The Role of Serum Procalcitonin as a Diagnostic and Prognostic Biomarker for Sepsis in Major Burn Patients: A Prospective Study

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Abstract

Background: Sepsis in burns worsens the patient's prognosis and increases the risk of organ failure and death. Multiple organ dysfunction syndrome (MODS), which is a direct response to sepsis is the main reason for death in burn patients. Identifying early sepsis is especially important, given that every 6h delay in the diagnosis of sepsis reduces survival by 10%. Complexity in diagnosing sepsis in the burn is due to the systemic response to the burn itself clinically simulating sepsis.

Objective: The aim of this study is: To investigate the diagnostic validity of PCT in burn sepsis as an early diagnostic tool and to identify its prognostic value in major burn patients with sepsis.

Patients and Methods: The study was a prospective study that was conducted in a six months period carried out in the Burn Intensive Care Unit (ICU) of Ain Shams University Hospitals on 30 patients that were admitted from October 2021 to March 2022 with major burn (more than 20% of TBSA) were included, the Local Ethics Committee approved the study, and informed consent was obtained from all participants or their guardians.

Results: It had been revealed that the first 3 samples that were drowned on admission and after 24 hours and then on day 3 of admission have no significant increase in PCT levels in relation to sepsis. However, the following 2 samples which had been withdrawn on day 5 show a significant increase in PCT levels, and these on day 7 are highly significant with a median (IQR) range of 9ng/dl and median (IQR) range of 13.2ng/dl respectively. Moreover, it had been noted that the PCT level on admission was significant for the prognosis of death with a median (IQR) range of 1.65ng/dl while in survivor patients the median was 0.45ng/dl.

Conclusion: Our study demonstrated that PCT level in major burn patients is a promising diagnostic biomarker in detecting sepsis that could facilitate ideal management and initiate

proper antimicrobial therapy and good prognostic value as an early predictor of mortality.

Key Words: *Serum procalcitonin – Sepsis – Major burn patients – Diagnosis – Intensive care unit.*

Introduction

Burn patients with sepsis have a worse prognosis and are more likely to experience organ failure. Multiple organ dysfunction syndrome (MODS), which is a direct response to sepsis is the main reason for death in burn patients [1].

The sepsis survival rate decreases by 10% for every 6 hours delay in diagnosis. Detecting sepsis in the burn is difficult, as the burn itself systemically induce sepsis [2].

Blood cultures are still the best way to detect sepsis, but they take 48–72 hours and cannot be used right afterwards. Additionally, the extremely low likelihood of positive blood culture detection would delay diagnosis due to the early administration of high-dose antibiotics [3].

Numerous other disorders, including trauma, surgery, tissue necrosis, and immune-mediated inflammatory illness, have an impact on the currently utilised indications of early identification of infection, such as CRP. Since severe burn patients do experience a systemic inflammatory response, it is crucial to create new techniques for differentiating between an inflammatory response alone and real sepsis brought on by microbial bloodstream invasion [4].

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Procalcitonin (PCT), a 116 amino acid protein, is a precursor to calcitonin, a substance involved in the metabolism of calcium. PCT is produced by Cells of the thyroid gland, and it is also synthesized in the liver, kidneys, lungs, and adipose tissues in response to endotoxins, cytokines, and other mediators [5].

Under normal circumstances, healthy individuals carry extremely low levels of PCT. However, in the presence of bacterial and fungal infections, dramatically increased levels of PCT may be seen. Past audits have concluded that procalcitonin (PCT) may be utilized as an assistant biomarker within the clinical conclusion of sepsis and a methodology to decrease introduction of anti-microbials to fundamentally sick patients [6] and may be the foremost promising biomarker of burn patients with sepsis [7].

Studies on the evaluation of the diagnostic and prognostic value of procalcitonin levels in severe burn sepsis are rare and still show inconsistent results. In 2012 Lavrentieva et al. [8] expressed that PCT is valuable as an early marker of sepsis in extreme burn patients. In the meantime, another study showed that PCT serum is not superior compared to CRP or blood leukocytes as a marker of sepsis in burn patients [9].

According to Kumar et al. [10] in 2021, PCT is a reliable indicator of sepsis, however the test's validity and predictability vary depending on the population. Thus, the present study was designed to find the diagnostic validity and the prognostic value of PCT in our burn population.

