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Laboratory Predictors for Morbidity and Mortality after Thermal Burns in Pediatrics

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Original Research Article

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ABSTRACT

Background: The utility of laboratory values to predict complications in pediatric burn patients is poorly understood. This study assessed the laboratory investigations' role in morbidities and mortalities prediction after moderate and severe thermal burn in pediatrics.
Methods: This prospective cohort study was carried out on 40 children with moderate and major thermal burn. All patients were subjected to clinical evaluation and laboratory investigations such as CBC, c-reactive protein (CRP), serum albumin, serum creatinine and urea.
Results: Patients were subdivided into two groups: uncomplicated group (n=25) and complicated group (n=15). CRP, serum albumin, platelet count, serum creatinine and urea can significantly predict sepsis incidence with AUC of 0.922, 0.912, 0.911, 0.807, 0.810, at cut off >12, ≤2, ≤194, >0.7, >23, with sensitivity of 100%, 90.91%, 100 %,100 %, 85.71%, specificity of 86.21 %, 86.21%, 79.31%, 24.24%, 39.39%, PPV of 73.3 %, 71.4%, 64.7%, 21.9% , 23.1% and NPV of 100 %, 96.2 %, 100 %, 100 % , 92.9% respectively. Serum creatinine and urea can significantly predict incidence of acute kidney injury (AKI) with AUC of 0.807, 0.810 At cut off >0.7, >23, with sensitivity of 100.00 %, 85.71%, specificity of 24.24%, 39.39%, PPV of 21.9%, 23.1% and NPV of 100.0%,

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92.9% respectively. Percent of burn, total ABSI, CRP, platelet, inhalation injury, albumin, creatinine and urea were dependent predictors for mortality. Sex, inhalation injury, percent of burn, total ABSI, hemoglobin, CRP, platelet, albumin, and creatinine were dependent predictors for sepsis. Sex, inhalation injury, percent of burn, total ABSI, CRP, hemoglobin, platelet, albumin and creatinine were dependent predictors for complication of acute kidney disease.
Conclusions: CRP, serum albumin, platelet count, serum creatinine and urea are good predictors of sepsis, AKI and mortalities after moderate to severe burn in pediatrics.

Keywords: Laboratory predictors; morbidities; mortalities; thermal burns; pediatrics.

1. INTRODUCTION

Burn injury is a major pathology resulting in profound morbidity and high fatalities [1]. It is a main cause of unexpected children death and injury, with minors being the most affected (less than 10%). A considerable percentage of children experience burns affecting more than 15% total body surface area (TBSA), resulting in systemic inflammatory response syndrome initiation [2].

Critical illness resulting from thermal injury leads to systemic inflammatory response syndrome (SIRS) involving a massive systemic cytokines' release that characterized by two at minimum of the listed four criteria: tachypnea, tachycardia , fever and leukopenia or leukocytosis [3]. This is coupled with an anti-inflammatory response as the body seeks homeostasis restoration, a condition known by the compensatory anti-inflammatory response syndrome (CARS) that results in a significant functional and numerical decrease of multiple immune cell types such as monocytes, neutrophils, lymphocytes, macrophages, and natural killer cells [4-6]. The usual post-traumatic cellular response is decrease in lymphocytic count and an increase in the neutrophils and white blood cells (WBC)count [3].

Severe burn injuries are correlated with an extensive inflammatory reaction, but the utilization of laboratory values to predict complications in pediatric cases with burn injuries is not well understood [3].

In other studies, the utilization of prognostic factors and multiple scales, such as the Abbreviated Burn Severity Index (ABSI), that includes age, sex , full-thickness injuries, body surface area burned (BSAB)and inhalation injury linked to burns and other variables have been utilized [7].

Thrombocytopenia is initially seen in cases suffering from burn injury during the first week post injury as a transient occurrence [8]. Hypoalbuminemia is also a frequent clinical deficiency and is accompanied with complications linked to elevated amount of extravascular fluid such as edema, sepsis susceptibility, and abnormal healing [7]. Acute kidney injury (AKI) is a frequent and morbid complication in cases suffering from severe burn [8]. C-reactive protein (CRP) is a useful sepsis indicator in cases with burns. CRP can be utilized, in combination with clinical sepsis markers, to initiate extensive monitoring and convenient antibiotic therapy [9].

The aim of this work was to assess the laboratory investigations' role in prediction of morbidities and mortalities after moderate and severe thermal burn in pediatrics.

