Significance of Early Acidosis In Predicting Early Mortality Among Flame Burned Patients In A Kenyan National Hospital

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Abstract

Introduction: Burn pathophysiology, fluid therapy and mortality have been assessed by various laboratory parameters including lactate and base deficit serum markers. This study targeted flame injured cohort with an objective to determine the significance of early acidosis, through measurement of three acid base indices at admission in predicting 5-day (early) mortality among the flame burned patients.

Methodology: A cohort study. Eighty flame injured patients presenting within 24 hours of incident were assessed for arterial blood pH, lactate and base deficit (BD). Mortality was recorded until day 28. Receiver operating characteristics curves were drawn; area under curve, cut offs, sensitivities and specificities for BD, lactate and pH were determined for 5-day mortality. The cut offs were used to derive contingency tables for calculation of predictive values. Odds ratios were calculated at 95% confidence interval. 28 day survival curve was generated. Level of significance was <0.05 .

Results: 28-day mortality was 39%. Five-day mortality was 24%. The latter was predicted by a lactate level of 2.36 mmol/L, BD of -10.05 mmol/L and pH of 7.344 with 75%, 74% and 95% sensitivities respectively. Odds of patients dying at these levels or worse were 6.3, 11.4 and 36.9 respectively all with significant p-values.

Conclusion: Arterial pH, base deficit and lactate are good predictors of 5-day mortality among fire victims.

Introduction

Burns is a type of trauma that has afflicted man since he first invented the use of fire 1.9 Million years ago (1). Major burns are a significant cause of morbidity and mortality in many hospitals. In one of the national referral hospitals in Nairobi Kenya, close to 600 major burns patients were admitted annually. Nearly 40% of these were as a result of open flames out of which 30% succumbed to their injuries. These fire related deaths accounted for up to 76% of overall burn mortality (2). Standard initial care included fluid and electrolyte therapy, intubation and oxygen supplementation in suspected inhalational injury and wound care. Alkali therapy was not part of standard of care in acidotic flame burned patients. Well known predictors of mortality among the many determinants of burn related deaths are total burn surface area, depth of the burn and presence of inhalational injury as described by J. Tobiasen et al in 1982 (3). These are more severe in flame burns compared to other burn mechanisms and cause greater derangement of physiology which begin soon after the burn incident (2). Key among these are perturbations in body fluids metabolism, peripheral perfusion, gaseous exchange and acute inflammatory response (4, 5). The resulting pathophysiology tends to cause acidosis and can be detected by various clinical and laboratory parameters including arterial blood pH, base deficit and lactate levels. These three parameters measured at admission formed the basis of this study. Their significance in predicting 5-day mortality was assessed premised on the fact that such early deaths would more likely be due to primary physiological effects of the burn as opposed to secondary complications such as wound sepsis (6).

Materials And Methods

This was a prospective observational cohort study which was carried out between April 2017 and February 2018. Data collection spanned six months. It involved flame burned patients aged 13 years or older presenting within 24 hours of fire incident to the accident and emergency department of the national referral hospital. All patients received standard of care according to the hospital's protocol.

The sample size was determined by Fisher's formula with finite population correction (7). The target population was fire casualties who presented to author's hospital in half a year. Mortality of these patients from previous studies done at the same centre was reported to be 30% (2). Therefore, the calculated sample size was 80 participants.

Requisite approvals, including publication of findings, were obtained from the institutional research and ethics committee.

Eligible participants were recruited consecutively as soon as they arrived at the accident and emergency department. Written consent was obtained either from the patients or their next of kin as appropriate.

Immediately thereafter, total burn surface area (%TBSA) was estimated using Lund- Browder chart. Two milliliters of arterial blood was drawn aseptically into heparinized syringe from the radial or femoral artery and submitted to the laboratory within 20 minutes. Among other parameters, three acid base indices of interest (the pH, base deficit and lactate) were measured using *Siemens RapidPoint^R 500* blood gas analysis machine. Mortality within the first 28 days of patients' admission was recorded with special interest of early deaths that occurred within the first 5 days.

