

Electrolyte Abnormalities in Neonates with Probable and Culture-Proven Sepsis and its Association with Neonatal Mortality

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ABSTRACT

Objective: To ascertain the frequency of electrolyte abnormalities in patients of probable and culture-proven sepsis on admission and assess any association of electrolyte disorders with mortality.

Study Design: Descriptive study.

Place and Duration of Study: NICU, Fazle-Omar Hospital, Rabwah, from October 2015 to September 2016.

Methodology: All neonates with the diagnosis of probable and culture-proven sepsis during the study period admitted in NICU, Fazle-Omar Hospital, were included in the study. Electrolyte levels were categorised as normal, high or low and recorded in the data form, with age and outcome. Fisher exact test was used to test association. SPSS 20 was used for data analysis.

Results: One hundred and fifty-one neonates were included in the study. Ten (6.6%) died. Among these, 114 (75.49%) had one or more electrolyte abnormalities. Median (IQR [interquartile range]) levels of sodium and chloride were, 140 (7.1), and 100.2 (7.4) mmol/L, respectively. Mean levels of potassium and calcium were 5.07 ± 0.76 mmol/L and 2.35 ± 0.338 mmol/L, respectively. Hyperkalemia was the commonest electrolyte disorder present in 60 (39.7%) neonates, followed by hypercalcemia in 50 (33.1%) and hypocalcemia in 20 (13.2%). None of the neonates without any electrolyte abnormality died ($p=0.053$).

Conclusion: Majority cases of neonatal sepsis have got electrolyte abnormalities. Hyperkalemia was the commonest electrolyte imbalance followed by hypercalcemia and hypocalcemia.

Key Words: Neonate. Sepsis. Electrolytes. Mortality.

INTRODUCTION

Neonatal sepsis is still one of the leading causes of mortality and morbidity all around the world, especially in the developing countries, such as Pakistan.^{1,2} Neonates with sepsis can present with respiratory distress, poor cry, poor sucking, reluctance or inability to take feed, lethargy, hypothermia, vomiting, and diarrhea.^{3,4} Some of these manifestations can lead to fluid and electrolyte abnormalities. Moreover, many neonates admitted in NICU (Neonatal Intensive Care Unit) require intravenous fluids. Inadequate fluid intake can lead to dehydration, hyperosmolarity, and renal failure; while excessive fluid administration may result in generalised edema, impairment of pulmonary function, patent ductus arteriosus, congestive cardiac failure, intraventricular hemorrhage, and bronchopulmonary dysplasia. The changes in mechanisms of homeostasis in early days of life is an important aspect of neonatal life, and kidneys play a vital role in this process. Besides the above mentioned problems, inadequate or excessive intake of fluids, less than optimum or excessive intake of

electrolytes, and abnormalities in the loss of electrolytes can lead to abnormal levels of electrolytes in the blood. Consequently, fluid and electrolyte management is an important aspect in the treatment of neonatal sepsis.^{5,6}

Studies have shown that among the neonates admitted in ICU (Intensive Care Unit), different electrolyte abnormalities like hyponatremia and hypocalcemia are associated with increased mortality.^{5,6} It is, therefore, important to ascertain the frequency of different electrolyte disorders among cases of neonatal sepsis, whether there is an association between electrolyte disorders and mortality. So far, no study has assessed the frequency of electrolyte disorders in cases of neonatal sepsis.

The objectives of this study were to ascertain the frequency of electrolyte abnormalities, i.e. of sodium, chloride, potassium and calcium, in neonates of probable and culture-proven sepsis on admission and whether there is an association between electrolyte disorders and mortality in such cases.

METHODOLOGY

This was a descriptive study. Medical records of all neonates with the diagnosis of probable and culture-proven sepsis from October 2015 to September 2016 were analysed. All neonates (0-30 days of age) of all gestational ages and categories of weight, with the diagnosis of probable and culture-proven sepsis were

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included. Neonates with birth asphyxia, congenital anomalies, metabolic disorders, respiratory distress syndrome, and those who received treatment from other centers prior to admission at Fazle Omar Hospital, were excluded from this study. Appropriate sample size was calculated using World Health Organization (WHO) sample size calculator. The calculations of sample size were based on the given prevalence of 11% for hyponatremia among neonates admitted in intensive care unit.⁵ At the prevalence of 6.4%, level of confidence 95%, at required precision of 5%, the sample size required was at least 151 cases.

