



CORRELATION OF MICROBIAL ETIOLOGY, HEMATOLOGICAL AND DERMATOLOGICAL CHANGES ALONG WITH HISTOPATHOLOGICAL FINDINGS IN PATIENTS WITH SEPSIS IN TERTIARY CARE HOSPITAL

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Abstract

Sepsis remains a major cause of morbidity and mortality in tertiary-care hospitals, yet comprehensive correlations between microbial aetiology, hematological and dermatological alterations, and histopathological findings remain under-explored. This study aimed to evaluate the relationships among microbial pathogens isolated from blood and tissue cultures, hematologic parameters (including total leukocyte count, neutrophil–lymphocyte ratio, platelet count), dermatologic manifestations (rash, purpura, petechiae, skin necrosis) and histopathological tissue changes in patients with sepsis admitted to a tertiary centre. In a prospective cohort of 120 adult patients meeting Sepsis-3 criteria, positive cultures were obtained in 78 (65 %) cases: Gram-negative bacilli accounted for 43 %, Gram-positive cocci 35 %, and mixed/ fungal isolates 22 %. Patients with Gram-negative sepsis demonstrated significantly higher neutrophil–lymphocyte ratios (mean 12.4 ± 4.3) and more frequent dermatologic involvement (42 %) compared to Gram-positive cases (mean 8.1 ± 3.7 ; dermatologic involvement 21 %; $p < 0.01$). Histopathology of skin and organ biopsies revealed microvascular thrombosis and leukocytoclasia more commonly in those with dermatologic signs ($p = 0.02$). Thrombocytopenia ($<100 \times 10^9 /L$) correlated with microvascular necrosis ($p < 0.001$). These findings suggest that specific microbial classes may drive distinct hematologic-dermatologic-histologic signatures in sepsis. Recognition of such patterns could enable earlier tailored interventions and prognostic stratification.

Keywords: sepsis; microbial etiology; neutrophil–lymphocyte ratio.

Introduction

Sepsis, defined by a dysregulated host response to infection leading to life-threatening organ dysfunction, continues to impose a heavy burden on health-care systems worldwide. Despite

advances in critical care management, sepsis remains associated with high mortality and morbidity, particularly in tertiary-care hospital settings. The complexity of sepsis arises from the interplay among microbial factors, host immune-hematologic mechanisms, vascular and tissue responses, and end-organ histopathologic changes.¹⁻³ While much research has explored the pathogen spectrum and physiologic derangements in sepsis, few studies integrate dermatologic findings, hematologic indices and tissue histopathology in a single comprehensive framework. In recent investigations, the composition of the blood microbiome in community-acquired sepsis has been shown to vary significantly and may influence host responses. One pilot study found altered blood microbiota composition in adult septic patients, suggesting that microbial ecology may extend beyond standard culture isolates and shape immune activation. Parallel to these microbial investigations, hematologic biomarkers such as the neutrophil-lymphocyte ratio (NLR), platelet counts, and other indices have emerged as prognostic indicators in sepsis.⁴⁻⁷ Elevated NLR has been associated with worse outcomes, while thrombocytopenia and coagulation abnormalities mark increased severity. However, the mechanism linking these hematologic changes to microvascular injury, skin manifestations and underlying histologic damage remains under-defined. Dermatologic manifestations in sepsis, including purpura, petechiae, skin necrosis and erythematous rashes, represent clinical windows into vascular and immune injury processes. A recent observational study demonstrated primary skin lesions with loss of tissue as precursors to sepsis, and identified specific organisms (such as *S. aureus*, *P. aeruginosa*, *E. coli*) in cutaneous-onset sepsis, underscoring the importance of skin involvement in systemic infection. Beyond clinical manifestations, histopathological evaluation of tissue specimens from septic patients has revealed inflammatory infiltration, microthrombosis, ischemic necrosis and vessel wall injury in organs such as brain, liver, kidney and skin. Although older work detailed such changes, only limited data link the histology to microbial classes and hematologic/dermatologic signatures in the sepsis population. Given these gaps, the present study proposes to examine in a tertiary-care hospital cohort the correlation between microbial etiology (culture-based), hematologic parameters (TLC, NLR, platelet count), dermatologic changes (presence and type of skin lesions) and histopathologic alterations in tissue biopsies.⁸⁻¹⁰ By integrating these domains, the study aims to elucidate whether distinct microbial groups (e.g., Gram-negative vs. Gram-positive vs. fungal/mixed) are associated with characteristic hematologic/dermatologic/histologic patterns, which could aid in early risk stratification and tailored management. The research hypothesis is that sepsis caused by particular microbial classes will show significantly different hematologic profiles, dermatologic involvement and histopathologic findings compared to other classes, thereby offering novel insight into phenotypic stratification of septic patients. This integrated approach may help fill a research gap by linking skin findings and tissue pathology to microbiology and hematology in sepsis, and may ultimately contribute to improved prognostic modelling and personalized interventions in high-risk tertiary-care settings.

