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# Outcome and Mortality Determinants of Hypernatremic Dehydration among Hospitalized Neonates in Tigray, Ethiopia

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## ABSTRACT

**Background:** Hypernatremic dehydration causes life-threatening complications, such as serious neurologic damage, acute kidney injury, and peripheral limb gangrene, and leads to death. However, there is limited data on hypernatremic dehydration among neonates in Sub-Saharan Africa in general and Ethiopia in particular. This study aimed to assess the clinical profile, outcome, and mortality determinants of hypernatremic dehydration among hospitalized neonates in Tigray, Ethiopia.

**Methods:** An institution-based cross-sectional study was conducted among neonates admitted with a diagnosis of hypernatremic dehydration at the Ayder Comprehensive Specialized Hospital (ACSH) between January and July 2022. All neonates admitted to the ACSH with a diagnosis of hypernatremic dehydration during the study period were included by using consecutive sampling. Data were prospectively collected using a pretested checklist. The collected data were coded, edited, cleaned, and analyzed using SPSS version 23. The results were described using tables, graphs, and charts. The chi-square test (P-value < 0.05) was used to test variables associated with mortality.

**Results:** The prevalence of hypernatremic dehydration among 670 consecutive hospitalized neonates was 7.8% (52/670) over seven months period. Fifty of these were included in the analysis, two cases were excluded (the outcome was unknown). Fever, failure to suck, and decrement in urine amount were the common presenting features, occurring in 78%, 54%, and 52% of them respectively. The median serum sodium level at admission was 161 mmol/l (IQR,154-169). Acute kidney injury was the common complication observed in 54% of neonates. In addition, three neonates had bilateral peripheral limb gangrene. The case fatality rate in the present study was 32% (16/50). Being lethargic at admission, the presence of acute kidney injury and hyperglycemia, and a hospital stay of less than a week were significantly associated with mortality.

**Conclusion:** Breastfeeding-associated hypernatremic dehydration has a high prevalence and mortality rate among neonates. Being lethargic at admission, the presence of acute kidney injury and hyperglycemia, and a hospital stay of less than a week were significantly associated with mortality. Antenatal and in-hospital screening of maternal and neonatal risk factors for lactational insufficiency combined with early post-delivery follow-up to identify excessive neonatal weight loss and inadequate elimination patterns is essential to prevent hypernatremia dehydration in neonates.

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**Abbreviations**

**ACSH:** Ayder Comprehensive Specialized Hospital
**AKI:** Acute Kidney Injury
**ANC:** Antenatal Care
**HDN:** Hypernatremic Dehydration
**IQR:** Interquartile Range
**NICU:** Neonatal Intensive Care Unit
**SCr:** Serum Creatinine

## Background

Exclusive breastfeeding is a natural way of feeding neonates and has become the standard of feeding infants in the first 6 months of life. Hypernatremic dehydration (HDN) is a well-recognized complication of lactational insufficiency in exclusively breastfed neonates [1]. In neonates, HDN is considered when there are clinical findings of dehydration with hypernatremia and a serum sodium concentration of ≥150 mmol/L. Neonates are adversely affected by HDN because of the immaturity of the kidney, which hinders their ability to excrete excess sodium. Moreover, babies have limited or no ability to express thirst, cannot feed themselves, and depend on caregivers to provide adequate

feed. HDN results from inadequate breast milk intake, hypertonic sodium gain (hypertonic infant formula), and hypotonic fluid loss (vomiting or diarrhea). Furthermore, radiant warmers increase renal loss and administration of sodium-containing solutions may cause neonatal HDN.

HDN is assumed to be rare; however, recent reports have suggested that its incidence is increasing. The incidence of hypernatremic dehydration in breastfed neonates has been reported to be 1.38% to 7.7%. This disease can cause serious neurological damage, including convulsions, vascular thrombosis, and intracranial hemorrhages. Other complications include acute renal injury, hyperglycemia/hypoglycemia, hyperkalemia, hypocalcemia, disseminated intravascular coagulation, and death. The common clinical features of neonates with HDN are weight loss, poor feeding, fever, lethargy, seizure, doughy skin, and decreased urine amount. Furthermore, other presenting features include jaundice, acute kidney injury, vascular thrombosis, and hyperglycemia. According to different studies, the case fatality rate of hypernatremic dehydration in neonates ranges from 6.8 to 9.8%. Serum Na+ level >160 mmol/L and rapid correction rate of serum Na (>0.5 mmol/L per hour) are independent risk factors of convulsion and death.