Blood samples of all the neonates were obtained for CBC (by Madonic CA 620 analyzer), CRP levels, urea, creatinine, serum electrolytes, i.e sodium, chloride, potassium, and calcium (by ion selective electrodes method Prolyte machine) and blood cultures, at the time admission. Urine samples of all the neonates were obtained at the time of admission and sent for routine examination and culture.

Probable sepsis was defined as the presence of clinical signs and symptoms of sepsis with at least one or more of the following: (1) Total leukocyte count $<5000/\text{cc mm}$ or $>30000/\text{cc mm}$. (2) C-Reactive Protein (CRP) $>6\mu\text{g/ml}$ (3) Prolonged rupture of membranes (PROM) >18 hours, maternal fever or foul smelling liquors. Culture proven neonatal sepsis was defined as the case with signs and symptoms of neonatal sepsis along with positive blood, urine or CSF cultures. Serum levels of sodium, potassium, calcium and chloride were checked on admission by Prolyte (Diamond diagnostics). Hyponatremia was defined as serum sodium <133 mmol/L and hypernatremia as >146 mmol/L. Hypokalemia was defined as serum potassium <3.7 mmol/L while hyperkalemia was defined as serum potassium >5.2 mmol/L. Hypochloridemia was defined as serum chloride <96 mmol/L and Hyperchloridemia as serum Chloride >108 mmol/L. Hypocalcemia was defined as serum calcium <2.0 mmol/L and hypercalcemia as serum Calcium >2.5 mmol/L. Name, age in days, gender, weight at admission, diagnosis, outcome, electrolyte levels were also recorded on the data sheet.

Shapiro-Wilk test was used to assess the normality of continuous variables. Mean value (\pm standard deviation) was used to measure the central tendency and spread of continuous variables with normal distribution, and median value (interquartile range [IQR]) was used to measure the central tendency and spread of continuous variables with non-normal distribution. Data of calcium and potassium levels showed normal, and data for sodium and chloride levels showed non-normal distribution. Median values of sodium and chloride were given with IQR, and mean values of potassium and calcium were given standard deviation (\pm SD). Chi-square test was used to assess association, if all the expected

cell counts were greater than 5; and Fisher exact test was used to test association, if expected cell count in any of the cells was less than 5. All p-values <0.05 were taken as significant. Data was analysed using SPSS version 20 and the study was conducted after approval by the Ethics Committee of Fazle Omar Hospital.

RESULTS

A total of 151 neonates were included in the study. Out of them, 100 (66.2%) were males and 51 (33.8%) were females. Probable and culture-proven sepsis was present in 66 (43.7%) and 85 (56.3%), respectively. Ten (6.6%) patients died while 129 (85.4%) cases were discharged and 12 (7.9%) left against medical advice. Among patients with culture-proven sepsis, 3 (3.5%) neonates died; and among cases with probable sepsis, 7 (10.8%) died. The difference was not significant ($p=0.053$).

Out of these, 114 (75.49%) neonates showed one or more than one electrolyte abnormality. Frequency of electrolyte abnormalities among the cases of neonatal sepsis at admission is shown in Table I. Hyperkalemia present in 60 (39.7%) patients, was the commonest electrolyte abnormality followed by hypercalcemia which was present in 50 (33.1%) and hypernatremia present in 20 (13.2%), and hypocalcemia present in 20 (13.2%) patients (Table I). Median (IQR) levels of sodium and chloride were 140 (7.1) and 100.2 (7.4) mmol/l. Mean (\pm SD) levels of calcium and potassium were 2.35 ± 0.338 and 5.07 ± 0.76 mmol/l. Maximum and minimum sodium levels were 165.10 and 123.90 mmol/l, respectively. Maximum and minimum chloride levels were 130.0 and 85.0 mmol/l, respectively. Maximum and minimum potassium levels were 7.51 and 3.48 mmol/l, respectively. Maximum and minimum calcium levels were 3.0 and 1.32 mmol/l, respectively.

Table I: Frequency of electrolyte abnormalities among cases of neonatal sepsis (n=151).