PCT can be used for early detection of sepsis and prediction of outcome after major trauma and surgery. PCT can be used as a diagnostic tool in patients with tissue necrosis, and immune-mediated inflammatory illness with or without bacteremia. Daily consecutive PCT measurements may be a valuable tool in monitoring the effectiveness of antibiotics where they have observed significant increase in PCT in septic patients in comparison to their pre-septic levels [19].

Aim of the work:
The aim of this study is:
To check the value of PCT in diagnosis of burn sepsis as an early diagnostic tool and to identify its prognostic value in major burn patients with sepsis.

Patients and Methods

The study was carried out in Burn Intensive Care Unit (ICU) of Ain Shams University Hospitals.

Patient details: Thirty patients with major burns (more than 20% of TBSA) were included, that was conducted in a six-month period. From September 2021 to March 2022.

The project had received ethical committee approval, and each participant gave their informed consent.

Type of study: Prospective study.

Inclusion criteria: Age: 3-65 years, gender: Both sexes, presented to ER with burns ≥20% of their TBSA and fluid Resuscitation started within 8 hours of injury.

Exclusion criteria: Extremes of Age, concomitant trauma, electric burn, inhalational Injury based on bronchoscopy evaluation, and medical Comorbidities, for example, hypertension, diabetes mellitus, liver, and kidney diseases.

The TBSA was calculated based on Lund and Browder Chart. Resuscitation liquid was calculated utilizing the Parkland equation. Half of this was managed over the primary 8 hours, and the rest was managed over another 16h. Lactated Ringer's was the liquid managed for resuscitation.

Study procedures:
I- *Assessment of the patient:*
Clinical assessment: Generally: Vital signs and full level of consciousness, burn: Cause, extent, distribution, depth, and time of presentation and burn wound infection and sepsis: According to American Burn Association guidelines.

Laboratory investigations: CBC, Renal, and liver function tests, Coagulation profile. Albumin level, Viral Markers, CRP. Procalcitonin Level on admission, 24 hours from admission then every 48 hours. Blood culture was done for all patients and measured in our study on admission of the patient to the ER, then after 24 hours every 48 hours and withdrawn before administration of antibiotics.

Resuscitation of the patient: Proper resuscitation using modified parkland formula to be monitored by urine output, pulse, temperature, and blood pressure.

Caloric requirement and Nutritional need of the patient: Curreri formula Empirical Antibiotic management with correction for any lab abnormalities Anti-inflammatory agents, Analgesics.

Sample collection: Procalcitonin was collected for each measurement, 5ml of venous blood was drawn into a red top tube. Specimen type: Whole blood (Venous). Transport: Within 60 minutes of venipuncture. The duration of follow-up varied from one patient to another. When the general condition improved the PCT was decreased. Follow-up samples were withdrawn at 0, 14, 28 days then every other day.

The plasma specimen was analyzed by the Automated immune analyzer (VIDAS®, bioMérieux, Marcy L'Etoile, France) (Fig. 1).
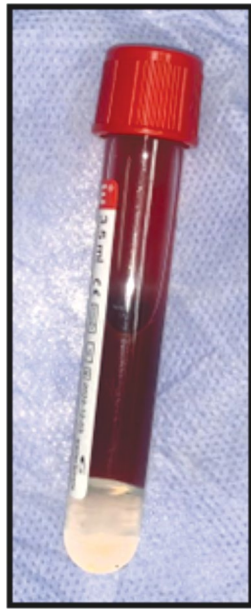
Fig. (1): Red top tube sample was collected.

Table (1): Sepsis criteria according to ABA (American Burn Association), Mann-Salinas novel predictors of sepsis, Sepsis-3 consensus definition for sepsis and septic shock [19].

ABA Sepsis Criteria
To fulfill these criteria, at least three of the following should be present:
- Temperature >39°C or <36.5°C.
- Progressive tachycardia (>110bpm).
- Progressive tachypnea.
- Thrombocytopenia.
- Hyperglycaemia.
- Inability to continue enteral feedings 24hours.
  Alongside infection, demonstrated by at least one of the following:
- Culture-positive infection.
- Pathological tissue source identified.
- Clinical response to antimicrobial agents.

Mann–Salinas novel predictors of sepsis Score comprises:
- Tachycardia >130bpm.
- MAP <60mmHg.
- Base deficit <–6mEq/l.
- Hypothermia <36°C.
- Use of vasoactive medications.
- Hyperglycaemia >150mg/dl.

