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CLINICO-INVESTIGATIVE PROFILE OF HYPERNATREMIA IN NEONATES OF RURAL WESTERN MAHARASHTRA.

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ABSTRACT

ORIGINAL RESEARCH ARTICLE

Objectives: To study the Clinico-investigative profile and outcome of hypernatremia in neonates.
Methodology: Observational descriptive, longitudinal study conducted at tertiary rural hospital during August 2021 to August 2022. All the babies with hypernatremia admitted to NICU during the above period were included in the study excluding the preterm babies presenting to our hospital for NICU care.
Results: The sex ratio of 1.3:1 was seen in our study with majority (69%) babies born to primigravida mothers and 58.7% of the mothers were subjected to LSCS. Majority of cases was admitted on 3rd to 5th day (mean age being 4.2 days). Feeding frequency was less than seven times a day in 91.3% babies, which could be due to inexperience and inadequacy. 88% of the neonates with hypernatremia had more than 10% weight loss due to dehydration. Fever, lethargy, and irritability were present in majority of the patients. CNS signs and symptoms at the time of presentation included seizures, decerebrate posturing and retrocollis.
Conclusion: The higher occurrence, as compared to other studies was due to a combination of factors such as summer months, inadequate feeding, early presentation or detection on 3rd or 4th day of birth.

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INTRODUCTION:

Electrolytes are essential content required for human beings' survival, involved in essential body functions. Of the electrolytes, sodium is the most abundant and one of the most important electrolytes, involved in all bodily metabolic functions. Sodium levels are tightly controlled in a healthy individual by regulating urine concentration and an intact thirst mechanism. The normal serum sodium level is 135-145 mEq/L [1].

An increase in sodium level is called Hypernatremia. It is a serum sodium level greater than 145 mmol/L [2]. Chumlea WC et

al. in their study, defined hypernatremia as a hyperosmolar condition caused by a decrease in total body water relative to electrolyte content/hypernatremia is a "water problem," not a problem of sodium homeostasis [3]. Thus, hypernatremia reflects a deficiency of water relative to total body sodium and is most often a disorder of water rather than sodium homeostasis [2,3].

Hypernatremic dehydration can affect both adults and infants; however, it is rare in newborns. In neonates, it can cause brain damage, including cerebral edema and intracranial hemorrhage, which is the probable reason for the brain damage.[3] Due to hypertonicity, water moves from the intra-cellular into the extracellular compartment to maintain intravascular volume, leading to intracellular volume contraction [4,5].

The principal types of hypernatremia include:

1. Hypovolemic Hypernatremia
2. Euvolemic Hypernatremia
3. Hypervolemic Hypernatremia

Hypernatremia associated with hypovolemia occurs when a greater body water loss accompanies sodium loss. Inadequate breast milk intake, diarrhea, radiant heat loss due to warmers, excessive sweating, renal dysplasia, and osmotic diuresis can lead to hypovolemic hypernatremia [3,5,6]. Hypernatremia with euvolemia is a decrease in total body water with near-normal total body sodium. Extrarenal causes of water loss, such as excessive sweating, resulting in some sodium loss, but because sweat is hypotonic, hypernatremia can result before significant hypovolemia. Hypernatremia, in rare cases, is associated with volume overload, resulting from a grossly elevated sodium intake associated with limited access to water [6]. Improperly mixed formula, NaHC03 administration, and NaCl administration can cause hypervolemic hypernatremia. Central diabetes insipidus and nephrogenic diabetes insipidus are infrequent.

Few authors reported that hypernatremia is more common in bottle-fed infants, especially those using concentrated formula feeds and undiluted cow milk [7,8]. Other authors reported that some normal healthy newborns developed neonatal hypernatremic dehydration, even if exclusively breastfed [9]. Weight loss of up to 5-7% of its birth weight during the first week of life is considered normal; however, in case of weight loss of more than 10% of birth weight, the neonate should be suspected of neonatal hypernatremic dehydration [10,11].

According to Adrogue HJ and Madias NE, majority of cases of hypernatremic dehydration, i.e., 90%, are reported in children less than two years of age, with the worst outcome in infants less than six months of age. The signs of Hypernatremic dehydration may not be specific because the initial manifestations are milder; neonates with hypernatremia are often brought with more profound dehydration [12,13]. In addition, neonates with hypernatremic dehydration are often lethargic and may be irritable when touched.

