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ORIGINAL ARTICLE

Characterization of Methicillin-Resistant *Staphylococcus Aureus* Resistance and Hematological Profiles in Diabetic Foot Infections

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SUMMARY

Background: **This study aimed to analyze the infection rate, drug-resistant phenotypes, and hematological index profiles of methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA) in patients with diabetic foot ulcers (DFUs). This study sought to provide insights for the early identification of MRSA infections and the optimization of antimicrobial strategies in patients with DFU.**

Methods: **The clinical data of patients with DFUs hospitalized from January 2022 through June 2023 were retrospectively reviewed. The detection rate and drug resistance profile of *S. aureus* were analyzed using bacterial culture and drug sensitivity testing. Additionally, the differences in hematological indices between the MRSA and MSSA infection groups were compared.**

Results: **A total of 1,385 patients with DFU underwent bacterial culture of secretions, with a positive rate of 50.25% (696/1,385) for pathogenic bacteria. The detection rate of *S. aureus* was 14.58% (202/1,385), out of which MRSA accounted for 38.12% (77/202). The MRSA group exhibited resistance to macrolides (clarithromycin: 64.94% vs. 36.00%; erythromycin: 70.13% vs. 39.20%; azithromycin: 66.23% vs. 38.40%), lincosamides (clindamycin: 68.83% vs. 31.20%), and quinolones (levofloxacin: 28.57% vs. 15.20%; moxifloxacin: 15.58% vs. 5.60%). These differences were statistically significant (all $p < 0.05$). Furthermore, hematological analysis revealed significant disparities between the two groups in erythrocyte mean corpuscular hemoglobin concentration (MCHC), D-dimer, albumin (ALB), alkaline phosphatase (ALP), and electrolytes (Na^+, Cl^-, Ca^{2+}) (all $p < 0.05$).**

Conclusions: **This study examined the characteristics of DFU-associated MRSA infection, particularly its multidrug resistance features. MRSA infection demonstrated 100% sensitivity to vancomycin and linezolid. The findings suggest that combined detection of MCHC, D-dimer, ALB, ALP, Na^+, Cl^-, and Ca^{2+} may serve as a valuable reference for the early identification of DFU-associated MRSA infection in clinical settings. Clinicians should be mindful of MRSA infection risks in patients with DFU and develop individualized anti-infection regimens based on drug sensitivity profiles to improve prognosis.**

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INTRODUCTION

Diabetic foot ulcer (DFU) is a serious complication of diabetes, with a lifetime risk of up to 34% among patients with diabetes [1,2]. In China, it is associated with significant disability and mortality, with annual amputation and mortality rates reaching 20% and 10%, respec-

tively [3,4]. The presence of diabetic foot infection (DFI) has been shown to substantially worsen patient prognosis [5]. A study by Henig et al. [6] revealed that among DFI isolates, multidrug-resistant organisms (MDROs) accounted for 56%, and approximately 30% of isolates were resistant to first-line antibiotics. This phenomenon significantly increases the risk of DFI. Antibiotic resistance is associated with delayed wound healing, treatment failure, readmission rates, and increased mortality [6]. MDROs are bacteria-resistant to three or more commonly used antibiotics [7]. Clinically, methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most prevalent antibiotic-resistant pathogens worldwide. Other common MDROs include vancomycin-resistant *Enterococci* and extended-spectrum β-lactamase-producing *Enterobacteriaceae* [8]. Research has identified several risk factors contributing to the development of MDRO infections in patients with DFU, including multiple hospitalizations, pre-admission antibiotic use, ulcer characteristics (e.g. size, depth, osteomyelitis), and vasculopathy [9,10].

