological results are not available for several days due to laboratory limitations, initial treatment of the infection is often experimental and is guided by clinical manifestations [9, 10]. On the other hand, the prognosis of many infectious diseases is similar, such as increased white blood cells, fever, restlessness, decreased level of consciousness, increased pulse, increased heart rate, and so on [11]. To select the initial antibiotics, physicians consider those bacteria that are more likely to be present, depending on the location of the infection [12]. Because in critically ill patients, the doctor usually does not wait for the laboratory results and starts the initial prescription of antibiotics [12].

If the source of bacteria or the site of infection is not known, several initial antibiotics are usually given until more accurate culture results are obtained, and alternative antibiotics are prescribed. If the source of infection is more specific, the correct choice of antibiotic is more likely to be faster [12]. The issue of diagnostic markers has been hotly debated for several years. In this regard, blood indicators such as RDW (red cell distribution width) and PDW (platelet distribution width) have been attractive indicators for researchers. However, their roles in the diagnosis and management of diseases are not known completely [13].

Studies have shown that inflammation and infection affect some blood indices [7, 8, 14] that could be used by physicians as diagnostic markers in diagnosing infectious diseases, including RDW, PDW, ESR (erythrocyte sedimentation rate), and CRP (C-reactive protein) [15, 16]. To diagnose common infections, immune cells are counted, especially neutrophils [17, 18]. These parameters could be estimated and evaluated by a complete blood count [14, 15] via a simple blood test, which is usually done routinely at the time of admission for patients, and no more specialized tests are needed [8]. The gold standard approach to diagnosing sepsis is blood culture. Although the report of blood culture test results takes 2-5 days, other markers could be used to quickly diagnose sepsis and decide on antibiotic treatment that should be started early [15, 19]. In the evaluation of many blood and platelet parameters assessed in this study, no additional costs are imposed on patients, because they are routinely determined by a complete blood count (CBC) test [20]. As mentioned earlier, given that the source of infection is very effective in choosing the type of initial antibiotic, comparing blood parameters in infectious diseases could help us find the source of infection and subsequently select the appropriate antibiotic. As far as we know, no research project has studied

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blood parameters simultaneously in several infectious diseases so far.

Objectives: The aim of this study was to compare blood indices in four important and prevalent infectious diseases, including urinary tract infection (UTI), septicemia, pneumonia, and diabetic foot infection. It is hoped that this study could be a good start for further similar studies to help physicians in diagnosing different types of infectious diseases.

Materials and Methods

In this study, 892 patients with a final diagnosis of urinary tract infection, septicemia, pneumonia, or diabetic foot infection were evaluated; they were hospitalized in Rasoul Akram hospital in Iran from August 2017 to February 2018. Questionnaires containing questions designed to collect patients' demographic, laboratory, and clinical information were prepared and made available to patients. Patients' demographic information was completed by the patients themselves. Also, information about laboratory results was obtained from Rasoul Akram hospital laboratory. Data were analyzed using SPSS software Version 20. Patients were assured about the confidentiality of the information they provided. In this study, patients with a history of the following diseases, affecting some blood indices, were excluded from the study, such as hypertension, liver disorders, kidney problems, diabetes, iron-deficiency anemia, hemoglobin-deficiency anemia, thalassemia minor, anisocytosis, decreased blood platelets, enlarged spleen, and secondary infection. By eliminating patients not meeting the study inclusion criteria, 202 patients were eventually evaluated. Afterwards blood indices including RDW, PDW, RBC (red blood cell), CRP, ESR, WBC (white blood cell), lymphocytes, monocytes, and neutrophils were evaluated. Also, for statistical analysis, one-way ANOVA and LSD post hoc tests were used to compare differences between groups.

Findings

In this study, more than 77% of patients with infectious diseases, including urinary tract infection, septicemia, pneumonia, or diabetic foot infection, were excluded from the study due to not meeting the study inclusion criteria. Therefore, 202 files related to patients with infectious diseases mentioned above were evaluated. Statistical analyses were performed, and the results were presented in tables. Demographic information including gender and age as well as information about patients' condition are presented in Tables 1 and 2. As shown in Table 1, the number of patients in five different age groups was evaluated (0-2, 3-20, 21-40, 41-60, 61<).