Many neonates had hypernatremic dehydration during day-to-day activities in the study area. One contributing reason for hypernatremic dehydration could be related to the ongoing war in the Tigray region of Ethiopia, which resulted in a widespread humanitarian crisis that led to widespread famine and food crises. The war mainly affected under-five children including neonates, and pregnant and lactating mothers. Moreover, the war resulted in the destruction of health facilities, which led to the absence of medications, poor antenatal care, supervised delivery, and postnatal and newborn care. Therefore, it is important to study hypernatremic dehydration and its death rate. Additionally, there is a scarcity of data on neonatal hypernatremic dehydration in sub-Saharan Africa in general, and Ethiopia in particular. Therefore, this study aimed to assess the clinical profile, treatment outcomes, and mortality determinants of hypernatremic dehydration among hospitalized neonates in Tigray, Ethiopia.

## Methods and Materials

### Study Design and Population

This study was conducted at the Pediatrics and Child Health Department of the Ayder Comprehensive Specialized Hospital (ACSH) in Tigray, Ethiopia. The department has 40-bed neonatal intensive care unit (NICU) that serves an average of 2000-2500 admissions per year. A high-risk infant clinic is attended by a neonatologist, pediatrician, and senior pediatric residents, with an average of 40-50 infants followed up every week. An institution-based cross-sectional study with prospective data collection was conducted among 1 to 28-days-old neonates who were admitted with a diagnosis of hypernatremia dehydration to ACSH from January to July 2022. Neonates who were premature (less than 34 weeks of gestation), neonates with lethal congenital malformation, perinatal asphyxia, or who went against medical advice (their outcome was unknown) were excluded. The treatment outcome (improvement or death) was considered a dependent variable. Age, birth weight, gestational age, presence of complications, sepsis, mother's age, antenatal care (ANC) follow-up, level of education, mode of delivery, parity, place of delivery, residence, creatinine level, glucose level, rate of correction, severity of hypernatremia, and type of fluid used were considered as independent variables. Hypernatremic dehydration was defined as a neonate born at ≥34 weeks of gestation who presented with a weight loss of ≥ 10% of birth weight or other clinical features of dehydration with serum sodium of ≥150 mmol/L [2,3].

### Sample Size and Sampling Procedure

All neonates admitted to the ACSH with a diagnosis of HDN between January and July 2022 were included in the study using consecutive sampling. There were a total of 52 cases and of them, 50 were included in the final analysis, two cases were excluded because their outcomes were unknown.

### Data Collection, Processing and Analysis

Data were collected from the mothers, charts, and electronic devices (smart care) of neonates using a pretested structured checklist. The collected data were cleaned, coded, and entered into Epi data version 4.6.0.2, and exported and analyzed using SPSS version 23. The results are described using text, tables, graphs, and charts, based on the type of data. The Chi-square test with a cut-off P-value < 0.05, was used to test variables associated with the mortality of neonates with hypernatremic dehydration.

### Management

Management of hypernatremic dehydration involves ensuring adequate calorie intake and correcting electrolyte imbalance through careful oral or intravenous rehydration. In cases of insufficient breast milk intake, complementary feeds were administered with expressed breast milk or formula, using a nasogastric tube or bottle with a wide-based nipple. Intravenous rehydration was administered if the neonate's serum sodium level was significantly elevated (≥ 160 mmol/L). All patients were initially treated with isotonic saline solution delivered intravenously at a dose of 10 – 20 mL/kg over 1 hour, once or twice, based on the response. Fluid therapy, which was calculated based on the degree of dehydration, was continued. The degree of dehydration was estimated based on the difference between the birth weight and weight on admission. Serum electrolyte levels were closely monitored to follow the predicted reduction in serum sodium level during therapy. The recommendation is to correct serum sodium by not more than 12 mmol/L in 24 hours (≤0.5mmol/L/hr.). Neonates who responded to the management of HDN and its acute complications during their hospital stay and were discharged were assumed to have improvement. Death was defined as if a neonate died during the treatment course of HDN and its acute complications.