S. aureus, the predominant causative agent of DFI (detection rates range from 47.3 to 76.3%), can result in severe local and systemic inflammatory reactions, increasing the risk of amputation by 154.5-fold [11-13]. Among the various strains of *S. aureus*, MRSA has been shown to have a particularly deleterious effect on the prognosis of patients with DFI due to its extensive drug resistance. This can result in prolonged wound healing, extended hospitalization, worsening infections, and an increased risk of amputation. Epidemiological surveillance data demonstrate that the detection rate of MRSA in patients with DFI in China has reached 8.24%, with an upward trend [14]. Consequently, dynamic monitoring of MRSA resistance characteristics can facilitate the initiation of effective antimicrobial therapy, and the early recognition of MRSA infection is crucial for improving prognosis.

While existing studies have predominantly concentrated on the disparities in drug resistance and clinical infection characteristics between MRSA and MSSA, the early warning value of hematological indicators remains to be elucidated. This study aimed to address this gap by comparatively analyzing the drug resistance characteristics of MRSA/MSSA isolates and the corresponding disparities in the levels of hematological indicators in patients with DFI. This objective will provide a novel perspective for the early identification and intervention of MRSA infection in patients with DFU and optimize therapeutic strategies.

MATERIALS AND METHODS

General information

The clinical and laboratory test data of patients with DFU admitted to our hospital between January 2022 and June 2023 were retrospectively analyzed. The inclusion criteria encompassed patients who met the WHO diagnostic criteria for diabetes mellitus, the criteria of the International Working Group on the Diabetic Foot, and those with DFUs located below the ankle protuberance. Additionally, patients with a minimum inhibitory concentration ≥ 4 mg/mL for oxacillin were included in the MRSA group. The exclusion criteria included acute complications of diabetes other than DFU. Furthermore, patients with non-DFUs due to vascular insufficiency, cardiac diseases, neurological diseases, and malignant tumors were excluded from the study. The study was approved by the Ethics Committee of the Air Force Hospital of the Eastern Theater Command, and all participants gave informed consent.

Research methods

Bacterial culture and drug sensitivity test

The process of wound specimen collection was conducted under strict aseptic conditions. For superficial ulcers, an antiseptic saline swab dipped in secretions or pus from the bottom of the ulcer was collected to avoid contamination of the skin around the wound. For deep ulcers, secretions or pus were collected with a sterile syringe after debridement. The samples were expeditiously transferred to the microbiology laboratory for bacterial culture and drug sensitivity testing. Bacterial identification and drug sensitivity test reagent plates, along with corresponding reagents, were obtained from Zhuhai Dier Biological Engineering Co. (Zhuhai, China). The quality control strains comprised *S. aureus* (ATCC25923), *Klebsiella pneumoniae* (ATCC700603), *Pseudomonas aeruginosa* (ATCC27853), *Enterococcus faecalis* (ATCC29212), and *Escherichia coli* (ATCC25 922). The results of the initial bacterial culture during hospitalization were then subjected to statistical analysis for all patients included in the study. The positive rates of bacterial culture, *S. aureus* culture, and MRSA culture and the difference in resistance characteristics between MRSA and MSSA of the specimens sent for examination were all statistically analyzed.

Analysis of blood and biochemical indicators

The initial test results upon patient admission were collected, including complete blood count, biochemical parameters, and coagulation profile (seven parameters). The following instruments and their supporting reagents were used: Hitachi 7600 automatic biochemistry analyzer (Hitachi Limited, Tokyo, Japan), Sysmex XN1000 automatic blood cell analyzer (Sysmex Corporation, Kobe, Japan), and Sysmex CS-5100 automatic coagulation analyzer (Sysmex Corporation, Kobe, Japan). A statistical analysis was conducted to compare the hematological marker levels between the MRSA and MSSA groups.

Statistical analysis

Statistical analysis was performed using SPSS 27.0 software (IBM Corp., Armonk, NY, USA). Measurement data following a normal distribution were expressed as mean ± standard deviation ($\bar{x} \pm s$), and a *t*-test was

Table 1. Demographic characteristics of MRSA- and MSSA-infection groups.

