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An Observational Study on Levels of Serum Fibrin Degradation Product (FDP), D-Dimer and Procalcitonin in Burn Sepsis

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Abstract

Background: Despite improvements in burn management, infection is still the biggest challenge in major burn cases globally. Burn causes extensive tissue destruction, immune dysfunction, increases the risk of infection and septicemia with high morbidity and mortality. The aim of this study was to observe the levels of serum fibrin degradation product (FDP), D-dimer and procalcitonin in patients with burn sepsis treated in intensive care unit (ICU).

Methods: This observational study was carried out in Department of Burn and Plastic Surgery, Dhaka Medical College Hospital, Dhaka from February 2018 to January 2019. Forty (40) patients with major burns, from (15% to 50% total body surface area burn) with burn sepsis, were recruited for the study. In all cases, plasma level of fibrin degradation product (FDP), D-dimer and procalcitonin were measured and recorded.

Result: Male predominance (57.5%) was observed in our study. Eighty five percent (85%) patients had total body surface area burn (TBSA) 20% to 50%. Sixteen patients (40%) suffered from flame burn, 13 (32.5%) patients from scalds and 11 (27.5%) patients had high voltage electric burn. The value of FDP was raised in 62.5% patients, D-dimer in 67.5% patients. Serum procalcitonin level was high (> 2ng/ml), indicating burn sepsis in 47.5% cases but it was not significant (2 sample t – test reveals no significant relationship between rise of serum level of procalcitonin and presence of burn sepsis)

Conclusion: Fibrin degradation product (FDP) and D- dimer were raised in two-thirds of burn cases while procalcitonin in two-fifths cases. Measurement of serum level of FDP, D-dimer and procalcitonin may give an idea regarding early onset of bacterial infection and burn sepsis and can serve as an indicator for burn sepsis.

Key words: Burn sepsis, Fibrin degradation product (FDP), D-dimer, Procalcitonin.

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Introduction:

Burn injury is one of the most critical and life-threatening injuries with high morbidity and mortality. Burn affects not only the skin but involves all systems of the body. Due to loss of skin barrier and alteration in the cellular and humoral immune responses, burn patients have increased susceptibility to infection. In extensive burn, more than 15-20% total body surface area (TBSA), due to persistent exposure to pathogens, patient may develop systemic inflammatory response syndrome (SIRS) and eventually lead to multiple organ failure (MODS) and death. Burn sepsis is the leading cause of mortality in adult and pediatric burn patients. Mortality following burn sepsis was noted up to 50%–84% in adult burn patients[1]. Systemic inflammation and burn-induced immunosuppression increase the risk of infection and sepsis, and these are major causes of morbidity and mortality in burn patients.

In clinical practice, diagnosis of burn sepsis depends on the use of combined clinical and laboratory findings. The presence of three or more of the following criteria indicates burn sepsis:

- temperature >39 °C or <36.5 °C

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- progressive tachycardia >110 beats per minute
- progressive tachypnoea >25 breaths per minute or minute ventilation >12 L/min,
- thrombocytopenia <100,000/mcl (does not apply until 3 days after burn)
- hyperglycaemia in the absence of pre-existing diabetes mellitus
- inability to continue enteral feedings >24 h (abdominal distension, enteral feeding intolerance, uncontrollable diarrhoea [>2500 ml/day]) and
- In addition, a documented infection is identified; defined as culture positive infection or pathologic tissue source identified or clinical response to antimicrobials[2].

Severe burn injury induces an inflammatory response, causes activation of all inflammatory pathways, disruption of cell-mediated immunity and alterations of mediators of the immune system such as cytokines, growth factors, vascular endothelium, and various immune-competent cell populations. The dysfunction of the immune system, a large cutaneous bacterial load, the possibility of gastro-intestinal bacterial translocation, prolonged hospitalization and invasive diagnostic and therapeutic procedures, all contribute to infection and sepsis[3,4]. Burn injuries are associated with high morbidity and mortality following infection and septic shock. According to the World Health Organization, in 2018 about 11 million burn cases occurred worldwide, claiming 180,000 lives[5].

Early diagnosis of sepsis is crucial for the management of burn patients to prevent complications and increase survival. Clinical and laboratory features of systemic inflammation such as changes in body temperature, leukocytosis, and tachycardia, used for diagnosis of sepsis are neither specific nor sensitive. The ideal parameter for diagnosis of sepsis should be sensitive, specific, reliable, and easy to measure. Serum fibrin degradation product (FDP), D-dimer and procalcitonin (PCT) may have some of these characteristics and can be a used as a sepsis marker in burn intensive care unit (ICU)[6].

