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Original Research Article

Base excess as a predictor of neonatal mortality in neonatal sepsis

Sushrutha K. P.[1], Hamsa M.[1]*, Lingaraju N.[2], Sampath Kumar C.[3]

[1]Department of Pediatrics, Chamarajanagara Institute of Medical Sciences, Chamarajanagara, Karnataka, India
[2]Department of ENT, Chamarajanagara Institute of Medical Sciences, Chamarajanagara, Karnataka, India
[3]Department of Pediatrics, DEIC, Mysore, Karnataka, India

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***Correspondence:**
Dr. Hamsa M.,
E-mail: drhamsa.m@gmail.com

ABSTRACT

Background: Neonatal sepsis is responsible for approximately 15% of all neonatal deaths in the world. Despite of availability in advanced medical healthcare facilities for mother and neonates, incidence of mortality secondary to sepsis especially in developing countries like India is more common. Metabolic acidosis is the most common form of acid base imbalance in neonatal sepsis which can be analyzed with increased levels of base excess. Hence early diagnosis of neonatal sepsis can be done by determining base excess.
Methods: This is a prospective observational study conducted in NICU at Cheluvamba Hospital, Mysore. 73 term neonates with suspected sepsis were enrolled in the study who were on regular follow-up and treatment till death/discharged from NICU. Base excess value is obtained from the arterial blood gas analysis from each subject and it was compared with survivor and non-survivor group along with other study parameter
Results: Out of 73 subjects, incidence of non survivors group with severe increase in base excess is 75%. To predict the mortality, we compared it with standard base excess which showed the prediction of more than 60%, with significant AOC (0.827) of very near to one in ROC curve, with statistically significant ($p<0.001$) sensitivity of 92.59%, specificity of 63.04%, positive predictive value of 59.5%, negative predictive value of 93.5%.
Conclusions: In present study we have proved that base excess is an important parameter for the early diagnosis and for early intervention in neonatal sepsis.

Keywords: Neonatal sepsis, Base excess, Neonatal mortality

INTRODUCTION

Neonatal sepsis (NS) remains the most common and important cause for neonatal morbidity and mortality. Despite of availability in advanced medical healthcare facilities for both mother and neonates, incidence of mortality secondary to sepsis especially in developing countries like India is more common.

Global burden

Neonatal sepsis is responsible for an estimated 4,30,000 neonatal deaths in 2013, accounting for approximately 15% of all neonatal deaths.[1]As per World health organization (WHO), neonatal sepsis is the third most frequent etiology of neonatal mortality.[2]

Indian data

The incidence of sepsis is 14.3% and culture positive sepsis was found to be 6.2% according to study done by Delhi national infection study (DeNIS) collaboration, and there were two-thirds of the cases diagnosed as early onset sepsis (EOS), caused by gram negative organisms and accounts for 25% of the total deaths.[3] According to data from National neonatal perinatal database (NNPD) 2002-

03 reported Neonatal sepsis as the commonest causes of neonatal mortality that contributes to 19% of all neonatal deaths.[4]In Karnataka a study from 2014 to 2018 by Dhaded SM, Somannavar MS, Moore JL, et al., the neonatal mortality rate was 24.5 per 1000 live births. The cause for the neonatal deaths was mainly due to prematurity (27.9%), birth asphyxia (25.1%), infection (23.7%) and congenital anomalies (18.4%).[5] Early diagnosis of Neonatal sepsis in neonate has remained a challenging even in the developed countries due to subtle and nonspecific signs and symptoms and hence prompt diagnosis of Neonatal sepsis is difficult. Even though blood culture is the gold standard for diagnosis, it is costly and requires at least 48hrs for the preliminary results and its yield is between 30-70%. Therefore, some of the neonates with sepsis may go undetected. If the diagnosis of the sepsis is delayed then it results in unnecessary and prolonged exposure of antibiotics that can even lead to mortality.[6,7] Sepsis in the neonate causes acid base imbalance and most common primary event being metabolic acidosis which can be seen in the form of increased levels of base excess in the arterial blood gas hence early diagnosis of neonatal sepsis can be done by detecting base excess. In this part of Karnataka that is in Mysore early diagnosis and adequate antibiotic treatment for neonatal sepsis are required because of the high rates of mortality and morbidity secondary to neonatal sepsis. This study is aimed to determine whether base excess value helps to diagnose sepsis and aid to know its association in predicting the mortality of Neonatal sepsis.

