Bacterial distribution and predictive value of blood routine parameters in elderly patients with bacteremia: a cross-sectional study

Shiyan Zhang[1], Ying Zhuo[1], Bu-Ren LI[2], Jing Shi[1], Zu-Shun Zheng[1], Ling-Yang Ling[3], and Ying-Ying Jiang[1]

[1]Fuding Hospital, Fujian University of Traditional Chinese Medicine, Fuding 355200, Fujian, China
[2]Fuding hospital, Fujian University of Traditional Chinese Medicine
[3]Fujian University of Traditional Chinese Medicine, Fuding 355200, Fujian, China

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Abstract

to assess the distribution of bacteremia pathogens in elderly patients, to evaluate the impact of gender on pathogen distribution, and to determine the predictive value of routine blood parameters for diagnosing bacteremia. Methods: A total of 151 elderly patients ([?]60 years old) who admitted to hospital from October 2022 to June 2023 were retrospectively studied. Routine blood test and blood culture were performed. ROC curve was used to analyze the diagnostic efficacy of blood routine parameters: white blood cell (WBC), neutrophil-to-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), red blood cell distribution width (RDW). Results: The subjects were categorized into either the culture-positive group (82 cases) and the culture-negative one (69 cases) according to blood culture results. There were no significant differences in age and gender between groups. The primary bacterial pathogens of bacteremia in the elderly were Escherichia coli, Klebsiella pneumoniae and Streptococcus. A significantly higher culture positivity rate for E. coli was found in elderly female patients compared to their male counterparts (P = 0.021). The area under the ROC curve of four parameters was: WBC, 0.851 (95% confidence interval (CI) 0.790 - 0.912); NLR, 0.919 (95% CI 0.875 - 0.963); PLR, 0.609 (95% CI 0.518 - 0.700); and RDW was 0.626 (95% CI 0.563 - 0.717). Conclusion: The most frequently pathogenic microorganism causing bacteremia was E. coli, with elderly female patients having a significantly higher rate of culture positivity. Routine blood parameters (WBC, NLR, PLR, and RDW) demonstrated predictive potential for bacteremia in elderly patients.

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Shi-Yan Zhang*, Ying Zhuo, Bu-Ren Li, Jing Shi, Zu-Shun Zheng, Ling-Yang Wang, Ying-Ying Jiang

Department of Clinical Laboratory, Fuding Hospital, Fujian University of Traditional Chinese Medicine, Fuding 355200, Fujian, China.

*Correspondence: Shi-Yan Zhang, Department of Clinical Laboratory, Fuding Hospital, Fujian University of Traditional Chinese Medicine, 120 South Road of Old City, Fuding, China. Email: myebox@139.com.

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Background: to assess the distribution of bacteremia pathogens in elderly patients, to evaluate the impact of gender on pathogen distribution, and to determine the predictive value of routine blood parameters for diagnosing bacteremia.

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Conclusion : The most frequently pathogenic microorganism causing bacteremia was *E. coli* , with elderly female patients having a significantly higher rate of culture positivity. Routine blood parameters (WBC, NLR, PLR, and RDW) demonstrated predictive potential for bacteremia in elderly patients.

KEYWORDS

Elderly, Blood culture, Neutrophil-to-lymphocyte ratio (NLR), ROC analysis, *Escherichia coli* , Bacteremia.

1 INTRODUCTION

Bacteremia, which can lead to sepsis, is a life-threatening organ dysfunction, caused by disorder of host response to infection, resulting in higher morbidity and mortality in the world[1]. In this condition, pathogenic bacteria penetrate the blood system, proliferate within the circulatory system, and discharge diverse metabolites, inciting a systemic inflammatory response. Bacteremia's rapid progression and high mortality rate lead to an estimated 8 million deaths annually, underscoring the urgency of early diagnosis and treatment to curtail its fatality[2]. Particularly vulnerable are the elderly, given their reduced immunity. Furthermore, bacteremia's course in older individuals is typically stealthy, with less apparent clinical symptoms. This leads to poor prognosis and increased mortality, so early detection and intervention are critical for this population[3].