## Results

### Socio-Demographic and Obstetric Characteristics of the Mothers and Neonates

Between January and June 2022, the magnitude of hypernatremic dehydration among hospitalized neonates was 7.8% (52/670); 50 neonates met the inclusion criteria and were admitted with serum sodium concentration of ≥150 mmol/L. Twenty-nine (58%) mothers were primiparous with a mean age of 29 (SD±6) years. Nearly all mothers (98%) had ANC follow-up. Thirty-one (62%) of the women had a spontaneous vaginal delivery and most of them (88%) gave birth at a health facility. The mean neonatal age at admission was 7.8 (SD±6.2) days, with a median gestational age of 40.1(IQR, 39 − 41) weeks. Nearly two-thirds (64%) of the neonates were admitted during the early neonatal period (Table 1). All neonates were exclusively breastfed prior to their current admission.

**Table 1: Sociodemographic Characteristics of Neonates (and their mothers) with Hypernatremic Dehydration Admitted at Ayder Comprehensive Specialized Hospital, January to July 2022(n = 50)**

| Characteristics | n (%) |
|---|---|
| **Age of mother in years** | |
| **<20** | 1(2) |
| **20-34** | 39(78) |
| **35+** | 10(20) |
| **Maternal education** | |

| | |
|---|---|
| **No formal education** | 10(20) |
| **Primary** | 13(26) |
| **Secondary** | 15(30) |
| **Tertiary** | 12(24) |
| **Residency** | |
| **Urban** | 34(68) |
| **Rural** | 16(32) |
| **ANC follow up** | |
| **Yes** | 49(98) |
| **No** | 1(2) |
| **Frequency of ANC visits** | |
| **<4 visits** | 10(20) |
| **≥4 visits** | 39 (78) |
| **Parity** | |
| **Primiparous** | 29(58) |
| **Multiparous** | 21(42) |
| **Mode of delivery** | |
| **SVD** | 31(62) |
| **CD** | 19(38) |
| **Gestational age** | |
| **Term** | 36(72) |
| **Near term** | 11(22) |
| **Post-term** | 3(6) |
| **Place of delivery** | |
| **Health facility** | 44(88) |
| **Home** | 6(12) |
| **Admission age** | |
| **ENP(1-7days)** | 32(64) |
| **LNP(8-27days** | 18(36) |
| **Sex** | |
| **Male** | 30(60) |
| **Female** | 20(40) |
| **Birth weight(gm)** | |
| **NBW** | 32(64) |
| **Unknown** | 11(22) |
| **LBW** | 5(10) |
| **Macrosomia** | 2(4) |

**ANC:** antenatal care; CD: cesarean delivery; ENP: early neonatal period; LNP: late neonatal period; LBW: low birth weight; NBW: normal birth weight; SVD: spontaneous vaginal delivery.

### Clinical Presentations and Physical Findings of Neonates

The median percentage of weight loss from birth weight in these neonates was 14.7% (IQR, 7.4-25.3). The mean weight of the neonates at admission was 2656.7(SD±505.4) grams. The common presenting complaints were fever, failure to suck, and decrement in urine amount seen in 39(78%), 27(54%), and 26(52%) neonates, respectively. The common presenting clinical signs were dry buccal mucosa 44(88%), weight loss 26(52%), and doughy skin 21(42%). At presentation, 39(78%) neonates were evaluated and empirically treated for presumed sepsis; treatment was then revised according to the culture results only for 35.8% (14/39) (due to limited availability of blood culture). The common presumed cause of dehydration was inadequate maternal breast milk seen in 25(50%) and poor oral intake seen in 18 (36%) neonates. None of the neonates had an oral abnormality such as a significant retrognathia cleft lip or palate. The median creatinine level was 1.01 mg/dl (IQR, 0.7-2.14), with a range of 0.35 to 9.16 mg/dl (Table 2). The median sodium level was 161 (IQR,154-169.25) mmol/L, and a majority (56%) of them had moderate to severe hypernatremia (Figure 1).