2. METHODS

This prospective cohort study was conducted on 40 children aged from 1 to 17 years old, with moderate and major thermal burn such as scald from hot liquids and steam, building fires, flammable liquids and gases at Emergency Department, Tanta University Hospitals from 1 December 2020 to 30 November 2021. Moderate burn in children was defined as (partial size thickness 10_20% or full-size thickness 2_10%) and major burn in children was defined as (partial size thickness more than 20% or full-size thickness more than 10%).

Exclusion criteria were associated polytrauma, comorbidities, old burn, patient who was discharged or died within 3 days.

All patients were subjected to: clinical evaluation (personal data, causative agent, concomitant inhalation injury which was suspected if there was a history of being trapped in a closed place, estimation of the extent of the burn according to the Lund and Browder chart [10], length of hospital stay, time of discharge, morbidities and vital signs).

Resuscitation according to ATLS guidelines by airway maintenance, breathing, ventilation, intravenous fluid resuscitation was performed using the modified parkland formula (Total amount of fluid =3 ml x body weight(kg) x % BSA (% of burnt area [11]) and nutritional protocol using the Hildreth formula (children <12 years: 1800kcal/m^2(TBSA)+1300kcal/m^2 (BSAB), children ≥12 years: 1500kcal/m^2(TBSA)+ 1500kcal/m^2 (BSAB)).

2.1 Laboratory Monitoring

All laboratory investigations were measured within 24 hours and twice per week from time of admission till discharge or death including complete blood picture (CBC), CRP, serum albumin, serum creatinine and urea. All laboratory investigations were done at admission, 3rd, 6th, 9th, 12th, 15th and 18th day.

Serum levels of CRP lower than 10 mg/dl is deemed normal for burn cases. Rise was determined by elevation from 3.9-9 mg/dl that remained for two measures, or a single day elevation of 10 mg/dl or more). serum albumin normal range is 3.5 to 5.5 g/dl).

We used kidney disease improving global outcomes (KDIGO) clinical practice guidelines for AKI staging. AKI was classified as stage 1 (SCr rise ≥ 1.5-1.9 times baseline or urine output < 0.5 mL/kg/h for 6-12 hours), stage 2 (SCr rise ≥ 2.0-2.9 times baseline or urine output < 0.5 mL/kg/h ≥12 hours), and stage 3 (SCr rise ≥ 3.0 times baseline, dialysis treatment for AKI, or eGFR < 35 mL/min/1.73m2 [if >3 months old] or urine output < 0.3 mL/kg/h for 24 hours, or anuric for≥ 12 hours)).

Follow up was to assess complications (sepsis, acute kidney injury, thrombocytopenia, hypoalbuminemia, and pneumonia), ABSI and mortality (as the percentage of deaths in the population). Systemic antibiotics were given to the patients, if indicated.

2.2 Sample Size Estimation

The sample size was estimated by MedCalc Software Ltd v. 20 with 80% power, 95% confidence limit, the expected AUC of the ROC curve of the albumin for prediction of 28-day mortality in severely burned patients was 0.76 and the null hypothesis AUC of the ROC curve was 0.5 according to a prior research [12]. Four cases were added to overcome dropout. Therefore, 40 cases were recruited.

2.3 Statistical Analysis

IBM's SPSS v26 (Chicago, Illinois, United States) was utilized for statistical analysis. Using an unpaired student t-test, the mean and standard deviation (SD) of parametric quantitative data were investigated. Using the Chi-square test, frequency and percentages were provided for qualitative variables (percent). The time to first postoperative analgesic demand was shown using a Kaplan Meier curve. To measure the degree of connection between two quantitative variables, Pearson correlation was performed. Using ROC curve analysis, the overall diagnostic performance of each test was evaluated. A two-tailed P value of < 0.05 was considered statistically significant.

3. RESULTS

Table 1 shows demographic data, burn characteristics, mortality and complication of the studied groups.

Patients were further subdivided into two groups: Uncomplicated group (n=25) and complicated group (n=15).

Platelets, albumin, hemoglobin at 3rd, 6th, 9th and 12th day were significantly lower in complicated group compared to another group (P ≤ 0.05). Creatinine and CRP at 3rd, 6th, 9th and 12th day were significantly higher in complicated group compared to another group (P ≤ 0.05). Urea at 6th was significantly higher in complicated group compared to other group (P value =0.016) while there is no significant difference between the two groups at admission, 3rd, 9th and 12th day. There was no significant difference between the two groups at admission regarding platelets, creatinine, albumin, hemoglobin and CRP.