Descriptive statistics of patients' gender and condition (improved / dead) are presented in Table 2. Total number of patients with urinary tract infection, pneumonia, septicemia, and diabetic foot infection was 74, 43, 38, and 46 cases, respectively.

In the following sections, blood indices including RDW, PDW, CRP, and ESR levels as well as WBC, lymphocyte, monocyte, and neutrophil counts were evaluated in patients with infectious diseases mentioned above, and the results are presented in Table 3. Statistical analysis was performed by employing one-way ANOVA and LSD post hoc tests to compare differences between groups. As shown in Table 3, the amount of measured parameters (neutrophil, WBC, and monocyte counts as well as RDW, PDW, and CRP levels) was higher in patients in the group of septicemia than in patients in the other three groups of infectious diseases. After performing one-way ANOVA analysis, comparison between different groups was performed using LSD post hoc test, and then the *p* value was calculated in each group for

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all blood parameters.

RDW: As shown in Table 3, the amount of RDW was significantly higher in the septicemia group than in the UTI (p=.000), diabetic wound (p=.001), and pneumonia groups (p=.035). Also, RDW level was higher in the UTI group (p=.05) compared to the diabetic wound group. In addition, the amount of RDW in the pneumonia group was higher than in the diabetic wound group (p=.002).

PDW: As shown in Table 3, there was a significant difference between the septicemia and pneumonia groups (p=.01) regarding the amount of PDW, which was higher in the septicemia group than in the pneumonia group.

ESR: The amount of ESR was significantly higher in the diabetic wound group compared to the UTI (p=.002) and pneumonia (p=.002) groups (Table 3).

Monocyte count: According to the results presented in Table 3, the amount of monocytes in the septicemia group was higher than in the pneumonia group (p=.002). Also, monocyte count was significantly higher in the diabetic wound group (p=.006) compared to the pneumonia group.

Basophil count: There was a significant difference regarding the amount of basophils between the UTI and pneumonia groups, which was higher in the UTI group (p=.001). Also, the amount of basophils was significantly higher in the diabetic wound group compared to the septicemia (p=.03) and pneumonia (p=.00) groups (Table 3).

Eosinophil count: As shown in Table 3, there was a significant difference between the UTI and septicemia groups (p=.04) regarding the amount of eosinophils, which was higher in the UTI group than in the septicemia group. Also, the amount of eosinophils in the pneumonia group was higher than in the septicemia group (p=.02). Furthermore, eosinophil count in the diabetic wound group was higher than in the septicemia group (p=.02).

Discussion

In this study, a significant number of patients (77%) were excluded from the study based on the inclusion and exclusion criteria, which was mostly due to the prevalence of the following diseases, affecting some blood indices, among the study population, including hypertension, liver disorders, kidney problems, diabetes, iron-deficiency anemia, hemoglobin-deficiency anemia, thalassemia minor, anisocytosis, decreased blood platelets, enlarged spleen, and secondary infection. The main advantage of the parameters assessed in this study is that they could be easily evaluated in emergency conditions [7]. In this study, most patients with infectious diseases, including urinary tract infection, septicemia, pneumonia, or diabetic foot infection, were in the age range of 61 years or older. In a study by Esme et al. (2019), the prevalence rate of infectious diseases, including respiratory infections, urinary tract infections, bacteremia, and sepsis-related infections, was higher in the elderly, which is consistent with the present study result [21]. In the current study, in terms of patients' gender, the highest prevalence rate of urinary tract infections was observed in women. UTIs have been found to be highly prevalent in women and affect them in all age groups regardless of socioeconomic status and education level [22]. This study showed that the mortality rate in sepsis cases was higher than in other cases (42.1%). A review study examining discharge data over a 22-year period and identifying 10 million sepsis cases in the USA in 2018 showed that there was an average of 13% increase in the incidence of sepsis annually. Also, studies have reported different mortality rate for sepsis, but what seems to be common in these studies is the high mortality rate in sepsis cases, which has been reported to be

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Table 1) Descriptive report of patients' age

Age Range (Year)	Septicemia N (%)	Pneumonia N (%)	Urinary Tract Infection N (%)	Diabetic Foot Infection N (%)
0-2	10(26.3)	9(20.4)	15(20.3)	0
3-20	0	4(9.1)	10(13.5)	0
21-40	2(5.3)	5(11.4)	6(8.1)	2(4.3)
41-60	6(15.8)	8(18.2)	5(6.8)	18(39.1)
61<	20(52.6)	18(40.9)	38(51.3)	26(56.5)
total	38(100)	44(100)	74(100)	46(100)