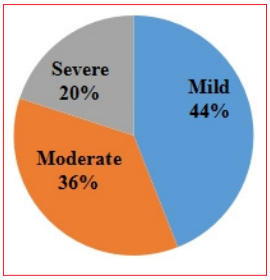


**Figure 1:** Degree of Hypernatremia in Neonates with Hypernatremic Dehydration Admitted at Ayder Comprehensive Specialized Hospital, January to July 2022 (n = 50)

**Table 2: Clinical Presentation and Laboratory Finding of Neonates with Hypernatremic Dehydration Admitted at Ayder Comprehensive Specialized Hospital, January to July 2022 (n = 50)**

| Fever | n(%) |
|---|---|
| Yes | 39(78) |
| No | 11(22) |
| Failure to suck | |
| Yes | 27(54) |
| No | 23(46) |
| Decrease in UOP | |
| Yes | 26(52) |
| No | 24(48) |
| Jaundice | |
| Yes | 12(24) |
| No | 38(76) |
| Presumed sepsis | |
| Yes | 39(78) |
| No | 11(22) |
| Weight loss | |
| ≥10% | 26(52) |
| <10% | 12(24) |
| Unknown | 12(24) |
| Dry buccal mucosa | |
| Yes | 44(88) |
| No | 6(12) |
| Lethargic at admission | |
| Yes | 23(46) |
| No | 27(54) |
| Doughy skin | |
| Yes | 21(42) |
| No | 29(58) |
| Depressed anterior fontanel | |
| Yes | 17(34) |

| | |
|---|---|
| No | 33(66) |
| Sunken eyes | |
| Yes | 11(22) |
| No | 39(78) |
| Presumed cause HDN | |
| Inadequate breast milk | 25(50) |
| Poor oral intake | 18(36) |
| Both** | 6(12) |
| GI loss | 1(2) |
| Serum sodium | |
| Median | 161 mmol/L |
| Minimum | 150 mmol/L |
| Maximum | 234 mmol/L |
| Serum creatinine | |
| Median | 1.03mg/dl |
| Minimum | 0.35 mg/dl |
| Maximum | 9.16 mg/dl |

UOP, urine output; GI, gastrointestinal; **, inadequate breast milk and poor oral intake; HDN, hypernatremic dehydration of the 50 neonates with hypernatremic dehydration, 34(68%) had one or more complications. Acute kidney injury 27(54%), seizure 16(32%), and hyperkalemia 14(28%) were the commonest complication observed. Three (6%) neonates had bilateral peripheral limb gangrene, and two of them had additional abdominal aorta thrombosis. Seven (14%) of them were critically ill and required mechanical ventilation; finally, all did not survive (Figure 2).

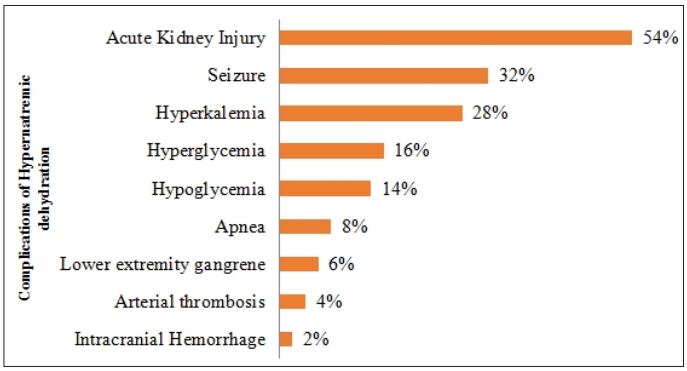


**Figure 2:** Complications of Hypernatremic Dehydration Among Neonates Admitted at Ayder Comprehensive Specialized Hospital, January to July 2022 (n = 50)