Hypernatremia may cause fever, hypertonicity, and hyperreflexia. The most common complication is seizures [13]. Among the organ systems involved, the brain is the most important. Plasma hypertonicity and the subsequent intracellular water loss cause the brain cells to shrink, leading to rupture of bridging vessels with hemorrhages in subarachnoid and brain parenchyma and thrombosis. Suppose an attempt is made to correct the high sodium concentration quickly [14,15]. In that case, there is a severe risk of osmotic changes in the brain, which can exacerbate cerebral edema, thus adding to potential brain damage. Therefore, care should be taken to that the process of rehydration should be earned out slowly to minimize or prevent damage to the brain [16].

Early diagnosis of neonatal hypernatremia is a necessary better prognosis.

However, it is a medical emergency that should not be overlooked. Because of this, we aimed to study various clinical manifestations and complications of hypernatremia in neonates, determine the maternal & neonatal risk factors for hypernatremia, and assess the outcome of the neonates diagnosed and managed as cases of hypernatremia in the NICU of PRH.

MATERIALS AND METHOD:

It was an observational descriptive, longitudinal study conducted from December 2020 to November 2021 on 150 patients admitted with the diagnosis of hypernatremia to the Neonatology Unit, Department of Pediatrics, after ethical approval from the institute and informed consent from the relatives.

INCLUSION CRITERIA:

- All those infants with hypernatremia admitted to NICU during the above period were included in the study.
- Neonates with the corrected gestational age of more than 34 weeks.

EXCLUSION CRITERIA:

- All neonates with Renal and/or other Congenital anomalies.
- All neonates whose parents or guardians were not willing to give consent.

A detailed history, including age, sex, mode of delivery, birth weight, feeding patterns, any past medical history, and maternal & neonatal history with specific emphasis on risk factors for hypernatremia, was obtained along with a complete physical examination. The laboratory investigations during the hospital stay were conducted. A detailed record was obtained regarding pregnancy and the pattern of feeding.

Management:

An initial bolus of normal saline (10-20 mL/kg) was given to all dehydrated patients. Boluses were repeated on a case-to-case basis to treat hypotension, tachycardia, and signs of poor perfusion (peripheral pulses, capillary refill time). All patients were given fluid sodium concentration of half-normal saline and a total fluid requirement of 20-30% greater than maintenance fluid. If signs or symptoms of volume depletion developed, the patient received additional boluses of isotonic saline. The glucose concentration of intravenous fluids was from 5% dextrose in water to 2.5% dextrose in water. The goal was to decrease the serum sodium by <12 mEq/L every 24 hour, a rate of 0.5 mEq/L/hr. 125% of the total fluid requirement was administered daily using a mixture of N/2 saline in 5% dextrose. An infusion of 3% saline was given to patients developing cerebral edema (confirmed by neurosonography or CT scan). Once serum sodium levels reached <150mEq/L, breastfeeding was established if the baby had sucking, rooting, and swallowing reflexes, and the balance of the fluid requirement was met with Isolyte P in 5% dextrose. Once breastfeeding was well established, the intravenous line was discontinued. Calculating total fluid requirements was according to the weight of baby, day of life, and insensible and radiant heat loss due to warmer were included. The underlying cause of the hypernatremia was detected and managed accordingly.

Monitoring of serum sodium level:

Serum sodium levels were monitored every 2-4 hours until the desired rate of decline in serum sodium was established. After this point, the frequency of the laboratory measurements was relaxed to every 4-6 hours until the serum sodium was less than 150mEq/L.

OUTCOME MEASURES:

Time taken for recovery, whether the baby recovered fully or developed problems or complications during recovery, duration of hospital stays, and mortality, if any, were studied and noted.

ANALYSIS OF DATA:

Data coding and entry were done in Microsoft Excel spreadsheets, and descriptive and inferential statistical analysis was done using SPSS (Statistical Package for Social Sciences) version 21 software.

RESULTS:

Out of 150 patients, 85 were male, and 65 were female, with male: female ratio of 1.3:1. 69% of the cases were babies of primigravida mothers, supporting that hypernatremia is more common in primigravida mothers (P<0.05). LSCS Mode of delivery has more cases of hypernatremia than vaginal delivery (P<0.05). The study suggests that occurrence is more during the Summer (64.7%) followed by Monsoon (28.7%) and Winter (6.6%) (p<0.005).

In present study most common feeding method found was breastfeeding, followed by formula feeding and then animal milk feed. Out of 150 mother and infants examined 40 mothers said they fed their child minimum 5 times a day i.e., 26.7%. 59/150 said they fed 6 times a day i.e., 39.3%, 38 out of 150 said they fed seven times a day i.e., 25.3% and only 13 mothers said they fed their infants more than 8 times a day. Most common maternal factor associated is maternal technical difficulty (48%) closely followed by absence of letdown reflex (44%) (p<0.05).