Demographic	MRSA (n = 77)	MSSA (n = 125)	χ^2/Z	p
Male (n, %)	67 (87.01%)	82 (65.6%)	11.289	< 0.001
Age (years)	66 (19)	61.23 ± 12.62	-1.868	0.062

MRSA - methicillin-resistant *Staphylococcus aureus,* MSSA - methicillin-sensitive *Staphylococcus aureus.*

Table 2. Antimicrobial susceptibility of *Staphylococcus aureus* to commonly-used antibiotics (n = 202).

Antibiotics	Susceptible (%)	Intermediate (%)	Resistant (%)
Penicillin	3.47 (7)	0 (0)	96.53 (195)
Erythromycin	45.54 (92)	4.46 (9)	50.00 (101)
Azithromycin	48.02 (96)	3.47 (7)	48.51 (99)
Clarithromycin	51.49 (104)	1.49 (3)	47.03 (95)
Clindamycin	54.46 (110)	0 (0)	45.54 (92)
Oxacillin	61.89 (125)	0 (0)	38.12 (77)
Levofloxacin	76.24 (154)	3.47 (7)	20.3 (41)
Tetracycline	77.72 (157)	5.94 (12)	16.34 (33)
Moxifloxacin	78.22 (158)	12.38 (25)	9.41 (19)
Gentamicin	88.61 (179)	3.47 (7)	7.92 (16)
Cotrimoxazole	94.55 (191)	0 (0)	5.45 (11)
Rifampicin	97.03 (196)	0 (0)	2.97 (6)
Teicoplanin	97.03 (196)	0 (0)	2.97 (6)
Chloramphenicol	96.53 (195)	1.49 (3)	1.98 (4)
Tigecycline	99.5 (201)	0 (0)	0.5 (1)
Amikacin	99.5 (201)	0 (0)	0.5 (1)
Linezolid	100 (202)	0 (0)	0 (0)
Vancomycin	100 (202)	0 (0)	0 (0)

used to compare the differences between groups. Non-normally distributed measurements were expressed as the median (interquartile range [IQR]). For between-group analysis, non-parametric tests were used; for categorical data, the number of cases or percentages was expressed, and the chi-squared test was used for analysis of the differences. $p < 0.05$ was considered statistically significant.

RESULTS

Results of bacterial culture of secretions from patients with DFUs

This study included 1,385 patients with diabetic foot who underwent examination of foot ulcer secretions between January 2022 and June 2023. Among these patients, pathogenic bacterial cultures yielded positive results in 696 patients, which corresponds to an overall positive rate of 50.25% (696/1,385). *S. aureus* was detected in 202 patients (14.58%, 202/1,385), out of which 77 patients (5.56%, 77/1,385) had MRSA infections. Among patients with positive pathogen culture, *S. aureus* infection accounted for 29.02% (202/696), and MRSA isolates accounted for 38.12% (77/202) of *S. aureus* strains.

A comparison of the demographic characteristics between the MRSA-infected group (n = 77) and the MSSA-infected group (n = 125) revealed that the mean age was 66 years (IQR = 19) in the MRSA group and 61.23 ± 12.62 years in the MSSA group. A subsequent analysis revealed no statistically significant disparity between the two groups ($p = 0.062$). Furthermore, the proportion of males in the MRSA group was 87.01% (67/77), which is considerably higher than the proportion of 65.6% (82/125) observed in the MSSA group

Table 3. Comparison of drug resistance phenotypes of MRSA and MSSA strains.