Management and its Outcome of the Neonates with Hypernatremia Dehydration

Fluid therapy was administered based on the degree of dehydration. The degree of dehydration was estimated based on the difference between the birth weight and weight on admission. Twenty-eight (56%) patients had received correction intravenous fluid and, in all of them, except for two, the serum sodium did not decline more than 12 mmol/L per day. Patients with mild hypernatremia were orally hydrated, and the drop was within the expected range. Eight neonates (16%) died before the correction of their hypernatremia. All 39 neonates with presumed sepsis had received empiric antibiotics. The median duration of hospital stay was 7 days (IQR, 1.5-13.3) (Table 3). Of the 50 neonates with hypernatremia dehydration, 34(68%) of them had improved and were discharged home, while 32% of them died. Half of the neonates with severe hypernatremia died (Figure 3).

**Table 3: Management and Outcome of Hypernatremic Dehydration Among Neonates Admitted at Ayder Comprehensive Specialized Hospital, January to July 2022 (n = 50)**

| **Parameters | n(%) |
|---|---|
| Received correction IV fluid | 28(56) |
| Type of correction fluid used | |
| ½ NS and D5W | 18(64.3) |
| NS | 10(35.7) |
| Type of Feeding offered | |
| Direct breastfeeding | 35(70) |
| Maintenance fluid | 11(22) |
| Formula feeding | 4(8) |
| Duration of correction | |
| 24 hrs. | 10(35.7) |
| 24-48 hrs. | 12(42.8) |
| ≥ 48 hrs. | 6(21.4) |
| Death before correction* | 8(22.2) |
| Rate of correction (IV fluid) | |
| ≤ 0.5mmol/L/hr. | 26(92.9) |
| > 0.5mmol/L/hr. | 2(7.1) |
| Received antibiotics | |
| Yes | 39(78) |
| No | 11(22) |
| Duration of hospital stay | |
| ≤ 1 week | 24(48) |
| 1-2 week | 14(28) |
| 2-3 weeks | 12(24) |
| Outcome | |
| Improved | 34(68) |
| Died | 16(32) |

D5W, dextrose 5% in water; IV –intravenous; MF, maintenance fluid; NS, normal saline; *correction of hypernatremia; **for those with IV correction.

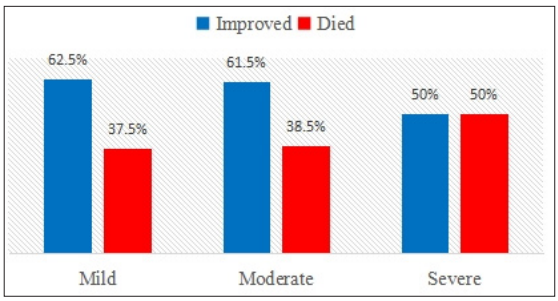


**Figure 3:** Outcome and degree of Hypernatremia Among Neonates Admitted at Ayder Comprehensive Specialized Hospital, January to July 2022 (n = 50)

Being lethargic at admission, the presence of acute kidney injury and hyperglycemia, and a hospital stay of less than one week were significantly associated with death (Table 4).

**Table 4: Cross Tabulation and X2 of Variables Associated with Mortality of HDN Among Neonates Admitted at Ayder Comprehensive Specialized Hospital, January to July 2022 (n = 50)**

