

Predisposing factors and outcome of hypernatremia in breastfed late preterm and term neonates

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ABSTRACT

Background: Inadequate breastfeeding results in hypernatremia in otherwise healthy neonates. **Objective:** This study finds out the predisposing factors and clinical outcome of hypernatremia in breastfed late preterm and term neonates. **Materials and Methods:** A descriptive study was conducted in a tertiary hospital with retrospective data from July 2013 to June 2016. Babies with serum sodium ≥ 150 mEq/L were identified. Breastfed babies with little or no formula feeds, gestational age ≥ 34 weeks, and birth weight ≥ 2000 g were included. Babies with congenital anomalies, sepsis, prior parenteral fluid therapy and renal or endocrine diseases causing fluid and electrolyte disturbances were excluded. Total weight loss $> 10\%$ or daily weight loss $> 5\%$ from the birth weight were considered as excess weight loss. **Results:** A total of 201 babies were studied. Hypernatremia was significantly more common in babies of primiparous mothers ($p < 0.01$). There was no difference in incidence between vaginal born and cesarean-born babies. Positive correlation was seen between age at presentation, percentage of weight loss ($p = 0.001$) and serum sodium ($p = 0.01$). Significantly more cases were seen in summer season ($p < 0.01$). Excess weight loss, jaundice, fever, and dehydration were the common symptoms. Complications observed were acute kidney injury, seizures, intracranial bleed, apnea, and bradycardia. Babies with complications mostly presented after 7 days of age, had $> 25\%$ weight loss and had serum sodium ≥ 170 mEq/L. There was no death. Three babies had neurodevelopmental problems on follow-up. **Conclusion:** Breastfed babies of primiparous mothers and born in summer are predisposed to hypernatremia. Babies presenting at a later age had severe weight loss, severe hypernatremia, and complications.

Key words: Breastfeeding, Hypernatremia, Primiparity, Summer season, Weight loss

Exclusive breastfeeding for the first 6 months of life is recommended by the World Health Organization to optimize the growth and development of the infants [1]. Breast milk in addition to nutrients provides various immunological factors that help to reduce the diarrheal and respiratory illness in children [2]. Breastfeeding is an instinct behavior and many mother-baby dyads accomplish it successfully [3]. However, some babies may not receive enough milk from their mothers due to various reasons. If breastfeeding is inadequate, then malnutrition and hypernatremic dehydration can occur in the baby [4]. Moritz *et al.* have termed this condition as “breastfeeding associated hypernatremia” (BFAH) [5].

An increase in the incidence of BFAH in otherwise healthy neonates has been observed in the past few years [5-8]. The clinical features and complications seen in these babies have been reported in various studies [9]. It has been found that daily weighing of the babies helps in the early recognition of this illness [10,11]. Thus, the discrepancy in clinical features and complications reported in various studies were probably related to weight monitoring practices and timing of presentation of the cases [10,11]. This study was planned to find out the predisposing

factors and outcome of hypernatremia in breastfed late preterm and term neonates in a hospital with regular weight monitoring practice.

MATERIALS AND METHODS

This descriptive study was done using retrospective data from July 2013 to June 2016. The study was conducted in an urban tertiary care medical college hospital with an average delivery rate of 2500 per year. Exclusive breastfeeding was promoted for all babies in the hospital. The mother-baby dyads were discharged at around 72 h after normal delivery and 120 h after cesarean delivery. As per hospital protocol, all babies were weighed daily. Excess weight loss was defined as total weight loss more than 10% from birth weight or weight loss per day more than 5% of birth weight [12]. Serum sodium level was checked for babies with excess weight loss. Hypernatremia was defined as serum sodium more than or equal to 150 mEq/L. Babies with hypernatremia were treated with liberal oral feeds, intravenous (IV) fluids, and other supportive therapies. Serum sodium < 150 mEq/L was considered an end point of treatment.

The Institutional Ethics Committee approved the study. Babies admitted during the study period with hypernatremia were identified from the hospital database. Their case records were scrutinized and babies who fulfilled the following criteria were included in the study: (1) Breastfed babies with little or no formula supplementation, (2) gestational age more than or equal to 34 weeks, and (3) birth weight more than or equal to 2000 g. The babies who had major congenital anomalies, blood culture positive sepsis, received IV fluids within 48 h before diagnosis of hypernatremia and renal or endocrine disorders which may affect the fluid and electrolyte balance were excluded from the study. The following data were collected: Gestational age as completed weeks, age at diagnosis as completed days, birth weight, weight at diagnosis, maternal age, obstetric details, details about baby feeding, clinical features, treatment, complications, condition at discharge, and neurodevelopment at follow-up.

