

## CASE SERIES

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# Postpartum severe hyponatremia in preterm birth and mature newborns: Dangers for mother and child?

Felix Sierra, Steffen Kunzmann, Niki Mouzakiti,  
Nafisa Sabarai, Franz Bahlmann

## ABSTRACT

**Introduction:** Sodium is the ion with the highest extracellular concentration and thus also determines the osmolality in the extracellular space. The lower the serum sodium, the more serious the dilemma.

**Case Series:** **Case 1:** A eutrophic female was born at 37+3 weeks gestation, birth by vacuum extraction, birth weight 2570-gram, umbilical cord blood gas analysis performed in delivery showed severe hyponatremia (sodium 122 mmol/L). **Case 2:** A eutrophic male was born at 40+4 weeks gestation, spontaneous labor, birth weight 3230-gram, suspicion of cerebral seizure, postpartum hyponatremia, perinatal metabolic acidosis, respiratory failure, and hypoxic ischemic encephalopathy. **Case 3:** A eutrophic male was born at 38+4 weeks gestation, spontaneous birth, birth weight 2895-gram, postpartum severe hyponatremia, suspicion of cerebral seizure, cyanosis attacks. **Case 4:** A preterm female was born at 31+1 weeks gestation, birth weight 1195-gram, sodium 125 mmol/L, potassium 6.3 mmol/L with respiratory disorder.

**Conclusion:** We recommend a quick diagnosis and stop the factors that cause hyponatremia. Laboratory

tests, history, and physical examination could reduce hyponatremia to ensure adequate treatment.

**Keywords:** Fetal hyponatremia, Laboratory tests include serum sodium, Maternal hyponatremia, Plasma osmolality, Urine sodium and osmolality

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## INTRODUCTION

Sodium is the ion with the highest extracellular concentration and thus also determines the osmolality in the extracellular space. The lower the serum sodium, the more serious the dilemma.

Although the laboratory definition may be slightly higher. Hyponatremia, defined as serum sodium concentration below 135 mmol/L, is a commonly electrolyte abnormality encountered in hospitalized patients. Hyponatremia is a clinical complication of a wide variety of diseases, surgical procedure, pregnancies, and drug treatments. Hyponatremia is primarily a disorder of water balance, with a relative excess of body water compared to total body sodium and potassium content [1, 2].

During pregnancy, hyponatremia can be caused by various mechanisms. An osmotic phenomenon is one of the physiologic changes that occur during pregnancy. Normal pregnancy is a state marked by avid sodium retention and plasma volume expansion. Increased

Felix Sierra<sup>1</sup>, Steffen Kunzmann<sup>2</sup>, Niki Mouzakiti<sup>1</sup>, Nafisa Sabarai<sup>1</sup>, Franz Bahlmann<sup>1</sup>

**Affiliations:** <sup>1</sup>Department of Obstetrics and Gynecology, Center for Ultrasound and Prenatal Medicine, Buergerhospital and Clementine Children's Hospital, Frankfurt am Main, Germany; <sup>2</sup>Department of Neonatology and Pediatric Intensive Care, Buergerhospital and Clementine Children's Hospital, Frankfurt am Main, Germany.

**Corresponding Author:** Felix Sierra, Department of Obstetrics and Gynecology, Center for Ultrasound and Prenatal Medicine, Buergerhospital and Clementine Children's Hospital, Frankfurt am Main, Germany; Email: sierrafelix303@gmail.com

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epithelial sodium channel activity in pregnancy may mediate these changes.

Prevention of sodium retention was associated with a decrease in maternal blood pressure and body weight, as well as fetal growth restriction. Taken together, these findings emphasize the importance of increased sodium channel activity during pregnancy in maintaining the pregnancy-mediated changes in sodium balance, volume status, and blood pressure. The reabsorption of water in the kidney is controlled by vasopressin, which in turn regulated by plasma osmolality. Vasopressin is eliminated due to increased osmolality, causing water retention that will restore osmolality [3, 4].

Reduction of plasma osmolality by  $\leq 10$  mOsm/kg occurs in early pregnancy mainly because of a decrease in plasma sodium by  $\leq 5$  mmol/L. By 11+6 weeks of gestation, the plasma osmolality remains low until after delivery.

On day of admission, serum sodium (mmol/L), osmolality in serum (mOsm/kg), sodium in urine, and osmolality in urine should be performed [5].

