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Original paper

The Diagnostic Value of Procalcitonin and Complete Blood Count Markers in Patients with Community-Acquired Pneumonia and Sepsis

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Abstract

Background: Community-acquired pneumonia (CAP) is a type of lung infection that people can acquire outside of the hospital. One of the most serious complications of bacterial pneumonia is sepsis. It is a life-threatening condition caused by the body's response to an infection**.** The aim of this research is to find potential diagnostic and prognostic markers for community-acquired pneumonia and sepsis. Specifically, the study examined the diagnostic value of procalcitonin (PCT) and complete blood count (CBC) markers.

Methods: One hundred twenty participants were selected and divided into 20 patients with sepsis due to CAP, 60 patients with bacterial CAP, and 40 control patients. All participants were between the ages of 23-95 years old. Blood samples were collected from both male and female patients. All samples were diagnosed by doctors specializing in respiratory and chest diseases and internal medicine. The study was conducted at Imam Al-Sadiq Hospital in Babylon Governorate and Imam Al-Hussein Medical City in Kerbela Governorate from December 2022 to June 2023.

Results: The results showed significant differences in PCT, white blood cells (WBC), lymphocytes (LYM), monocyte, granulocyte (GRA), haematocrit, platelet-to-lymphocyte ratio (PLR), and neutrophil-to-lymphocyte ratio (NLR). Haemoglobin also showed significant differences, except for platelets, which did not show significant differences. The study found that PCT, WBC, GRA, NLR, and PLR were valuable markers for diagnosing patients with CAP and sepsis due to CAP. Other CBC parameters were found to be less useful.

Conclusion: The study highlights the importance of using PCT and CBC markers to diagnose and manage patients with community-acquired pneumonia and sepsis.

Keywords: Community Acquired Pneumonia, Complete Blood Count, Procalcitonin, Sepsis.

Introduction

Lower respiratory tract infections (LRTIs), including pneumonia, are a serious health issue. They refer to acute inflammation resulting from infections within the lungs, which can be caused by several infectious factors, including bacteria, fungi, viruses or parasites. These infections can occur in one or both lungs and kill more than two million people worldwide, with most of them being children under five years of age or people over 70 years old [1]. Pneumonia is classified into four categories: community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), ventilation-associated pneumonia (VAP), and aspiration pneumonia. Community-acquired pneumonia (CAP) is an acute infection of the pulmonary tissues in a patient who did not contract it from a healthcare system or within the first 48 hours after being hospitalized [2].

Depending on the severity, age, and immune system of the patient, pneumonia can have a range of effects from mild infections to fatal organ failure from sepsis [3]. Sepsis is a medical condition characterized by a dysfunctional response of the body's organs to an infection, which can be life-threatening [4]. Sepsis has been declared a worldwide health crisis by the World Health Organization

(WHO). There are 11 million sepsis fatalities and 48.9 million cases globally across 195 nations and territories. In severe cases, sepsis causes multiple organ dysfunction and death [5].

Procalcitonin (PCT) is a hormone that helps in the production of calcitonin. During bacterial infections, the level of PCT increases in response to a pro-inflammatory stimulus. However, this increase does not lead to a rise in serum calcium levels or calcitonin. In the first two days of life, there is a small physiological increase in PCT levels due to bacterial colonization of the gastrointestinal tract and endotoxin translocation through the bowel wall. Nonetheless, this increase is minor compared to that seen in bacterial infections. Additionally, non-infectious perinatal events such as maternal preeclampsia, perinatal asphyxia, and intracranial hemorrhage may also cause an increase in PCT concentrations [6].

Complete blood counts (CBC) are a simple, low-cost laboratory test that provides information about the composition of blood cells. This test is commonly used as a routine examination technique. Proper interpretation of CBC results is crucial for the early detection of various clinical conditions, which may require further laboratory and clinical analysis. These parameters have been suggested as indicators of systemic inflammation and infection. Studies have investigated the diagnostic value of blood parameters in patients with community-acquired pneumonia (CAP) and sepsis caused by CAP [7].