CRP can significantly predict incidence of sepsis with AUC of 0.922, P value<0.001. At cut off >12, it's a significant predictor with 100.0% sensitivity, 86.21 %specificity, 73.3 % PPV and 100.0 % NPV. Serum albumin can significantly predict incidence of sepsis with AUC of 0.912, P value<0.001. At cut off ≤2, it's a significant predictor with 90.91% sensitivity, 86.21% specificity, 71.4% PPV and 96.2 % NPV. Platelet count can significantly predict incidence of sepsis with AUC of 0.911, P value<0.001. At cut off ≤194, it's a significant predictor with 100.00 % sensitivity, 79.31% specificity, 64.7% PPV and 100.0 NPV.

Table 1. Demographic data, burn characteristics, mortality and complication of the studied groups (N=40)

		N=40
Age (years)		8.87 ± 4.73
Sex	Male	21 (52.5%)
	Female	19 (47.5%)
Temperature (˚c)		37.14 ± 1.07
Mode of burn	Scald	21(52.50%)
	Flame	19(47.5%)
Type of burn	Partial thickness	16 (40%)
	Mixed thickness	7 (17.5%)
	Full thickness	17 (42.5%)
Percentage of burn	2-10%	18 (45.00%)
	11-20%	15 (37.50%)
	21-30%	7 (17.50%)
Degree of burn	Moderate	31 (77.5%)
	Major	9 (22.5%)
Inhalation injury		17 (42.5%)
TBSA(m^2)	<20%	38 (95.00%)
	>20%	2 (5.0%)
Total ABSI	Very low (2-3)	19(47.50%)
	Moderate (4-5)	21 (52.50%)
Mortality		7 (17.5%)
Complication	Complication	15 (37.5%)
	No complication	25 (62.5%)
Hospital stays (days)		11.175 ± 40.05

Data are presented as mean ± SD or frequency (%). TBSA: Total body surface area, ABSI: abbreviated Burn Severity Index

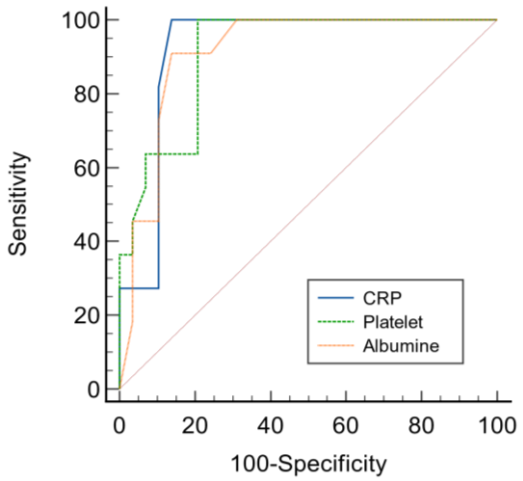

Fig. 1. ROC curves of CRP, serum albumin, platelet counts as predictors for sepsis

Serum creatinine can significantly predict incidence of AKI with AUC of 0.807, P value=0.013. At cut off >0.7, it's a significant predictor with 100.00 % sensitivity, 24.24%specificity, 21.9% PPV and 100.0% NPV. Urea can significantly predict incidence of AKI with AUC of 0.810, P value=0.005. At cut off >23, it's a significant predictor with 85.71% sensitivity, 39.39%specificity, 23.1% PPV and 92.9% NPV.

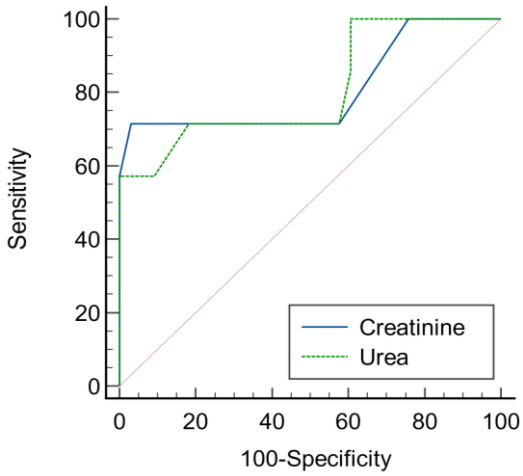

Fig. 2. ROC curves of serum creatinine and urea in prediction of AKI

The mean survival was significantly higher in the uncomplicated group compared to complicated group regarding sepsis and Acute kidney injury (AKI) (P=0.025, P<0.001 respectively).