Antibiotics	MRSA strains (n = 77)	MSSA strains (n = 125)	χ^2	p
Clindamycin	68.83% (53)	31.20% (39)	27.206	< 0.001
Clarithromycin	64.94% (50)	36.00% (45)	16.014	< 0.001
Erythromycin	67.50% (52)	39.20% (49)	15.240	< 0.001
Azithromycin	66.23% (51)	38.40% (48)	12.175	< 0.001
Rifampicin	7.79% (6)	0% (0)	NA	0.003
Moxifloxacin	15.58% (12)	5.60% (7)	6.092	0.014
Levofloxacin	28.57% (22)	15.20% (19)	5.066	0.024
Gentamicin	11.69% (9)	5.60% (7)	2.634	0.105
Chloramphenicol	3.90% (3)	0.80% (1)	2.449	0.114
Teicoplanin	5.19% (4)	1.60% (2)	2.136	0.144
Cotrimoxazole	7.79% (6)	4.00% (5)	1.331	0.249
Penicillin	100% (77)	94.40% (118)	1.244	0.265
Tetracycline	19.50% (15)	14.40% (18)	1.116	0.291
Amikacin	1.30% (1)	0% (0)	NA	0.330
Tigecycline	0% (0)	0.80% (1)	NA	1.000
Linezolid	0% (0)	0% (0)	NA	NA
Vancomycin	0% (0)	0% (0)	NA	NA

NA - not applicable.

Table 4. Comparison of blood routine parameters of patients in MRSA group and MSSA group.

Index	MRSA group	MSSA group	Z	p
MCHC (g/L)	331.03 ± 9.57	335 (14)	-2.371	0.018
Hb (g/L)	112 (31)	116 (25)	-1.518	0.129
Plt ($\times 10^9$/L)	224 (113)	243.34 ± 81.18	-0.974	0.330
WBC ($\times 10^9$/L)	8.1 (5.2)	8.3 (4.75)	-0.250	0.803
NEUT ($\times 10^9$/L)	5.9 (5.2)	6.30 (4.15)	-0.040	0.968

MCHC - mean corpuscular hemoglobin concentration, Hb - hemoglobin, Plt - platelet count, WBC - white blood cell count, NEUT - neutrophil count.

Table 5. Comparison of coagulation indices of patients in MRSA group and MSSA group.

Index	MRSA group	MSSA group	Z/t	p
D-D (mg/L)	0.76 (1.15)	0.62 (0.74)	-2.287	0.022
PT (s)	12.4 ± 1.08	12 (1.6)	-1.470	0.142
INR	1.08 ± 0.1	1.04 (0.14)	-1.443	0.149
AT III (%)	85.95 ± 15.89	89.39 ± 17.07	1.406	0.161
APTT (s)	27.9 (3.2)	27.4 (3.2)	-1.337	0.181
FIB (g/L)	4.9 (2.2)	4.6 (1.9)	-1.033	0.302
TT (s)	17.33 ± 1.49	17.43 ± 1.43	0.438	0.662

D-D - D-dimer, PT - prothrombin time, INR - international standardized ratio, AT III - antithrombin III, APTT - activated partial thromboplastin time, FIB - fibrinogen, TT - thrombin time.

Table 6. Comparison of biochemical indices of patients in MRSA group and MSSA group.

Index	MRSA group	MSSA group	Z/t	p
Na^+ (mmol/L)	136.69 ± 4.5	139 (5.2)	-2.929	0.003
Cl^- (mmol/L)	99.85 ± 4.73	101.42 ± 4.26	2.422	0.016
ALB (g/L)	31.76 ± 6.15	33.75 ± 5.28	2.346	0.02
ALP (U/L)	101.25 (39.8)	95.55 (34.42)	-2.017	0.044
Ca^{2+} (mmol/L)	2.24 ± 0.14	2.28 ± 0.14	2.031	0.044
TC (mmol/L)	3.61 ± 1.09	3.94 ± 1.1	1.902	0.059
HDL-C (mmol/L)	0.95 (0.42)	1.10 (0.43)	-1.75	0.08
CREA (mmol/L)	79.7 (70.1)	70 (59.1)	-1.609	0.108
LDL-C (mmol/L)	2.02 ± 0.8	2.21 ± 0.8	1.506	0.134
CRP (mg/L)	32.2 (78.4)	19.1 (65.1)	-1.227	0.22
DBIL (mmol/L)	8.91 (5.32)	7.79 (6.27)	-1.204	0.229
AST (U/L)	15.8 (12.6)	13.80 (7.93)	-1.068	0.286
ALT (U/L)	14.45 (16.7)	13.5 (12.95)	-0.986	0.324
FPG (mmol/L)	9.85 (7.54)	8.64 (6.09)	-0.97	0.332
TBIL (mmol/L)	9.42 ± 4.46	7.79 (6.27)	-0.837	0.402
UA (mmol/L)	286.5 ± 101.89	298.02 ± 100.81	0.783	0.434
GGT (U/L)	28.1 (31.7)	25.65 (22.92)	-0.765	0.444
K^+ (mmol/L)	4.11 ± 0.48	4.06 (0.75)	-0.47	0.638
LDH (U/L)	183.48 ± 48.7	169.5 (50.4)	-0.34	0.734
BUN (mmol/L)	6.54 (4.74)	6.80 (4.26)	-0.316	0.752
IBIL (mmol/L)	6.27 ± 3.14	5.63 (4.53)	-2.69	0.788
TG (mmol/L)	1.16 (0.54)	1.15 (0.56)	-0.209	0.834
CK (U/L)	48.9 (59.7)	49.6 (46.45)	-0.115	0.908