Changes in plasma sodium concentration are therefore a reflection of abnormal water balance, rather than the dysregulation of sodium intake and excretion. The neonatal electrolyte disorders account for 10% of seizures at the newborn, 25% ill newborns developed a mild hyponatremia, and 1% a moderate hyponatremia [6, 7]. The water content of the body depends on age. In the first year of life there is a rapid and later slower decrease in body water. The total body fluid in preterm infants is 80% of body mass in the 28th week of pregnancy, decreases to 70–75% in term infants, 65–70% in infants, 60% in children, adolescents, and adults [8–11].

Postnatally there is an adaptation of the newborn, which proceeds according to a characteristic pattern. The prediuretic phase comprises the first two days of life. The newborn loses fluid mainly through the “perspiratio insensibilis” (release of water through the breath and skin). In this phase, the amount of urine is minimal and independent of the amount of fluid applied. This transepidermal loss of fluid is particularly high in premature babies. Increased water loss is also caused by sweating, fever, hyperventilation, or tachypnea [10, 11]. The kidneys play an increasingly important role in fluid regulation. The urine production is adjusted to the amount of fluid administered. The influence of the skin on the fluid balance decreases through the stratum corneum (34 weeks of pregnancy), whereby the fluid balance in this phase is mainly regulated by the kidneys [11]. The physiologically induced weight loss after birth is also due to the loss of sodium and water through the kidneys and thus a loss of extracellular fluid [11, 12]. The weight loss in premature babies is up to 15%, in term babies around 10% [13, 14]. However, this is not seen as dehydration, but as a physiological adaptation to extrauterine life. Furthermore, the pulmonary vascular resistance drops postnatally, which increases the left atrial venous return. This results in a stretching of the atrial muscles, which in

turn leads to the release of the “atrial natriuretic peptide” (ANP). Diuresis, natriuresis, and weight loss are the results [13, 15].

## CASE SERIES

### Case 1

#### Diagnosis

A eutrophic female was born at 37+3 weeks gestation, birth by vacuum extraction, birth weight 2570-gram, umbilical cord blood gas analysis performed in delivery showed severe hyponatremia (sodium 122 mmol/L). Her arterial pH was 7.2, body temperature 36.2°C, breathing rate 27/min, heart rate 117/min, blood pressure 71/46 mmHg, and left dacryocystocele. The newborn was transferred to Neonatal Intensive Care Unit (NICU) due to the hyponatremia.

Hypocalcemia (ionized calcium 1.23 mmol/L) and hyponatremia (sodium 126 mmol/L) were confirmed by laboratory analysis as well as blood glucose 86 mg/dL, lactate 2.6 mmol/L, urine osmolality 287 mOsm/kg, sodium urine 32 mmol/L, and interleucin 6 84 pg/mL. We started an intravenous slow sodium correction as follows: [sodium deficit (set point) – sodium actual value  $\times$  total body water  $\times$  0.3 = deficit of sodium in mmol/L] for 24–48 hours.

The skull ultrasound showed no evidence of past or recent bleeding, no calcification, no evidence of a liquor circulation disorder and Doppler of the anterior cerebral artery was normal. The ultrasound showed normal bilateral kidneys. Figures 1 and 2 show the electrolyte and saturation changes for seven days.

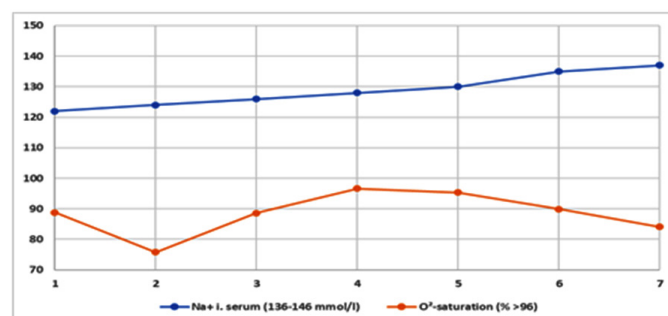


Figure 1: Newborn serum sodium concentration (mmol/L) and saturation (%) during seven-days balance study.