Statistical package for social sciences (SPSS) version 23 was used for analysis. Receiver operating characteristic (ROC) curves were generated to determine cut off values and associated sensitivity and specificity for base excess, lactate and pH. The cut offs were used to derive contingency tables with 5-day mortality as the primary outcome. Positive predictive value (PPV), negative predictive value (NPV) and odds ratios (OR) at 95% confidence interval were calculated. Kaplan Meier survival curve was generated for 28 days' survival. All statistical tests were considered significant at a p-value of < 0.05.

Results

Demographics

Eighty patients were studied; 56% were males (n = 45) and 44% (n = 35) females. Majority (84%) aged between 18–45 years [Table 1].

Table 1
Demographic characteristics of
the fire casualties

Frequency n (%)	
Gender	45 (56.3)
Male	
Female	35 (43.7)
Age Group	
< 18	4 (5.0)
18–25	28 (35.0)
26–35	27 (33.8)
36–45	12 (15.0)
> 45	9 (11.3)

Total burn surface area (%TBSA)

Cutaneous total burn surface area of the patients ranged from 6–100% with a median of 25.5% and a mean of 30.9% [Table 2].

Table 2
Cutaneous total burn surface area
(%TBSA) of flame burned patients

%TBSA	Frequency (%)
< 10	3 (3.8)
10–19	21 (26.3)
20–29	22 (27.5)
30–39	18 (22.5)
40–49	5 (6.3)
50+	11 (13.8)
Mean (30.9%)	80 (100.0)

Arterial blood acid base parameters

Three arterial blood gas parameters were targeted: the pH, base deficit and lactate. These had a mean of 7.30, -7.87mmol/L and 2.91mmol/L respectively [Table3].

Table 3
Arterial blood gas analysis findings of 3 selected indices

Frequency n (%)	
pH	
< 7.15	10 (12.5)
7.15–7.24	7 (8.8)
7.25–7.34	21 (26.3)
7.35–7.44	39 (48.8)
> 7.45	3 (3.8)
Mean (7.30)	80 (100.0)
Base Excess (mmol/L)	
>-2.00	5 (6.3)
-6.00 to -2.00	26 (32.5)
-10.00 to -6.01	23 (28.7)
≤ -10.01	26 (32.5)
Mean (-7.87)	80 (100)
Lactate (mmol/L)	
0-1.9	21(53.9)
2 to 3.9	7(17.9)
4 to 5.9	8(20.5)
≥ 5.9	3(7.7)
Mean (2.91)	39 (100.0)*
<i>* A study limitation where only 39 samples of the 80 were tested for lactate levels.</i>	

The three blood gas parameters were correlated with %TBSA. All were found to worsen with increasing %TBSA on Pearson's moment product correlation [Table 4].

Table 4
Pearson's moment-product correlation for %TBSA vs acid base indices

	Correlation with %TBSA (r)	p-value
Arterial base Excess	0.538	< 0.001
Arterial lactate	0.695	< 0.001
Arterial blood pH	-0.588	< 0.001

Mortality and survival

Twenty eight day mortality was found to be 38.8% (n = 31) with the median mortality at day 5. Twenty three

percent (n = 7) of all deaths occurred within 24 hours of admission, 61.3% (n = 19) by day 5 and 67.8% (n = 21) by day 7. Twenty-eight-day mean survival of flame burned patients was 20.81 (95% CI, 1.37 – 23.50) days [figure 1]

Receiver operating characteristics graphs for 5-day mortality

Receiver operating characteristics (ROC) graphs for 5-day mortality prediction were drawn for arterial base deficit, lactate and pH. The area under the curve (AUC) was examined for each of the graphs. Cut off values were derived based on sensitivity and specificity for each graph as follows:

Base deficit

Base deficit (BD) AUC value was 0.80 (95% CI, 0.69–0.91) and a cut off value of -10.05mmol/L with sensitivity of 73.7% and specificity of 80.3% (p < 0.001) hence good in predicting 5-day mortality [figure 2].

Arterial lactate

The AUC for arterial lactate was 0.75 (95% CI, 0.56–0.94). The cut off was 2.36 mmol/L with a sensitivity of 75.0% and specificity of 67.7% (p = 0.034) hence fair in predicting 5-day mortality [figure 3].