Most frequent urination was 5 times a day (40.7%) followed by 6 times a day (40%). Lesser frequency was suggestive of hypernatremic dehydration in present study (p<0.005). 88% of patient had more than 10% weight loss. Mean weight loss 14.6. >10% Weight loss is highly significant to hypernatremic dehydration(P<0.001)

Dehydration (some or severe) was present in 81.3%, (p<0.001) which is highly significant. More than 50% patients were not having any sepsis. 68% of patients developed hyperbilirubinemia along with hypernatremia, which is significant association (p<0.05).

Table no 1: Distribution of demographic data of the study population.

VARIABLES	**NUMBERS [%]**
Gender	
Male	85 (56%)
Female	65 (44%)
Gravida	
Primigravida	103 (69%)
Multigravida	47 (31%)
Mode of delivery	
Vaginal	62 (41.3%)
LSCS	88 (58.7%)
Season	
Summer (March- June)	97 (64.7%)
Winter (November - February)	10 (6.6%)
Monsoon (July – October)	43 (28.7%)
Frequency of feeding	
< 7 times	13 (8.7%)
> 7 times	137 (91.3%)
Feeding type	
Breast feeding	84 (56%)
Formula feeding	36 (24%)
Animal milk	30 (20%)
Urine frequency	
< 5 times	84 (56%)

> 5 times	66 (44%)
Weight loss	
<10%	18 (12%)
>10%	132 (88%)
Severity of dehydration	
No	18 (12%)
Some	90 (60%)
Severe	42(28)
Sepsis	
Yes	74 (49.3%)
No	76 (50.7%)
Hyperbilirubinemia	
Yes	103 (68%)
No	47 (32%)

In our study fever was seen in 89 cases i.e., 59.3%, CNS findings were observed in 56 patients (37.3%), lethargy was present in 67 cases (44.7%), irritability in 58 cases (38.7%), depressed anterior fontanel was seen in 132 cases i.e., 88% and doughy abdomen in 16 cases (10.7%). Most common symptom with which the baby presented was fever (59.3%) whereas, most common sign was depressed anterior fontanel (88%).

Table 2: Distribution of the clinical features among the study population.

Sign/Symptom	**No (%)**
Fever	89(59.3)
CNS Findings (Decerebrate posturing, Retrocollis, Seizures, Altered tone)	56(37.3)
Lethargy	67(44.7)
Irritability	58(38.7)
Depressed Anterior fontanel	132(88)
Doughy abdomen	16(10.7)

***Renal profile of cases*.**

Most common urea level was ranged 40-50 (81.3%). Most patients presented with normal creatinine level (96%). This indicates that azotemia was mainly due to pre-renal failure. The most common range of sodium level was 156-160 (41%) closely followed by 151-155 mEq/l (36%) and only 7% cases had sodium level <150mEq/l. Most patients presented with normal potassium level (85.3%).

Table 3: Renal profile of the study population	
Urea	
<40	22 (14.7%)
40-50	122 (81.7%)
>50	6 (4%)

Creatinine	
<0.5	32 (21.3%)
0.5-1	112 (74.7%)
>1	6 (4%)
Sodium	
<150	11 (7%)
151-155	54 (36%)
156-160	62 (41%)
>160	23 (16%)
Potassium	
<5.5	128 (85.7%)
>5.5	22 (14.3%)

Most patients recovered from hypernatremia around 28 hours after admission. Mean value being 28±2.6. ($p<0.05$) with rate of correction being 0.45mEq/L/hour. The gradual reduction in sodium levels resulted in good recovery with minimal complications.

Most common time of discharge from hospital was within 5 days (48%) followed by 6-10 days (39.3%). Those patients who developed complications during correction therapy were observed and investigated. Out of 150 patients in study total 8 developed seizures of which 2 were diagnosed as having cerebral edema. There was 1 mortality observed during the study which was due to cerebral edema.

Table 4: Outcome and Complications seen in the study population

Recovery Time (Hours)	
<12	36 (24)
13-24	46 (30.7)
25-48	50 (33.3)
>48	18 (12)
Duration of stay in hospital	
< 5 days	72 (48%)
6-10 days	59 (39.3%)
> 10 days	19 (12.7%)
Complication	
Nil	142 (94.7)
Seizures	6 (4)
Cerebral Edema	2 (1.3)
Outcome	
Survived	149 (99.3%)
Death	1 (0.7%)

DISCUSSION:

Out of a total of 10541 newborn managed at Neonatology Unit, Department of Pediatrics, 150 were diagnosed and studied as cases of hypernatremia during the period of August 2021 to July 2022. All these cases of hypernatremia were due to hypernatremic dehydration. In the present study, 7.66 per 1000

patients developed hypernatremic dehydration which was like other similar studies as shown in table 5 whereas few studies found much higher prevalence [17,18,19].