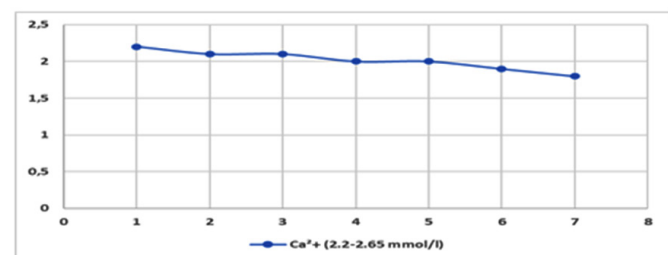


Figure 2: Newborn serum calcium concentration (mmol/L) during seven-day balance study.

### Maternal characteristics

A 32-year-old mother, gravida 1, para 1, blood group A rhesus positive, suspected fulminant preeclampsia, hyponatremia (120 mmol/L), after labor transferred to intensive care unit.

### Case 2

#### Diagnosis

A eutrophic male was born at 40+4 weeks gestation, spontaneous labor, birth weight 3230-gram, suspicion of cerebral seizure, postpartum hyponatremia, perinatal metabolic acidosis, respiratory failure, and hypoxic ischemic encephalopathy.

Good postnatal adaptation, APGAR score 9/10/10, arterial pH 7.21. The newborn was given to the mother for bonding, after 1 hour we found a livid apneic and bradycardic newborn (20–30/min). Rapid heart rate increases with bagging, and we decided on endotracheal intubation.

The umbilical cord blood gas analysis performed in delivery room showed hyponatremia (sodium 127 mmol/L), arterial pH 6.88, BE-25, lactate 14. The newborn was transferred to NICU, blood gas analysis performed showed hyponatremia, arterial pH 7.13, BE-19, lactate 16. The mother’s sodium was 126 mmol/L.

The skull ultrasound showed a cerebral edema stage II, end-systolic and end-diastolic flow velocities increased, diffuse echogenicity increased in parenchyma.

After 7 hours there was a decrease in oxygen saturation of up to 20% and a generalized increase in tone. Despite the substitution, we assessed the result as a seizure with renewed hyponatremia. Due to hypothermia, the newborn was reintubated and sedated.

The hypotension was supported with norepinephrine, the newborn was extubated successfully without additional oxygen requirement.

Due to the withdrawal symptoms, dexmedetomidine was administered after extubation therapy and therapy with ampicillin and gentamicin was carried out for 5 days which led to the control of cerebral edema stage II. The newborn was transferred to the Children’s Hospital in good general condition. Figure 3 shows sodium, lactate, and saturation changes for nine days.

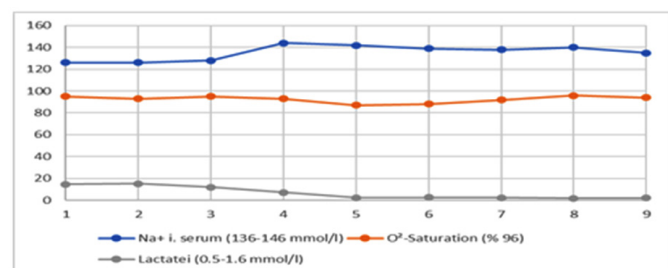


Figure 3: Newborn serum sodium, lactate concentration (mmol/L), and saturation (%) during nine-days balance study.

### Maternal characteristics

A 41-year-old mother, gravida 1, para 1, blood group A rhesus positive, pre-existing arterial hypertension, insulin resistant diabetes, obesity, and hypothyroidism, spontaneous birth in skull position, and pulpy amniotic fluid.

### Case 3

#### Diagnosis

A eutrophic male was born at 38+4 weeks gestation, spontaneous birth, birth weight 2895-gram, postpartum severe hyponatremia, suspicion of cerebral seizure, cyanosis attacks, APGAR score 9/10/10, arterial pH 7.25, temperature 36.3°C, blood pressure 63/38, breathing rate 70/min, heart rate 134/min, saturation 98% under room air, sodium 118 mmol/L, potassium 5.1 mmol/L, calcium 1.15 mmol/L, lactate 3.6 mmol/L. Presentation at the age of 2 hours because of a drop in oxygen saturation and labored breathing. Admission to NICU for recurring deep desaturations.