Table 2. laboratory investigations between complicated and uncomplicated patients

Platelets count (10^9/L)			
	Uncomplicated (n=25)	**complicated (n=15)**	**P-value**
At admission	254.32 ± 28.85	257.6 ± 22.83	0.710
3rd day	236.28 ± 27.32	212.6 ± 17.70	0.005*
6th day	217.44 ± 25.77	181.4 ± 15.57	<0.001*
9th day	278.09 ±12.76	257.9 ±29.32	0.038*
12th day	381.5 ± 15.46	335.6 ± 8.90	<0.001*
15th day	0 ± 0	471.86 ± 40.11	---
18th day	0 ± 0	483 ± 39.6	---
Serum creatinine (mg/dL)			
At admission	0.74 ± 0.17	0.75 ± 15	0.864
3rd day	0.8 ± 0.15	1.13 ± 0.58	0.010*
6th day	0.83 ± 0.15	1.48 ± 0.88	0.001*
9th day	0.77 ± 0.22	0.89 ± 0.88	0.012*
12th day	0.65 ± 0.15	0.89 ± 0.95	0.033*
15th day	0 ± 0	1.44 ± 1.15	---
18th day	0 ± 0	1.65 ± 1.48	---
Serum albumin (g/dL)			
At admission	3.31 ± 0.35	3.16 ± 0.22	0.069
3rd day	3.07 ± 0.48	2.33 ± 0.37	<0.001*
6th day	2.87 ± 0.49	1.83 ± 0.38	<0.001*
9th day	2.39 ± 0.44	1.79 ± 0.27	0.001*
12th day	2.8 ± 0.4	2.2 ± 0.33	0.004*
15th day	0 ± 0	2.41 ± 0.33	---
18th day	0 ± 0	2.65 ± 0.21	---
Hemoglobin (gm/dL)			
At admission	13.07 ±1.97	12 ±1.96	0.105
3rd day	14.08 ± 0.59	8.5 ± 1.15	<0.001*
6th day	12.63 ± 0.33	7.33 ± 0.49	<0.001*
9th day	11.82 ± 1.58	7.4 ± 0.52	<0.001*
12th day	10.22 ± 3.43	7.15 ± 0.85	<0.001*
15th day	0 ± 0	6.89 ± 0.42	---
18th day	0 ± 0	6 ± 0	---
CRP (mg/L)			
At admission	9.48 ± 1.88	8.73 ± 1.53	0.260
3rd day	10.05 ± 1.59	12.93 ± 1.98	<0.001*
6th day	9.76 ± 1.62	20.27 ± 3.43	<0.001*
9th day	5.24 ± 5.07	15.07 ± 11.23	<0.001*
12th day	2.9 ± 4.06	15.27 ± 11.4	<0.001*
15th day	0 ± 0	15.67 ± 9.86	---
18th day	0 ± 0	15 ± 4.24	---
Urea (mg/dL)			
At admission	22.2 ±7.68	22.27 ± 6.75	0.978
3rd day	22.25 ± 7.8	28.33 ± 13.77	0.067
6th day	25.92 ± 8.63	36.53 ± 18.72	0.016*
9th day	15.75 ± 15.13	17.2 ± 14.2	0.284
12th day	9.79 ± 12.05	16.47 ± 13.24	0.681
15th day	0 ± 0	24.43 ± 5.74	---
18th day	0 ± 0	24 ± 8.49	---

*Data are presented as mean ± SD, *: significant as P value ≤0.05. CRP:C-reactive protein*

Percent of burn, total ABSI, CRP, platelet, inhalation injury, albumin, creatinine and urea were dependent predictors for mortality. Sex, inhalation injury, percent of burn, total ABSI,

hemoglobin, CRP, platelet, albumin, and creatinine were dependent predictors for sepsis. Sex, inhalation injury, percent of burn, total ABSI, CRP, hemoglobin, platelet, albumin and creatinine were dependent predictors for complication of acute kidney disease.

4. DISCUSSION

In the present study, Platelets at 3rd, 6th, 9th and 12th day were significantly lower in complicated group compared to other group while there is no significant difference between the two groups at admission. Platelet count can significantly predict incidence of sepsis with AUC of 0.911, at cut off ≤194, with 100.00 % sensitivity, 79.31% specificity, 64.7% PPV and 100.0 NPV.

Our findings are supported by Cato et al. [13], they observed that both nadir and peak platelet count were significantly lower in sepsis and mortality groups than non. Housinger et al. [14] found that 31 of the 32 no survivors had a platelet count below $0.1x10^{12}$/L. Only 10 of the survivors had a similar occurrence. Platelet count decline preceded other signs of sepsis in all cases. A platelet counts less than $0.1x10^{12}$/L for more than 4 days was usually associated with mortality.