Currently, the clinical "gold standard" for diagnosing bacteremia is a laboratory blood culture [4]. However, this method's significant drawback is its prolonged duration, taking about 5-7 days. Moreover, positive culture results necessitate contamination exclusion, and negative results do not entirely rule out bacteremia, increasing the risk of missing optimal diagnosis and treatment windows.

Medical practitioners continuously seek rapid biomarkers for diagnosing bacteremia, such as procalcitonin (PCT), C-reactive protein (CRP), and interleukin-6 (IL-6). While they can aid in bacteremia's early detection, their moderate diagnostic efficacy, extended turnaround time, and high cost impose limitation.

Routine blood parameters, which are cost-effective, straightforward to operate, and suitable for primary hospitals, hold potential in predicting bacteremia. Numerous studies across the globe have highlighted routine blood's value in identifying patients at high risk for bacteremia early and anticipating adverse outcomes[5].

However, the correlation between routine blood parameters and geriatric bacteremia, as well as the correlation between routine blood parameters and various bacterial pathogens of geriatric bacteremia, remain underexplored in China. This paper aims to report the associations between white blood cell (WBC), neutrophil-to-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), red blood cell distribution width (RDW), and geriatric bacteremia, along with its bacterial pathogens.

2 MATERIALS AND METHODS

The clinical and laboratory data of 151 consecutive inpatients aged over 60 years old who were tested by blood culture were retrospectively analyzed from October 2022 to June 2023 at our hospital. If the patient's diagnosis at the time of admission or during hospitalization was sepsis or septic shock, they were included according to the Survival Sepsis Exercise Guidelines [6]. Subjects who received their first dose of antibiotics more than 24 hours before screening for inclusion in this investigation were excluded. Exclusion criteria included pregnant women, immune-compromised patients receiving radiation therapy or cytotoxic drugs, patients with AIDS, organ transplant patients, patients with inherited immunodeficiency diseases, patients with chronic kidney disease (baseline serum creatinine [?]2mg /dL) or chronic liver failure (Child-Pugh grade C), patients with bacterial endocarditis who require long-term treatment, and patients with conditions impacting hematologic indices, such as hematologic diseases, tumors, autoimmune diseases, and trauma. The study protocol was approved by the Medical Ethics Committee of Fuding Hospital (The ethnical approval number: Fuding Hospital 2022325).

Blood samples (2 ml) were drawn from the median elbow vein of patients before treatment, and EDTA was used for anticoagulation. The Japanese SYSMEX XE 2100 fully automated hematocrit analyzer and associated reagents were employed for testing complete blood cell counts. Neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were calculated based on the patient's neutrophil count, lymphocyte count, and platelet count obtained from routine blood tests. The procedures were strictly adhered to, according to standard operating procedures (SOPs), and all tests were completed during in-house quality control.

Two sets of bilateral double vials were taken for blood culture, and aerobic and anaerobic cultures were performed simultaneously. Blood samples were obtained extracted from peripheral venous puncture of the patients, directly injected into Bactec vials, and incubated in a Bactec incubator (BD Diagnostics, Franklin Lakes, NJ, USA). Blood culture vials were incubated at 37@C for 7 days. Positive cultures were Gram-stained and subcultured on solid media for subsequent analysis. Microbial identification using conventional techniques and API systems (bioMerieux, BacT/ALERT 3D, France).

A positive blood culture result from a single vial on one side was considered positive for bacteria. When coagulase negative*staphylococcus, Propionibacterium, Corynebacterium,* etc. are isolated in blood culture, the same strain should be isolated unilaterally or repeatedly at the same time, otherwise it is considered as contaminated with colonizing bacteria of skin.