The significance of studying the diagnostic value of PCT and CBC markers in CAP (community-acquired pneumonia) and sepsis is to improve patient care and outcomes. Accurate and timely diagnosis of CAP and sepsis is crucial for initiating appropriate treatment strategies. By utilizing these biomarkers, healthcare professionals can make informed decisions regarding the need for antibiotics, the selection of appropriate antibiotics, and the duration of therapy. This approach helps optimize antibiotic stewardship, reduce unnecessary healthcare costs, and minimize the risk of adverse effects associated with antibiotic use. Additionally, the use of PCT and CBC markers can assist in risk stratification, predicting the severity of the infection, and identifying patients at higher risk of complications or mortality [8].

This research aimed to find potential diagnostic and prognostic markers for community-acquired pneumonia and sepsis. Specifically, the study examined the diagnostic value of procalcitonin (PCT) and complete blood count (CBC) markers

Materials and Methods

The Design and Setting.

A case-control study was conducted at Imam Al-Sadiq Hospital in Babylon Governorate and Imam Al-Hussein Medical City in Karbala Governorate by physicians specialists to diagnosis bacterial CAP based on non-culture methods including the clinical findings (e.g., fever, pulse rate, respiratory rate (SPO_2), blood pressure, purulent or hemorrhagic sputum production and/or pleural pain and shortness of breath and also by the radiological findings by X-ray and/or computed tomography scan evidence of consolidations consistent with bacterial pneumonia to diagnosis sepsis with CAP and CAP patients (9) during the period from December 2022 to June 2023. The study involved the use of Up-converting Phosphor Technology (UPT) and immunochromatography (China) for detecting sepsis due to CAP and automated hematology analyzers Sysmex XN-2000 (Japan) for obtaining CBC results.

Study participants and sampling:

In this study used 120 participants of adults of both genders (55 males and 65 females), including 20 sepsis patients due to CAP, 60 patients with bacterial CAP, and 40 healthy individuals. Each participant provided informed consent and completed a detailed questionnaire, including their name, age, gender, onset of disease, and other medical conditions. Finally, 4 mL venous blood samples were collected from all groups using disposable syringes and placed in both the gel and EDTA tubes for further analysis.

Exclusion criteria

The study did not include individuals infected with other diseases, such as cancer, kidney disease, thyroid gland diseases, chronic or immune disorders including HIV, pregnant women, and those on long-term oral corticosteroid anti-inflammatory therapy. Additionally, neonates, children, and teenagers below 18 years of age were excluded from the trial. Patients who had a history of pneumonia caused by fungal infections by culture on Sabouraud's dextrose agar and viral infections such as COVID-19 were also excluded, as well as patients with Hospital Acquired Pneumonia and Ventilations Acquired Pneumonia.

Ethics Approval and Consent to Participate

Written approval had been gained from the Ethics Committee of the Ministry of Health, Babylon Health Department, Imam Al-Sadiq Hospital Ethics (No. 1723 on 5/12/2022), and Karbala Health Department Imam Al-Hussein Medical City Ethics

(No. 3107 in 7/12/2022). Data was used for research purposes only. Information consent and Verbal from every participant were taken with detailed explanations on how to take the samples and some information about the study and its benefit for future health improvement.

Statistical Analysis

Data were collected, summarized, analyzed, and presented using the Statistical Package for the Sciences of Society (SPSS) version 26 and Graph Pad Prism 8. The level of probability was indicated as $P < 0.05$, $P < 0.01$ $P < 0.001$, and $P < 0.0001$.

Results

Table 1 presents the results of our study on patients with pneumonia. We found that the number of patients with pneumonia increased with age. The highest ratio of patients was in the age group of 41-60 years, with 21 patients (35.0%), and in the age group of 61-80 years, with 19 patients (31.70%) for patients with CAP. For sepsis patients due to CAP, the age group of 41-60 years had only 1 patient (5.0%), while the age group of 61-80 years had 13 patients (65.0%) and those over 81 had 5 patients (25.0%). We also found significant differences between the ages of patients and the control groups ($P < 0.000$). Furthermore, our study showed that there were 60 patients with CAP (30 males and 30 females), 20 patients with sepsis due to CAP (7 males and 13 females), and 40 healthy controls (18 males and 22 females). We found no significant differences between the genders ($P = 0.503$), and the demographics, vital signs, and medical history of the study population were summarized in Table 1.