The total weight loss and weight loss per day were calculated as a percentage of the birth weight. Axillary temperature more than 38°C was considered as fever. The rate of decline in serum sodium was calculated using the sodium before and after treatment and the time taken to achieve it. Acute kidney injury (AKI) was diagnosed if serum creatinine increased by >0.3 mg/dl in 24 h or if it was >1.5 mg/dl with normal maternal renal functions [13]. Jaundice treated with phototherapy was considered as significant. At the time of discharge, babies were said to have improved if their serum sodium level was <150 mEq/L and was taking feeds well. At follow-up, their neurodevelopment was said to be normal if gross motor, fine motor, language, and social milestones were appropriate for age and had no other neurological problem.

SPSS software version 24 was used for analysis. Numerical data were presented as mean±standard deviation or median±interquartile range as appropriate. Categorical data were presented as percentages and analyzed using Chi-square test. Ordinal data were analyzed with Mann–Whitney U-test or Student's t-test. Correlation was done with Spearman rank correlation coefficient where appropriate. $p < 0.05$ was considered as significant.

RESULTS

There were 213 babies with hypernatremia satisfying the inclusion criteria during the study period. 12 babies were excluded due to various reasons. The remaining 201 babies were considered for analysis (Fig. 1). During the study period, there were 7613 live births, with 4570 vaginal births, and 3043 cesarean births. There were 4463 primiparous and 3150 multiparous mothers. Hypernatremia was seen in 2.4% of vaginally born babies and 3.1% of cesarean-born babies. This difference was not statistically significant. 3.1% babies of primiparous mothers and 1.6% babies of multiparous mothers had hypernatremia, and this difference was statistically significant (Chi-square 16.7, $P < 0.01$). All babies were born of singleton pregnancy. Most of the (80%) mothers had no problem in breastfeeding their babies (Table 1).

Serum sodium had a negative correlation with mother's age ($r = -0.23$, $p = 0.01$) and baby's gestational age ($r = -0.2$,

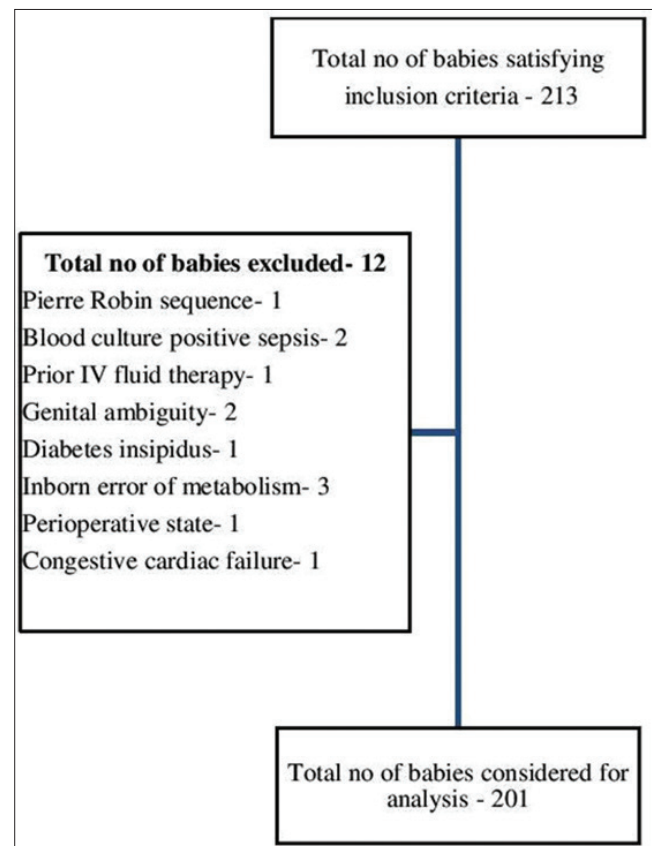


Figure 1: Flow of cases in the study

$p = 0.004$). No correlation was seen between serum sodium level and birth weight. A positive correlation was seen between age at presentation and total weight loss ($r = 0.65$, $P = 0.001$). Serum sodium at admission had a positive correlation with age at presentation ($r = 0.704$, $p = 0.01$) and percentage of total weight loss ($r = 0.652$, $p = 0.001$). More than 50% of the cases were seen during the summer season in this study. This seasonal variation in the incidence of cases was statistically significant (Chi-square-26.9, $p < 0.01$) (Table 1).