In the NICU, we observed seizures with staring gaze, changes in skin color, a drop in oxygen saturation and breathing difficulties. The amplitude-integrated electroencephalogram (aEEG) showed no evidence of focal or generalized convulsive activity. The severe hyponatremia was normalized by sodium substitution. In the further course the electrolytes were normal. The mother also had hyponatremia of 131 mmol/L, potassium value was 3.9 mmol/L at the time of delivery. We assume syndrome of inappropriate antidiuretic hormone (SIADH) symptoms were highly likely during childbirth. Figure 4 shows changes of potassium and lactate for thirteen days. Figure 5 shows the course of sodium, chloride concentration (mmol/L), saturation (%), and arterial pH blood gas analysis (mmHg) for 13 days.

### Maternal characteristics

A 24-year-old mother, gravida 1, para 1, blood group A rhesus positive, conditions after rupture of membranes, spontaneous birth in skull position.

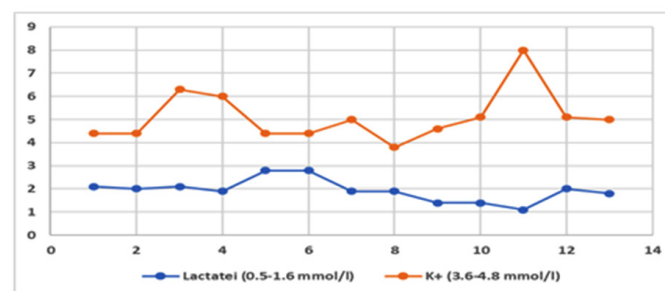


Figure 4: Newborn serum potassium and lactate concentration (mmol/L) during 13-days balance study.

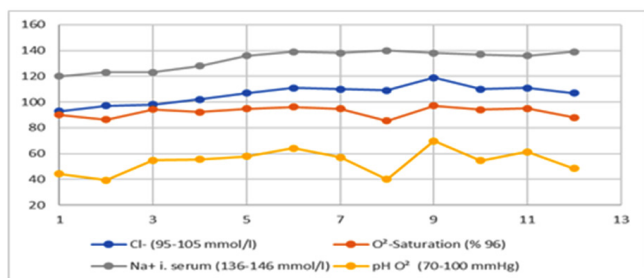


Figure 5: Newborn serum sodium, chloride concentration (mmol/L) saturation (%), and arterial pH blood gas analysis (mmHg) during 12-days balance study.

## Case 4

### Diagnosis

A premature female was born at 31+1 weeks gestation, birth weight 1195-gram, sodium 125 mmol/L, potassium 6.3 mmol/L with respiratory disorder, APGAR score 8/9/10, arterial pH 7.35, temperature 36.8°C, blood pressure 41/20 mmHg, heart rate 162/min, breathing rate 50/min, and saturation 91%.

Neonatal echocardiogram revealed a muscular ventricle septum defect (VSD) with left-right shunt as well as atrium septum defect (ASD II) with left-right shunt, retrograde flow in the descending aorta with Vmax 162 cm/s and slight pleural effusion. The metabolic screening showed an abnormal finding of 17-hydroxyprogesterone (OH) progesterone, which is the biochemical marker for diagnosing Adrenogenital syndrome (AGS).

### Maternal characteristics

A 38-year-old mother, gravida 1, para 1, blood group A rhesus positive, HBsAg negative, cytomegalovirus (CMV) positive, inpatient admission due to suspected gestosis. As develops hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome, so decision for caesarean section was taken.

The maternal osmolality in serum was 277 mOsm/kg at day 3, 265 mOsm/kg at day 6, total protein in urine was 498 mg/24 h and sodium in urine was 53 mmol/L. The placenta showed a chorangiosis type I. Figure 6 shows maternal and neonatal serum sodium concentration (mmol/L) for 13 days and Figure 7 shows maternal and neonatal serum calcium concentration (mmol/L) for 8 days.

## DISCUSSION

The risks and dangers of maternal hyponatremia in pregnancy and during labor have previously been recognized [16–18]. Maternal hyponatremia can also be reflected in the fetus and may increase the incidence of respiratory distress and hyperbilirubinemia in

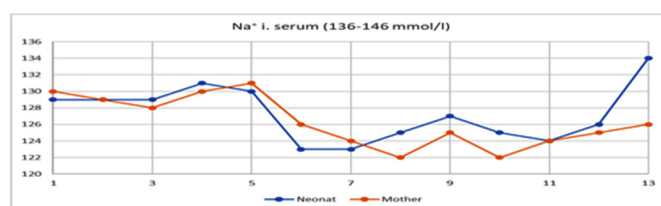


Figure 6: Maternal and neonatal serum sodium concentration (mmol/L) during 13-days balance study.

