Base Deficit as a Predictor of Mortality in Sepsis and Septic Shock

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ABSTRACT

Introduction: Sepsis is a common problem encountered in emergency room which needs to be intervened early. It is always difficult to have quick prognostic marker of sepsis in busy emergency. So this study was conducted to determine whether base deficit can be used as an indicator of mortality among septic patients in emergency room setup like ours.

Methods: It was a hospital based descriptive cross sectional study done at Tribhuvan University Teaching Hospital, Kathmandu from March 2018 to December 2018. Acute physiology and chronic health Evaluation II score (APACHE II), Base deficit, Sequential Organ Failure Assessment (SOFA) score on first day of arrival in emergency room was calculated. The association of 28-day outcome with acute physiology and chronic Health Evaluation II score, Base deficit value and SOFA score were derived.

Results: Out of 229 patients with septic shock 62 died (27%) and among 71 patients without septic shock, 12 died (16.9%). Overall mortality was 24.66 % (n= 74). The area under the ROC curve for Base deficit(0.864;95% C.I.=0.822-0.906), APACHE II (0.782; 95% C.I=0.718-0.848, SOFA (0.689;95% C.I=0.620-0.757) were greater than 0.7 except for SOFA which signifies these test to have fair efficacy to predict mortality.

Conclusions: High base deficit value predicts mortality in patients with sepsis and septic shock. The base deficit could be used as an alternate marker to predict mortality in septic patient. We recommend for large multicenter study with randomization so that the findings can be applied to general population and of different geographical situations.

Keywords: Base Deficit; Sepsis; Septic Shock, Predictor, Mortality

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INTRODUCTION

Sepsis is one of the commonest presentations in emergency room with high mortality rate. It has been called one of the oldest and most elusive syndrome in medicine. The most effort in sepsis has been given by Surviving Sepsis Campaign (SSC) guidelines which undoubtedly improved the process of care and outcome in the past decade. One of the important way to decrease the mortality is early identification of sepsis and start early management. 

Base deficit is one of the important parameter in sepsis and septic shock investigation and management in current days. If we can predict the mortality of patients with sepsis in emergency room and aggressively resuscitate them, the mortality rate can be decreased. In recent days base deficit is being investigated for its prognostic value in septic patients. Base deficit is assumed to be the first accurate index of the non-respiratory component of acid base balance. Therefore base deficit value can provide a prognostic index that correlates with infection and easily available test in emergency room. The aim of this study is to determine whether the base deficit can be used in septic patients in our emergency set up to predict mortality.

METHODS

This hospital based, descriptive cross sectional study was conducted at Department of General Practice and emergency medicine, Tribhuvan University Teaching Hospital (TUTH) Nepal, From March 2018 to December 2018. Written consent was obtained from participants or from legal guardian when patients are too sick. Patient of greater than 18 years presented in TUTH emergency with diagnosis of sepsis were included. SOFA score of more than two was used to diagnose sepsis. Patients with an age less than 18 years, do-not-resuscitate order, pregnancy, left against the medical advice, were excluded. For each patient, at emergency vital signs were recorded with conscious level, temperature, heart rate, respiratory rate and systemic blood pressure. Laboratory parameters viz. haematocrit, blood glucose, total leucocyte count, serum sodium, serum potassium, serum creatinine and platelets count; were recorded. Patient arterial blood gas report was recorded with arterial pH, serum bicarbonate, FiO2, serum lactate and base deficit.

Sample size was calculated by \( N = \frac{Z^2pq}{d^2} \) with Applying the sample size calculation formula based on hypothesis testing for two means from mortality of 59.6% in sameet et al, and from article published in Scientific Reports in 2017, November with 14 % mortality where \( z = 1.96 \) at 95% confidence level, \( p = 86.7\% \) p = percent area under the curve, \( q = 100-p = 13.3\% \), \( d = \) allowable error = 5% of \( p = 4.3 \). So, calculating by using above formula, the sample size of this study (n) is 300.

Descriptive statistics of demographic and laboratory variable were calculated with mean and percentages. Receiver operating characteristics (ROC) curve and Area under the receiver operating characteristics curve was used to evaluate the efficiency of base deficit in comparison to APACHE II and SOFA score; in predicting mortality within 28 days of hospital admission.