Sepsis-3 consensus definition for sepsis and septic shock Score comprises:
- Altered mental status (Glasgow coma scale score <13).
- Systolic blood pressure ≤100mmHg.
- Respiratory rate ≥22 breaths per minute.
- sSuspected or documented infection and qSOFA ≥2 and/or SOFA ≥2; SOF variables are PaO2/FiO2 ratio, Glasgow coma scale, mean arterial pressure, vasopressor requirements, serum creatinine or urine output, bilirubin and platelet count.

The criteria for septic shock are:
- Vasopressors required to maintain MAP >65mmHg.
- Lactate >2mmol/l (after adequate fluid resuscitation).

Results

Out of 30 patients 14 were males and 16 were females. Their median age was 19 years, where the range was from (3-61) years. And the cause of burn in our study was 53.3% flame burn and 46.7%-scald burn. And the median TBSA burn injury of the study population was 22% where the range was from (20%-60%).

As shown in Table (1) there were a statistically significant (p-value <0.01) in the comparison between PCT levels between every sample that was withdrawn on admission, day 1, day 3, day 5 and day 7 respectively as the median for the first sample was (0.87), While in sample 2 (4.28), Sample 3 (5.05), Sample 4 (4.97) and sample 5 (4.23).

In the current study it has been revealed that 24 of the studied patients showed bacterial growth according to their blood cultures, gram-negative bacterial growth was found in 83.3% while 16.7% showed gram-positive, 26.7% of the studied patient has Actinobacter bacterial growth, Staphylococcus coagulase negative and Klebsiella pneumonia bacterial growth in 16.7%.

As shown in Table (2) it has been found that the first 3 samples that were withdrawn on admission, in the first day and in the third day have no significant increase in PCT levels in relation to sepsis. However, the following 2 samples which had been withdrawn in day 5 show significant increase in PCT levels and those of day 7 on admission are highly significant with Median (IQR) range 9ng/dl and Median (IQR) range 13.2ng/dl respectively.

As shown in Table (3) the PCT level on admission was significant for the prognosis of death with Median (IQR) range 1.65ng/dl while in survivor patients was 0.45ng/dl and highly significant for prognosis of death in day 7 with Median (IQR) range 12.2ng/dl.

As shown in Table (4), there was non-significant change between survivors and non-survivors CRP samples with p-value >0.05: Non-significant, there was a meaningful change between survivors and non survivors regarding gram cultures with p-value 0.032, There was a highly significant difference between survivors and non survivors regarding sepsis with p-value 0.004.

Statistical analysis: Our study has divided the studied patients into 2 groups according to the outcome also according to the development of sepsis with qualitative data was done by using the Chi-square test and/or Fisher exact test was used instead of the Chi-square test when the expected count in any cell was found less than 5.

The comparison between two independent groups with quantitative data and parametric distribution was done by using the independent t-test.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. The p-value was considered significant as the following: $p > 0.05$ = Non-significant (NS), $p < 0.05$ = Significant (S), $p < 0.001$ = Highly significant (HS).

Table (2): Comparison between procalcitonin samples that had been withdrawn from the studied patients.

Procalcitonin	Sample 1	Sample 2	Sample 3	Sample 4	Sample 5	Test value≠	p-value	Sig.
Median (IQR)	0.87 (0.24-1.65)	4.28 (2.58-6.52)	5.05 (1.46-33.03)	4.97 (1.23-21.49)	4.23 (1.23-14.2)	42.098	<0.001	HS (Highly Significant)
Range	0-100	0.06-100	0-100	0.23-100	0.09-100			

Table (3): Comparison between sepsis and non-sepsis cases regarding and procalcitonin levels.

Distribution	Non sepsis No.=18 ——— 4 (22.2%)	Sepsis No.=12 ——— 9 (75.0%)	Test value	p-value	Sig.
Procal. (Sample 1):					
Median (IQR)	0.7 (0.23-1.6)	1.13 (0.7-1.85)	–1.165≠	0.244	NS
Range	0.05-5.1	0-100			
Procal. (Sample 2):					
Median (IQR)	4.68 (1.2-9.3)	3.72 (2.68-6.23)	–0.423≠	0.672	NS
Range	0.12-31.04	0.06-100			
Procal. (Sample 3):					
Median (IQR)	3.63 (0.88-41.52)	7.35 (3.82-28.91)	–0.741≠	0.459	NS
Range	0.1-100	0-100			
Procal. (Sample 4):					
Median (IQR)	2.66 (0.9-15.3)	9 (3.59-39.83)	–2.244≠	0.025	S
Range	0.23-45.23	1.27-100			
Procal. (Sample 5):					
Median (IQR)	2.22 (1.01-8.99)	13.2 (6.4-45.12)	–2.599≠	0.009	HS
Range	0.09-35.37	1.53-100			

Table (4): Shows the Procalcitonin of the studied patients regarding the outcome.