| Parameter | Outcome | | $\chi 2$ | P-value |
|---|---|---|---|---|
| | Died n(% ) | Improved n(%) | | |
| Severity of HDN | | | | |
| Mild | 6(12) | 16(32) | 1.86 | 0.39 |
| Moderate | 5(10) | 13(26) | | |
| Severe | 5(10) | 5(10) | | |
| Acute kidney injury | | | | |
| Yes | 15(30) | 12(24) | | 0.001 |
| No | 1(2) | 22(44) | 14.96 | |
| Hyperglycemia | | | | |
| Yes | 7(14) | 1(2) | 13.481 | 0.001 |
| No | 9(18) | 33(66) | | |
| Sex | | | | |
| Male | 11(22) | 19(38) | 0.31 | 0.57 |
| Female | 5(10) | 15(30) | | |
| Residency | | | | |
| Urban | 12(24) | 2244) | 0.16 | 0.68 |
| Rural | 4(8) | 12(24) | | |
| Parity | | | | |
| Primiparous | 12(24) | 17(34) | 1.86 | 0.17 |
| multiparous | 4(8) | 17(34) | | |
| Lethargic at admission | | | | |
| Yes | 11(22) | 12(24) | | 0.027 |
| No | 5(10) | 22(44) | 4.9 | |
| Gestational age | | | | |
| Term | 11(22) | 25(50) | | 0.4 |
| Near term | 3(6) | 8(16) | 1.84 | |
| Post-term | 2(4) | 1(2) | | |
| Duration of hospitalization | | | | |
| <1 week | 13(26) | 11(22) | | 0.005 |
| 1-2 weeks | 2(4) | 12(24) | | |
| 2-3 weeks | 1(2) | 11(22) | 10.5 | |

## Discussion

In the present study, we report on 50 neonates who developed hypernatremic dehydration attributable mainly to insufficient or inadequate breastfeeding during the seven-month study period. The magnitude of hypernatremic dehydration among admitted neonates in this study was 7.8%, significantly higher than in previous studies. The incidence of hypernatremic dehydration in breastfed neonates has been reported to be 1.4% to 7.7% (4–8). Despite the short study period (7 months) and the fact that the patient flow to our hospital had decreased significantly (due to the ongoing war and siege), the magnitude of hypernatremic dehydration in our study was high compared to previous reports. This could be due to the high burden of the problem. This could also be partially explained by the fact that neonates with concomitant sepsis were included in the current study, unlike previous studies.

The mean age at presentation was 7.85 days (SD±6.28), which is similar to that in a study conducted in British Colombia's Children's Hospital. The affected newborns were born primarily through vaginal delivery to primiparous mothers, which is consistent with previous studies. This may represent a compounding factor because these mothers lacked experience and failed to recognize the severity of their babies' illnesses early. Moreover, the high incidence of breastfeeding-associated hypernatremia among infants born to first-time mothers may be related to the fact that primiparous women produce significantly less milk than multiparous women do during the first postpartum week. Despite, nearly all (98%) mothers having antenatal care follow-up and most mothers giving birth at a health facility, a significant number of neonates have presented with hypernatremic dehydration, indicating a gap in breastfeeding practices.

The median percentage of weight loss was 14.7(IQR,7.4-25.25) and more than half of them had ≥10% weight loss, which is consistent with a previous study. Twelve neonates (24%) were with an unknown weight loss because birth weight was not identified (born at home or

transferred from another facility). Weight loss is a significant marker of dehydration in the early neonatal period. Literature has shown that a weight loss of up to 10% during the first week is acceptable. Babies with more than expected weight loss should be screened for hypernatremia. Furthermore, it is estimated that 33% of breastfed infants with weight loss exceeding 10% have hypernatremic dehydration.

Most neonates in our study presented with fever, failure to suck, and decrement in urine amount seen in 78%, 54%, and 52% of them respectively. Our findings are consistent with other studies. These clinical findings are non-specific, and hypernatremic dehydration can be difficult to clinically recognize. This is because infants with hypernatremic dehydration have better-preserved extracellular volume and, therefore, have less pronounced clinical features of dehydration. The common presenting clinical signs were dry buccal mucosa, significant weight loss, lethargy, and doughy skin present in 88%, 52%, 46%, and 42% of neonates, respectively, which is a similar finding to the previous reports. The combination of elevated serum glucose, blood urea nitrogen levels, and hypernatremia results in extremely elevated osmolality. These factors combine to produce lethargy, confusion, neuromuscular irritability, seizure, coma, and death. Weight loss, inadequate urination, and stooling are sensitive indicators of infant dehydration. Therefore, these should be included in the history of all infants presenting for the evaluation of jaundice, fever, weight loss, and lethargy.