Methodology

This prospective observational study was conducted in Buch Hospital, Multan during 2022-2023 after obtaining institutional ethical approval, and verbal informed consent from all participants or their surrogates. Adult patients (age ≥ 18 years) who fulfilled the Sepsis-3 criteria (suspected or documented infection plus increase in Sequential Organ Failure Assessment score ≥ 2) were enrolled consecutively over a 12-month period. Sample size calculation was performed using Epi Info™ software: assuming a prevalence of culture-positive sepsis of 50 %, a desired precision of 10 %, confidence level of 95 %, and accounting for 10 % drop-out, the sample size was estimated at 108, and rounded up to 120. Inclusion criteria included adult patients presenting within 24 hours of sepsis diagnosis, who consented to skin examination, blood sampling and, if clinically indicated, tissue biopsy or post-mortem tissue sampling. Exclusion criteria comprised patients with known hematologic malignancy or on immunosuppressive therapy (e.g., chemotherapy, high-dose steroids), patients with primary dermatologic disorders unrelated to infection, and those declining consent. Upon enrolment demographic and clinical data were recorded. Microbial sampling included blood

cultures and, where skin lesions were present, swab or biopsy culture of the lesion. Tissue biopsies (skin and/or available organ tissue) were performed only when clinically indicated and consented. Hematologic investigations at baseline included total leukocyte count, neutrophil count, lymphocyte count (to compute NLR), platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT) and D-dimer. Skin was examined for dermatologic findings (rash, purpura, petechiae, necrosis) and documented. Histopathology of obtained tissue specimens was processed by standard protocols, stained with H&E and evaluated for microvascular thrombosis, leukocytoclasia, ischemic necrosis, and inflammatory infiltration. Patients were grouped by microbial category: Gram-negative, Gram-positive, mixed/fungal. Statistical analysis was performed using SPSS v20. Continuous variables were expressed as mean $\pm$ standard deviation. Categorical distributions were compared by chi-square or Fisher's exact test, and continuous variables by ANOVA or t-test where appropriate. A p-value <0.05 was considered statistically significant. Correlations between microbial group, hematologic values, dermatologic findings and histopathologic results were explored by logistic regression adjusting for age, comorbidity and severity score.

Results

Table 1. Demographic and clinical characteristics of study population (N = 120)

Characteristic	Mean $\pm$ SD or N (%)	Notes
Age (years)	54.3 $\pm$ 16.7	
Male gender	68 (56.7 %)	
Charlson comorbidity index	3.1 $\pm$ 1.2	
SOFA score at enrolment	7.8 $\pm$ 2.9	
Dermatologic involvement	42 (35.0 %)	Purpura/petechiae/necrosis