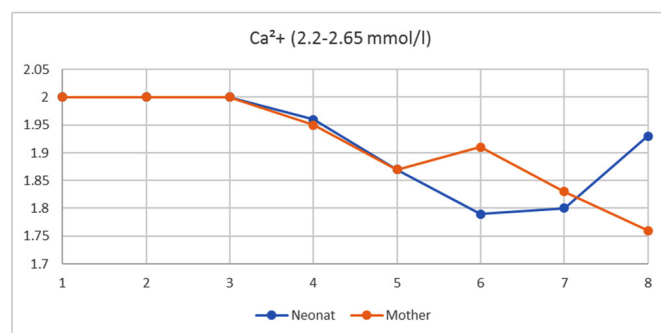


Figure 7: Maternal and neonatal serum calcium concentration (mmol/L) during eight-days balance study.

hyponatremic neonate [19, 20]. Acute hyponatremia in our cases reflected maternal pre-delivery hyponatremia and the neonate reflected those of mother. Administration of oxytocin with glucose infusion causes in neonate hyponatremia, and the same with excessive oral water intake during labor and other medications [21–23]. Sodium-active drugs use like diuretics, angiotensin converting enzyme (ACE) inhibitors, and selective serotonin reuptake inhibitors (SSRIs) could be provoking a maternal hyponatremia [19, 24]. Diagnostic difficulties during labor are obvious as initial symptoms of hyponatremic encephalopathy are nonspecific and may easily be confused with symptoms of pre-eclampsia [17]. The symptoms of lower sodium levels can occur during pregnancy and a reduction in brain size [25]. Although the importance of this reduction remains to be explained, it could be due to an intracellular adaptation to pregnancy.

When life threatening symptoms (vomiting, irritability, headache, nausea, brain edema, and coma) occur, therapy must aim at quick restitution of serum sodium and osmolality [26].

Severe hyponatremic can cause encephalopathy, respiratory failure, and death [20, 27]. Hyponatremia is a rare complication of preeclampsia. The pathogenesis of the severe hyponatremia in our case is not fully understood as most women with preeclampsia do not develop hyponatremia. It is hypothesized that the non-osmotic stimulation of vasopressin in the setting of a hypovolemic state with low effective circulating plasma volume is the main mechanism of hyponatremia. Previous case reports have described hyponatremia with pre-eclampsia with and without nephrotic syndrome [28, 29].

A fall in serum osmolality suppresses the release of antidiuretic hormone, allowing excretion of the excess water in dilute urine [11].

We know that higher fluid administration during labor may cause significant hyponatremia in women. Oral fluid intake during labor should be documented to avoid intravenous administration of hypotonic solutions [30, 31].