Table 2 and Figure 1 reveal a significant increase ($P < 0.000$) in the mean levels of PCT for both patient groups with community-acquired pneumonia and sepsis due to community-acquired pneumonia, compared to the control group. For the community-acquired pneumonia group, the mean and standard deviation were 0.38±0.06. For sepsis due to community-acquired pneumonia, the mean and standard deviation were 9.34±13.66, while for the control group, it was 0.08±0.06. Additionally, Table 2 shows that the WBC levels in community-acquired pneumonia and sepsis due to community-acquired pneumonia groups increased significantly compared to the control group. The mean and standard deviation of the three groups were 9.45±4.69, 14.70±7.29, and 6.90±1.16, respectively ($P<0.000$). The results also show a significant decrease ($P < 0.000$) in the lymphocyte count for community-acquired pneumonia and sepsis due to community-acquired pneumonia groups compared to the control group.

Table 1. The Demographics, vital signs, and medical history of the study population.

Variable		Community Acquired Pneumonia	Sepsis and Community Acquired Pneumonia	Control	P-value
Demographics (NO. (%))					
Age	21-40	16 (26.7)	1(5.0)	10(25.0)	0.000***
	41-60	21(35.0)	1(5.0)	20(50.0)	
	61-80	19(31.7)	13(65.0)	10(25.0)	
	>80	4(6.6)	5(25.0)	0(0.0)	
Gender	Males	30(50.0)	7(35.0)	18(45.0)	0.503ns
	Females	30(50.0)	13(55.0)	22(55.0)	
Vital Signs					
Pulse Rate	Low	2(3.3)	0(0.0)	0(0.0)	0.000***
	Normal	49(81.7)	10(50.0)	40(100.0)	
	High	9(15.0)	10(50.0)	0(0.0)	
Respiratory Rate	Low	22(36.7)	14(70.0)	0(0.0)	0.000***
	Normal	38(63.3)	6(30.0)	40(100.0)	
Blood Pressure	Low	8(13.3)	0(0.0)	0(0.0)	0.000***
	Normal	15(25.0)	17(85.0)	40(100.0)	
	High	37(61.7)	3(15.0)	0(0.0)	
Shortness of Breath	No	2(3.3)	1(5.0)	40(100.0)	0.000***
	Yes	58(96.7)	19(95.0)	0(0.0)	
Fever	No	0(0.0)	0(0.0)	40(100.0)	0.000***
	Yes	60(100.0)	20(100.0)	0(0.0)	
Productive Cough	No	0(0.0)	0(0.0)	0(0.0)	0.000***
	Yes	60(100.0)	20(100.0)	40(100.0)	
Chest Pain	No	1(1.7)	7(35.0)	40(100.0)	0.000***
	Yes	59(98.3)	13(65.0)	0(0.0)	
Medical History					
Diabetic Militates	No	29(48.3)	10(50.0)	40(100.0)	0.000***
	Yes	31(51.7)	10(50.0)	0(0.0)	
Hypertension	No	33(55.0)	7(35.0)	40(100.0)	0.000***
	Yes	27(45.0)	13(65.0)	0(0.0)	
Heart Diseases	No	50(83.3)	14(70.0)	40(100.0)	0.003**

***P < 0.05, **P < 0.01, *** P < 0.001**

Table 2. Comparison among study groups based on the studied parameters.