Significant jaundice was seen in 57.2% babies, but none required exchange transfusion. Phototherapy (median duration 24 h) before the onset of hypernatremia was given to 26 babies. Other common clinical findings observed were fever (33.8%) and dehydration (17.4%). No symptom other than excessive weight loss was seen in 21.4% of babies. Severe hypernatremia with serum sodium ≥ 170 mEq/L was seen in only five babies, and all other babies (98%) had moderate hypernatremia (serum sodium 150–169 mEq/L). About 89% of babies improved after treatment and got discharged. There was no death in the study population (Table 2). The babies who improved had a median birth weight of 3000 g (2800–3300), median admission weight of 2700 g (2460–2930), and median discharge weight of 2800 g (2540–3070).

Five babies (2.5%) had complications during the course of hypernatremia. One male baby with serum sodium of 151 mEq/L had apnea after vomiting of feeds and developed aspiration pneumonia. He improved with mechanical ventilation and antibiotics. All other four babies presented after 7 days of life

Table 1: Baseline characteristics of hypernatremic babies

Characteristics	Observation
Median maternal age (years) (n=183)*	26.9 (23-29)
Number of babies born to primiparous mothers	138/188 (73.4%)
Number of babies born to cesarean mothers	108 (53.7%)
Number of mothers reported problem in breastfeeding	42 (20.1%)
Male to female ratio	1.34:1
Median gestational age (weeks) (n=189)*	38 (37-39)
Median age at diagnosis (days)*	3 (2–18)
Number of babies presented on 2–3 days age	161 (80.1%)
Median birth weight (g)*	3080 (2810-3410)
Median weight at diagnosis (g)*	2710 (2470-3020)
Median daily weight loss (%)*	3.9 (3.3-4.7)
Median total weight loss from birth (%)*	11.3 (10-12.8)
Number of babies with 10–15% weight loss	139 (69.2%)
Season and number of babies admitted	
a. March to June (Summer)	103 (51.2%)
b. July to October	40 (19.9%)
c. November to February (Winter)	58 (28.9%)
Number of babies on exclusive breastfeeding	177 (88.1%)

*Median (IQR). IQR: Interquartile range

Table 2: Clinical features and outcome of hypernatremic babies

Characteristics	Observations
Median serum sodium at diagnosis (mEq/L)*	153 (151–155)
Serum sodium range and number of babies	
a. 150–159 mEq/L	184 (91.5%)
b. 160–169 mEq/L	12 (6%)
c. ≥ 170 mEq/L	5 (2.5%)
Mean time to normalize serum sodium	
a. 150–159 mEq/L (n=161)	17.8 h
b. 160–169 mEq/L (n=12)	26.6 h
c. 170–179 mEq/L (n=3)	48.8 h
d. ≥ 180 mEq/L (n=2)	71.3 h
Outcome	
a. Improved	178 (88.6%)
b. Left against medical advice	23 (11.4%)
Neurodevelopment problem at follow-up	3/154 (1.9%)

*Median (IQR). IQR: Interquartile range

with weight loss more than 25% of birth weight and severe hypernatremia (serum sodium ≥ 170 mEq/L). Complications observed were AKI (4), seizures (2), apnea (2), intracranial hemorrhage (1), and bradycardia (1). Peritoneal dialysis was done for one baby with AKI. No baby had peripheral or cerebral vessel thrombosis. Neurosonogram done for one baby with seizures showed increased white matter echogenicity. Another baby with seizures had normal neurosonogram. The treatment and outcome details of babies with severe hypernatremia are given in Table 3.

Follow-up details were available in 154 cases (76.6%) for a median duration of 1.5 months (0.5–11 months). Three babies had abnormal neurodevelopment. One female baby with serum sodium 150 mEq/L had a prolonged period of jaundice requiring phototherapy for 9 days. At follow-up, she had a global developmental delay with a seizure disorder. One male baby with serum sodium 150 mEq/L was found to have hyperactivity and aggressive behavior at 3 years. Neuroimaging was not available for these two babies. Another female baby had severe hypernatremia with AKI, seizures and normal neurosonogram in the neonatal period; and on follow-up at 1 year was found to have left hemiparesis and magnetic resonance imaging of the brain showed chronic infarct in right front parietal region and white matter changes in subcortical and deep cerebral white matter.

DISCUSSION

In this study, we have found BFAH to be more common among babies of primiparous mothers. Although breastfeeding is an instinct behavior, mothers have to learn the technique and need social support to successfully breastfeed their babies [3]. Systematic review on BFAH has found cesarean delivery, primiparity and absent previous breastfeeding experience as risk factors for BFAH [9]. However, there was no difference between cesarean babies and vaginally born babies in this study. Similarly, two studies had found no significant difference in mode of delivery among hypernatremic babies compared to control group [5,14].