Table 5: Comparison of variables with similar studies.

Variables	Present study	Uras N et al [20]	Farhat A S et al [21]	Bolat F et al [19]	Penalver Giner O et al [22]	Zachariassen G et al [16]	Trotman H et al [23]	Boskabadi et al [24]	Reilev et al [25]
Total patients	10541	1150	731	4280	115	54	100		8924
Hypernatremia	150	64	44	81	115	54	100		
GRAVIDA									
Primigravida	69	22	30		83.33	70.45	79		
Multigravida	31	42	14		16.67	29.55	21		
Mean sodium level(mg/dl)	159	152	151	160	160	153	158	152.75	
Weight loss (%)	14.4	7			13.7	12.3	10	16.3	10.3
Age on admission	4.2±0.22 days	3.5±1.5 days		6±1.5 day	5±2 days		7.4±3.8 days		
Feeding frequency	6 per day	7 per day		5 per day	6 per day	5 per day	7 per day	7 per day	
HYPERBILIRUBINEMIA									
Present	68	30	15.86	21	18		42		
Absent	32	70	84.14	79	82		58		
COMPLICATION									
Seizure	4						13		12.5
Cerebral edema	1.3						4		3.1
Mortality	0.7		9.1				4		

Our study suggests that majority of the cases of hypernatremia was seen in primigravida mothers' which was consistent with other studies as shown in table 5. The probable reason for primigravida preponderance could be relative inexperience of primigravida mothers and lack of proper breastfeeding techniques.

This study suggests that 88% of patient had weight loss of >10% body weight, with an average weight loss being 14.4% of body weight, which is similar to that of other studies. In Boskabadi et al [24] average weight loss was observed to be 16.3%, Penalver Giner O et al [22] observed 13.7% whereas Reilev et al [23] experienced weight loss up to 10.3%. Some studies suggest that weight loss of more than 10% has sensitivity of 93% in diagnosing hypernatremia with majority of them showing some sort of association of weight loss with neonatal hypernatremic dehydration [22,23,25].

The Mean sodium level in present study was 159mEq/dl which was consistent with other studies shown in table 5. This higher level of serum sodium levels can be attributed to dehydration as the primary cause of

electrolyte imbalance. This can be attributed to the feeding practices, which was shown in our study as less frequent feeding babies had more chances of developing hypernatremia compared to more frequent feeding babies.

In our study, features of dehydration (i.e., depressed anterior fontanel) were the most common signs, while the most common presenting symptom was fever (59.3%) consistent with Penalver Giner O et al. [22] whereas the most common sign seen was CNS finding, which could be due to early diagnosis of cases in our study preventing them to develop CNS features. In present study hyperbilirubinemia was markedly higher in contrast to other studies which can be due to factors like breast feeding jaundice and being presented on 3rd/4th day of neonatal period when physiological jaundice is at its peak.

In our study, most patients recovered from hypernatremia around 24-30 hours after admission with mean duration being 28±2.6 hours. ($p<0.05$). The Recovery rate observed in the present study was <0.5mEq/L/hour which was consistent with similar studies. Erdemir A et al [26] used the intravenous therapy along with oral feeding and compared them, which suggested that the low level of hypernatremia can be treated with oral feeds but to treat hypernatremia with complications or with higher level of sodium >150mEq/l intravenous therapy is better than the oral feeding.

The occurrence of hypernatremia is significantly associated with seasonal changes as it is in the present study ($p<0.005$). This was confirmed in other studies too. This may be due to insensible loss of water is more during summer. Those patients who developed complications during the correction therapy were observed and investigated. In present study out of 150 patients, 8 patients had episode of seizure amongst them 2 were diagnosed with cerebral edema which was less than the similar studies as shown in table 5. The lesser complication in our study, can be attributed to early detection, close observation and monitoring and standardized management protocols. There was 1 mortality observed during the study period which was due to cerebral edema. As seen in table 5, the mortality rates were comparable to other studies, with our study having lesser rates compare to others.

CONCLUSION:

All the cases in our study were due to dehydration which was seen in primigravida babies which can be reduced by proper breastfeeding techniques, early diagnosis, and management of the cases. Educating the mothers before discharge about proper handling and feeding of the babies can drastically reduce the number of cases specially during the summer season.

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