Na^+ - sodium, Cl^- - chloride, ALB - albumin, ALP - alkaline phosphatase, Ca^{2+} - calcium, TC - total cholesterol, HDL-C - high-density lipoprotein cholesterol, CREA - creatinine, LDL-C - low-density lipoprotein cholesterol, CRP - C-reaction protein, DBIL - direct bilirubin, AST - aspartate aminotransferase, ALT - alanine aminotransferase, FPG - fasting plasma glucose, TBIL - total bilirubin, UA - uric acid, GGT - transglutaminase, K^+ - potassium, LDH - lactate dehydrogenase, BUN - blood urea nitrogen, IBIL - indirect bilirubin, TG - triglyceride, CK - creatine kinase.

($p < 0.001$). A more detailed demographic comparison is provided in Table 1.

Antimicrobial drug susceptibility characteristics of *S. aureus*

The results of antimicrobial drug susceptibility tests of 202 *S. aureus* clinical isolates were statistically analyzed. The findings demonstrated a high susceptibility rate (> 90%) of *S. aureus* isolates to cotrimoxazole, tigecycline, vancomycin, rifampicin, linezolid, chloramphenicol, amikacin, and teicoplanin. Additionally, the study observed a macrolide resistance rate exceeding 40%, with resistance rates of 50.00% for erythromycin, 48.51% for azithromycin, and 47.03% for clarithromycin. The penicillin resistance rate was remarkably high at 96.53% (195/202). A comprehensive overview of these findings is provided in Table 2.

Comparative analysis of drug resistance between MRSA group and MSSA group

The *S. aureus* clinical isolates were categorized into two groups: MRSA (n = 77) and MSSA (n = 125). This categorization was based on the resistance of the isolates to oxacillin. The results of the chi-squared test revealed statistically significant differences ($p < 0.05$) in resistance rates to 12 commonly-used antibiotics between the two groups. The variation in resistance to clindamycin emerged as the most pronounced ($p < 0.001$), exhibiting a 68.83% resistance rate in the MRSA group, compared to 31.20% in the MSSA group. A detailed resistance phenotype comparison is provided in Table 3.

Comparison of hematological indices of patients in MRSA group and MSSA group

Analysis of blood routine parameters

Following the exclusion of four cases with missing data, 198 patients were included in this study (77 in the

MRSA group and 121 in the MSSA group). The data were statistically analyzed based on five core hematological indicators (screened from 22 indicators). The Mann-Whitney U test revealed a statistical difference in mean corpuscular hemoglobin concentration (MCHC) ($p = 0.018$) between the two groups. However, no significant differences were observed for the remaining indicators ($p > 0.05$). A comparative summary of blood routine parameters between the two groups is provided in Table 4.