Table 2) Descriptive report of patients' gender and condition (improved / dead)

Disease	Patient's Condition		Gender	
	Improved N (%)	Dead N (%)	Men N (%)	Women N (%)
Urinary tract infection	2(2.7)	72(97.3)	48(64.9)	26(35.1)
Pneumonia	4(9.1)	40(90.9)	16(36.4)	28(63.6)
Septicemia	16(42.1)	22(57.9)	22(57.9)	16(42.1)
Diabetic foot infection	1(2.2)	45(97.8)	18(39.1)q	28(60.9)

up to 74% [23-25].

Since the current study considered both the pediatric and adult populations, leukocytosis was defined as a WBC count of >10,000 cells/mm^3, although in the pediatric population, leukocytosis is usually defined as a WBC count of >15,000 cells/mm^3 [17, 26]. In the current study, leukocytosis was observed in the first laboratory test report of 42% of patients with urinary tract infection, septicemia, pneumonia, or diabetic foot infection. Therefore, due to the high white blood cell count in infected patients, there was no significant difference regarding the number of white blood cells between the four groups of infectious diseases studied. Chaudhary et al. (2016) found that 34.1% of patients with urinary tract infection had a high WBC count [2]. In another study by Furer et al. (2011), about 74.4% of all patients with bacteremic pneumococcal pneumonia had leukocytosis [17]. The difference in the prevalence rate of leukocytosis could be due to the difference in age, gender, type of infectious disease, considering a WBC count of >10,000 cells/mm^3 as leukocytosis, or other items.

Laboratory findings associated with urinary tract infections usually show an increase in leukocyte count, neutrophil count, red blood cell deposition, and ESR or CRP levels [27, 28]. In infectious diseases, the number of monocytes increases because macrophages and monocytes play an important role in the secretion of inflammatory cytokines and are involved in all stages of inflammation and

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Table 3) Assessment of blood indices in patients with urinary tract infections, pneumonia, septicemia, and diabetic foot infection

Variable	Urinary Tract Infection (UTI) Mean ± SD	Septicemia Mean ± SD	Diabetic Wound Mean ± SD	Pneumonia Mean ± SD	df	F	Sig.
RDW	14.53±2.37	16.43±2.54	13.73±1.54	15.19±2.11	4	6.40	0.00*
RDW	11.83±2.4	12.53±2.18	11.72±1.69	11.09±1.4	4	1.70	0.048*
RDW	3.97±0.61	3.91±0.77	4.04±0.99	4.05±0.74	4	0.81	0.51
CRP	36.85±34.69	50.86±36.12	34.18±34.13	43.14±36.13	4	1.37	0.24
ESR	43.26±26.61	47.82±30.19	64.70±31.51	39.71±25.62	4	3.53	0.009*
WBC count[a] ($\times 10^3/mm^3$)[b]	10.08±4.67	10.39±3.89	9.37±3.66	9.99±3.89	4	0.44	0.77
Neutrophil count (%)	62.28±19.57	67.57±16.89	65.73±10.83	66.93±16.79	4	1.31	0.26
Lymphocyte count (%)	27.21±16.72	22.91±13.60	24.25±9.87	22.21±14.57	4	1.35	2.52
Monocyte count (%)	6.67±6.09	8.07±2.87	7.92±2.90	4.99±3.66	4	2.48	0.046*
Basophil count (%)	2.22±1.79	1.78±1.52	2.83±1.84	1.12±1.32	4	5.43	0.00*
Eosinophil count (%)	2.8±1.91	1.8±0.81	3.05±1.9	3.02±2.24	4	2.11	0.048*

a: Low WBC (<$4x10^3/mm^3$): 1.5%, normal WBC ($4x10^3/mm^3$-$10x10^3/mm^3$): 56.5%, high WBC (>$10x10^3/mm^3$): 42%
b: WBC range in all patients ($\times 10^3/mm^3$): 2.3 -25.6
*: Statistically significant

infection [29]. In this study, the amount of monocytes in the septicemia (p=.022) and diabetic wound (p=.006) groups was higher than in the pneumonia group. Also, this study indicated that basophil and eosinophil counts were significantly different in different groups of infectious diseases; however, in a study conducted by Tartar and Balin in 2019, no significant difference was observed between bacteremic and non-bacteremic patients regarding WBC and neutrophil counts [7]. In the present study, changes in parameters such as RDW, PDW, and ESR levels as well as monocyte, basophil, and eosinophil counts were significant among patients with different infectious diseases such as urinary tract infection, septicemia, pneumonia, and diabetic foot