Arterial blood pH

The AUC for blood pH was 0.82 (95% CI, 0.74–0.91). The cut off was 7.344 with a sensitivity of 94.7% and specificity of 67.2% (p < 0.001) hence good in predicting 5-day mortality [figure 4].

Prediction of 5-day mortality based on cut off values for the three acid base indices

The cut off values for each of the three acid base indices were used to generate contingency tables. Positive

predictive values, negative predictive values and odds ratios were calculated at 95% confidence interval with 5-day mortality as the primary outcome [Table 5].

Table 5

Contingency table for the prediction of 5-day mortality based on ROC cut off values for the three acid base indices

Acid Base Parameter	Dead	Alive	Odds Ratio ^a	p-value	PPV ^b (%)	NPV ^c (%)
BD cut off value (mmol/L)						
≤ -10.05	14	12			53.8	
>-10.05	5	49				90.7
Total	19	61	11.4 (3.4–37.9)	<0.001		
Lactate Cut Off value (mmol/L)						
≥ 2.36	6	10			37.5	
< 2.36	2	21				91.3
Total	8	31	6.3 (1.1–36.9)	0.045		
pH Cut Off value						
≤ 7.344	18	20			47.4	
> 7.344	1	41				97.6
Total	19	61	36.9 (4.6-296.4)	<0.001		
^a Odds ratio was calculated at 95% confidence interval and level of significance pegged at < 0.05.						
^b PPV- positive predictive value.						
^c NPV- negative predictive value.						

Discussion

Burn injury induces complex physiological stress to the victim and untold anguish. Many determinants of burn mortality have been studied and include extremes of age, presence of comorbid conditions and inadequate or delayed resuscitation (8, 9). However, strong determinants of burn mortality are %TBSA, depth of the burn and presence of inhalational injury (3). The resulting burn pathophysiology lead to derangements in fluid metabolism, circulatory and respiratory perturbations, systemic inflammatory and metabolic responses. These alterations are worse in fire injuries due to greater thermal energy transfer and the potential for inhalational injury. These account for many deaths in fire victims which tend to occur at the scene of incident or in early course of hospitalization compared to deaths from other burn mechanisms (6, 10).

The burned skin loses its fluid conservation quality resulting in transdermal exudation of fluid and electrolytes (11). Moreover, blood vessels in the burned tissue suffer endothelial necrosis and breakdown causing further fluid and even blood loss (12). Thirdly, the burn injury initiates acute inflammatory process locally which is associated with vasodilation, increased vascular permeability and thereby third spacing of body fluids. The locally released cytokines may lead to systemic inflammatory response syndrome (SIRS). Furthermore, catecholamine surge due to the injury causes vasoconstriction that increases total peripheral resistance (13). These factors lead to contracted vascular volume and reduced perfusion resulting into hypovolemic and redistributive shock of various degrees. A reduction of oxygen tension in tissues and accumulation of metabolic waste in the interstitial fluid follows. If present, physicochemical inhalation injury to the respiratory epithelium leads to ventilation-perfusion mismatch which worsens hypoxemia. Besides, should there be asphyxiants such as carbon monoxide in the inhaled smoke, further hypoxemia results. These perfusion, inflammatory and respiratory disturbances lead to metabolic derangements including acidosis which was the target for this study.

The basic burns profile and mortality findings in this study were similar to prior studies carried out at the same institution involving the flame injured cohort. The mean %TBSA was 30.9%. Overall 28-day mortality was 38.8%. Sixty-one percent of the deaths occurred within the first five days and additional 7% occurring by day 7 of admission.

All the three acid base indices taken at admission were noted to worsen with increasing %TBSA indicating worsening pathophysiology. At derived cut offs, odds of early (5-day) mortality were significantly high.