Data normality was evaluated using the Shapiro-Wilk test, with non-normally distributed measurements expressed as median and quartiles (P_{25}-P_{75}). Nonparametric tests were utilized for intergroup comparisons: the Mann-Whitney U test for two groups and the Kruskal-Wallis H test for multiple groups. Data that conformed to a normal distribution were reported as mean ± standard deviation, and the t-test was employed for mean comparisons between groups. Categorical variables were measured using chi-square test (χ^2) or exact Fisher's tests, as appropriate, and were reported as count (%). Receiver operating characteristic (ROC) curve analyses were conducted for blood routine parameters. The area under the ROC curve (AUC) for blood routine parameters was calculated to determine the standard error and 95% confidence interval (95% CI). The sensitivity, specificity, accuracy, positive predictive value, and negative predictive value were calculated according to the ROC curves. Statistical processing was carried out using SPSS 22.0 statistical software (IBM SPSS, Armonk, NY, USA). A P - value of less than 0.05 was considered statistically significant.

3 RESULTS

Shapiro-Wilk Test: The Shapiro-Wilk test was employed to assess data normality in each group. All groups exhibited a P -value less than 0.05, indicating non-normal distribution. Data were subsequently organized using median and quartiles.

Baseline Characteristics: There were no statistically significant differences in the age and gender of the two groups ($P>$ 0.05). Detailed data are presented in Table 1.

Analysis of WBC, NLR, PLR, and RDW Measurements: Comparisons revealed the positive group had significantly higher values than the negative control group, with a statistically significant difference ($P<$ 0.05). Further details can be found in Table 2.

Distribution and Composition of Bacterial Pathogens: A total of 82 bacterial strains were isolated from the blood specimens of 82 hospitalized elderly patients. The total proportion of Gram-negative bacteria isolated from elderly female patients with bacteremia (n=61, 74.4%) was significantly higher than that in elderly male patients with bacteremia (n=21, 25.6%) ($P = 0.021$) (Table 5).

The distribution of bacterial pathogens included 42 strains of *E. coli* , 15 strains of *K. pneumoniae* , 10 strains of*Streptococcus,* and 9 strains of *Staphylococcus aureus* . Six strains of other bacteria (including *Enterococcus faecium* 2 strains, *Bacteroides fragilis* 2 strains, *Proteus mirabilis*1 strain, *Moraxella osloensis* 1 strain), accounted for 7.3% of the isolates. Details can be found in Table 4 and Figure 1.

Tables 1, 2, 3, and 4 provide detailed data analysis, with clear statistical representation of the comparisons between the groups and the outcomes of various measurements. These tables summarize the characteristics and results of the study groups, including statistical significance, detailed counts of various cell types, and the effectiveness of different markers. Note that in Table 3, the ROC curve and related parameters are used to determine optimal cutoff values, sensitivities, specificities, accuracies, and predictive values for various blood cell parameters. In Table 4, the Kruskal-Wallis H test was used to examine differences among various pathogens and their relationships with the routine blood parameters.

4 DISCUSSION AND CONCLUSION

This retrospective study of 82 elderly patients with bacteremia, compared with a control group of 69 patients, identified *E. coli, K. pneumoniae,* and *streptococcus* as the most prevalent gram-negative bacteria. These findings align with prior research conducted by Guarno et al. [7]. Similarly, an investigation by Daniela Dambroso et al. [8]indicated that 47.7% of bloodstream infections were due to Gram-positive bacteria and 52.3% to Gram-negative bacteria, with the Enterobacteriaceae family, particularly *E. coli* (26.5%) and*K. pneumoniae* (19.7%), being the most prevalent. Further support for these results was offered by a study conducted in Japan[9], which identified *E. coli* (28/58, 48%) as the leading causative bacteremia pathogen, followed by *K. pneumoniae* (6/58, 10%), and *Staphylococcus* (5/58, 8%).