RESULTS

The age range of participants were 18 years to 101 years and mean age of 49.6 +/- 18.25years in survival groups and 60.6 +/- 17.26 years in mortality group. The overall mortality in septic patient was 24.7% (n=74) and the mortality in sepsis only was 16% and septic shock was 27%.There is increase in mortality rate as age increases with highest mortality of 54 % in age group of more than 77 years and minimum of 11 % in age group of 18-37 years(Fig 2).Most of the patients lie in severe base deficit(≥15) group (42.6%) followed by moderately high base deficit(-11 to-15) group(25%) and mild base deficit (≤ -10) group(32.3 %) (Table 3).Mean base deficit was -12.15 +/- 5.19 in survival group and -19.42 +/- 3.93 in mortality group.

In correlating between APACHE II score and base deficit ratio (Figure 1) shows positive deflection with correlation coefficient of 0.45 indicating that base deficit shows good mortality prediction.
The area under the ROC curve for base deficit (0.864;95% C.I = 0.822-0.906), APACHE II (0.782;95% C.I = 0.718-0.848), SOFA (0.689;95% C.I = 0.620-0.757) were greater than 0.7 except for SOFA score which signifies these score to be a fair test to predict mortality among septic patients (Table 1). As base deficit has highest area under the curve among other prediction scores, it is the superior to other scores to predict mortality among septic patients. Bivariate logistic regression analysis was done to analyse effect of confounding factors like age, sex, presence of septic shock on mortality. Patients were further divided into two groups sepsis and septic shock. Out of 229 patients with septic shock 62 died (27%) and among 71 patients without septic shock, 12 died (16.9%). (Table 4). Overall mortality was 24.66% (n=74).

Base deficit subgroups analysis showed 8% mortality in moderate base deficit group (-11 to-15) and 52 % in severe base deficit group (>15) (Table 3). This shows increase trend of mortality with increase in base deficit value and vice versa.

Figure 1: Relationship between base deficit and APACHE II score
Figure 2: Outcome of septic patient in 28th day follow-up as per age group

Figure 3: Receiver Operating characteristics curve analysis for base deficit, SOFA and APACHE II score to predict mortality in sepsis
### Table 1: Area under the curve

<table>
<thead>
<tr>
<th>Test Result Variable(s)</th>
<th>Area</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>Base Deficit</td>
<td>.864</td>
<td>.822</td>
</tr>
<tr>
<td>APACHEII Score</td>
<td>.782</td>
<td>.718</td>
</tr>
<tr>
<td>SOFA</td>
<td>.689</td>
<td>.620</td>
</tr>
</tbody>
</table>

### Table 2: Sensitivity, specificity, positive likelihood ratio and negative likelihood ratio for base deficit to predict mortality in sepsis

<table>
<thead>
<tr>
<th>Base Deficit</th>
<th>Sensitivity</th>
<th>PLR</th>
<th>Specificity</th>
<th>NLR</th>
</tr>
</thead>
<tbody>
<tr>
<td>-5.2</td>
<td>1.00</td>
<td>1.09</td>
<td>0.08</td>
<td>0.00</td>
</tr>
<tr>
<td>-10.1</td>
<td>0.99</td>
<td>1.66</td>
<td>0.41</td>
<td>0.03</td>
</tr>
<tr>
<td>-15.05</td>
<td>0.91</td>
<td>3.35</td>
<td>0.73</td>
<td>0.13</td>
</tr>
<tr>
<td>-18.1</td>
<td>0.55</td>
<td>3.79</td>
<td>0.85</td>
<td>0.52</td>
</tr>
</tbody>
</table>

### Table 3: Binary logistic regression of base deficit subgroup and outcome

<table>
<thead>
<tr>
<th>Base Deficit Classification</th>
<th>Cured (N = 226)</th>
<th>Mortality (N = 74)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>Row %</td>
<td>Column %</td>
</tr>
<tr>
<td>Low &lt;5</td>
<td>4</td>
<td>100%</td>
<td>1.76%</td>
</tr>
<tr>
<td>Mild 5-10</td>
<td>92</td>
<td>98.9%</td>
<td>40%</td>
</tr>
<tr>
<td>Moderate 11-15</td>
<td>69</td>
<td>92%</td>
<td>30%</td>
</tr>
<tr>
<td>Severe &gt;15</td>
<td>61</td>
<td>47%</td>
<td>26%</td>
</tr>
</tbody>
</table>