Following sepsis, different local and systemic response systems are activated, such as coagulation and fibrinolysis. D-dimer acts as a marker of fibrin degradation and reflects the turnover of the coagulation system and can be used as a marker of microcirculatory failure. FDP is the breakdown product of fibrinogen and increased value indicates enhance fibrinolysis. Elevated FDP is used to confirm the presence of disseminated intravascular coagulation (DIC). Procalcitonin (PCT) is one of the most studied biomarkers in bacterial infections and sepsis. Procalcitonin levels increase as early as 3 hours after bacterial infection and reach a peak at around 20 hours and have been used as a biomarker for infection and sepsis since the year 1990s[1].

In a developing country like Bangladesh, burn injury becomes one of the most dangerous health hazards now a day. Morbidity and mortality from major burns is very high. The severity of burn, lack of isolation of the patient, inadequate maintenance of sterility and late identification of septicemia increase the risk. Wound swab for culture and sensitivity and blood culture to diagnose septicemia are time consuming, not readily available and cause diagnostic delay. The aim of the current study was to estimate serum level of FDP, D-dimer and procalcitonin in burn sepsis patients.

Materials and Methods:

An observational study was carried out in the Department of Burn and Plastic Surgery, Dhaka Medical College Hospital, Dhaka from February 2018 to January 2019. A total of 40 cases, with major burn, (15 - 50%) total body surface area (TBSA) with burn sepsis treated in intensive care unit (ICU), were included in the study. Patients presented with more than 50% total body surface area (TBSA) burn and patients with multiple co-morbidities were excluded from the study due to high mortality. In all patients, plasma level of FDP, D-dimer and procalcitonin were measured and recorded in a data collection sheet. Only a single sample at the onset of clinical features of burn sepsis were sent and no further follow up test was done. Samples were sent between the 4th to 12th post burn days. In addition, routine laboratory investigations, wound swab for culture and sensitivity and in some cases blood culture was done as an adjuncts.

In this study, we categorized serum level of fibrin degradation product (FDP) value into two types:

- Value less than 200ng/ml is considered as negative.
- Value >200ng/ml is considered as positive.

We categorized serum procalcitonin level into 3 types:

- Cat 1: Less than 0.5 ng/ml indicates no sepsis,
- Cat 2: 0.5 -2 ng/ml indicates presence of infection and
- Cat 3: more than 2 ng/ml indicates presence of burn sepsis.

Results:

Male predominance was observed in our study; 57.5% was male and 42.5% was female. Eighty five percent (85%) patients had total body surface area burn (TBSA) 20% to 50%. Sixteen patients (40%) suffered from flame burn, 13 patients from scalds (32.5%), and 11 patients (27.5%) had high voltage electric burn. Regarding the outcome, 60% patients survived, and 40% patients died.

Serum level of fibrin degradation product (FDP) value was negative (value <200ng/ml) in 15 patients (37.5%) and was positive (value > 200mg/ml) in 25 patients (62.5%).

D-dimer was positive in 27 patients (67.5%), and negative in 13 patients (32.2%).

Though serum level of fibrin degradation product was increased in patients with positive wound swab culture, we did not find any significant relation between rise of serum level of FDP and presence of septicemia.

We found about 47.5% (19) patients showed high(>2ng/ml) procalcitonin level, indicating presence of sepsis while the 47.5% (19) patients with procalcitonin level 0.5-2 ng/ml indicating presence of infections (Table 2). Though procalcitonin level was increased in presence of infection and burn sepsis, we did not find any significant relationship among PCT levels using two sample t- tests.

Wound swab for culture and sensitivity isolates single microorganism in 26 patients, multiple organisms in 12 patients and no growth in 2 patients. The most common organism found was pseudomonas. Blood culture was positive in 50% of cases. Antibiotics were given according to culture sensitivity.

Table-I

Relation between positive wound swab culture and rise of FDP.