Distribution	Outcome		Test value	p-value	Sig.
	Survivors No.=17	Non-survivors No.=13			
Procal (on admission):					
Median (IQR)	0.45 (0.23-1.3)	1.65 (0.73-1.9)	–2.010≠	0.044	S
Range	0.05-100	0-5.1			
Procal (day 1):					
Median (IQR)	3.93 (1.2-6.51)	4.32 (2.78-6.52)	–0.377≠	0.706	NS
Range	0.12-100	0.06-31.04			
Procal (Day 3):					
Median (IQR)	2.4 (0.88-33.03)	9.5 (4.6-31.4)	–1.423≠	0.155	NS
Range	0.1-100	0-100			
Procal (day 5):					
Median (IQR)	1.27 (0.97-5.78)	9.62 (3.98-23.9)	–1.737≠	0.082	NS
Range	0.23-100	0.44-48.53			
Procal (day 7):					
Median (IQR)	1.53 (1.01-3.56)	12.2 (6.4-32.1)	–2.662≠	0.008	S
Range	0.09-100	4.23-46.29			

Table (5): Comparison between samples of CRP level and bacterial growth in survivors and non survivors regarding outcome.

| | Outcome | | Test value | *p*-value | Sig. |
	Survivors No.=17	Non-survivors No.=13			
CRP:					
Median (IQR)	66.5 (49.4-153.1)	180.4 (45.2-274.4)	–0.984≠	0.325	NS
Range	0-275.3	0-407.4			
Gram:					
Negative	12 (70.6%)	13 (100.0%)	4.588*	0.032	S
Positive	5 (29.4%)	0 (0.0%)			
Sepsis:					
Non sepsis	14 (82.4%)	4 (30.8%)	8.167*	0.004	HS
Sepsis	3 (17.6%)	9 (69.2%)			

Discussion

Our study had also clarified that most of the mortality cases died because of sepsis, the causative organisms were gram negative bacteria which can clearly be significant in our results as 80% of the studied patients had bacterial growth according to the blood cultures and 20% of the studied cases has no bacterial growth. Lin [11] and his co-workers in 2020 agreed with our study that the increase in PCT level can detect a Gram-negative bloodstream infection in severe burn patient which helps in accurate clinical decision-making to start the proper antimicrobial therapy. Moreover, in 2012, Lavrentieva [8] and his co-workers also supported the rise of PCT could help in detection of Gram-Negative bacteria.

It has been revealed in the present study that the main finding is the rise in PCT level can divide patients with major burn into sepsis and non-sepsis patients also the patients can be divided into survivors and non survivors. Regarding their age, extent, gender & distribution.

Early detection of sepsis can facilitate an ideal management and initiate proper antimicrobial therapy Although, Delays in treating infections are associated with poorer outcomes and increased costs [12].

Sepsis resulted from burns makes the patient's prognosis worse and raises the possibility of multi-organ dysfunction syndrome (MODS) which is the direct cause of death [1]. Sepsis must be diagnosed as soon as possible because every six hours that pass before a diagnosis reduces survival by 10% [2]. Blood culture remains the gold standard for identifying sepsis, but due to early use of high-dose antibiotics, the positive detection rate of blood cultures is extremely low, which will delay the diagnosis [3].

In 2012, Lavrentieva [8] said that during an ICU stay, PCT can be used as a diagnostic tool for patients who have infectious complications with or without bacteremia. Where they have observed a significant increase in PCT in septic patients in comparison to their pre-septic levels, daily consecutive PCT measurements may be a useful tool for monitoring the effectiveness of antibiotics. At the onset of sepsis, the median PCT concentration was 7.2ng/ml, and in septic shock patients, it reached 23.9ng/ml.

In the current study it has been found that the first 3 samples that were withdrawn on admission, in the first day and in the third day have no significant increase in PCT levels in relation to sepsis. However, the following 2 samples which had been withdrawn in day 5 show significant increase in PCT levels and those of day 7 on admission are highly significant with Median (IQR) range 9ng/dl and Median (IQR) range 13.2ng/dl respectively.