Analysis of coagulation indices

This study analyzed seven distinct coagulation indices in 198 patients diagnosed with *S. aureus* infections (77 in the MRSA group and 121 in the MSSA group). The Mann-Whitney U test revealed that D-dimer levels were considerably elevated in the MRSA group compared to the MSSA group (0.76 [IQR 1.15] vs. 0.62 [0.74] mg/L, $Z = -2.287$, $p = 0.022$). The disparities between the two groups for the remaining indicators were not statistically significant ($p > 0.05$). The statistical data of coagulation indices between the two groups are shown in Table 5.

Analysis of biochemical indicators

A comparative analysis of 23 biochemical indices was conducted among the 198 patients with *S. aureus* infections (MRSA: n = 77, MSSA: n = 121). The results identified five biochemical parameters with statistically significant differences ($p < 0.05$) between the two groups, including alkaline phosphatase (ALP), albumin (ALB), Na^+, Cl^-, and Ca^{2+}. The comparative analysis of biochemical indices between the two groups is shown in Table 6.

DISCUSSION

MRSA infection is recognized as one of the three most challenging infectious diseases, along with viral heaptitis and acquired immune deficiency syndrome [15]. Microcirculatory disorders in DFUs delay ulcer healing, while the high glucose microenvironment and immunosuppressive state facilitate bacterial proliferation, often leading to the development of DFI. The standard approach to managing DFI involves the administration of antibiotics, and the presence of MRSA infection is associated with a prolonged healing cycle, extended hospitalization, and increased healthcare costs [16].

We reported a 29.02% prevalence of *S. aureus* infection in patients with DFI (202/696), with MRSA accounting for 38.12% of these patients (77/202). This rate exceeded the data from peer studies in India (23.7%) and Pakistan (26.76%) but was notably lower than the 78% prevalence reported in Iran [17,18]. This geographic heterogeneity suggests that regional differences in healthcare resource allocation, antibiotic stewardship practices, and nosocomial surveillance control capacity significantly impact MRSA prevalence. Demographic characterization showed that the mean age of the MRSA and MSSA groups was > 60 years, with no statistical difference between the two groups ($p = 0.062$). Previous studies have indicated that males with diabetes have a higher risk of DFI compared to females, which may be attributable to estrogen-mediated protection, lifestyle differences between sexes, and occupational exposure risk gradient [19]. We further observed that the proportion of males in the MRSA group was significantly higher than in the MSSA group (87.01% vs. 65.6%, $p < 0.001$), underscoring the importance of developing gender-specific prevention and control strategies.

The treatment of DFI should be based on adequate debridement and effective antimicrobial application. The extent of infection, depth of involvement, complications, and regional epidemiologic characteristics should be comprehensively evaluated at the initial stage to guide empirical anti-infective treatment [20,22]. Subsequent adjustments to the treatment regimen should be made in accordance with the results of drug sensitivity testing and the actual efficacy of the treatment. The emergence of multidrug-resistant phenotypes of *S. aureus* is a major challenge in the treatment of DFI. The long-term use of broad-spectrum antibiotics in current clinical practice has increased the detection rate of multidrug-resistant strains, highlighting the value of MRSA identification and dynamic monitoring of resistance characteristics in the empirical treatment phase of DFI. In this study, we conducted a retrospective analysis of the resistance characteristics of 202 DFI-associated *S. aureus* isolates. The results demonstrated that *S. aureus* exhibited absolute sensitivity to linezolid and vancomycin, as well as high sensitivity (> 85%) to seven drugs, including amikacin and ticlopidine, which is consistent with the recommended medications outlined in international guidelines. Conversely, penicillin and macrolide antibiotics (erythromycin, azithromycin, and clarithromycin) exhibited a high resistance rate (> 45%), underscoring the necessity for a meticulous evaluation of clinical drug utilization based on regional resistance monitoring data. Tigecycline demonstrated a sensitivity rate of 99.50% in *in vitro* drug susceptibility testing. However, its utilization in the treatment of DFI is explicitly restricted by current international guidelines. This restriction is primarily due to its 44% incidence of dose-dependent adverse reactions (including rash and diarrhea) and the potential risk of inducing resistance [23,24].