Wound swab for culture	FDP < 200		FDP >200		P-value*	Total	
& sensitivity	N	%	N	%		N	%
No growth	3	21.43	o	0.00	-	3	07.50
Single organism	8	57.14	18	69.23	0.55	26	65.00
Multiple organism	3	21.43	8	30.77	0.76	11	27.50
Total	14	100.00	26	100.00	-	40	100.00

*Two sample t-test

Table-II

Relation between positive wound swab culture and rise of serum procalcitonin level.

Wound swab for culture &	PCT level <0.5	PCT level 0.5 to 2	PCT level >2	P-value*	Total
sensitivity	N (%)	N (%)	N (%)	N (%)	
Multiple organism	-	5	6	0.78	11
Single organism	2	11	13	0.73	26
No growth	-	3	0		3
Total	2	19	19	-	40

*Two sample t-test

Discussion:

For a better outcome, early detection of sepsis is essential. It should be performed routinely through a simple, inexpensive test with a high sensitivity and specificity[5]. The use of biomarkers provides a novel approach to diagnose infection, its severity and treatment response. Sepsis is a common complication in burn intensive care units and delayed diagnosis is associated with increased morbidity, mortality, duration of hospital stays, and cost. Early diagnosis of sepsis and prompt administration of antimicrobials and manage-ment of hemodynamic alterations and other organ dysfunction increases patients' survival. A single biomarker that fulfills all these requirements has not yet been identified[1]. Several inflammatory markers, such as leukocyte cell count, C reactive protein (CRP), and cytokines (TNF-á, IL-1â, or IL-6), have been used for diagnosis of sepsis but none of them are specific and may increase in different situations. So, we need a more specific biomarker[7].

Coagulation activation is almost always present in infections and systemic host response is indicated by elevated plasma levels of D-dimer. D-dimer can be used as a marker of microcirculatory failure and related to organ dysfunction and outcome. Fibrin degradation product (FDP) assays measure the breakdown product of fibrinogen or fibrin and increases in DIC.

PCT seems to have valuable characteristics to be a reliable marker for identifying systemic infection and sepsis in burn patients[5]. PCT is one of the most studied biomarkers in bacterial infections and sepsis. In a pioneer study including nine burn patients[1], the author reported increased serum levels of PCT after burn injury and described the association of serum PCT levels with the development of infections, sepsis, and septic shock. Other recent studies also support the use of PCT as an adjunct in the early detection of sepsis in burn patients. In a study done in Singapore on 37 patients from 2013 to 2016, established that serum procalcitonin can serve as a reliable early predictor of bacteremia. They were able to identify a statistically significant positive correlation between raised serum PCT within the first 48 hours of admission and the presence of bacteremia within the first 10 days of admission[8]. Present studies showed that serum PCT is the most promising sepsis marker in critically ill patients, capable of complementing clinical signs and routine lab parameters suggestive of severe infection at the time of ICU admission[9,10].

The elevated level of D-dimer is associated with increased mortality in patients with infection or sepsis[11]. In addition, FDP, D-Dimer and PCT level can be used for monitoring patients with sepsis. Procalcitonin is a powerful marker of sepsis and is sensitive, specific, reliable, and easy to measure and offers an opportunity to burn intensive care specialists to make an early decision of any changes in the antimicrobial regimen[6,12]. Serum PCT levels could be a diagnostic biomarker for sepsis in major burn patients[13,14].

In this study, we found that there was a rise of serum level of FDP, D-dimer and PCT in patients with burn sepsis, but not significant (by 2 sample t- test). Value is rising, and this value was also high in patients with positive wound swab culture and blood culture. Together with good clinical judgments and judicious use of antimicrobial agents; FDP, D-dimer and PCT should serve as a valuable adjunct in the diagnosis and management of burn sepsis.

Conclusion:

FDP, D-dimer and procalcitonin are raised in burn sepsis patients. Measurement of serum level of FDP, D-dimer and procalcitonin may give us an idea regarding early onset of infection and burn sepsis and can serve as an early indicator for bacterial infection and burn sepsis with important diagnostic potential. So, it can be done routinely for all patients with major burns. Changes in serum level of fibrin degradation product (FDP), D-dimer and procalcitonin will help in the management of burn patients by early prediction of burn sepsis and thus decrease the morbidity and mortality.

Conflict of Interest

No conflict of interest was reported.

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Author Contribution:

Conceptualization: Nurunnahar Begum, Mahbub Hasan; Data collection: Nurunnahar Begum, Methodology: All author. Writing, Review & Editing: Nurunnahar Begum, Tanveer Ahmed, Abul Kalam

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