Test	Cases	Number	Mean	Standard Deviation	P-value	Least Significant Differences.
Procalcitonin	CAP	60	0.38	0.06	0.000***	0.789
	Sepsis and CAP	20	9.34	13.66		0.000
	Control	40	0.08	0.06		
	Total	120	1.77	6.43		0.000
White Blood Cell	CAP	60	9.45	4.69	0.000 ***	0.006
	CAP and Sepsis	20	14.70	7.29		0.000
	Control	40	6.90	1.16		
	Total	120	9.48	5.17		0.000
Lymphocyte	CAP	60	1.58	0.85	0.000***	0.000
	Sepsis and C.A.P	20	1.16	0.75		0.000
	Control	40	2.34	0.78		
	Total	120	1.76	0.91		0.000
Monocyte	CAP	60	0.46	0.39	0.000***	0.142
	Sepsis and C.A.P	20	1.29	0.78		0.000
	Control	40	0.59	0.17		
	Total	120	0.65	0.52		0.000
Granulocyte	CAP	60	7.27	3.78	0.000***	0.000
	Sepsis and C.A.P	20	12.63	5.76		0.000
	Control	40	4.02	0.79		
	Total	120	7.08	4.58		0.000
Lymphocyte	CAP	60	17.51	9.28	0.000***	0.000
	Sepsis and C.A.P	20	10.44	5.96		0.000
	Control	40	33.65	7.82		
	Total	120	21.71	12.11		0.001
Monocyte	CAP	60	5.11	3.16	0.000***	0.000
	Sepsis and C.A.P	20	7.33	4.12		0.059
	Control	40	8.86	1.55		
	Total	120	6.73	3.37		0.004
Granulocytes	CAP	60	77.02	10.22	0.000***	0.000
	Sepsis and C.A.P	20	83.13	8.41		0.000
	Control	40	57.42	8.91		
	Total	120	71.51	13.92		0.014
Hemoglobin	CAP	60	12.33	1.72	0.002**	0.001
	Sepsis and C.A.P	20	12.35	3.00		0.013
	Control	40	13.62	1.11		
	Total	120	12.76	1.92		0.966
Haematocrit	CAP	60	38.16	4.72	0.000***	0.000
	Sepsis and C.A.P	20	38.66	8.76		0.010
	Control	40	42.42	3.27		
	Total	120	39.66	5.54		0.715
Platelets	CAP	60	257.90	125.55	0.094 n.s	0.646
	Sepsis and C.A.P	20	197.95	96.45		0.089
	Control	40	247.90	74.48		
	Total	120	244.58	107.60		0.031
Neutrophil/Lymphocytes Ratio	CAP	60	6.30	5.18	0.000***	0.000
	Sepsis and C.A.P	20	15.93	10.77		0.000
	Control	40	1.91	.76		
	Total	120	6.44	7.35		0.000
Platelates/Lymphocytes Ratio	CAP	60	226.61	189.62	0.001**	0.001
	Sepsis and C.A.P	20	252.74	203.45		0.002
	Control	40	115.99	38.13		
	Total	120	194.09	167.55		0.526

*P < 0.05, **P < 0.01 *** P < 0.001

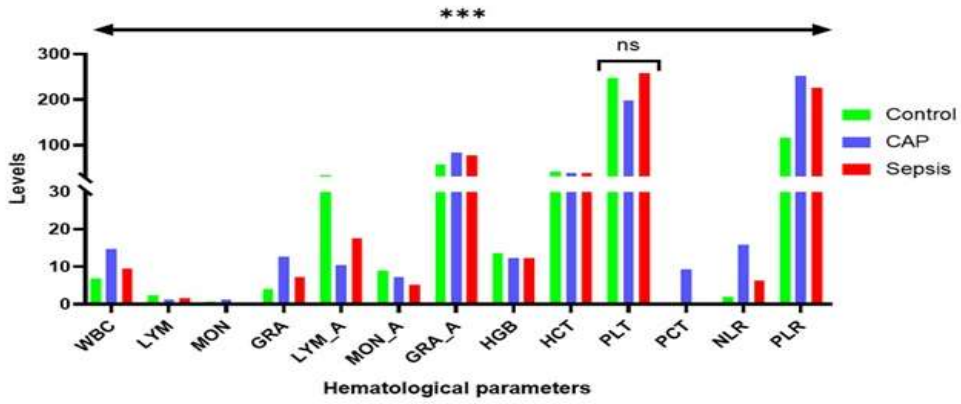

Figure 1. Comparison among study groups based on the studied of procalcitonin (PCT), white blood cell (WBC), granulocyte (GRA), monocyte (MON), haemoglobin (HGB), haematocrit (HCT), neutrophil/lymphocytes ratio (NLR), and platelet to lymphocyte ratio (PLR).