MRSA has a broader resistance spectrum than MSSA, and the results of this study validate the evidence-based foundation of international guidelines, providing clinical insights into the selection of antimicrobial drugs for the empirical treatment of DFI. Glycopeptides and oxazolidinones are still the core therapeutic choices for MRSA infections. The high rate of resistance to macrolides requires strict adherence to sensitivity-directed precision therapy, and there is a pressing need to establish multidisciplinary collaboration in antimicrobial drug management. To effectively prevent and control

drug resistance, it is essential to develop a multidisciplinary antimicrobial stewardship system, which should include the standardization of bacterial culture frequency for wound assessment, the establishment of a regional drug resistance monitoring network, the promotion of antimicrobial drug hierarchical management, and the development of rapid identification methods.

As MRSA infection is a complex pathophysiological process, the systemic responses it triggers may be characterized in the peripheral circulation. Therefore, this study explored characteristic differences in MRSA infection using common clinical hematological indicators. The difference analysis revealed statistically significant differences ($p < 0.05$) between the two groups in MCHC, D-dimer, ALB, ALP, and electrolytes (Na^+, Cl^-, Ca^{2+}). The results indicated that the MRSA-infected group exhibited more severe metabolic disorders and pathological progression, which might be linked to the following mechanisms: first, an imbalance of nutrient metabolism, with significantly lower levels of MCHC ($p = 0.018$) and ALB ($p = 0.02$) in the MRSA group, suggests that iron metabolism disorders were associated with insufficient protein synthesis. Alternatively, the overconsumption of nutrients could be implicated, which was presumably associated with the infection-induced negative nitrogen balance. Second, coagulation function abnormalities were observed, with significantly higher D-dimer levels in the MRSA group, presumably related to MRSA infection leading to prolonged wound healing and deep tissue injury exacerbated by prothrombin release, further promoting a prethrombotic state. Third, ALP levels were significantly higher in the MRSA group, suggesting underlying bone metabolism abnormality and renal impairment. In addition, the mechanism of electrolyte disorders may involve impaired tubular reabsorption in severe infectious states and the release of inflammatory mediators from tissue damage affecting electrolyte transport across membranes. The paucity of data regarding ulcer classification poses a significant challenge in establishing a causal relationship between MRSA infection and the observed alterations in hematological indices. This challenge persists in determining whether these alterations are a direct consequence of MRSA infection or if highly graded DFUs exhibit a heightened propensity to be associated with MRSA infection. This study systematically unveils, for the first time, that patients with MRSA-associated DFI exhibit a distinctive pattern of hematological alterations, which offers a potential biomarker for the early clinical recognition of MRSA infection and prognostic assessment.

The current study has certain limitations. First, the data were collected from a single center, which may limit the external validity of the conclusions; therefore, a multicenter, large-sample study should be carried out for subsequent validation. Second, the inherent missing data in retrospective studies may lead to selection bias, potentially affecting the accuracy of the analysis. Third, conventional hematological indices are susceptible to interference from individual differences and comorbidities, necessitating improvements in the diagnostic specificity of MRSA infection.

In summary, this study offers two key contributions. First, based on a detailed resistance profile analysis, it was confirmed that DFI-associated MRSA isolates exhibited a wider range of resistance phenotypes than MSSA strains, particularly regarding resistance to macrolides and quinolones. This finding underscores the importance of dynamic resistance monitoring in guiding clinical antimicrobial therapy. Second, the study employed an innovative approach by exploring common hematological indicators of MRSA infection in patients with DFI, highlighting their potential to enhance diagnostic specificity. For the first time, this study identified a correlation between MRSA-associated DFI and alterations in MCHC, D-dimer, ALB, ALP, and electrolyte (Na^+, Cl^-, Ca^{2+}) levels. These findings provide a new perspective for the early identification and intervention of MRSA infection in patients with DFUs and contribute to optimizing therapeutic strategies.

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