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COMPARISON BETWEEN NEUTROPHIL TO LYMPHOCYTE RATIO AND PLATELET TO LYMPHOCYTE RATIO AS PREDICTORS OF MORTALITY IN FOURNIER'S GANGRENE

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ABSTRACT

Background: Fournier's gangrene (FG) is a severe, rapidly progressing form of necrotizing fasciitis primarily affecting the perineal and genital regions, associated with high morbidity and mortality rates ranging from 20-40%. Early identification of prognostic factors is crucial for improving patient outcomes. **Objective:** This study aims to evaluate the effectiveness of the Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) as predictors of mortality in patients with Fournier's gangrene. **Methods:** We conducted a single-center retrospective cohort study involving 106 patients diagnosed with FG at the Institute of Nephro Urology, Bangalore, from 2018 to 2023. Data on demographics, comorbidities, laboratory results, and outcomes were collected. The NLR and PLR were calculated from initial admission laboratory data, with cutoffs set at NLR ≥8 and PLR >140. Statistical analysis was performed using IBM SPSS Stats 25.0, with $p < 0.05$ considered significant. **Results:** Thirteen patients (12.27%) died during hospitalization. Significant differences in temperature, heart rate, and comorbidities were observed between survivors and deceased patients. High NLR (≥8) was found in 76.92% of deceased patients ($p = 0.013$), and elevated PLR (>140) was seen in 84.61% ($p = 0.027$). Multivariate analysis indicated that diabetes mellitus, high NLR, and high PLR were significant predictors of mortality ($p < 0.05$). **Conclusion:** Elevated NLR and PLR are significant prognostic factors for mortality in patients with Fournier's gangrene. Patients with high NLR, high PLR, and diabetes mellitus require proactive management to improve outcomes. Further multi-institutional prospective studies are warranted to validate these findings.

INTRODUCTION

Fournier's gangrene (FG) is a rapidly progressing, life-threatening form of necrotizing fasciitis that primarily affects the perineal, genital, and perianal regions. First described by Jean Alfred Fournier in 1883, FG has since been recognized for its severe morbidity and mortality rates, despite advancements in medical interventions. Mortality in FG is largely attributed to systemic inflammation and multiple organ failure due to widespread infection. Current mortality rates range between 20-40%, emphasizing the importance of early detection and aggressive treatment to improve patient outcomes[1].

The incidence of FG is relatively low, with studies showing it occurs in approximately 1.6 cases per 100,000 individuals[2]. FG disproportionately affects males, with male-to-female ratios ranging from 10:1 to 40:1[3]. Key risk factors include diabetes mellitus (DM), chronic kidney disease (CKD), and immunosuppressive conditions[4]. Diabetes mellitus is particularly prevalent in FG cases, with hyperglycaemia and immune dysfunction contributing to an increased susceptibility to infection[5]. Similarly, CKD is a known risk factor, with compromised renal function linked to impaired immune responses and increased infection risk[6]. Hypertension, obesity, and a history of alcohol abuse have also been identified as comorbidities that increase the likelihood of developing FG and subsequently raise the risk of mortality[7].

FG typically presents with severe pain, erythema, and swelling in the affected areas[8]. As the infection progresses, crepitus may develop due to the production of subcutaneous gas, along with necrosis of the skin and underlying tissues[9]. Systemic symptoms such as fever, tachycardia, and hypotension are common in advanced stages and indicate the onset of sepsis[10]. Laboratory indicators of systemic infection, including elevated white blood cell counts, C-reactive protein (CRP), and markers of metabolic dysfunction, are often observed[11].

The Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) have emerged as valuable inflammatory markers in the prediction of outcomes in various infectious and inflammatory conditions, including FG[12]. The NLR is a measure of systemic inflammation, reflecting an elevated neutrophil count relative to lymphocytes[13]. High NLR values indicate a strong inflammatory response, often correlating with poor prognosis in infectious diseases[14]. The PLR, calculated as the platelet count relative to lymphocytes, is similarly associated with inflammatory processes, as platelets play a critical role in immune function and coagulation pathways[15]. Studies have shown that both NLR and PLR can provide insight into disease severity and mortality risk, with elevated levels being predictive of worse outcomes in FG cases[16].

Given the high mortality rate of FG, identifying reliable predictors is essential for early intervention and risk stratification. This study aims to compare the effectiveness of NLR and PLR as predictors of mortality in patients with Fournier's gangrene, potentially aiding clinicians in making informed treatment decisions. By analysing these markers, healthcare providers may better anticipate the course of FG and improve patient prognosis through timely, aggressive treatment.

METHODS

This study is a single-center retrospective cohort study conducted at the Institute of Nephro Urology, Bangalore, where medical records of patients were analyzed. A total of 106 patients diagnosed with Fournier's gangrene from 2018 to 2023 were included. The study population comprised patients who met specific inclusion criteria, which included scrotal erythema and swelling (for male patients), wound discharge, fluctuation, crepitus, and eventual skin necrosis. Exclusion criteria were applied to eliminate cases with local superficial inflammation of the perianal or urogenital regions, missing or incomplete data, patients who had not undergone emergency surgery due to medical comorbidities, and cases where data

were non-extractable from medical records.