Our research also revealed a significant predominance of gram-negative bacteria in elderly female patients with bacteremia (74.4%), compared to their male counterparts (25.6%) ($P = 0.021$) (Table 5). Interestingly, a higher positivity rate for *E. coli* was found in the female patient population, making *E. coli* the most common bacteremia pathogen among this demographic. This is in alignment with existing literature that identifies *E. coli* as a predominant human pathogen with the capability to colonize, infect, and invade various human tissues, leading to severe *E. coli* disorders and potential mortality [10]. *E. coli* is the leading cause of bacteremia among adults in the world and is the common frequent of sepsis and subsequent hospitalization or deaths in the United States[11]. The risk of invasive *E. coli* infections, which consisted of sepsis and bacteremia, and increased with the growth of the age [12].

The comparative evaluation of blood cell parameters in our study revealed a statistically significant increase in leukocyte count, NLR, PLR, and RDW among bacteremia patients. From the ROC curves, NLR emerged as the most effective predictor of bacteremia in geriatric patients. While the total white blood cell count is traditionally used as an indicator of bacterial infection, its efficacy is limited by the influence of other conditions such as hematological diseases, non-infectious inflammatory diseases, surgery, and trauma[13]. In our study, the sensitivity and specificity of WBC in diagnosing bacteremia in elderly patients were determined to be 74.4% and 87.0%, respectively. RDW, a measure of the variation in red blood cell volume size, is primarily used for diagnosing anemia. Elevated RDW may reflect better residual bone marrow hematopoiesis during severe anemia [14]. In conditions such as sepsis, oxidative stress and inflammation can disrupt erythrocyte maturation, leading to an increased RDW[15]. A previous study by Professor Dogan P et al. showed that an RDW cut-off of >19.50% was associated with a sensitivity of 87% and a specificity of 81% for predicting late-onset Gram-negative sepsis ($P < 0.001$)[16]. In our study, the diagnostic value of RDW demonstrated an

RDW cut-off of >13.0% with the sensitivity of 78.0% and the specificity of 52.2% for predicting bacteremia. The difference in the results of the two investigations were mainly due to the difference in the enrolled subjects.

Finally, our study underscores the value of NLR as a reliable indicator of systemic inflammatory response, which has potential predictive value for bacteremia. While NLR can be influenced by several factors, including age, obesity, and various diseases [5], its efficacy in diagnosing bacteremia is supported by several studies, including our own.

The insights provided by this study make a compelling case for utilizing these routine blood parameters as cost-effective, straightforward, and rapid indicators for bacteremia in the elderly. However, it's important to acknowledge the study's limitations. Our focus was on bacterial pathogens, excluding others such as fungi, mycoplasma, chlamydia, parasites, and viruses. Moreover, the single-center nature of the study limits the generalizability of our findings. Future studies should aim for a multi-center approach with larger sample sizes to provide a more comprehensive understanding of geriatric bacteremia infections. These studies should also further investigate the distribution of microorganisms and the predictive value of routine.

AUTHOR CONTRIBUTIONS

Shi-Yan Zhang: Conceptualization (lead); writing – original draft (lead); formal analysis (lead); writing – review and editing (equal). Software (lead).**Ying Zhuo, Bu-Ren Li:**Conceptualization (supporting); Writing – original draft (supporting); Writing – review and editing (equal). **Jing Shi, Zu-Shun Zheng:**Methodology (lead); writing – review and editing (equal).**Lin-Yang Wang, Ying-Ying Jiang:** Software (equal); writing – review and editing (equal).

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Research data are not shared.