The presumed causes of hypernatremic dehydration in the present study were insufficient breast milk production (50%), poor oral intake (36%), and a combination of both (12%). The assumed reasons were incorrect breastfeeding techniques and some of the mothers had surgical and medical problems, such as postoperative pain and preeclampsia. Most of the mothers were primiparous, so they were novices to breastfeed. Poor oral intake may be a manifestation of dehydration or other comorbidities such as sepsis. The fact that more than two-third of the neonates had presumed sepsis supports this finding. Different studies support that the common causes of neonatal hypernatremic dehydration are inappropriate breastfeeding techniques and contributions from underlying diseases such as sepsis.

This study revealed that the median serum sodium level was 161 (IQR, 154-169) mmol/L, which is similar to previous studies. Of the 50 neonates with hypernatremic dehydration in the present study, more than two-thirds had one or more short-term complications, AKI being the most common (54%). Likewise, AKI has been reported to be one of the most common complications of hypernatremic dehydration, at least in the initial stage, mainly due to hypovolemia [4-9]. Seizure was the second most common complication, witnessed in 32% of the neonates, and all except one had a seizure at admission before treatment was started. Seizure usually occurs during the correction of hypernatremia, which is generally caused by rapid correction. Contrary to other studies, in our study, only one neonate experienced a seizure during correction due to intracranial hemorrhage. Three neonates (6%) had bilateral lower extremity gangrene. In addition, two patients had abdominal aorta thrombosis and one had bilateral renal artery thrombosis. Finally, all the patients died. Hypernatremic dehydration is a known cause of thrombosis due to hypertonicity and hypo-perfusion. Moreover, sepsis (all our cases with thrombosis were septic), hypercoagulable state, prematurity, asphyxia, umbilical artery cannulation, low serum albumin level, and maternal diabetes are known risk factors for thrombosis.

In the case of mild hypernatremia, complementary feeds were administered with expressed breast milk or formula using a nasogastric tube or bottle with a wide-based nipple. Intravenous rehydration was administered if the neonate's serum sodium level was significantly elevated (□160 mmol/L). Fluid therapy was calculated based on the degree of dehydration, which was estimated from the difference between the birth weight and weight on admission. Twenty-eight (56%) patients had received correction intravenous fluid based on the local hospital protocol developed following the modification of different studies. Slow correction of high serum Na levels will prevent serious complications such as brain edema, brain damage, convulsions, and death, as it will decrease the osmolality in brain cells in balance with serum osmolality. A decrease in serum Na+ level of 10-15 mmol/L in 24 hours (≤0.5mmol/L/hr) has been reported to be safe. The majority of the neonates (78%) were evaluated and treated for presumed sepsis at presentation. Blood culture was performed only for 35.5% (14/39) neonates, of whom 35.7% (5/14) samples had bacterial growth (Klebsiella oxytoca-2, Klebsiella Pneumonea-1, Citrobacter-1, and Staphylococcusaureus-1). All neonates with presumed sepsis were started on empiric antibiotics and then revised according to growth for those having bacterial growth. A similar approach has been used previously. The mortality rate (32%) in the present study was significantly higher than in previous studies [10-14]. Unlike in previous studies, neonates with proven or suspected sepsis were included in our study, which may have contributed to the high mortality rate. It was also observed that delayed presentation of patients with severe clinical and laboratory findings can negatively affect the prognosis. Moreover, seven neonates were critically ill and required mechanical ventilation, and all died, similar to previous studies [15].

Regarding the severity of hypernatremia, mortality rates were as follows; 37.5%, 38.5%, and 50%, respectively, which is consistent with a similar previous study[11-16]. Eight (16%) neonates have died before hypernatremia correction of hypernatremia, which implies early detection and intervention are crucial for a better outcome. Almost all the patients who died had one or more complications. More than half (55.6%) of the neonates with AKI have died which is similar to another former report. Previous studies have reported that peritoneal dialysis is effective in patients with hypernatremic dehydration and AKI requiring dialysis [17-20]. In our study, peritoneal dialysis was not offered to the candidates because of the lack of dialysis fluid and catheters associated with the current crisis in Tigray.