The mean and standard deviation for the community-acquired pneumonia group were 1.58±0.85, for sepsis due to community-acquired pneumonia, it was 1.16±0.75, and for the control group, it was 2.34±0.78.The monocyte counts for the community-acquired pneumonia group decreased significantly compared to the control group and sepsis due to community-acquired pneumonia patients. The mean and standard deviation were 0.46±0.39 for the community-acquired pneumonia group, 1.29±0.78 for sepsis due to community-acquired pneumonia, and 0.59±0.17 for the control group (P<0.000). Furthermore, the granulocyte count increased significantly in community-acquired pneumonia and sepsis due to community-acquired pneumonia patients compared to the control group. The mean and standard deviation were 7.27±3.78 for the community-acquired pneumonia group, 12.63±5.76 for sepsis due to community-acquired pneumonia, and 4.02±0.79 for the control group (P<0.000). The lymphocyte percentage decreased significantly in community-acquired pneumonia and sepsis due to community-acquired pneumonia groups compared to the control group. The mean and standard deviation were 17.44±9.28, 10.44±5.96, and 33.65±7.82, respectively (P < 0.000). The monocytes percentage also decreased significantly in the community acquired pneumonia and sepsis due to community acquired pneumonia groups compared to the control group. The mean and standard deviation were 5.11±3.16, 7.33±4.12, and 8.86±1.55, respectively (P<0.000). Additionally, the granulocytes percentage increased in the community acquired pneumonia, sepsis due to community acquired pneumonia, and control groups. The mean and standard deviation were 77.02±10.22, 83.13±8.41, and 57.42±8.91, respectively (P<0.000). The hemoglobin count decreased significantly in community-acquired pneumonia and sepsis due to community-acquired pneumonia groups compared to the control group. The mean and standard deviation were 12.33±1.72, 12.35±3.00, and 13.62±1.11, respectively (P<0.002). The hematocrit counts also decreased significantly in community-acquired pneumonia and sepsis due to community-acquired pneumonia groups compared to the control group. The mean and standard deviation were 38.16±4.72, 38.66±8.76, and 42.42±3.27, respectively (P < 0.000). The platelet count increased significantly in the community-acquired pneumonia group compared to the sepsis due to community-acquired pneumonia and control groups. The mean and standard deviation were 257.90±125.55 for community-acquired pneumonia, 197.95±96.45 for sepsis due to community-acquired pneumonia, and 244.58±107.60 for the control group (P 0.094 with non-significant). The neutrophil-lymphocyte ratio increased significantly in community-acquired pneumonia and sepsis due to community-acquired pneumonia groups compared to the control group. The mean and standard deviation were 6.30±5.18 for community-acquired pneumonia, 15.93±10.77 for sepsis due to community-acquired pneumonia, and 1.91±0.76 for the control group (P < 0.000). The platelets lymphocyte ratio also increased significantly in community-acquired pneumonia and sepsis due to community-acquired pneumonia groups compared to the control group. The mean and standard deviation were 226.61±189.62 for community-acquired pneumonia, 252.74±203.45 for sepsis due to community-acquired pneumonia, and 115.99±38.13 for the control group (P<0.001). Table 3 reveals an ROC curve of PCT, WBC, GRA, NLR, and PLR, where the Area Under the Curve (AUC) of PCT was 1.0 (95% CI: 1.0-1.0), and the cut-off point for PCT levels was 0.24.

Table 3. The cut-off point of procalcitonin, white blood cell, granulocyte, eutrophil/lymphocytes ratio and neutrophil/lymphocytes ratio levels for discrimination patients with CAP and sepsis due to CAP compared healthy persons.