Objectives

Objectives were to determine base excess in neonates with suspected sepsis and to study the correlation between base excess and mortality of neonate admitted in NICU with sepsis.

METHODS

Sample size and sampling method

A total of 73 neonates with sepsis were taken up for the study which was calculated based on the prevalence of 5% of neonatal mortality due to sepsis amongst term neonates admitted in Cheluvamba hospital, at 0.05 significance level using the formula;

$$Sample\ size = Z2pq/d2$$

Where Z=1.96, p is the prevalence of disease, d=95% confidence interval, q=1-p. Purposive sampling was utilized as sampling method.

Study design, duration and location

Current study is a prospective observational study conducted for a period of 12 months (1 January 2020 to 1 January 2021) at Cheluvamba hospital, Mysore Medical College, Mysore.

Inclusion criteria

All term neonates admitted for suspected sepsis at NICU, Cheluvamba hospital, MMC & RI, Mysore were included.

Exclusion criteria

Exclusion criteria were; Preterm neonates <37 weeks, Neonates associated with birth asphyxia, Neonates with meconium aspiration syndrome, Neonates with congenital Anomalies, Neonates with renal failure, congenital heart disease and Neonates with Inborn error of metabolism.

Procedure

All neonates satisfying the inclusion criteria was included in the study. For each neonate, a detailed history from the mother or other reliable care-giver was recorded using a preset questionnaire along with particulars of the neonates. Before enrollment parent of each child was given a detail explanation about the nature and purpose of the study and informed consent was taken. Complete history including antenatal risk factors like leaking pervagina, uterine tenderness, foul smelling discharge, status of the amniotic fluid, mode of delivery was taken from maternal record. Other details regarding neonate like, cried after birth or not, birth weight, gestational age, APGAR score at 1min, 5min, whether resuscitation required or not, vitamin k given or not, breast fed within 1 hour or not and baby's information on admission including age on admission, general condition of the baby (alert/lethargic/comatose), h/o bottle feeding, h/o loose stools, vomiting, temperature, GRBS and baby's vitals like heart rate, peripheral pulses, CRT, respiratory rate, grunting/chest in drawing, SpO2, cry, suck, activity, tone, presence of convulsion, bleeding, jaundice, umbilical discharge, skin pustules were noted. Presence of any one of the risk factors with or without presence of 3 or more abnormalities in the above-mentioned vitals, neonates were labelled to have suspected sepsis. For all the neonates with suspected sepsis, septic screen, blood culture and sensitivity was done. Enrolled neonates were also analyzed for the blood gas status where 0.5ml of arterial sample was taken with all aseptic precaution in the heparin flushed disposable syringe within 12-24 hrs of admission as well as other necessary investigations including, complete blood count, chest X-ray, renal function test, serum electrolytes, CSF analysis were done as a part of management. Base excess from the arterial blood gas analysis was compared with the outcome of the each neonate.

Statistical analysis

A total sample size of 73 neonates with suspected sepsis was selected and regular follow up was done till the neonate get discharged or succumbed. Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies (f) and proportions. Chi-square test or Fischer's exact test (for 2x2 tables only)

was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. ANOVA was used as test of significance to identify the mean difference between more than two quantitative variables. Receiver operating characteristic (ROC) and optimal cut-off points were chosen for the calculation of sensitivity, specificity, positive and negative predictive values. A test that predicts an outcome no better than chance has an area under the ROC curve of 0.5. An area under the ROC curve above 0.8 indicated fairly good prediction. Graphical representation of data: MS Excel and MS word were used to obtain various types of graphs. P value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests. Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

RESULTS

Subjects were grouped as survivors and non-survivors. Out of 73 neonates 63% were survivors, i.e., neonates who got discharged from the hospital and 37% were non-survivors (Figure 1).