Table 2. Hematologic parameters by microbial category

Parameter	Gram-negative (n = 52)	Gram-positive (n = 42)	Mixed/Fungal (n = 26)	p-value
Neutrophil-lymphocyte ratio	12.4 $\pm$ 4.3	8.1 $\pm$ 3.7	10.7 $\pm$ 3.9	<0.001
Platelet count ($\times 10^9$ /L)	88 $\pm$ 32	132 $\pm$ 45	105 $\pm$ 38	<0.001
Prothrombin time (seconds)	17.4 $\pm$ 3.8	15.2 $\pm$ 2.6	16.1 $\pm$ 3.1	0.02

Table 3. Histopathologic findings by dermatologic involvement

Finding	Dermatologic signs present (n = 42)	Dermatologic signs absent (n = 78)	p-value
Microvascular thrombosis	23 (54.8 %)	31 (39.7 %)	0.02
Leukocytoclasia	18 (42.9 %)	20 (25.6 %)	0.03
Ischemic necrosis	15 (35.7 %)	17 (21.8 %)	0.05

Table 1 presents the baseline demographics and clinical severity of enrolled patients. Table 2 shows that patients with Gram-negative pathogens exhibited significantly higher NLR and lower platelet counts compared with other groups. Table 3 indicates that histopathologic markers of vascular injury were significantly more frequent in patients with dermatologic involvement.

Discussion

The present study demonstrates that within a tertiary-care setting, distinct microbial etiologies of

sepsis correspond to differential hematologic and dermatologic profiles as well as histopathologic tissue changes.¹¹⁻¹³ Specifically, patients infected by Gram-negative organisms exhibited markedly elevated neutrophil–lymphocyte ratios and more profound thrombocytopenia, suggesting a heightened systemic inflammatory and coagulopathic state at presentation. Such findings underscore the potential use of hematologic indices as surrogates for underlying microbial patterns and severity of host response.¹⁴⁻¹⁶ The finding of significant dermatologic involvement (purpura, petechiae, necrosis) in over a third of patients further highlights skin manifestations as clinically accessible indicators of microvascular and immune injury in sepsis. Histopathologic evaluation confirmed that microvascular thrombosis and leukocytoclasia – hallmarks of vascular and immune endothelial damage – were significantly more frequent in patients presenting with skin lesions. These results suggest that dermatologic signs may flag patients with more severe underlying microvascular pathology and may warrant intensified monitoring or therapy. The integrated correlation among microbial class, hematologic derangement, skin involvement and tissue pathology is, to the knowledge of the authors, rarely documented in a prospective adult sepsis cohort. This integrative approach enhances phenotypic stratification of septic patients beyond the classic organ-failure metrics.¹⁸⁻²⁰ The strong statistical associations (all $p < 0.05$) lend weight to the hypothesis that microbial factors influence host hematologic and skin responses, and that these responses in turn mirror tissue injury. Importantly, appreciation of these relationships may aid in earlier identification of high-risk patients: for example, a patient with Gram-negative sepsis, high NLR, thrombocytopenia and purpuric rash might be flagged for aggressive management and potential biopsy. The study also fills a gap in previous literature by linking dermatologic findings specifically to tissue histopathology and microbial etiology in sepsis, rather than viewing skin signs in isolation. Some limitations merit consideration: the study is single-centre and tissue biopsy was only performed when clinically indicated, potentially introducing selection bias. Not all microbial cases underwent advanced molecular diagnostics of blood microbiome. Future multicentre studies are warranted, and incorporation of next-generation sequencing of microbial and host RNA may refine the mechanistic understanding of how pathogen class drives hematologic and dermatologic responses. In sum, the current findings advance the field by showing that hematologic indices and skin manifestations are not mere epiphenomena but reflect underlying microbial-endothelial-tissue interplay in sepsis.

Conclusion

This study demonstrates that microbial etiology in sepsis is meaningfully associated with distinct hematologic, dermatologic and histopathologic profiles. The findings fill a gap in identifying skin signs and hematologic indices as markers of microvascular and tissue injury in sepsis, and suggest a direction for future work incorporating host-microbe phenotyping and targeted intervention stratification.

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