

The predictive value of systemic inflammatory response syndrome on the outcome of soft tissue infections in adults

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Abstract

Objective: The study aims to identify whether the Systemic Inflammatory Response Syndrome (SIRS) provides a good predictive value to determine and correlate with the outcome of soft tissue infections in adults with diabetic foot infection (DFI).

Design: Retrospective study collected the data of 311 cases using the criteria of SIRS.

Setting: Surgical ward and intensive care unit (ICU) of Al-Noor Specialist Hospital in Mecca, Saudi Arabia.

Material and Methods: 277 participants with severe diabetic foot infection, gas gangrene or necrotizing fasciitis were retrospectively reviewed from 2014 to 2016.

Main Outcome Measures: The SIRS criteria were used to define the severe infection.

Results: The SIRS criteria were positive in patients with longer stay in ICU and there was no significant relationship between the SIRS criteria and amputation in case of DFI. SIRS criteria had a good correlation with NF scoring system, which both can help in the diagnosis of NF.

Conclusion: SIRS criteria for severe infections in diabetic patients with soft tissue infections were not associated with worse outcomes other than longer hospital stay. The relationship between SIRS criteria and total score of NF was statistically significant.

Keywords: Diabetic foot infection, Systemic Inflammatory Response Syndrome (SIRS), necrotizing fasciitis

Introduction:

Systemic inflammatory response syndrome (SIRS) refers to a defensive response of the body to a toxic inflammatory infection affecting the whole body, particularly, immune system.¹ The occurrence of SIRS can be identified if at least two or more of the following conditions are present: Fever $> 38^{\circ}\text{C}$ or $< 36^{\circ}\text{C}$, Heart rate > 90 beats/min, respiratory rate > 20 breaths/min or $\text{PaCO}_2 < 32$ mm Hg or White blood cell count $> 12,000/\mu\text{L}$ or $< 4,000/\mu\text{L}$ or the presence of $> 10\%$ immature forms.^{2,3} In severe conditions, abnormality in circulatory system can occur by dropping blood pressure, ultimately leading to the patient's death.⁴

Soft tissue infection is a very common medical condition and its complications may include: necrotizing fasciitis, lymphadenitis, myositis,

osteomyelitis, endocarditis and septicaemia or sepsis.⁵ Hine et al.⁶ have found higher incidence of infections in Type 2 patients except herpes simplex. Glaudemans, Uçkay and Lipsky⁷ indicated that diagnosing the incidence of infection in the foot of a diabetic patient can somewhat be a complicated task. Very few studies have been done on SIRS and found its relationship with the outcome of the soft tissue infection in adults. However, a number of studies are found related to SIRS criteria, diabetic foot infection, and necrotizing fasciitis separately.^{4,8-10}

Necrotizing fasciitis (NF) is a rare but a rapidly progressive devastating soft tissue necrosis in which fascia and subcutaneous tissues with a significant hospital morbidity and mortality are involved. It affects about one in every 100,000 people per year globally.¹⁰ It is a rare and fatal

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soft-tissue infection, which involve the superficial fascial layers of the perineum, extremities, or abdomen. Evolution to septic shock can happen gradually with its related high mortality and morbidity.¹¹ For early distinction of NF, the Laboratory Risk Indicator for NF (LRINEC) is used from six routinely performed laboratory tests. Multiple studies have assessed that the LRINEC can be utilized for the early diagnosis, identification, and classification of NF patients into different risk categories to facilitate the appropriate management of hospital resources.¹²

Due to the lack of studies related to SIRS and its association to the outcome of soft tissue infection, this study aims to find out whether the SIRS criteria give a good predictive value to determine the outcome of common soft tissue infections in adults and therefore estimate the extent of SIRS validity in predicting the morbidity and mortality of common soft tissue infections in clinical settings.

