



Dynamics of Urine Electrolytes in Term Neonates during the 1st Week of Life

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Background: Urine electrolyte assessment is vital for diagnosing and managing neonatal conditions. However, the challenge of urine collection in neonates has resulted in a lack of standardized urine electrolyte reference values. **Aim:** This study seeks to explore the reference levels and potential trends in serum and urine electrolytes to better understand how the kidneys handle these substances. **Methods:** Healthy neonates were prospectively enrolled following normal births. Using biochemical methods, blood and urine samples were collected and analyzed on the 1st and 5th postnatal days. Statistical analysis was performed using descriptive statistics and the Wilcoxon matched-pairs signed-rank test. **Results:** This prospective study enrolled 55 healthy neonates. Significant changes in serum electrolyte concentrations were observed between the 1st and 5th days after birth. Notably, sodium, creatinine, urea nitrogen, and uric acid levels decreased, whereas potassium, calcium, and phosphate levels increased. Urine analysis revealed significant increases in the tubular maximum phosphate reabsorption per glomerular filtration rate and decreases in the fractional excretion of potassium and uric acid by Day 5. **Conclusion:** This study challenges prevailing assumptions about the stability of neonatal urine electrolytes and highlights dynamic changes in the first postnatal week. These insights lay the groundwork for further research into electrolyte disorders in newborns and have potential implications for improving neonatal care practices.

Key words: Urine, calcium, phosphate, uric acid, sodium, potassium, chloride, neonate

INTRODUCTION

Clinical indicators assessing renal function often provide short-term insights, relying on isolated blood and urine test values at specific time points. However, the intricate nature of renal function is dynamic, necessitating a thorough understanding of its changes over time. The transition from intrauterine to extrauterine circulation involves rapid increases in systemic blood pressure and renal blood flow after birth, accompanied by metabolic conditions that deviate significantly

from fetal life. This results in substantial fluctuations in postnatal blood and urine metabolites.¹ Despite the clinical significance of these changes, the existing literature lacks a comprehensive exploration of the impact of postpartum metabolic alterations in neonates. The clinician's ability to make this critical distinction can significantly influence diagnostic accuracy and patient outcomes.

The evaluation of urine electrolytes is a readily accessible, expeditious, and cost-effective diagnostic approach for the care and treatment of critically ill individuals. Urine electrolytes are widely recommended for diagnosing conditions such as hypovolemia, acute kidney injury, and imbalances in acid-base and other electrolytes. Their use has become significantly

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prevalent in adult intensive care units.² The process of renal tubular development persists postnatally in both term and preterm neonates.^{3,4} Closely monitoring urine electrolyte levels in neonates is crucial for assessing renal tubular function and identifying potential abnormalities. Specifically, the levels of urine sodium and the ratio of urine sodium to potassium can be utilized as indicators of acute pyelonephritis.⁵ The urine sodium to creatinine ratio has been employed as a means to approximate the overall sodium content in the body of newborns experiencing intestinal failure.⁶ Evaluating the levels of electrolytes in the plasma and urine can also be used as a measure of fluid management in neonates.⁷ Nevertheless, the usefulness of urine electrolytes in newborns is subject to debate due to the absence of standardized reference values and challenges in interpretation.

Recognizing the pivotal role of neonatal renal function in clinical practice, we initiated a longitudinal study covering the period from birth to 5 days of age. The study involved a comprehensive examination of blood and urine samples. The primary objective is to elucidate the abrupt changes in renal function after birth, exploring the adaptation of neonatal kidneys to the postnatal environment and identifying subtle alterations in renal function. This study contributes to advancing our understanding of neonatal metabolic physiology and sheds light on the complexities of renal adaptation during the early stages of life while acknowledging the dynamic changes in electrolyte levels after birth.