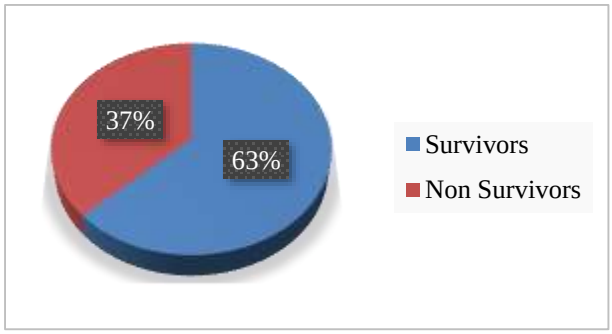

Figure 1: Distribution of subject according to outcome.

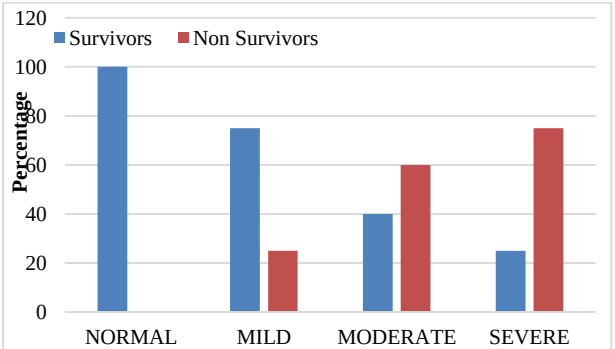

Figure 2: Distribution of subject according to outcome and base excess.

Out of 73 newborns 15 subjects had normal base excess among them all survived. 24 newborns had base excess between -3 to -7 (mild), among them 6 were non survivors i.e., 25% of mortality in newborns with mild increase in base excess.

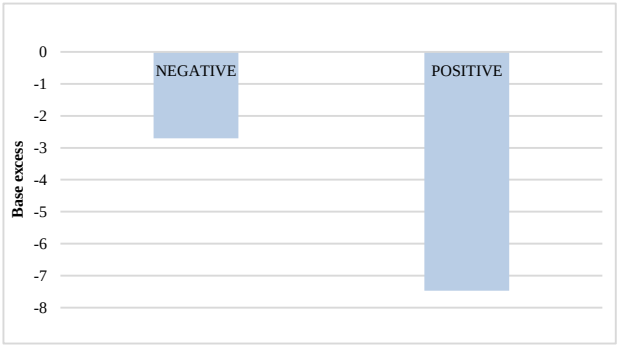

Figure 3: Comparison of base excess with septic screen.

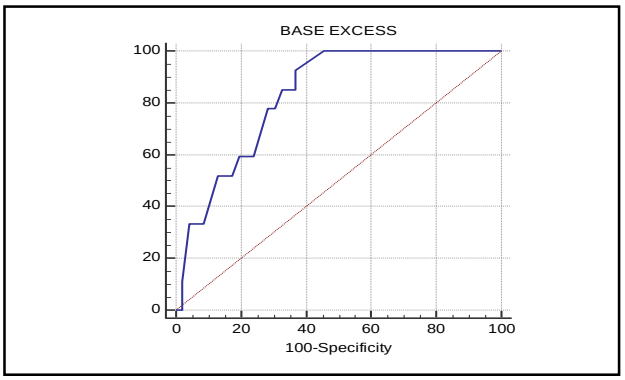

Figure 4: ROC for base excess in predicting mortality.

Similarly, there were 30 newborns with moderate increase in base excess (-7 to -12) and among which 60% were non-survivors. There were 4 newborns with severely increased base excess (>-12), among them 75% were non survivors. p<0.001, there was a statistically significant difference found between outcome and base excess. The same is depicted in (Figure 2). Out of 73 subjects, 67 newborns had positive septic screen who had mean base excess of -7.46. While patients with negative septic screen had mean base excess of -2.7. The p value is 0.003, there was a statistically significant difference found between septic screen and base excess which is shown in (Figure 3). An area under the ROC curve above 0.8 indicated fairly good prediction of mortality by base excess, which is depicted in (Figure 4).

Table 1: ROC parameters.