Moreover, Cabral [7] and his colleagues in 2017 had showed that PCT kinetics in addition to that during the first few days after a burn injury, a clinical examination may be helpful in diagnosing sepsis. As in the present study there were a statistically significant (*p*-value <0.01) in the comparison between PCT levels between every sample that were withdrawn during the first days of burn as the median for the first sample was (0.87), While in sample 2 (4.28), Sample 3 (5.05), Sample 4 (4.97) and sample 5 (4.23).

Furthermore, In 2018, Kumar [10] and his colleagues reported that PCT is thought to be a useful biomarker for diagnosing sepsis in burns with a hypermetabolic response and has the potential to bridge the gap between clinical signs and confirmatory culture results, also in 2019, Kundes and Kement [13], showed that ss In children with burn injuries, high PCT levels may serve as a biomarker for the onset of sepsis. PCT Median (IQR) in the

5th day of admission of sepsis cases was 9ng/dl, whereas PCT Median (IQR) in the 7th day of admission of sepsis cases was 13.2ng/dl. This finding is consistent with the findings of the current study, which found a rise in PCT levels in sepsis patients in comparison to non-sepsis patients.

There is a correlation between all-cause short-term mortality and serum PCT levels when patients with severe sepsis are admitted to the intensive care unit. In 2009, Meng [14] and his colleagues reported that serum PCT values of >10ng/mL at the time of ICU admission are superior to CRP and TLC values in their ability to predict all-cause short-term mortality., which was agreed in the current study that the PCT level on admission was significant for the prognosis of death with Median (IQR) range 1.65ng/dl while in survivor patients was 0.45ng/dl and highly significant for prognosis of death in day 7 with Median (IQR) range 12.2ng/dl, While TLC and CRP level weren't significant for the prognosis of death with Median (IQR) for CRP 180.

Moreover, in 2014, The mortality rate in sepsis remains high, according to Jain [15] and his colleagues, despite the use of better support and strategy. At admission, a higher level of procalcitonin than high sensitivity CRP is a better indicator of mortality. Which was proved in the current study that the prognosis of death of sepsis patient is highly significant with *p*-value 0.004 as 9 sepsis cases were died out of 12 case that had been studied.

Also, Liu [16] and his co-workers in 2015 admitted that rise in PCT levels and PCT non-clearance were accompanied with a higher risk of death in patients with sepsis. However, PCT may not be useful as a single index for assessing prognosis because of its moderate diagnostic accuracy, though it may be helpful in addition to the patient's overall conditions and other clinical indexes. Moreover, in 2012 Lavrentieva [8] and his co-workers have shown that maximum procalcitonin level has prognostic value in burn patients.

The aim of all interventions is still patient survival. However, the patient has a pre-existing set of morbidity variables that affect his response to burn insult and therefore the result of these interventions may differ from patient to another.

The currently used indicators of early diagnosis of infection like CRP are also greatly affected by many other conditions such as trauma, surgery, tissue necrosis, and immune-mediated inflammatory diseases. Patients with severe burns are present with systemic inflammatory reactions. Therefore, it is particularly important to develop new methods of differential diagnosis between a simple inflammatory response and true sepsis due to microbial entry into the body [4].

In 2013, Jeschke and his colleagues found, in agreement with the current study, that CRP alone does not predict sepsis or severe infection; however, when used in conjunction with other factors like the cytokine expression profile, hormones, and other proteins, it may be more helpful for the overall evaluation of severely burned patients. Moreover, Permatasari [2] and his co-workers in 2021 according to their results they showed that PCT has a better diagnostic test value than CRP, its use in deciding treatment for patients should be applied with caution and correlated with clinical and other laboratory findings. As in the present study it has been noticed the non-significance role of conventional inflammatory biomarkers, including CRP in detection of sepsis with Median (IQR) 56.1mg/L with *p*-value >0.05.

Kundes and Kement [13], in 2019 had demonstrated that pediatric patients with larger TBSA (>30%) and non survivors showed significantly higher levels of PCT as well as Abdel-Hafez et al. [17] study in 2007, showed that higher PCT levels were related to higher TBSA, more positive blood cultures, higher requirement of antibiotics and intensive care unit, and also longer hospitalization time, in agreement with the present study it was noted that the increase of burned TBSA would increase the mortality rate as the Median (IQR) of the extent in Non survivor cases was 32% which is significant with *p*-value 0.038 but in the contrary it might not suspect the sepsis as Median (IQR) was 29.5% with *p*-value >0.05 which is not significant.

This study has its limitations: A small sample size will lead to less accurate estimates of the accuracy of serial serum procalcitonin. Second, it included patients with a large total body surface area burned and PCT had been elevated in addition to the other inflammatory markers.