MATERIALS AND METHODS

This prospective study recruited neonates from the maternity ward of Tungs' Taichung MetroHarbor Hospital in Taichung, Taiwan. Eligible participants were those who had normal births, with Apgar scores of >7 at 5 min, gestational age of >36 weeks, and <24 h postnatal age. These neonates were born either via cesarean section or vaginal delivery. Newborns in this study were fed on demand, receiving either breastmilk or the World Health Organization (WHO) standard infant formula based on individual needs, without fortifiers or nutritional supplements. Exclusion criteria included guardians declining participation, maternal diabetes or gestational diabetes, maternal hyperthyroidism or hypothyroidism, neonatal asphyxia, intrauterine growth retardation, premature birth before 37 weeks of gestation, and congenital anomalies in neonates. This study was conducted in accordance with the Declaration of Helsinki and was approved by the institutional review board of the Tungs' Taichung MetroHarbor Hospital (IRB# R960330-1/96002), and informed consent was obtained from the parents or legal guardians.

Venous blood samples (2 mL each) were collected from the neonates within 24 h and again on the 5th day postpartum.

Aseptic techniques were used during the blood collection, employing serum separator containers. The collected blood samples were centrifuged to obtain serum samples, which were subsequently stored for further analysis. Concurrently, spot urine samples were collected within 2 h using an external collection device. Urine collection was resumed if leaks occurred, with each collection lasting a minimum of 120 min. Urine samples were then preserved by being placed on ice and subsequently frozen.

Laboratory analysis

Blood and urine samples underwent biochemical analysis using an automated chemistry analyzer (Hitachi-7107, Hitachi HiTech, Tokyo, Japan), measuring substances including sodium (Na⁺), potassium (K⁺), chloride (Cl⁻), total calcium (Ca), phosphate (Pi), glucose, urea nitrogen, creatinine (Cr), uric acid (UA), and albumin in blood, and Cr, UA, Na⁺, K⁺, Cl⁻, total Ca, and Pi levels in urine. The serum total calcium (Ca) levels were adjusted based on serum albumin using the formula: Adjusted Ca = (0.8 × [4 – serum albumin]) + serum Ca.

Data analysis

We determined the fractional excretion (FE) of Na (FENa), K (FEK), Cl (FECl), Ca (FECa), and UA (FEUA), using the formula: $FE_x = ([U_x/P_x]/[UCr/PCr]) \times 100$. In this formula, UCr and PCr are the Cr concentrations in urine and plasma, respectively, and “x” represents the specific substance being measured in both urine (U) and plasma (P), respectively. In addition, we determined the urine Ca-to-Cr ratio (UCA/UCr), and the tubular maximum phosphate reabsorption per glomerular filtration rate (TmP/GFR), calculated as: $\text{Serum Pi} - (\text{urine Pi} \times \text{serum Cr}) / \text{urine Cr}$.

Data analysis employed descriptive statistics to compute medians, interquartile ranges (IQRs), and urine electrolyte excretion rates. The Wilcoxon signed-rank test was used to evaluate differences between the two-time points for the same patient. All statistical analyses and graphical presentations were performed using GraphPad Prism 10.1 (GraphPad Software, MA, USA).

RESULTS

This prospective study included 55 neonates recruited from Tungs' Taichung MetroHarbor Hospital in Taichung, Taiwan, from July 1, 2007, to January 11, 2008. The median gestational age at enrollment was 38 2/7 weeks (IQR 37 5/7–39 1/7 weeks), with a median birth weight of 3309 g (IQR 3000–3535 g). All birth weights fell within the ≥10th percentile according to the WHO Child Growth Standards.⁸ The cohort comprised 54 males and 1 female, with their basic

characteristics, as summarized in Table 1. The electrolyte and biochemical parameters in the blood and urine of these healthy neonates, collected on the 1st and 5th days after delivery are summarized in Table 2.

Substantial discrepancies in serum electrolyte concentrations between the 1st and 5th days after birth

As illustrated in Table 2 and Figure 1, serum concentrations of Na⁺, Cr, urea nitrogen, and UA were significantly lower on

Table 1: The demographic data of full-term healthy neonates (*n*=55)

Characteristic	
Gestational age (weeks)	38 ^{2/7} (37 ^{5/7} –39 ^{1/7})
Gender (male; %)	98.2
Body weight (g)	3309 (3000–3535)
Weight on Day 5 (g)	3186 (2883–3409)
Apgar scores	
1 min	8 (8–8)
5 min	9 (9–9)

These data are presented as median with 25th and 75th percentiles

the 5th day compared to the first postpartum day. Conversely, a remarkable increase in serum K⁺, adjusted total Ca, Pi, and glucose levels was noted. No significant differences were observed in blood albumin levels between the two-time points.