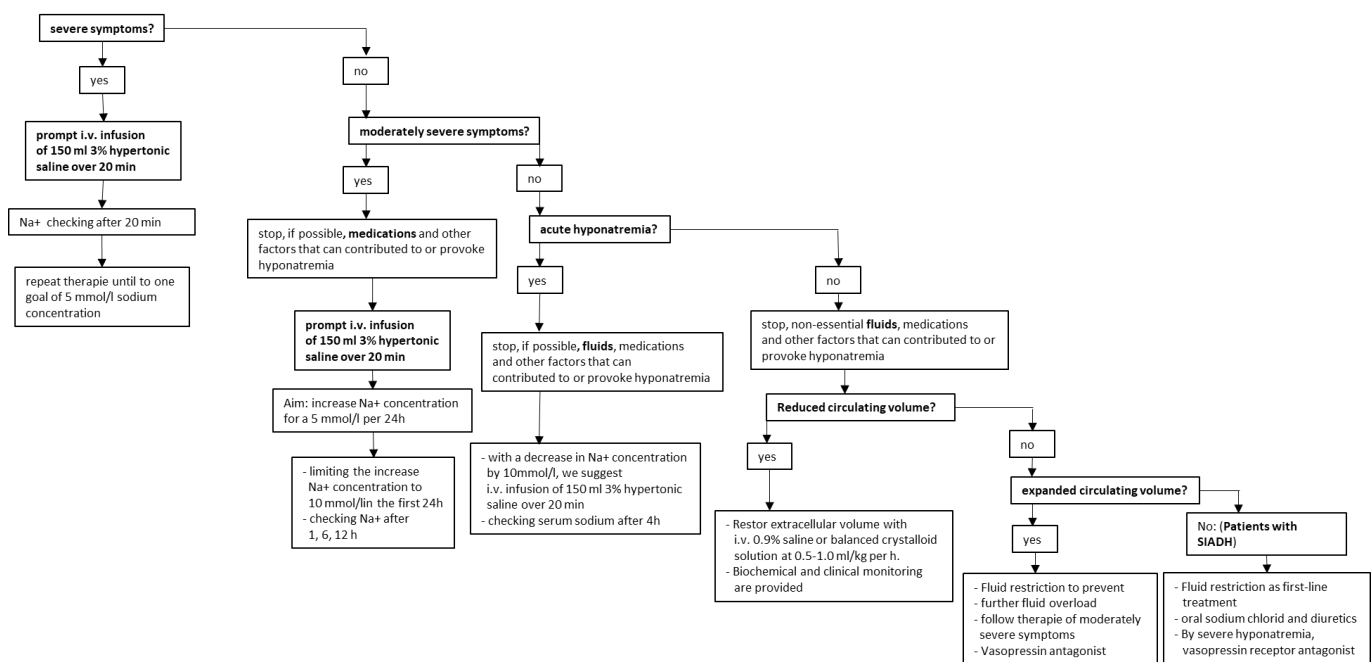
We know that the common clinical problem of hyponatremia is frequently developed in hospitalized patients [32]. Although morbidity varies widely in severity, serious complications can arise from the disorder itself as well as from errors in management [30]. The manifestation of hyponatremia is largely related to dysfunction of the central nervous system, and it is more conspicuous when the decrease in the serum sodium concentration is large or rapid [33]. Massive fluid intake

during labor can cause hyponatremia due to sodium loss through sweating and fluid retention [34].

Complications of severe or rapidly evolving hyponatremia include seizures, coma, permanent brain damage, respiratory arrest, brain-stem herniation, and death. These complications often occur with excessive water retention in patients who are essentially euvoletic [27].

The management of hypotonic, hypertonic hyponatremia requires balancing the risks of hypotonicity, and hypertonicity against those of therapy. The presence of symptoms and their severity largely determine the pace of correction [35]. At patients with symptomatic hyponatremia and concentrated urine osmolality ( $\geq 200$  mOsm/kg of water) and clinical euvolectia or hypervolemia require infusion of hypertonic saline.

### Algorithm for the management and therapy of hypotonic hyponatremia befor and during pregnancy.



## CONCLUSION

The therapeutic options for treating hyponatremia have recently expanded. Clinicians should be familiar with the diagnosis and management of various forms of hyponatremia, and the therapeutic approach should primarily be based on the severity of the symptoms. Laboratory assessment should include plasma osmolality, urine osmolality, and urine sodium. Additionally, we recommend tests of thyroid and adrenal function which may also be necessary. All these tests are required for the differential diagnosis of hyponatremia. For clinical practice, it should be noted that if a sudden increase in urine output to  $>100$  ml/h

signals of rapid rise in serum sodium concentration. If vasopressin activity is suddenly suppressed, as happens when intravascular volume is restored in hypovolemia, free water clearance can dramatically increase, resulting in serum sodium concentration rising more rapidly than expected. We recommend prompt diagnostic assessment, and stop if would be possible, medications and other factors that can contribute to or provoke hyponatremia. The cause of cases of hyponatremia can be deduced from the history, physical examination, and basic laboratory tests. In addition, the etiology of hyponatremia must be systematically determined to ensure adequate treatment.