However, Aguayo-Becerra et al. [7] observed that platelet concentration showed non-significant difference between survivors and deceased patients.

In the present study, creatinine at 3rd, 6th, 9th and 12th day were significantly higher in complication compared to no complication while there is no significant difference between complication and no complication at admission.

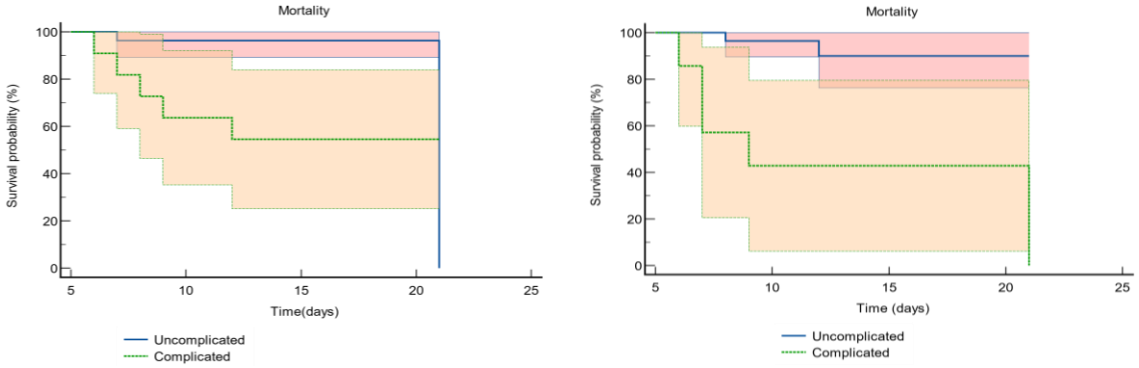

Fig. 3. Overall survival rate of the studied group regarding (A) sepsis, (B) AKI

Table 3. Logistic regression of different variables for prediction of mortality, sepsis, AKI

	Mortality		Sepsis		AKI	
	Odds ratio	95% CI	Odds ratio	95% CI	Odds ratio	95% CI
Age (years)	1.030	0.867-1.225	0.956	0.821-1.113	0.898	0.767 - 1.052
Sex	1.600	0.308-8.300	8.550	1.541-47.409	8.550	1.541-47.409
Inhalation injury	3.521	1.130-3.427	1.363	1.236-7.838	0.292	1.118 - 1.251
Percent of burn	1.476	1.130-1.927	1.141	1.014-1.283	1.143	1.014-1.283
Hospital stay	0.903	0.713-1.143	1.129	0.950-1.342	1.061	0.873 - 1.289
Total ABSI	3.648	1.564-11.508	3.112	1.236-7.838	3.112	1.236-7.838
CRP	2.234	1.023 -4.877	1.489	1.169-1.898	1.505	1.121 - 2.021
Hemoglobin	0.355	0.119-1.061	0.250	0.062-0.999	0.356	2.121 - 3.021
Platelet	0.938	0.887-0.993	0.889	0.817-0.9677	0.967	1.929 - 2.005
Albumin	0.0225	0.001-0.491	0.018	0.001-0.252	0.076	0.009 - 0.686
Creatinine	7.907	1.690-36.98	3.890	1.092-13.847	43.005	1.289 - 1435.361
Urea	1.074	1.011-1.140	1.038	0.988-1.091	1.038	0.988-1.091

**: significant as P value≤0.05. ABSI: abbreviated Burn Severity Index, CRP:C-reactive protein*

Similarly, Aguayo-Becerra et al. [7] observed higher creatinine level in deceased cases than survivors.

In the current study, albumin at 3rd, 6th, 9th and 12th day were significantly lower in complication compared to no complication while there is no significant difference between complication and no complication at admission.

Similarly, De Tymowski et al. [12] found that in a context of early exogenous supply of albumin, admission and 4hour Albuminemia (Alb4 h) were significantly lower in deceased cases. Aguayo-Becerra et al. [7] reported that deceased patients had significantly lower albumin level than survivors.

In this study, Hemoglobin at 3rd, 6th, 9th and 12th day were significantly lower in complicated group compared to the other group. Hemoglobin at admission was insignificantly different between uncomplicated and complicated group.

Similarly, Aguayo-Becerra et al. [7] reported that Hb in deceased patients was lower compared to survivors.