Material and Methods:

The study has collected data of patients admitted to surgical ward and intensive care unit (ICU) of Al-Noor Specialist Hospital in Mecca, Saudi Arabia, a tertiary teaching hospital serving approximately 12,000 patients in different departments annually. This retrospective study collected the data of 311 cases using the criteria of SIRS. Data were collected from the existing files using a data collection sheet from Al-Noor Specialist Hospital. All patients between January 1st, 2014 to January 1st, 2016 were reviewed and included in the study. Patients included in the study were aged more than 18 years and diagnosed on admission with one of the following: DFI, gas gangrene or necrotizing fasciitis whether survived or died during hospitalization. Among 311 cases, 277 cases fulfilled the criteria. Whereas, patients with age 18-years or less and cases that lacked the complete data for SIRS criteria and an outcome measure were excluded from the study (34 cases). An approval from the ethical committee at the faculty of medicine in Umm Al-Qura University and the ethical committee of biological researches at Al-Noor Specialist Hospital was taken prior to data collec-

tion.

Personal data including (age, gender, nationality, comorbidities and diagnosis), admission data (vital signs, investigation and ER procedures), location of admission (surgical ward vs. intensive care unit), interventions (medical and surgical), and outcome were retrieved from the electronic medical records or files for all patients. All variables were predefined before retrieving the data and recording in a standardized format during information collection. The SIRS criteria were established for more than one of the following parameters;

- (1) white blood cell count greater than 12,000/mm³ or below 4,000/mm³
- (2) body temperature more than 38 or less than 36° C
- (3) tachypnoea with respiratory rate more than 20 bpm, and
- (4) heart rate more than 90 bpm. The SIRS criteria were met as defined by the ACCP/SCCP in 1992.

To assess the relationship between SIRS criteria and final outcome of each patient, the study looked at certain data including location of admission (surgical ward or ICU), length of hospital stays, the need for a surgical procedure (e.g. amputation vs. debridement), and survival (30 days survival rate).

Statistical analysis was performed with SPSS 21. The demographics and characteristics of patients were summarized using descriptive analysis. Number and percentages were used to present categorical variables. Categorical variables were examined using Chi-square or Fisher exact test, when needed. T-test was used to find out the relationship between SIRS criteria and site of admission in the study.

Results:

From 2014 to 2016, 311 patients were admitted in surgical ward or ICU with SIRS. A total of 277 patients were included who met the in-

Table 1: The relationship between SIRS criteria and outcome in the study

Outcome		SIRS Criteria		
		Negative SIRS	Positive SIRS	Total
Survived	N	171	85	256
	%	94.5%	88.5%	92.4%
Died	N	10	11	21
	%	5.5%	11.5%	7.6%
Total	N	181	96	277
	%	100.0%	100.0%	100.0%
Chi-square	X ²		2.999	
	P-value		0.083	

Table 2: The relationship between SIRS criteria and site of admission in the study [surgical ward duration of stay, duration of ICU stays, total duration of admission (days)]

	SIRS Criteria	SIRS Criteria			T-test	
		Range	Mean	SD	t	P-value
Duration Surgical Ward (days)	Negative SIRS	1 - 268	10.173	23.341	-0.286	0.775
	Positive SIRS	1 - 82	10.942	12.462		
Duration of ICU	Negative SIRS	1 - 44	11.778	13.184	0.852	0.400
	Positive SIRS	1 - 24	8.895	6.463		
Duration of admission	Negative SIRS	1 - 274	10.956	24.519	-0.259	0.796
	Positive SIRS	1 - 90	11.660	13.217		