## REFERENCES

1. Modi N, Bétrémieux P, Midgley J, Hartnoll G. Postnatal weight loss and contraction of the extracellular compartment is triggered by atrial natriuretic peptide. *Early Hum Dev* 2000;59(3):201–8.
2. Anderson RJ. Hospital-associated hyponatremia. *Kidney Int* 1986;29(6):1237–47.
3. Arieff AI, Guisado R. Effects on the central nervous system of hypernatremic and hyponatremic states. *Kidney Int* 1976;10(1):104–16.
4. Modi N. Hyponatraemia in the newborn. *Arch Dis Child Fetal Neonatal Ed* 1998;78(2):F81–4.
5. Berl T. Treating hyponatremia: Damned if we do and damned if we don't. *Kidney Int* 1990;37(3):1006–18.
6. Loman AMW, ter Horst HJ, Lambrechtsen FACP, Lunsing RJ. Neonatal seizures: Aetiology by means of a standardized work-up. *Eur J Paediatr Neurol* 2014;18(3):360–7.
7. Marcialis MA, Dessi A, Pintus MC, Irmesi R, Fanos V. Neonatal hyponatremia: Differential diagnosis and treatment. *J Matern Fetal Neonatal Med* 2011;24 Suppl 1:75–9.
8. Spasovski G, Vanholder R, Allolio B, et al. Clinical practice guideline on diagnosis and treatment of hyponatraemia. *Nephrol Dial Transplant* 2014;29 Suppl 2:i1–39.
9. Reynolds RM, Padfield PL, Seckl JR. Disorders of sodium balance. *BMJ* 2006;332(7543):702–5.
10. Lindheimer MD, Davison JM. Osmoregulation, the secretion of arginine vasopressin and its metabolism during pregnancy. *Eur J Endocrinol* 1995;132(2):133–43.
11. Brace R. Fluid and electrolyte metabolism. In: Polin R, Fox W, Abman S, editors. *Fetal and Neonatal Physiology*. Philadelphia: Saunders Elsevier; 2004. p. 1341–50.
12. Modi N. Clinical implications of postnatal alterations in body water distribution. *Semin Neonatol* 2003;8(4):301–6.
13. Steurer MA, Berger TM. Infusion therapy for neonates, infants and children. [Article in German]. *Anaesthesist* 2011;60(1):10–22.
14. Sulyok E. Renal aspects of sodium metabolism in the fetus and neonate. In: Polin R, Baumgart S, Guignard J, et al. editors. *Nephrology and Fluid/Electrolyte Physiology - Neonatology Questions and Controversies*. Philadelphia: Saunders Elsevier; 2008. p. 2353.
15. Burrell C, de Swiet M. Severe hyponatraemia and pre-eclampsia. *BJOG* 2004;111(9):1020–2.
16. Adrogué HJ, Madias NE. Aiding fluid prescription for the dysnatremias. *Intensive Care Med* 1997;23(3):309–16.
17. Magriples U, Laifer S, Hayslett JP. Dilutional hyponatremia in preeclampsia with and without nephrotic syndrome. *Am J Obstet Gynecol* 2001;184(2):231–2.
18. Frizzell RT, Lang GH, Lowance DC, Lathan SR. Hyponatremia and ultramarathon running. *JAMA* 1986;255(6):772–4.
19. Tarnow-Mordi WO, Shaw JC, Liu D, Gardner DA, Flynn FV. Iatrogenic hyponatraemia of the newborn due to maternal fluid overload: A prospective study. *Br Med J (Clin Res Ed)* 1981;283(6292):639–42.
20. Omigbodun AO, Fajimi JL, Adeleye JA. Effects of using either saline or glucose as a vehicle for infusion in labour. *East Afr Med J* 1991;68(2):88–92.
21. Bauer K. Body fluid compartments in the fetus and newborn infant with growth aberration. In: Polin R, Baumgart S, Oh W, et al. editors. *Nephrology and Fluid/Electrolyte Physiology - Neonatology Questions and Controversies* Philadelphia: Saunders Elsevier; 2008. p. 155–60.
22. Johansson S, Lindow S, Kapadia H, Norman M. Perinatal water intoxication due to excessive oral intake during labour. *Acta Paediatr* 2002;91(7):811–4.
23. West CR, Harding LE. Maternal water intoxication as a cause of neonatal seizures. *J Paediatr Child Health* 2004;40(12):709–10.
24. Paul SP, Basude S, Smith-Collins AP. Maternal over-hydration in labor can cause dilutional hyponatremia in neonates. *Indian J Pediatr* 2014;81(7):637–8.
25. Spencer SA, Mann NP, Smith ML, Woolfson AM, Benson S. The effect of intravenous therapy during labour on maternal and cord serum sodium levels. *Br J Obstet Gynaecol* 1981;88(5):480.
26. Valerio E, Fantinato M, Giovannini IAB, Baraldi E, Chiandetti L. Severe asymptomatic maternal antepartum hyponatremia leading to neonatal seizures: Prevention is better than cure. *Matern Health Neonatol Perinatol* 2015;1:25.
27. Singhi SC, Chookang E. Maternal fluid overload during labour; transplacental hyponatraemia and risk of transient neonatal tachypnoea in term infants. *Arch Dis Child* 1984;59(12):1155–8.
28. Rascher W. Wasser- und Mineralhaushalt. In: Lentze M, Schaub J, Schulte F, et al. editors. *Pädiatrie*. 3ed. Heidelberg: Springer; 2007. p. 236–44.
29. Sterns RH, Spital A, Clark EC. Disorders of water balance. In: Kokko JP, Tannen RL, editors. *Fluids and electrolytes*. 3ed. Philadelphia: W.B. Saunders; 1996. p. 63–109.
30. Rose BD. Hypoosmolar states – hyponatremia. In: *Clinical Physiology of Acid-Base and Electrolyte Disorders*. 4ed. New York: McGraw-Hill; 1994. p. 651–94.
31. Singhi S, Chookang E, Hall JS. Intrapartum infusion of aqueous glucose solution, transplacental hyponatraemia and risk of neonatal jaundice. *Br J Obstet Gynecol* 1984;91(10):1014–18.
32. Oatridge A, Holdcroft A, Saeed N, et al. Change in brain size during and after pregnancy: Study in healthy women and women with preeclampsia. *AJNR Am J Neuroradiol* 2002;23(1):19–26.
33. Ayus JC, Achinger SG, Arieff A. Brain cell volume regulation in hyponatraemia: Role of sex, age, vasopressin, and hypoxia. *Am J Physiol Renal Physiol* 2008;295(3):F619–24.
34. Oh MS, Kim HJ, Carroll HJ. Recommendations for treatment of symptomatic hyponatremia. *Nephron* 1995;70(2):143–50.
35. Moen V, Brudin L, Rundgren M, Irestedt L. Hyponatremia complicating labour—rare or unrecognized? A prospective observational study. *BJOG* 2009;116(4):552–61.