Parameters			Values	
Area under the ROC curve (AUC)			0.827	
95% Confidence interval			0.720 to 0.905	
P value			<0.0001	
Cut off	**Sensitivity**	**Specificity**	**+PV**	**-PV**
≤-6	92.59%	63.04%	59.5 %	93.5%

DISCUSSION

Neonatal sepsis represents most important and most common cause for neonatal mortality and morbidity in the world which accounts for about 15% of neonatal deaths.[1] There are many laboratory investigations to diagnose neonatal sepsis, gold standard being blood culture and sensitivity. Standard base excess is one such parameter helps to diagnose neonatal sepsis and to predict neonatal mortality secondary to sepsis. In sepsis because of decrease organ perfusion there will be acid base imbalance mainly metabolic acidosis secondary to anaerobic metabolism.

Table 2: Comparison of the outcome with other studies.

Studies	Present study	Yusuf et al.[9]	Ahmed et al.[10]
Survivors (%)	63	58	66
Non-Survivors (%)	37	41	33.9

Table 3: Comparison of base excess and mortality with various studies.

Studies	Present study	Yusuf et al.[9]
Non-Survivors (%)	41%	37%
Mean base excess (%)	-13.21	-9.5

This acid base imbalance is more severe in newborns, since the acid production is more. Many studies have showed detection of sepsis by increased base excess which in other words amount of acidosis helps to prevent mortality of newborns with early intervention.[8] Present study is prospective observational study, and included 73 term neonates for this study.

In present study non-survivors are 37%. Which when compared to other studies percentage of population required to interpret results in non-survivor group is adequate. In a study Seema et al. showed that the study subjects had mean pH of 7.27 with mean base excess of -6.6 and states that increase in base excess can be used for the early detection of neonatal sepsis.[8] In present study as the newborns who had positive septic screen had increased base excess. Hence increase in base excess can be used to identify sepsis early for early intervention and to prevent mortality secondary to sepsis.

Metabolic acidosis is the most common acid base imbalance which occur in newborn with sepsis. In study by Yusuf et al stated that Metabolic acidosis with base excess <5mmol/l is frequently seen in non-survivors and in critically ill patients it serves as a powerful marker for poor prognosis.[9] In the present study it was also found that patient who presented with lethargy had increase level of base excess with a p value of 0.011. Presence of septic shock and requirement of inotropes also correlated with increased level base excess with p value 0.001 for both. It is evident from the present study that more severe the base excess worse is the outcome, similar to various studies mentioned earlier. If the initial value of base excess is more we can predict the poor outcome in terms of mortality and morbidity, hence one can plan for early intervention in terms of antibiotics, bolus and inotropes. With the early identification of poor outcome, by increased base excess value and with early intervention for such newborn one can prevent mortality and morbidity associated with neonatal sepsis. In our study to predict the mortality we compared it with standard base excess which showed the prediction of more than 60%, with significant AOC (0.827) of very near to one in ROC curve, with statistically significant ($p<0.001$) sensitivity of 92.59%, specificity of 63.04%, positive predictive value of 59.5%, negative predictive value of 93.5%.

Strength and limitations

Strengths were; the study was done with term neonates with sepsis excluding those who had history of birth asphyxia, which is an important cause for metabolic acidosis in the neonatal period. Sepsis in subjects is not only diagnosed based on septic screen but also is proved with blood culture and sensitivity for majority of the neonates. Arterial blood gas was done for every subject after taking consent from the patient's attenders. Venous blood sample was not taken and hence maintained uniformity among subjects. Limitations were; Serum lactate level was not measured in study subjects to confirm acidosis, other parameters like contribution of PCo_2, PaO_2, phosphate with respect to neonatal sepsis, were not measured and Study was limited to term neonates where sepsis is common in preterm infants also.

CONCLUSION

Despite of having advanced medical care for newborns in developing countries like ours availability of such medical care for every newborn is difficult. Neonatal sepsis is the most common cause for neonatal mortality and morbidity early identification and early intervention in-terms of antibiotics, bolus and inotropes are required to prevent mortality and thus to decrease the global burden of neonatal mortality. In present study we have proved that base excess is an important parameter for the early diagnosis and for early intervention in neonatal sepsis. Our study also showed that increasing severity of base excess is associated with increasing mortality, hence increased levels of base excess can be used as a predictor or indicator for neonatal mortality in neonatal sepsis.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

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