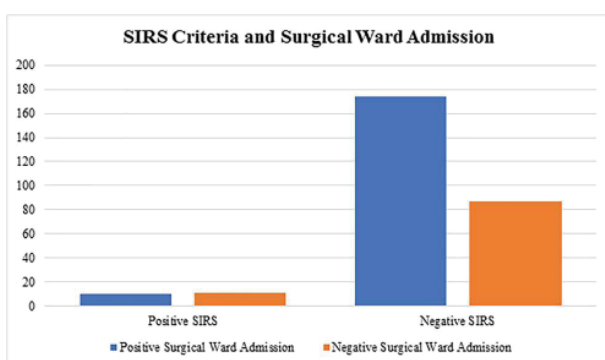


Figure 1: Relationship between SIRS Criteria and surgical ward stay

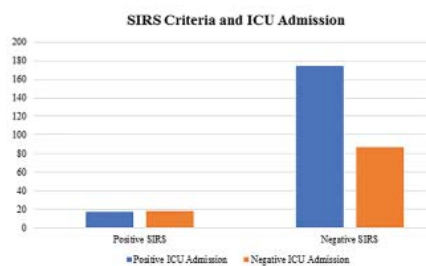


Figure 2: Relationship between SIRS Criteria and ICU admission

clusion criteria as proposed in the figure 1. Findings illustrated that only 256 patients survived while 21 patients lost their life. However, out of these 256 survived patients, 171 had negative and 85 had positive SIRS criteria. The SIRS criteria were also followed in 21-patients who did not survive, in which 10 had negative, while 11 had positive SIRS criteria as shown in table-1. A total of 261 patients stayed in the surgical ward, among whom 174 had negative while 87 had positive SIRS criteria as shown in figure-1.

Inclusion criteria: Adults aged > 18 years old, Alive or dead, diagnosed with one of the following: DFI, Gangrene or NF

Excluding criteria: Adults ages < 18 years old, cases that lacks SIRS criteria and outcome measures.

Total number of cases 311 in which 277 were included and 34 cases were excluded.

Regarding ICU admissions, 35 patients had to stay in the ICU (17 with positive and 18 with negative SIRS criteria) as shown in figure-3. Figure 3 shows that there was no significant relationship between SIRS Criteria and surgical ward stay where $X^2=3.034$ and $p\text{-value}=0.069$ was more than 0.05. A total of 164 patients showed negative SIRS and negative ICU admission. 78-patients showed positive SIRS and negative ICU admission. 17-patients showed negative SIRS and positive ICU admission. 18-patients showed positive SIRS and positive ICU admission.

Table 2 demonstrates the relationship between SIRS criteria and the overall admission in the hospital. A total of 118 patients went through amputations, of whom 70 had negative while 48 had positive SIRS criteria as shown in Figure 2. Figure 3 also shows that there was no significant relationship between SIRS criteria and amputation where $X^2=3.277$ and $p\text{-value}=0.07$ was more than 0.05. The level of amputation was determined among 112 patients as follows: 58 went through toe amputations, 11 had a trans-metatarsal amputation, two had a Syme's

Table 3: The relationship between SIRS criteria and level of amputation

Level of amputation		SIRS Criteria		
		Negative SIRS	Positive SIRS	Total
Negative	N	114	51	165
	%	63.0%	53.1%	59.6%
Toes	N	37	21	58
	%	20.4%	21.9%	20.9%
Trans-metatarsal	N	8	3	11
	%	4.4%	3.1%	4.0%
Syme's	N	1	1	2
	%	0.6%	1.0%	0.7%
Below-the- knee	N	12	12	24
	%	6.6%	12.5%	8.7%
Knee disarticulation	N	1	0	1
	%	0.6%	0.0%	0.4%
Above-the- knee	N	8	8	16
	%	4.4%	8.3%	5.8%
Total	N	181	96	277
	%	100.0%	100.0%	100.0%
Chi-square	X2		6.384	
	P-value		0.382	

Table 4: The relationship between SIRS criteria and total score of NF in the study

SIRS Criteria	Total score of NF			T-test	
	Range	Mean	SD	t	P-value
Negative SIRS	0 - 9	3.564	1.622	-3.471	±
Positive SIRS	1 - 9	4.295	1.725		±