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### Author Contributions

Felix Sierra – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Steffen Kunzmann – Acquisition of data, Analysis of data, Interpretation of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Niki Mouzakiti – Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Nafisa Sabarai – Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related

to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Franz Bahlmann – Analysis of data, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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### Consent Statement

Written informed consent was obtained from the patient for publication of this article.

### Conflict of Interest

Authors declare no conflict of interest.

### Data Availability

All relevant data are within the paper and its Supporting Information files.

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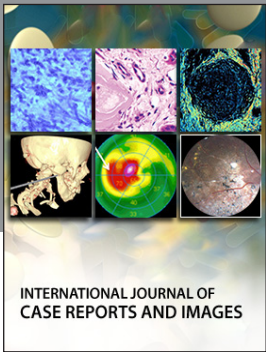
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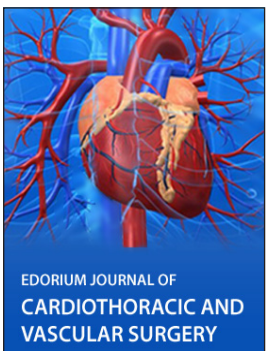
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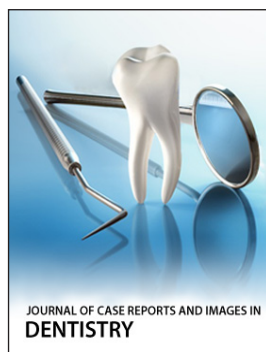
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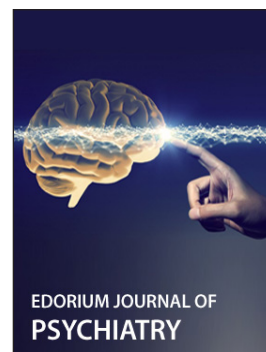
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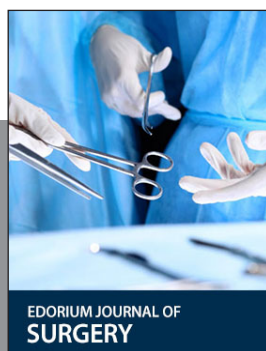
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