ORCID

Shi-Yan Zhang http://orcid.org/0000-0003-4305-8213

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Table 1. Clinical baseline parameters of the blood culture positive and negative groups [median (P_{25}-P_{75})]

Groups (cases)	Age	Male	Female
Positive (82)	73.0 (70.0–80.3)	38 (46.3)	44 (53.7)
Negative (69)	72.0 (68.5–75.5)	34 (49.3)	35 (50.7)
Mann-Whitney U /χ^2 test	-1.793	0.129	0.129
P-value	0.073	0.719	0.719

Table 2. Comparison of blood cell parameters between the two groups [median (P_{25}-P_{75})]

Item	Positive (n=82)	Negative (n=69)	*Z*-value	*P*-value
WBC (10^9/L)	10.93 (7.32 – 16.23)	5.96 (4.80–7.18)	-10.407	0.000
Neutrophils (10^9/L)	8.58 (5.67 – 14.75)	3.69 (2.76–4.54)	-8.407	0.000
Lymphocytes 10^9/L)	1.00 (0.59 - 1.49)	1.70 (1.38–2.18)	-6.307	0.000
RDW (%)	13.70 (13.00-15.00)	12.90 (12.30- 14.00)	-2.676	0.007
NLR	10.52 (5.50–18.44)	2.01 (1.36–3.07)	-8.853	0.000
PLR	188.61 (97.64–250.00)	135.86 (97.66–187.50)	-2.312	0.021

Note: The non-parametric test between the two groups was performed using the Mann-Whitney U test.

WBC: White blood cells; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; RDW: Red cell distribution width.

Table 3. Area under the receiver operating characteristic (ROC) curve and related parameters.

Item	WBC	NLR	PLR	RDW
Optimal Cutoff	8.0	4.0	205.9	13.0
Youden index (%)	61.3	69.4	26.7	30.2
Sensitivity (%)	74.4	85.4	42.7	78.0
Specificity (%)	87.0	84.1	84.1	52.2
Accuracy (%)	80.1	84.8	61.6	66.2
PPV (%)	87.1	86.4	76.1	66.0
NPV (%)	74.1	82.9	55.2	66.7
AUC (95%CI)	0.851 (0.790-0.912)	0.919 (0.875-0.963)	0.609 (0.518-0.700)	0.626 (0.536-0.717)
Standard Error	0.031	0.022	0.046	0.046
P- value	0.000	0.000	0.021	0.008

Note: AUC: Area under the receiver operating characteristic (ROC) curve; 95%CI: 95% confidence interval; WBC: White blood cells; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; RDW: Red cell distribution width; PPV: Positive predictive value; NPV: Negative predictive value.

Table 4. Kruskal-Wallis H test of routine blood-related parameters and different pathogens.

Pathogen (Strains)	Number Rank Average WBC	Number Rank Average NLR	Number Rank Average PLR	Number Rank A RDW
Escherichia coli (42)	43.79	38.90	41.48	40.90
Klebsiella pneumoniae (15)	43.90	48.80	39.60	36.23
Streptococcus (10)	32.30	37.50	43.00	35.70
Staphylococcus (9)	33.06	42.78	44.11	57.61
Other bacteria (6)	47.50	46.17	40.00	44.33
H-value	3.544	2.447	0.267	5.618
p-value	0.471	0.654	0.992	0.230

Note: The non-parametric test Kruskal-Wallis H test was used to compare the five groups of routine blood parameters and different pathogens. All$P > 0.05$, there is no statistically significant difference, so the Bonferroni method is not used to correct the significance level for post-hoc pairwise comparisons. WBC: White blood cell count; NLR: Neutrophil-to-lymphocyte ratio; PLR: Platelet-to-lymphocyte ratio; RDW: Red cell distribution width. Other bacteria: *Enterococcus faecium* (2 strains), *Bacteroides fragilis* (2 strains), *Proteus mirabilis* (1 strain),*Moraxella osloensis* (1 strain).