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infection, while there was no significant difference in terms of changes in some parameters such as WBC, neutrophil, and lymphocyte counts and CRP level between patients with different infectious diseases mentioned above. It is worth noting that WBC, neutrophil, and lymphocyte counts could be considered as a good indicator for comparison between healthy and infected persons, but could not be considered as a good indicator for comparison between patients with different types of infections evaluated in this study, including urinary tract infection, septicemia, pneumonia, and diabetic foot infection.

In addition, changes in RDW are extremely associated with changes in inflammatory markers such as ESR and CRP levels. Therefore, changes in RDW during treatment may be associated with the outcomes of inflammatory diseases and thus could be used as a marker of the progression of inflammatory diseases[6, 30].

The present study findings indicated significant differences between different infectious diseases in terms RDW and PDW parameters; for example, the level of PDW in the septicemia group was significantly higher than in the pneumonia group (p=.01). In general, the present study results revealed that the amount of measured parameters (WBC, neutrophil, and monocyte counts as well as RDW, PDW, and CRP levels) was higher in patients in the group of septicemia than in patients in the other three groups of infectious diseases.

Platelets also play an important role in the pathogenesis of infectious/ inflammatory disorders. Platelet count and mean platelet volume (MPV) have been studied as inflammatory markers associated with disease activity [27,28]. Studies have shown that there is a significant relationship between a PDW of 13 ≥and the presence of infection in patients [31]. Also, Aktar et al. (2016) showed that RDW and PDW levels in patients with infectious diseases were significantly higher than in patients in the non-infectious group [32]. Also, in a study in 2018, it was found that PDW level was significantly higher in patients with diabetic foot infection than in patients without diabetic foot infection [8]. Furthermore, in the present study, RDW level in the septicemia group was higher than in the UTI (p=.001), pneumonia (p=.035), and diabetic foot infection (p=.00) groups. Studies on sepsis have shown that RDW level increases in patients within 72 hours after hospitalization. Thus, RDW could be considered as a promising prognostic indicator for patients with severe sepsis [33]. Also, in a study by Mohan et al. (2019), RDW and PDW were identified as sepsis biomarkers [15]. Another study in 2019 showed that RDW could be used as the most sensitive hematology marker for predicting infant mortality due to sepsis [17]. In addition, studies have shown that RDW is associated with the outcomes of community-acquired pneumonia[34].

Conclusion

It seems that the range of blood parameters varies in different types of infectious diseases. The present study showed that the amount of some parameters such as WBC, neutrophil, and monocyte counts as well as RDW, PDW, and CRP levels was higher in patients in the group of septicemia than in patients in the other three groups of infectious diseases. Due to the differences in the range of typical blood parameters in different types of infectious diseases, the doctor could employ routine blood parameters along with other diagnostic indicators to more accurately diagnose the type of infection and prescribe more appropriate antibiotics. It is recommended that more extensive studies be performed on blood indices in different types of infectious

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diseases with larger statistical populations so that blood parameters could be used as important diagnostic biomarkers along with other diagnostic factors.

Abbreviations

UTI: urinary tract infection
RDW: red cell distribution width
PDW: platelet distribution width
ESR: erythrocyte sedimentation rate
CRP: C-reactive protein
RBC: red blood cell
WBC: white blood cell

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Conflicts of interest: The authors declare they have no conflict of interests.

Authors Contribution: Conceptualization: AM and SSM ; data curation: NAP and SF; formal analysis: SSM; funding acquisition: AM; investigation: NAP and SRK; methodology: AM, SSM and SRK; project administration: AM and SSM; resources: SSM and SF; software: SSM, SF and SRK; supervision: AM and SSM; writing of the original draft: SSM and NAP; writing-review and editing: AM and SSM.

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