Furthermore, a chi-square test (cut-off $p < 0.05$) was used to test variables associated with mortality[21-27]. The presence of AKI, lethargy at admission, hyperglycemia, and a hospital stay of less than a week was significantly associated with mortality. All our patients who died, except for one, had AKI. It is well known that even a small increase in serum creatinine level, especially in severe AKI (stage 3), is associated with an increased mortality rate among critically ill patients, particularly in developing countries such as Ethiopia, where the availability of renal replacement therapy is very limited [28,29]. Being lethargic at admission, one of the neonatal danger signs, and a shorter survival period between hospital admission and death indicate that they were brought to the health facility late in the course of the illness, which is in line with previous studies [30,31]. Hyperglycemia is significantly associated with mortality in neonates [32]. This could be due to increased oxidative stress or a pro-inflammatory state resulting from hyperglycemia. Moreover, a high serum glucose level has a prothrombotic effect and reduces endothelial nitric oxide production, thus reducing tissue perfusion [33].

In summary, breastfed neonates should be evaluated by a well-trained health professional at 3 to 5 days of age and they should be evaluated with a weight check, assessment of hydration status, and evaluation of breastfeeding and neonatal elimination patterns. Most breastfeeding-associated hypernatremia can be prevented if neonates with excessive weight loss or inadequate breast milk transfer are carefully given expressed breast milk if available and formula, if necessary, until breast

milk production increases and breastfeeding difficulties are addressed. Furthermore, the prevention of hypernatremic dehydration in breast-fed neonates begins with prenatal and early postpartum screening to identify possible maternal and neonatal factors that could interfere with successful lactation and breastfeeding, as well as with anticipatory guidance regarding basic breast-feeding techniques.

**Limitations**

This study used a small sample size because the disease is rare. The current crisis (war and siege) in Tigrai, Ethiopia (lack of basic services, banking, transportation, telecommunication, and frequent interruption of electric power) has contributed to low service utilization by mothers. Moreover, the ongoing crisis had a negative effect on the management protocol of neonates with HDN due to the absence of complete investigations (blood culture, blood gas analysis, and frequent determination of serum electrolytes) and appropriate management options, such as peritoneal dialysis and medications. The present study assessed only short-term outcome/complications during the hospital stay and did not assess the long-term effect of hypernatremic dehydration, especially neurological outcomes after discharge.

**Conclusion**

Breastfeeding-associated hypernatremic dehydration has a high prevalence and mortality among neonates. Being lethargic at admission, the presence of acute kidney injury and hyperglycemia, and a hospital stay of less than one week was significantly associated with mortality. Pediatric healthcare providers should be aware of this potentially serious but completely preventable complication of insufficient breastfeeding. Antenatal and in-hospital screening of maternal and neonatal risk factors for lactational insufficiency combined with early post-delivery follow-up to identify excessive neonatal weight loss and inadequate elimination is important to prevent hypernatremic dehydration in neonates. Moreover, primiparous mothers are novices at breastfeeding; therefore, they should be taught breastfeeding techniques and warning signs of dehydration. Furthermore, the materials needed for emergency peritoneal dialysis (dialysis set and fluids) should be available for those in need.

**Declarations**

**Ethics Approval**

Ethical clearance was obtained from the Institutional Review Board of Mekelle University, College of Health Science, with the protocol approval number MU-IRB 2001/2022. Informed consent was obtained from each parent and/or legal guardian for participation in the study before the data collection. Data were collected after providing clear information about the study objectives and other methodological issues. During data collection, the names of the participants were kept anonymous using only the study record number. All Methods Were Performed in Accordance with the Relevant Institutional Guidelines and Regulations.

**Consent for Publication:** This is not applicable

**Availability of Data and Materials:** Please contact the corresponding author for data requests

**Competing Interest:** There is no conflict of interest

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**Authors' Contribution**

This work was carried out in collaboration with all the authors. HGH, YLG, AHB, and KTG contributed to the conception, initiation, and drafting of the manuscript. HHL, MMM, and DSG reviewed the data and were involved in the preparation and critical revision of the manuscript. AHA and GFA were involved in the data analysis and interpretation. All the authors have read and approved the final manuscript.

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