Test Result Variable(s)	Area (95 CI)	Cut off	Sensitivity	Specificity	P. value
Procalcitonin	1.0 (1.0-1.0)	0.24	100	100	0.000***
White Blood Cell	0.745(0.656-.833)	8.05	70	90	0.000***
Granulocyte	0.850(0.779-0.920)	5.55	71	100	0.000***
Granulocyte	0.938(0.898-0.977)	70.35	76	100	0.000***
Neutrophil/Lymphocytes Ratio	0.914(0.867-0.962)	3.48	69	100	0.000***
Neutrophil/Lymphocytes Ratio	0.674(0.580-0.768)	175.96	46	100	0.002**

*P < 0.05, **P < 0.01 *** P < 0.001

The sensitivity and specificity of PCT were both 100% at p < 0.000 and the cut-off point for WBC was 8.05, with a sensitivity of 70% and a highly specific value of 90% at p < 0.000. Similarly, the AUC for the granulocyte (GRA) count was 0.850 with a 95% CI of 0.779-0.920. The cut-off point for GRA was 5.55, with a sensitivity of 71% and a strongly specific value of 100% at p < 0.000.

The AUC for the percentage of GRA was also 0.850 with a 95% CI of 0.779-0.920. The cut-off point for the GRA percentage was 5.55, with a sensitivity of 71% and a specificity of 100% at p < 0.000. The AUC for the neutrophil-to-lymphocyte ratio (NLR) was 0.914 with a 95% CI of 0.867-0.962, and the cut-off point for NLR was 3.48. The sensitivity was 69%, and the specificity was 100% at p < 0.000. Finally, the AUC for the platelet-to-lymphocyte ratio (PLR) was 0.674 with a 95% CI of 0.580-0.768. The cut-off point for PLR was 175.96, with a sensitivity of 46% and a specificity of 100% at p < 0.002 (Figure 2).

Discussion

The present study has shown that procalcitonin (PCT) is a more effective diagnostic marker than white blood cell count (WBC), granulocytes (GRA), granulocyte percentage (GRA%), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) for diagnosing patients with community-acquired pneumonia (CAP) and sepsis due to CAP. The area under the curve (AUC) of PCT was 1.0 (95% CI: 1.0-1.0), and the cut-off point for PCT levels was 0.24. The sensitivity and specificity of PCT were both 100% at P<0.000. PCT was able to differentiate bacterial pneumonia from other types of pneumonia, making it a promising marker for detecting bacterial pneumonia and facilitating early diagnosis (10). The PCT team in CAP has focused on predicting mortality rates and evaluating the effectiveness of antibiotics in the short term [11].

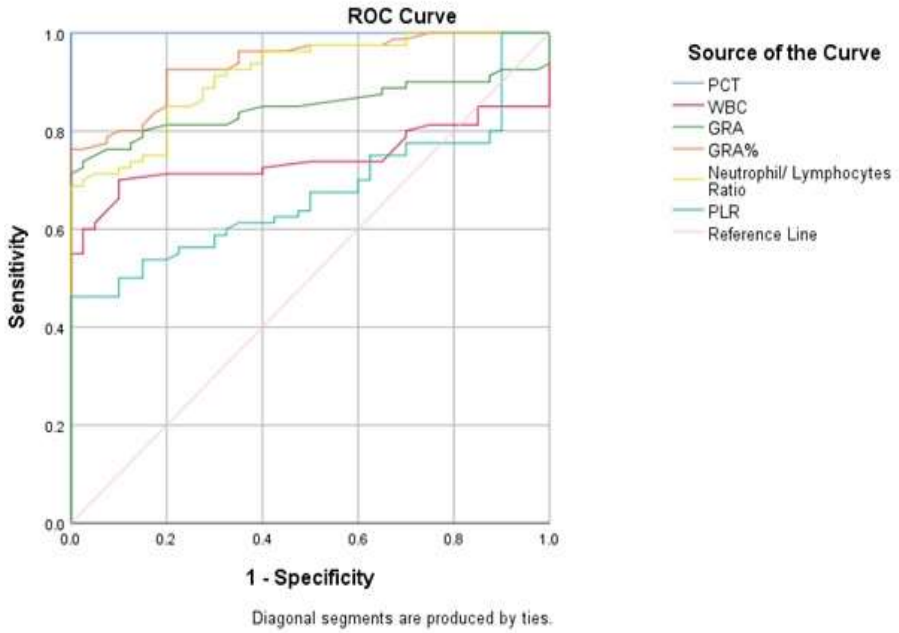

Figure 2. Receiver operating characteristic curves of procalcitonin (PCT), white blood cell (WBC), granulocyte (GRA), neutrophil/lymphocytes ratio, and platelet to lymphocyte ratio (PLR).