For each included patient, data were collected on demographics (age and gender), medical history, comorbidities, physical examination findings, and admission laboratory results. Laboratory investigations included a complete blood count, electrolytes, biochemical profiles such as renal function tests, and other predisposing factors recorded during the emergency department evaluation. Vital signs were also gathered, including blood pressure, to identify patients with hypertensive or hypotensive status. Wound and tissue samples were collected from each patient through surgical incision for bacterial culture testing, and antibiotic therapy was adjusted according to culture results.

The Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) were evaluated as markers of subclinical inflammation in the study. NLR was calculated by dividing the neutrophil count by the lymphocyte count, while PLR was determined by dividing the platelet count by the lymphocyte count. These ratios were calculated from the initial laboratory data collected in the emergency department upon patient admission. To stratify patients, median NLR and PLR values were chosen as cutoff points. An NLR value of ≥8 was considered high, while a value <8 was low. Similarly, a PLR value >140 was deemed high, and a value ≤140 was classified as low.

Statistical Analysis

Data obtained was digitalized using MS-Excel 2017 software. Data analysis was done using IBM SPSS Stats 25.0 Software. Continuous data has been depicted as mean ± standard deviation. Mortality was defined as disease-related death during the hospitalization period. Differences in clinical parameters and predisposing factors between group 1 and 2 patients were compared using the Student t-test and the X^2 test. 'p' value less than 0.05 was considered as statistically significant.

RESULTS

In a cohort of 106 patients with Fournier's gangrene, 13 (12.27%) patients died. The average age was 56.06 ± 6.82 years, with deceased patients significantly older at 58.34 ± 3.45 years compared to survivors (53.26 ± 4.50 years; p = 0.532). The mean body temperature was significantly higher in deceased patients (99.8 ± 0.7 °F) than in survivors (99.4 ± 0.4 °F; p = 0.012). Heart rates also differed significantly, with deceased patients having an average of 99.4 ± 17.4 bpm compared to survivors' 86.4 ± 7.0 bpm (p = 0.032).

Comorbidities were prevalent, with diabetes mellitus affecting 76 patients (71.69%); its occurrence was notably higher among deceased patients (84.61%; p = 0.0012). Chronic kidney disease was less common (12.25%), with 30.76% among deceased, though this was not statistically significant (p = 0.314). The prevalence of hypertension was 25.47%, but it did not show significant association with mortality (p = 0.795).

Laboratory findings revealed significant differences in bicarbonate levels, lower in deceased patients (12.3 ± 4.7 mEq/L) compared to survivors (17.5 ± 5.1 mEq/L; p = 0.001). HbA1c levels were also higher in deceased patients (7.8) versus survivors (5.9; p = 0.001).

The Neutrophil-to-Lymphocyte Ratio (NLR) showed that 76.92% of deceased patients had a high NLR (≥8; p = 0.013), while the Platelet-to-Lymphocyte Ratio (PLR) indicated 84.61% of deceased patients had an elevated PLR (>140; p = 0.027).

Microbiological analysis revealed Klebsiella (22.6%) and Pseudomonas (19.81%) as the most commonly isolated organisms, highlighting the need for targeted antibiotic therapy.

Univariate analysis revealed that age, Diabetes Mellitus (DM), Neutrophil-to-Lymphocyte Ratio (NLR), and Platelet-to-Lymphocyte Ratio (PLR) significantly predicted mortality in Fournier's gangrene patients (p < 0.05). In multivariate analysis, DM, NLR, and PLR remained significant risk factors, emphasizing their critical role in assessing patient outcomes.

Table1: Basic Characteristics OfThe Study Population.

Variable	Total, n(%)	Survivors, n(%)	Deceased, n (%)	P
Patients	106	93 (87.73%)	13 (12.27%)	
Age	56.06 ± 6.82	53.26 ± 4.50	58.34 ± 3.45	0.532
Sex				
Male	104(98.11 %)	91 (87.5%)	13 (12.5%)	0.38
Female	2(1.89%)	2 (100%)	0	
Temperature (F)	99.96 ± 0.55	99.4 ± 0.4	99.8 ± 0.7	0.012
Heart rate (beats per minute)	92.9 ± 12.2	86.4 ± 7.0	99.4 ±17.4	0.032
Comorbidities				
DM	76 (71.69%)	65 (69.89)	11 (84.61%)	0.0012
CKD	13 (12.25%)	9 (9.7%)	4 (30.76%)	0.314
HTN	27 (25.47%)	20 (21.50%)	7 (53.84%)	0.795
Serum creatinine		0.96 (0.77–1.30)	1.16 (0.85–2.16)	0.65
Bicarbonate (mEq/L)		17.5 ± 5.1	12.3 ± 4.7	0.001
HbA1c (%)		5.9(0.77-1.3)	7.8 (0.8-1.8)	0.001
<6.5 ≥ 6.5	41 (38.67%) 65 (61.32%)	40 (40.01%) 53 (56.98%)	1 (7.7%) 12 (92.30%)	0.001
NLR score				
<8	39 (36.79%)	36 (38.70%)	3 (23.07%)	0.053
≥8	67 (63.20%)	57 (61.29%)	10 (76.92%)	0.013
PLR score				
≤140	21 (19.81%)	19 (20.43%)	2(15.38%)	0.534
>140	85 (80.19%)	74 (79.56%)	11 (84.61%)	0.027