Table 5. Comparison of the distribution of pathogenic bacteria between male group and female group. (n %)

Pathogen (Strains)	Pathogen (Strains)	Male (37)	Female (45)	χ^2	P value
Gram-stain (82)	Positive (21)	14 (37.8)	7 (15.6)	5.292	0.021[a]
	Negative (61)	23 (62.2)	38 (84.4)		
Escherichia coli (42)	Positive	13(35.1)	29 (64.4)	6.981	0.008[a]
	Negative	24 (64.9)	16 (35.6)		
Klebsiella pneumoniae (15)	Positive	9 (24.3)	6(13.3)	1.641	0.200[a]
	Negative	28 (75.7)	39 (86.7)		
Streptococcus (10)	Positive	7 (18.9)	3 (6.7)	-	0.089[b]

	Negative	30 (81.1)	42 (93.3)		
Staphylococcus (9)	Positive	5(13.5)	4 (8.9)	-	0.725[b]
	Negative	32 (86.5)	41 (91.1)		
Other bacteria (6)	Positive	3 (8.1)	3 (6.7)	-	1.000[b]
	Negative	34(91.9)	42 (93.3)		

Note: [a]Chi-square test. [b]Fisher's exact test. Other bacteria: *Enterococcus faecium* (2 strains),*Bacteroides fragilis* (2 strains), *Proteus mirabilis* (1 strain), *Moraxella osloensis* (1 strain).

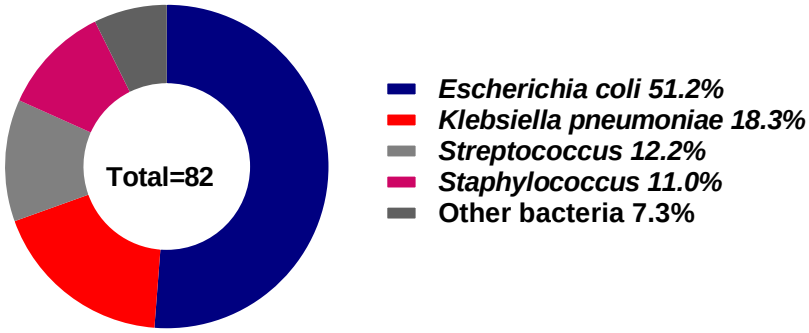

Figure 1. The distribution of isolated pathogens

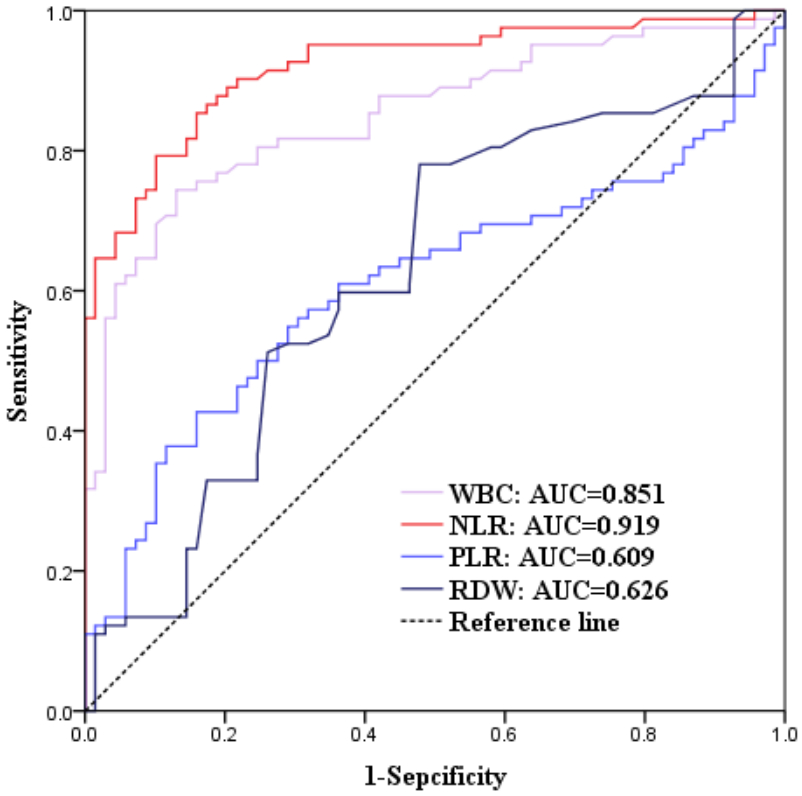

Figure 2. ROC curve