### Table 4: Bivariate logistic regression analysis of confounding factors and prognostic predictive scores

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Improved/Cured (N = 226)</th>
<th>Mortality (N = 74)</th>
<th>95% Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Row %</td>
<td>n</td>
</tr>
<tr>
<td>Age</td>
<td>49.64</td>
<td>75.3%</td>
<td>226</td>
</tr>
<tr>
<td>Base Excess</td>
<td>-12.1</td>
<td>75.3%</td>
<td>226</td>
</tr>
<tr>
<td>APACHE II</td>
<td>16.61</td>
<td>75.3%</td>
<td>226</td>
</tr>
<tr>
<td>SOFA</td>
<td>8.16</td>
<td>75.3%</td>
<td>226</td>
</tr>
<tr>
<td>Chloride</td>
<td>103.9</td>
<td>75.3%</td>
<td>226</td>
</tr>
<tr>
<td>Sex: Male</td>
<td>71%</td>
<td>116</td>
<td>28.8%</td>
</tr>
<tr>
<td>Female</td>
<td>80%</td>
<td>119</td>
<td>19.7%</td>
</tr>
<tr>
<td>Septic</td>
<td>Yes</td>
<td>72.9%</td>
<td>167</td>
</tr>
<tr>
<td>Shock</td>
<td>No</td>
<td>83.1%</td>
<td>59</td>
</tr>
</tbody>
</table>
DISCUSSION

With the early resuscitation and hour bundle care in the management; which decreases mortality in sepsis and septic shock, the focus has now moved to predicting mortality in septic patients. Our study showed that in the patients with sepsis and septic shock base deficit level obtained at admission in the emergency room can be used as an independent predictor of 28 day mortality. Lots of study have been done to investigate the biomarkers to predict mortality in sepsis but only few studies have evaluate the prognostic significance of base deficit level in a septic patient. In-hospital mortality in our study was 24.7% which is nearly equal to study done by Cohen J et al with mortality of 25-30%. With our study mortality in younger age group was 11% in 18-37 years group compared to 54% in old age group above 77 years whereas study done by Nasa P et al showed mortality of 45.6% (n=387) in younger age group as compared to 60.7% in old age group and 78.9% in very old age group. So sepsis is significant burden on society and disproportionally affects the older adults and more than 60% of sepsis diagnosis are made in adults aged more than 65 years which is similar finding to our study.

Base deficit is assumed to be the first accurate index of the non-respiratory component of acid-base balance. It is defined as the amount of strong acid that must be added to each litre of fully oxygenated blood to return the pH to 7.40 at a temperature of 37 degree centigrade and pCO\textsubscript{2} of 40 mmHg. The measurement of single lactate value in emergency room has several limitation, like in trauma, diabetic ketoacidosis, liver dysfunction level of lactate is high. So base excess value is more important as it isn’t much influenced by above factors and gives the proper interpretation value in metabolic acidosis in septic patients. In our study overall mortality till 28\textsuperscript{th} day follow up was 74 (24.7%) and 27% with septic shock. It shows that one in every four patient diagnosed as sepsis or septic shock are dying, similar results were found in study done by Harm-Jan with 65 septic shock RCTs in 2018.

APACHE II and SOFA scoring system were used widely to assess outcome in septic patient but this is time consuming and difficult to assess immediately in busy emergency room situation. So we used base deficit as a marker of outcome in sepsis. It is found that increase in base deficit increases mortality in septic patients. Our study finding were similar with study done by Min Ho Seo in 2016 with hypoalbuminemia, low base excess value and tachypnoea to predict 28 day mortality in severe sepsis and septic shock patient in emergency department, which found that mortality in patients with sepsis and septic shock correlates with increased base excess level. It is found that base excess has slight higher area of under the ROC curve (AUROC=0.864) in comparison with APACHE II (AUROC = 0.782) which correlates with the above study done by Min Ho Seo. Study done by Min Ho Seo showed the AUC of the APACHE II score to be 0.6177(95% CI,0.5423-0.6931) whereas albumin, base deficit and respiratory rate combined had AUC of 0.8173(95% CI,0.7605-0.8741) and conclude that, base excess can be chosen for predicting mortality then APACHE II. Our study had mean APACHE of 16 (S.D = 5.92) in survival group and 23.3 (S.D = 6.94) in mortality group, while study done by Sundaramoorty et al had mean APACHE of 24.3 in survival group with S.D of 6.48 and 32.39 in mortality group with S.D of 5.09.

Limitation of Study: Sensitivity analysis of all confounders that could cause increase mortality in sepsis was not perform. Patients were generalized once they come to emergency room in spite of their level of treatment outside the hospital. It was a single center non-randomized study which has chances of biasness.

CONCLUSION

High base deficit value predicts mortality in patients with sepsis and septic shock. The base deficit could be used as an alternate marker to predict mortality in septic patient. We recommend for large multicenter
study with randomization so that the findings can be applied to general population and of different geographical situations.

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