Electrolyte	Low	Normal	High	Total
Calcium	20 (13.2%)	81 (53.6%)	50 (33.1%)	151
Sodium	13 (8.6%)	118 (78.1)	20 (13.2%)	151
Potassium	3 (2%)	88 (58.3%)	60 (39.7%)	151
Chloride	12 (7.9%)	125 (82.8%)	14 (9.3%)	151

Mean calcium levels in probable and culture-proven neonatal sepsis were 2.35 ± 0.35 and 2.35 ± 0.33 mmol/l, respectively. Mean potassium levels in probable and culture-proven neonatal sepsis were 5.1 ± 0.74 and 5.06 ± 0.78 mmol/l, respectively. Median (IQR) sodium levels in probable and culture-proven neonatal sepsis were 140.10 (8.20) and 140.0 (7.0) mmol/l, respectively. Median (IQR) chloride levels in probable and culture-proven neonatal sepsis were 100.85 (8.05) and 100.0 (6.25) mmol/l, respectively.

After excluding the patients who left against medical advice, 109 neonates showed one or more than one

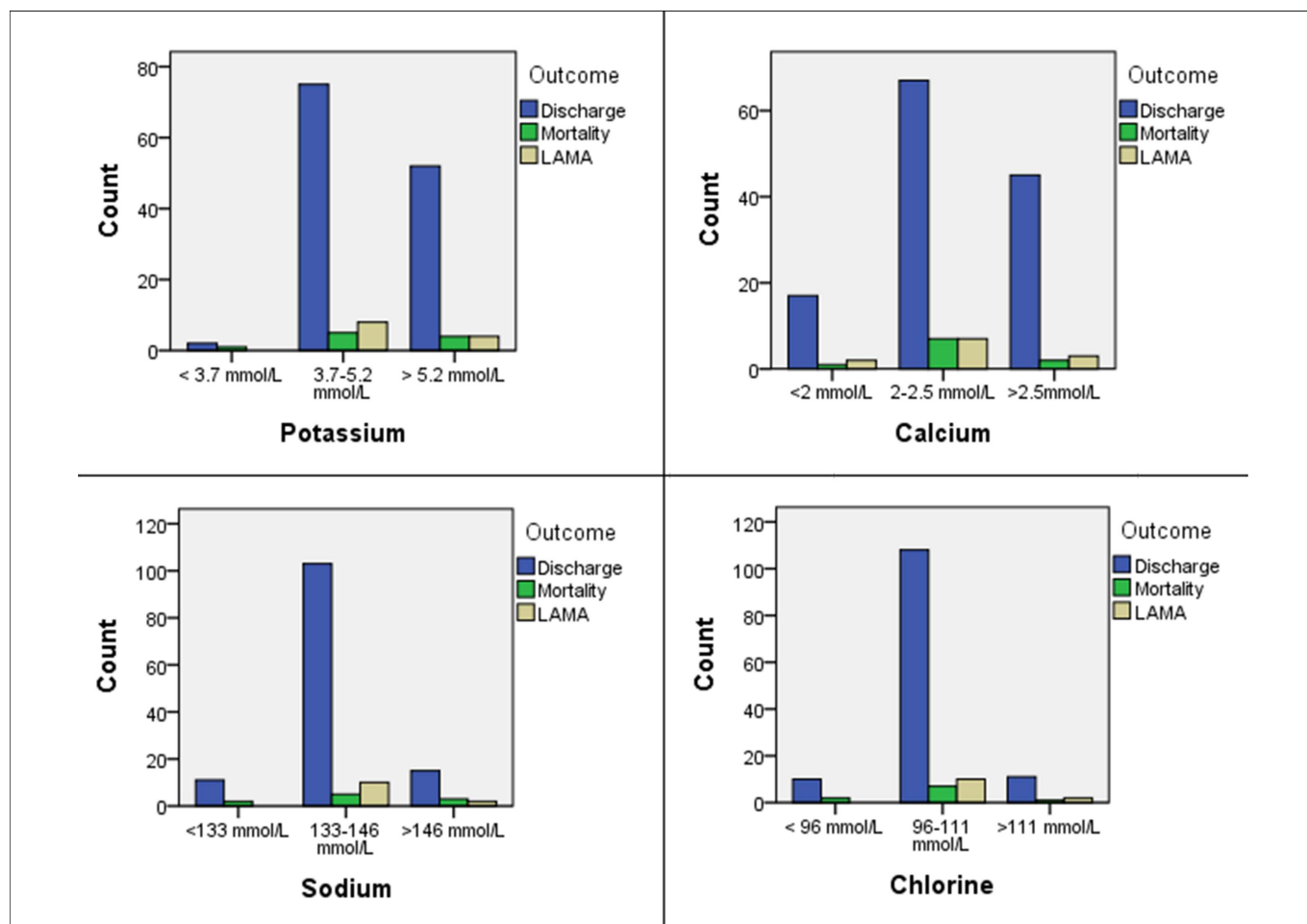


Figure 1: Bar charts showing outcomes according to levels of potassium, calcium, sodium, and chloride.