Conclusion:

The study admits that PCT levels in major burn patients are a good biomarker in detecting sepsis and good prognostic value as early detection of sepsis can facilitate an ideal management and initiate proper antimicrobial therapy.

References

1- Greenhalgh D.G.: Sepsis in the burn patient: A different problem than sepsis in the general population. Burns & trauma, 5, 2017.

2- Permatasari A.Y., Sanjaya I.H., Widiana I.G.R., Niryana I.W., Asmarajaya A.N., Hamid A.R.R. and Adnyana M.S.: Role of Procalcitonin and C-reactive Protein as Marker of Sepsis in Major Burn Patients: A Systematic Review and Meta-analysis. Open Access Macedonian Journal of Medical Sciences, 9 (F): 197-203, 2021.

3- Chiesa C., Panero A., Osborn J.F., Simonetti A.F. and Pacifico L.: Diagnosis of neonatal sepsis: A clinical and

laboratory challenge. Clinical Chemistry, 50 (2): 279-287. 2004.

4- Barati M., Alinejad F., Bahar M.A., Tabrisi M.S., Shamshiri A.R. and Karimi H.: Comparison of WBC, ESR, CRP and PCT serum levels in septic and non-septic burn cases. Burns, 34 (6): 770-774, 2008.

5 Xu Y., Jin X., Shao X., Zheng F. and Zhou H.: Valuable prognostic indicators for severe burn sepsis with inhalation lesion: Age, platelet count, and procalcitonin. Burns & Trauma, 6, 2018.

6- Mann E.A., Wood G.L. and Wade C.E.: Use of procalcitonin for the detection of sepsis in the critically ill burn patient: A systematic review of the literature. Burns, 37 (4): 549-558, 2011.

7- Cabral L., Afreixo V., Santos F., Almeida L. and Paiva J.: A. Procalcitonin for the early diagnosis of sepsis in burn patients: A retrospective study. Burns, 43 (7): 1427-1434, 2017.

8- Lavrentieva A., Papadopoulou S., Kioumis J., Kaimakamis E. and Bitzani M.: PCT as a diagnostic and prognostic tool in burn patients. Whether time course has a role in monitoring sepsis treatment. Burns, 38 (3): 356-363, 2012.

9- Jeschke M.G., Finnerty C.C., Kulp G.A., Kraft R. and Herndon D.N.: Can we use C-reactive protein levels to predict severe infection or sepsis in severely burned patients? International journal of burns and trauma, 3 (3): 137, 2013.

10- Kumar H.R.N., Barreto E., Paul M.K. and Gupta A.K.: Procalcitonin: Promising biomarker to detect sepsis in burns A prospective study. Indian Journal of Burns, 26 (1): 87, 2018.

11- LIN J.C., CHEN Z.H. and CHEN X.D.: Elevated serum procalcitonin predicts Gram-negative bloodstream infections in patients with burns. Burns, 46 (1): 182-9, 2020.

12- Wu J., Hu L., Zhang G., Wu F. and He T.: Accuracy of presepsin in sepsis diagnosis: A systematic review and meta-analysis. PLoS One, 10 (7): e0133057, 2015.

13- Kundes M. and Kement M.: Value of procalcitonin levels as a predictive biomarker for sepsis in pediatric patients with burn injuries. Nigerian Journal of Clinical Practice, 22 (7): 881, 2019.

14- Meng F.S., Su L., Tang Y.Q., Wen Q., Liu Y.S. and Liu Z.F.: Serum procalcitonin at the time of admission to the ICU as a predictor of short-term mortality. Clinical biochemistry, 42 (10-11): 1025-31, 2009.

15- Jain S., Sinha S., Sharma S.K., Samantaray J.C., Aggrawal P., Vikram N.K., Biswas A., Sood S., Goel M., Das M. and Vishnubhatla S.: Procalcitonin as a prognostic marker for sepsis: A prospective observational study. BMC research notes, 7 (1): 1-7, 2014.

16- Liu D., Su L., Han G., Yan P. and Xie L.: Prognostic value of procalcitonin in adult patients with sepsis: A systematic review and meta-analysis. PLoS one, 10 (6): e0129450, 2015.

17- Abdel-Hafez N.M., Saleh Hassan Y. and El-Metwally T.H.: A study on biomarkers, cytokines, and growth factors in children with burn injuries. Ann. Burns Fire Disasters, 20: 89-100, 2007.