Several studies have confirmed that the levels of procalcitonin (PCT) can be used as a biomarker in sepsis. These studies have also noted that initiating antibiotic treatment early in patients with elevated PCT levels can help reduce mortality rates, length of hospital stay, and associated treatment costs. Moreover, treating sepsis has been found to decrease antibiotic usage and result in significant cost savings [12-13], and the study coincided with the results by Huang et al. (2022) when showed that PCT was a high diagnostic value for sepsis patients [14].

When investigating sepsis, the complete blood count (CBC) can be a valuable tool due to its simplicity, accessibility in all healthcare facilities, and its frequent use in all clinical settings as a first-line laboratory test [7]. The rapid screening test for CBC is an important indicator for the early detection of sepsis, providing a preliminary indication of conditions that may cause it [15]. The study of Cizmecioglu et al. (2022) showed that WBC count was found to be increased in pneumonia patients (14.07) compared to healthy controls (7.29) at $P<0.001$ [16]. According to Abed et al. (2018), significant differences were observed in WBC, GRA (%), and LYM (%) between bacterial pneumonia and control groups ($P < 0.001$) [10]. The study conducted by Kadim and Al-Dahmoshi in 2023 found that WBC, LYM, and GRA counts can aid in the early detection of the causative agent of sepsis [17]. The LYM and GRA cells respond to microbial infections. During infection, there is an increase in GRA count and a decrease in LYM count. The GRA count usually increases significantly with the severity of the infection, as we found in our study [7,18].

The LYM and GRA cells respond to microbial infections. During infection, there is an increase in GRA count and a decrease in LYM count. The GRA count usually increases significantly with the severity of the infection, as we found in our study [19]. Based on the calculation of the WBC, NLR is a readily accessible biomarker that has been used as a marker for assessing patients with various clinical conditions [20-21]. The role of the neutrophil-lymphocyte ratio (NLR) as a predictor of adverse outcomes in patients with CAP is described in this study as a simple, inexpensive, and easy-to-use marker [22-23]. Huang et al. (2018) found that NLR was higher in patients with CAP than healthy individuals. NLR had a higher diagnostic value for CAP than other blood parameters [24]. According to Kartal and Kartal (2017), NLR and PLR are significantly increased in Community Acquired Pneumonia (CAP) [25]. They proposed that both can be used as predictors for the presence of CAP. The NLR can be used as an index of systemic inflammation that predicts prognosis in elderly adults treated for CAP [26]. The NLR is a tool that is easily accessible and is recommended to evaluate patients suffering from sepsis [27].

Limitations

The first limitation of the studies is they were conducted in the Kerbala and Babylon Governorate of Iraq which limits the generalizability of the results to other Iraq Governorates. Another limited was the difficulty conducted blood cultures on the patients due to taking antibiotics and relying on non-culture methods to diagnose patients and the number of samples of study taken on sepsis patients was low, as well as the enslavement of patients whose stay in the hospital to take treatments more than three days. It is difficult to obtain samples from some patients when some patients refuse to give a blood sample. Other things, the study was seasonal and limited to some months of the year and our study sampling of patients was within a specific time frame.

Conclusion

This study revealed that WBC count and differential are useful in differentiating CAP with sepsis from CAP alone. Nevertheless, PCT was more effective than hematological parameters as revealed by ROC analysis.

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Author contribution: Conceptualization: S.J.R.; **Methodology:** N. H. K..; **Formal analysis and Investigation:** H.A.A.; **Supervision:** M. A. A. **Writing:** J.S.J.

Declaration of patient consent: All participants were voluntary and signed a consent form.

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