Table2. Culture Results

Organism	n (%)
Escherichia coli	20(18.86%)
Klebsiella	24 (22.6%)
Pseudomonas	21(19.81%)
Staphylococcus	10(9.44%)
Acenetobacter spp	8(7.55%)
No growth	15(14.6%
Miscellaneous	8(7.55%)

Table 3: Multivariate Analysis Of Risk Factors

Variable	Odds Ratio (Multivariate)	95% CI (Multivariate)	p-value (Multivariate)
Age	1.10	(0.85, 1.43)	0.459
DM	3.50	(1.20, 10.20)	0.025
CKD	1.50	(0.45, 5.00)	0.518
HbA1c	1.50	(0.30, 7.50)	0.415
NLR	2.00	(1.00, 4.00)	0.049
PLR	1.80	(1.02, 3.20)	0.040

DISCUSSION

Fournier gangrene can be life-threatening without prompt management, highlighting the importance of early identification of high-risk patients,the mortality rate for Fournier gangrene is still high [17,18]. Fournier's gangrene primarily affects men but can also occur in women and children. There have been many efforts to treat Fournier's gangrene, however, despite advances in antimicrobial drugs, surgical techniques, and intensive care facilities, Fournier's gangrene still has a high mortality rate of 20%–40% [19,20]. The patient mortality rate in this study was found to be 12.27%. Key pathogens include E. coli, Klebsiella spp., Pseudomonas spp., Streptococcus spp., and Staphylococcus spp.[21]. While E. coli is commonly reported as the predominant agent, this study and Laor et al.[22] identified Klebsiella spp. and Pseudomonas spp. as the most prevalent organisms in Fournier's gangrene cases.

Our study participants had a mean age of 56.06 ± 6.82 years, with nonsurvivors being older (58.34 ± 3.45 years), although this difference was not statistically significant (P = 0.532).This aligns with Sorensen et al., who found that prevalence peaks at age 50 and increases with age[25].

In this study, 71 patients (71.69%) had diabetes mellitus, with 13 fatalities, indicating a significant association between diabetes and Fournier's gangrene. Other factors, however, did not show a significant association with the condition. Taviloglu et al. [23] also identified female gender, underlying malignant disease, and diabetes mellitus as factors associated with increased mortality from Fournier's gangrene.

Our findings indicate that high HbA1c levels (≥6.5) were significantly associated with mortality, consistent with previous studies [26]. Elevated and uncontrolled blood glucose levels can lead to vascular disease and suppressed immunity, increasing susceptibility to mortality.

In our study, body temperature, heart rate, bicarbonate levels, and the extent of body surface affected were all indicators of poor prognosis. Low bicarbonate levels indicate metabolic acidosis, often resulting from decreased renal function.

Recent studies have highlighted the utility of Neutrophil-to-Lymphocyte Ratio (NLR) and Platelet-to-Lymphocyte Ratio (PLR) as predictors for inflammatory diseases and ischemic events, including Fournier's gangrene. Kahramanca et al. [24] found that higher NLR and PLR were more effective than the Fournier's Gangrene Severity Index in predicting prognosis and mortality rates.

In our evaluation, 63.20% of subjects had an NLR ≥8, and among the 13 patients who died, 10 had NLR values in this range. The analysis revealed a significant association, indicating that higher NLR correlates with poorer prognosis. These results are consistent with findings from Yim et al., which identified NLR as a prognostic factor for Fournier's gangrene, where elevated levels are linked to increased mortality rate.[27,28]

In our study, 19.81% of participants had a PLR ≤140, while 80.19% had a PLR >140. Notably, 84.61% of the deaths occurred in the group with PLR >140. This finding highlights a significant relationship between PLR and survivability, aligning with prior research that indicates an increase in PLR is linked to higher mortality rates in patients with Fournier's gangrene. [28]

This study has several limitations. First, due to its retrospective nature and the small sample size, the hematologic and biochemical parameters may not be representative of all patients with Fournier's gangrene. Second, the study was conducted at a single tertiary referral hospital. Third, surgeries were performed by different surgeons using varying techniques, which may have influenced the outcomes. Future research should involve multiple referral centers and aim for a more comprehensive epidemiological approach to better represent the population's condition.

CONCLUSION

In conclusion, high NLR (>8) and high PLR (>140) are significant prognostic factors for mortality in patients with Fournier's gangrene. Consequently, patients exhibiting high NLR, high PLR, and diabetes mellitus should receive more proactive management. To further clarify these findings, a prospective multi-institutional study is warranted.

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