electrolyte abnormality. Out of these, 10 (9.1%) died. There was no mortality among 30 cases of neonatal sepsis without any electrolyte abnormality. Fisher exact test showed that the difference was non-significant ($p=0.11$). Fisher exact test was applied to test association between levels of potassium, calcium, sodium and chloride levels and outcome. P values were found to be 0.36, 0.24, 0.18, and 0.24, respectively for these electrolytes, leading to the conclusion that none of the electrolyte abnormality was associated with mortality. Figure 1 exhibits the bar charts showing outcome according to the levels of potassium, calcium, sodium and chloride.

DISCUSSION

Many studies have ascertained electrolyte disorders among critically ill patients and in patients with bacteraemia. A study by Elisaf *et al.* showed that among febrile patients with bacteraemia, electrolyte disturbance is a common phenomenon. Hypophosphataemia was most frequent electrolyte disturbance (33%), followed by hypokalemia (26.5%) cases.⁷ Senterre *et al.* studied frequency of electrolyte disturbances among very low birth weight neonates receiving optimum parental

nutrition. This study showed that hypophosphataemia was the commonest electrolyte disorder (37.3%) followed by hyponatremia (30.3%), hypernatremia (15.7%), hypocalcemia (13.7%), and hypercalcemia (12.7%).⁸ No previous study had ascertained the frequency of electrolyte imbalance in cases of neonatal sepsis though this is a very common complication among such cases. This study showed that 75.49% patients of neonatal sepsis suffer from one or more than one electrolyte imbalance. Hyperkalemia, hypercalcemia and hypernatremia were found to be the three most common electrolyte abnormalities.

There can be a number of possible reasons for hyperkalemia being the commonest electrolyte disorder in this study. Hemolysis in pediatric specimens is common due to difficult draws and small bore needles. This falsely elevates potassium level.⁹ Secondly, metabolic acidosis and renal failure are common occurrence among the neonates with sepsis, and these factors can also account for high frequency of hyperkalemia in this study.^{10,11}

Hypercalcemia was the second-most common electrolyte abnormality while hypocalcemia was the third-most

common abnormality, equal in occurrence to hypernatremia. A study by McNeilly *et al.* also showed that hypercalcemia is a common electrolyte imbalance among neonates, specially the neonates with sepsis. This study showed that patients of neonatal age group had the highest frequency of hypercalcemia. Sepsis was reported as the most common cause (41%) of neonatal hypercalcemia.¹² Another study by Forster *et al.* showed that hypercalcemia can occur in critically ill surgical patients. It was ascertained that these cases initially developed shock and sepsis, and this stimulated the increase in parathyroid hormone levels, which ultimately increased the calcium levels.¹³ Lucas *et al.* showed that hypocalcemia after severe shock or sepsis stimulates release of parathyroid hormone, which abates with recovery. Sustained sepsis with multiple organ failure, however, may cause a resurgent release of PTH and life-threatening hypercalcemia.¹⁴

Hypernatremia was the third commonest electrolyte disorder in our study along with hypocalcemia (13.2%). Senterre *et al.* showed similar frequency of hypernatremia i.e. 15.7%,⁸ but it is worth noting that in this study the frequency of hyponatremia was 30.4%. In this study, the frequency of hyponatremia was only 8.6%. One possible reason for more frequent hypernatremia, in this study as compared with the study by Senterre *et al.*, which included included very low birth weight neonates who were already receiving intravenous fluids and optimum parenteral nutrition; while in this study, electrolytes were checked on admission before administration of any intravenous fluids. Studies have shown that hypernatremic dehydration in breast-fed newborns is usually secondary to insufficient lactation, and neonates with sepsis usually present with reluctance to take feed and insufficient lactation.¹⁵

Different studies have shown that hypernatremia, hyponatremia, hypophostemia, hypokalemia and hypocalcemia are associated with increased mortality in different ailments.¹⁶⁻²² The present study showed that none of the electrolyte disorder was associated with increased mortality among cases of probable and culture-proven neonatal sepsis.

CONCLUSION

Among cases of neonatal sepsis, 75.49% cases had one or more than one electrolyte imbalance. Hyperkalemia was found to be the commonest electrolyte disorder followed by hypercalcemia. No significant association was found between electrolyte imbalance and mortality.

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