Significant changes in urine electrolyte excretion rates between the 1st and 5th days after birth

Data presented in Table 2 and Figure 2 indicate a substantial increase in UCa/UCr levels exhibited on the 5th day after birth compared to the first. However, FECa remained consistent, suggesting that, despite a significant increase in the urine Ca on the 5th day, the FE remained remarkably low. The TmP/GFR, indicative of Pi reabsorption capacity, was high at birth and even higher by the fifth postnatal day. In contrast to the initial postpartum day, the FEUA values significantly decreased by the 5th day. Nevertheless, no notable differences were observed in FENa and FECl between the initial and 5th days after birth.

DISCUSSION

Our study offers a unique contribution to the understanding of neonatal urine electrolyte dynamics, especially among

Table 2: Medians and interquartile ranges of blood biochemistries and urine electrolytes in healthy neonates

Variables	Day 1	Day 5	<i>P</i>
Serum			
Na ⁺ (mmol/L)	141 (139–142)	139 (138–140)	0.0022
K ⁺ (mmol/L)	4.40 (4.10–4.75)	4.75 (4.60–5.20)	<0.0001
Cl ⁻ (mmol/L)	112.8 (110.3–115.2)	112.9 (109.5–114.3)	0.0953
Adjusted total Ca (mg/dL)	8.78 (8.25–9.24)	9.74 (9.40–10.07)	<0.0001
Pi (mg/dL)	5.90 (5.38–6.43)	6.70 (6.20–7.25)	<0.0001
Uric acid (mg/dL)	5.25 (4.68–6.13)	2.50 (2.20–2.90)	<0.0001
Creatinine (mg/dL)	0.80 (0.60–0.93)	0.30 (0.20–0.40)	<0.0001
Urea nitrogen (mg/dL)	9.10 (7.15–11.35)	4.70 (3.65–6.35)	<0.0001
Albumin (g/dL)	3.50 (3.30–3.63)	3.50 (3.30–3.68)	0.7979
Glucose (mg/dL)	60.50 (51.00–74.75)	70.0 (65.00–81.00)	0.001
Urine			
FENa (%)	0.18 (0.095–0.43)	0.18 (0.095–0.34)	0.1305
FEK (%)	12.0 (7.0–35.0)	5.2 (2.8–8.6)	<0.0001
FECl (%)	0.54 (0.27–0.825)	0.45 (0.255–0.670)	0.0609
FEUA (%)	36.2 (24.35–45.92)	13.81 (8.715–19.94)	<0.0001
FECa (%)	0.073 (0.048–0.138)	0.122 (0.042–0.178)	0.1387
UCa/UCr	0.085 (0.0555–0.1355)	0.397 (0.1155–0.9120)	<0.0001
TmP/GFR	5.85 (5.40–6.30)	6.45 (5.99–7.02)	0.013

Days 1 and 5 indicate the duration in days following childbirth. Data are presented as medians with 25th and 75th percentiles. The statistical significance of the examined parameters between the 1st and 5th days of life are analyzed by the Wilcoxon signed-rank test. Na⁺=Sodium; K⁺=Potassium; Cl⁻=Chloride; Ca=Calcium; Pi=Phosphate; FE=Fractional excretion; FEUA=Fractional excretion of uric acid; UCa/Cr=Urine calcium-to-creatinine ratio; TmP/GFR=Tubular maximum phosphate reabsorption per glomerular filtration rate