In the present study, CRP at 3rd, 6th, 9th and 12th day were significantly higher in complication compared to no complication while there is no significant difference between complication and no complication at admission.

Similarly, John et al. [9] found a significant higher value of CRP in septic patients.

In the present study, urea at 6th was significantly higher in complication compared to no complication while there is no significant difference between complication and no complication at admission, 3rd, 9th and 12th day.

Similarly, Aguayo-Becerra et al. [7] stated that urea level in deceased patients was significantly higher than survivors.

In the current study, CRP can significantly predict incidence of sepsis with AUC of 0.922, at cut off >12, with 100.0% sensitivity, 86.21 % specificity, 73.3 % PPV and 100.0 % NPV.

Similarly, John et al. [9] documented that rise in serum CRP level predicted sepsis with an efficacy of 87%, while the specificity was found to be 80% and the sensitivity was 93% , with a significant odds ratio of 56. Also, a pre-defined elevation in CRP predicted sepsis onset about 2 days prior to the clinical onset.

In our study, serum albumin can significantly predict incidence of sepsis with AUC of 0.912, P value < 0.001. At cut off ≤ 2, it is a significant predictor with 90.91% sensitivity, 86.21% specificity, 71.4% PPV and 96.2 % NPV.

Similarly, Bandeira et al. [15] reported that the rate of hypoalbuminemia was 41.8% for the standard level with 11.8% of the cases at or below the cut-point of 2.2 g/dL. The rate of mortality for those cases with serum albumin ≤ 2.2 g/dL was 43.7% (7/16).

In the present study, serum creatinine can significantly predict incidence of AKI with AUC of 0.807, at cut off >0.7, with 100 % sensitivity, 24.24%specificity, 21.9% PPV and 100% NPV.

Similarly, Brusselaers et al. [16] found that S-Cr was defined by a cutoff value in 19 trials with S-Cr equal to or more than 2 mg/dl as the most frequent cutoff. The highest cutoff was 5.0 mg/dl and the lowest was 1.1 mg/dl. Clark et al. [8] observed that the base line serum creatinine was 0.80 ± 0.36 and its concentration increased in TBSA >40% to 0.82 ± 0.36 so elevation of serum creatinine is associated with severity and complications.

In the present study, in regression analysis, percent of burn, Total_ ABSI, CRP, platelet, albumin, creatinine, urea and inhalation injury were independent predictors for mortality. In regression analysis, age, sex, hospital stay, and hemoglobin were independent predictors for mortality.

Similarly, Lip et al. [17] found that gender and age were insignificant predictors for mortality. Aguayo-Becerra et al. [7] observed that there was no significant difference between cases older and younger than 40 years or in relation to marital status, gender, or occupation. Clark et al. [8] documented that presence of inhalation injury, and any stage of AKI were significantly associated with hospital mortality. Taylor et al. [18] found that TBSA, age and inhalation injury were significant mortality predictors.

However, Dhopte et al. [19] concluded that factors found to be significant on univariate firth analysis were female gender, older age , higher TBSA , suicidal burns, inhalation injury presence, higher burn depth, and positive microbial cultures. On multivariate analysis, higher TBSA was described as an independent risk factor for mortality.

In the present study, sex, percent of burn, total ABSI, hemoglobin, CRP, platelet, albumin, inhalation injury and creatinine were dependent predictors for sepsis. Age, hospital stay, urea were independent predictors for complication of sepsis.

Similarly, Cato et al. [13] observed that TBSA affect the multivariable model, with a 5%-point elevation in TBSA corresponding to an 18% elevation in the risk of having sepsis. However, even when adjusted for R-Baux the nadir platelet count still shows some relation to sepsis.

In the current study, the mean survival was significantly higher in uncomplicated compared to complicated.

Similarly, Cato et al. [13] reported that % survived was significantly lower in complicated group (sepsis) than non-complicated.

Limitations: It was a single-center study, and the results may differ elsewhere. Also, sample size was relatively small.

5. CONCLUSIONS

Laboratory investigations such as CRP, serum albumin, platelet count, serum creatinine and urea are good predictors of sepsis, AKI and mortalities after moderate to severe burn in pediatrics. Percent of burn, total ABSI, CRP, platelet, albumin, creatinine, urea and inhalation injury are significant risk factors for mortality while age, sex, hospital stay, and hemoglobin are insignificant predictors for mortality.

CONSENT AND ETHICAL APPROVAL

Informed written consent was taken from parents after explanation of benefits and risks. The trial was conducted after approval from the Ethics Committee of Faculty of Medicine, Tanta University.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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