Base deficit was found to be a good predictor of 5-day mortality at cut off value of -10.05 mmol/L ($p < 0.001$) with odds ratio of 11.4 (95% CI, 3.4–37.9). Choi et al reported that abnormal increase in BD (< -6 mmol/L) after a burn injury represents mal-perfusion state which may not be recognized by traditional parameters such as urine output (5). Similarly, Mutschler et al reported that BD increases with deepening degrees of hypovolemic shock in trauma patients. He noted that a BD of ≤ -10 mmol/L represented Class IV hypovolemic shock (14). Furthermore, patients with high BD (< -6 mmol/L) measured within 24 hours of burn injury have more florid SIRS, more prevalent acute respiratory distress syndrome and experience

more severe multiple organ dysfunction syndrome compared to those with BD of >-6 mmol/L. This translates to a higher mortality outcome (5). Our study echoes Choi and Mutschler's finding such that a BD of -10.05 mmol/L predicted mortality with a sensitivity of 73.7% and specificity of 80.3%.

Cochran et al reported that an early rise in serum lactate was an independent risk factor for death after a burn injury (15). This was demonstrable in our study where at 2.36 mmol/L or more, lactate showed an acceptable discrimination for 5-day mortality with 6.3 times more likelihood of death compared to patients with < 2.36 mmol/L (95% CI, 1.1–36.9). Therefore, just as BD, lactate elevations at day 0 is a useful parameter to separate survivors from non survivors of burns a position also observed by Andel et al (16).

The BD and lactate lower the blood pH. A pH of 7.344 or less predicted early mortality with a sensitivity of 94.7% and specificity of 67.2% ($p < 0.001$). The odds of burn patients dying at these levels was 36.9 times more than those with a higher pH (95% CI, 4.6-296.4). A higher pH predicted 5-day survival of up to 97.6%.

From the foregoing, the three acid base parameters discussed can be utilized to identify burned patients at higher risk of death. Additionally, literature highlights importance of lactate and BD in particular, in estimating fluid requirement and adequacy of resuscitation in major burns. However, except for the work by Peaston, in 1968 there is paucity of information on utility of alkali therapy in treatment of acidosis in burns as applied to other causes of severe acidosis (14, 16, 17, 18). Therefore, whether or not alkali therapy can help better outcomes in severe acidosis associated with flame burns may be a potential area of study.

Conclusion

Flame burned patients undergo complex pathophysiological processes that explain the tendency for an elevated arterial blood base deficit (BD), a raised lactate and a lower pH. Measured at admission, these parameters can predict five-day mortality with good sensitivity and high odds of death at cut offs of -10.05 mmol/L, 2.36 mmol/L and 7.344 respectively. Therefore, these tests can help identify early, burned patients at higher risk of death and help inform and guide a more vigorous early resuscitation and enhanced treatment. It is plausible to deduce that an alkali may be a useful addition to therapy for these patients presenting with severe acidosis.

Study Limitation

Only 39 of the 80 recruited participants had their samples tested for lactate due to frequently unavailable reagent for lactate measurement at the study hospital. None the less, the results and analysis obtained were significant and therefore included in this article.

Recommendations

Findings of this study may be used to identify physiologically high risk flame injured patients for a more aggressive fluid therapy and enhanced treatment. Due to paucity of information on utility of alkali therapy for severe metabolic acidosis among acutely burned patients, a study may be conducted to assess the impact of alkali therapy on morbidity and mortality of such patients.

Declarations

Competing interests

Authors declare that they have no competing interests.

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Ethics and consent to participate

The joint Kenyatta National Hospital and University of Nairobi Ethics and Research Committee's approval

was obtained to carry out the study and to publish the results under reference number P744/10/2016.

Availability of data and materials

The datasets analyzed during the current study are available from the corresponding author on reasonable

request.

Consent of publication

There was no individual person's data featured in this study.

Authors' contribution

ENM was the principal investigator, drafted the manuscript and is the Corresponding author.

SOK did the concept paper and edited the draft manuscript.

JMN reviewed literature and did the second manuscript.

COA helped interpret and contextualise the laboratory data and typeset the final draft of the manuscript.

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Figures

Figure 1

28-day survival curve of flame burned patients

Figure 2

ROC curve for arterial base excess (mmol/L) vs 5-day mortality

Figure 3

ROC curve for arterial lactate (mmol/L) vs 5-day mortality

Figure 4

ROC curve for arterial blood pH vs 5-day mortality