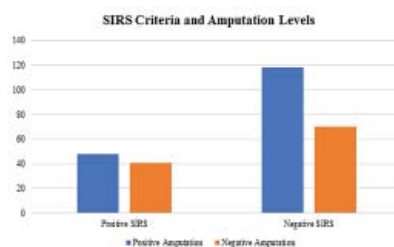


Figure 3: Relationship between SIRS Criteria and Amputation

amputation, 24 went through below-the-knee amputation, one had a knee disarticulation, and 16 had an above-the-knee amputation (Table 3). Table-3 shows that there was no significant relationship between SIRS criteria and level of amputation where $X^2=6.384$ and $p\text{-value}=0.382$ was more than 0.05.

The relationship between SIRS criteria and the patients' laboratory results including WBC count and serum creatinine, haemoglobin, glucose, and sodium levels have also been studied. Other results that were statistically analysed included the relationship between SIRS criteria and different medical conditions such as DM, hypertension, coronary artery disease (CAD) and renal disease. Regarding the NF scoring system, the study has found a significant relationship between positive and negative SIRS criteria and the total score of the disease ($p = 0.001$) (Table 4). Table 4 shows that there was a significant difference between negative SIRS and positive SIRS regarding total score of NF (increased NF score with positive SIRS) ($t = 3.471$, $p = 0.001$). In negative SIRS cases, the total score of NF ranged from 0 to 9 by 3.471 ± 1.622 . In positive SIRS cases, the total score of NF ranged from 1 to 9 by 4.295 ± 1.725 .

Figure 4 shows that there was a significant relationship between SIRS criteria and serum sodium level (decreased serum sodium level) ($X^2 = 6.124$, $p = 0.013$). The study has found 91 cases with 50.8% negative SIRS and with serum $Na < 135$ meq/L, whereas 63 cases with 66.3% positive SIRS and with serum $Na < 135$ meq/L.

Figure 6 shows that there was a significant relationship between SIRS criteria and haemoglobin level (decreased Hb level) ($X^2 = 8.889$, $p = 0.012$). The study showed 27 patients with positive SIRS and $Hb > 13.5$ g/dL, 47 patients with positive SIRS and with Hb level ranging from 11 to 13.5 g/dL, and 91 patients showed positive SIRS and with Hb level less than 11 g/dL.

Discussion:

The results indicated that SIRS criteria were not related to the survival of patients ($p\text{-value} =$

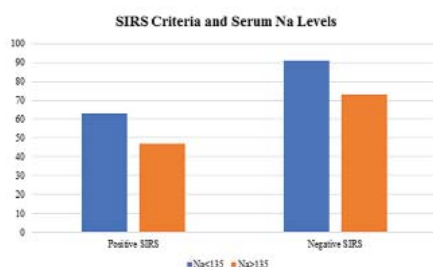


Figure 4: Relationship between SIRS criteria and Serum Sodium Level

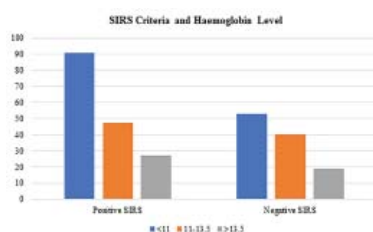


Figure 5: Relationship between SIRS criteria and haemoglobin level

0.083). Mixed results were evidently reported regarding the relationship between the outcome of diabetic foot infection and other aspects such as serum albumin level, serum sodium level, haemoglobin and WBC count in previous studies. For instance, Hadadi et al.¹⁴ have found no relationship between the outcome of diabetic foot infections (DFI) and several other aspects. In the present study, the length of stay was proven to be related to have a positive SIRS criteria as patients with positive SIRS criteria had a longer admission in the ICU (p -value > 0.05), while length of stay in the surgical ward did not have a statistically significant relationship with SIRS criteria (p -value = 0.069).