It is stated that the parents of hypernatremic babies have poor recognition of their baby's illness [7,15]. About 80% of our baby's mothers have not felt any problem with their baby's feeding behavior. Excess weight loss gave a clue to identify these cases early. Thus, majority of our cases were identified at an early age, had less severe weight loss and less severe hypernatremia. Many studies report that babies presenting at a later age have higher weight loss and more severe hypernatremia [16,17]. Hence, daily weighing of babies along with appropriate lactation support during the first 4–5 days of life has been suggested for early detection of BFAH [10,11,18]. The seasonal variation in the incidence of hypernatremia was reported in some studies [12,19-21]. This was attributed to excess insensible water loss due to the hot climate in summer and overuse of room heaters in winter [9,21]. In this study, we have found significantly more number of cases during the summer season. This seasonal variation may be related to hot environmental temperature during summer seen in Tamil Nadu state of India where the study was done.

At admission, jaundice, fever, and dehydration were common symptoms in our study population. Lavagno *et al.* through systematic review have found jaundice, poor feeding, and dehydration each seen in about 45% of all reported cases [9]. Yang *et al.* have showed that percentage of weight loss within first 3 days of life has a positive correlation with jaundice at 72 h after birth in healthy term breastfed babies [22]. The hypernatremia and the resultant hyperosmolar state may damage the blood-brain barrier and facilitates bilirubin entry into nervous tissues at

Table 3: Clinical features and outcome of babies with severe hypernatremia

Gestational age (weeks)	Birth weight (g)	Total weight loss (%)	Day of diagnosis	Maximum Sr. sodium (mEq/L)	Complications	Treatment	Time to correct Sr. sodium (h)	Outcome at follow up
40	2700	25.9	12	182	Seizures, AKI, apnea, bradycardia	½ DNS+oral feeds; peritoneal dialysis; anticonvulsant	57	Normal
40	3630	14.3	4	173	Nil	½ DNS	43	Normal
37	2510	37.5	18	174	AKI, cerebral hemorrhage	NS bolus, ½ DNS	69.75	Normal
36	3060	27.5	8	173	AKI	½ DNS+oral feeds	33.5	Normal
Term	2700	24.1	17	186	AKI, seizures	NS bolus, DNS, ½ DNS; anticonvulsants	85.5	Left hemiparesis

AKI: Acute kidney injury

lower serum bilirubin level [5,23]. This has to be considered in one baby with neurodevelopmental impairment in our study who had hypernatremia and prolonged jaundice. About 20% of our babies had no symptoms at admission except for excess weight loss. Similarly Uras *et al.* and Korgali *et al.* have found that 14% and 2.4% of their hypernatremic babies were asymptomatic at admission, respectively [24,25].

Four out of five babies with severe hypernatremia had neurological and/or renal complications. Similarly, Ahmed *et al.* have found that babies with AKI presented at a later age, had higher weight loss and higher serum sodium [26]. However, less number of babies in this study had complications compared other studies [5,8,9,20,25-27]. This may be due to earlier age at presentation and a lesser degree of hypernatremia seen in the large proportion of babies in our study. There was no death in our study population and on follow-up only three babies had a neurodevelopmental problem. Mortality rate of 1-5% has been reported by various authors [8,26-28]. Koklu *et al.* have reported neurodevelopmental impairment in 47.8% cases [27]. Similarly, a high rate of neurodevelopmental impairment is also reported by Bolat *et al.* and Ergenekon *et al.* [29,30]. This emphasizes the need for formal neurodevelopmental follow-up of hypernatremic babies.

In this study, we have reported the correlation of serum sodium level with various other clinical parameters in babies with BFAH. Our study has the following limitations due to retrospective nature of the study: Some data were incomplete and long-term formal neurodevelopmental assessment was not done. Our study was hospital based, and many babies had a less severe degree of hypernatremia with fewer complications. A larger scale prospective study with neurodevelopmental follow-up is needed to have a clear understanding of the risk factors, complications and long-term effects of BFAH.

CONCLUSION

Breastfed late preterm and term babies born to primiparous mothers and born in summer season have predisposition to develop

hypernatremia. These babies commonly presented with excess weight loss, jaundice, fever, and dehydration. Babies presenting beyond 7 days of age and with more than 25% weight loss are likely to have severe hypernatremia. Neurological complications and AKI were common complications observed with severe hypernatremia. These babies are at risk of neurodevelopmental impairment. Prospective study with long-term follow-up is needed.

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