These findings were supported with a previous study where patients with severe DFI had a longer stay in the hospital by four days than patients with moderate DFI.¹⁴ However, the previous study did not define the hospital admissions as ICU or surgical ward. Nevertheless, they found that patients with severe DFI required more hospital admissions in general. Regarding surgical amputation, the results of this study showed no significant relationship between SIRS and the need for amputation (p -value=0.07).¹⁴ However, it was found that patients with severe diabetic foot infection experienced a 2.55-fold higher risk of an amputation.⁸ However, this

study could not find any statistical data that studied the relationship between SIRS criteria and the number of surgical procedures needed in general, whether it was surgical amputation or debridement only.

In this study, patients underwent different categories of amputation in the hospital such as with toes, trans-metatarsal, Syme's, below-the-knee, knee disarticulation and above-the-knee. Similarly, this study did not find any significant relationship between the level of amputation and the presence of SIRS criteria ($p = 0.382$). This study has found a significant relationship between positive SIRS criteria and a decreased serum level of sodium and haemoglobin with a p -value of 0.013 and 0.012, respectively. A total of 63-patients reported positive SIRS criteria and a decreased serum sodium level (less than 135 meq/L), while 61 cases with positive SIRS criteria had a decreased serum haemoglobin level (less than 11 g/dL).

Previous studies have found a positive relationship between major amputations and varied laboratory results such as ESR, low serum albumin level, serum sodium level, and WBC count.^{15,16} Several medical conditions were included in this study to find the relationship between positive SIRS criteria and the general health condition of the patients such as DM, hypertension, CAD and renal disease. However, none of them was found to be statistically significant. Hence, they showed no relationship with SIRS criteria in determining patients' outcome of soft tissue infection. Other studies did not focus on the relationship between SIRS criteria and medical conditions; therefore, the study could not conduct a fair comparison between the results of this study and previous studies in this regard. A scoring system for necrotizing fasciitis has been used to assist physicians in the diagnosis of NF.^{17,18} In this study, patients with positive SIRS criteria had higher NF score than SIRS-negative patients with a p -value of 0.001. SIRS criteria can help in identifying patients whom at high risk to have NF on presentation to the emergency department, which could be a challenge to diagnose on initial presentation due to wide

spectrum of clinical manifestation.

The weaknesses of this study should be discussed. Firstly, SIRS criteria did not predict the outcome of patients with DFI. Secondly, absence of relevant literature limited the study to only collected data, therefore, it failed to examine the theoretical implications of previous studies in this regard. The strength of this study is the examination and identification of the relationship between SIRS criteria and other aspects of major amputations and variable laboratory results such as ESR, serum albumin level, serum sodium level and WBC count, which occur in diabetic patients.

The present findings examined the previously existing data of patients with severe skin and soft tissue and diabetic foot infection and found that there was no significant association between SIRS criteria for severe infections in diabetic patients with soft tissue infections with outcomes other than longer ICU stay. The study was able to find out a significant relationship between SIRS criteria and longer ICU stay and decreased sodium and haemoglobin serum levels. SIRS criteria had a good correlation with NF scoring system, which both can help in the diagnosis of NF.

Conclusion:

Based on the findings of this study, it was recommended that additional studies should be conducted regarding the relationship between SIRS criteria and the outcomes of patients with soft tissue infections but in large group of patients. This will assist medical staff and experts in diagnosing the infection at the earliest and to provide better facilities to patients.

List of abbreviations:

SIRS: Systemic Inflammatory Response Syndrome

DFI: Diabetic Foot Infection,

ICU: Intensive Care Unit,

ACCP: American College of Chest Physicians,

SCCP: Society of Critical Care Medicine,

DM: Diabetes Mellitus,

NF: Necrotizing Fasciitis,

WBC: White Blood Cells,

ESR: Erythrocyte Sedimentation Rate,

CAD: Coronary Artery Disease

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Role and contribution of authors:

Dr Hassan Adnan Bukhari, collected the data, references and did the write up.

Dr Rani Abdullah ALSairafi, critically review the article and made final changes,

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