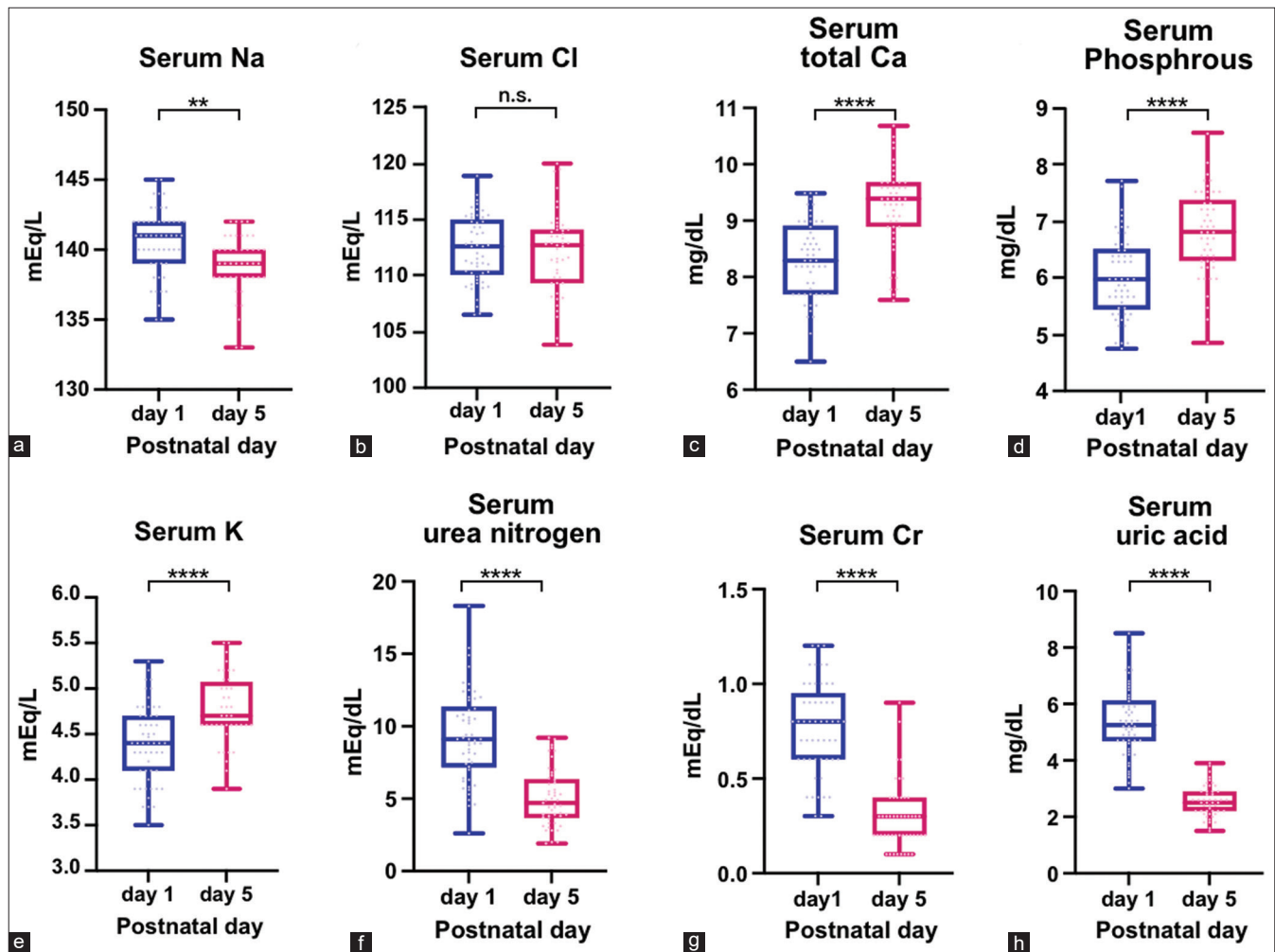


Figure 1: (a-h) Box plots of serum electrolytes and biochemistries in healthy term neonates on the 1st and 5th days after birth. Serum levels of electrolytes and biochemistries were evaluated on the 1st and 5th postnatal days with the Wilcoxon signed-rank test. Significance levels are denoted as * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$. Na⁺ = Sodium; K⁺ = Potassium; Cl⁻ = Chloride; Ca = Calcium; Pi = Phosphate; UA = Uric acid; Cr = Creatinine

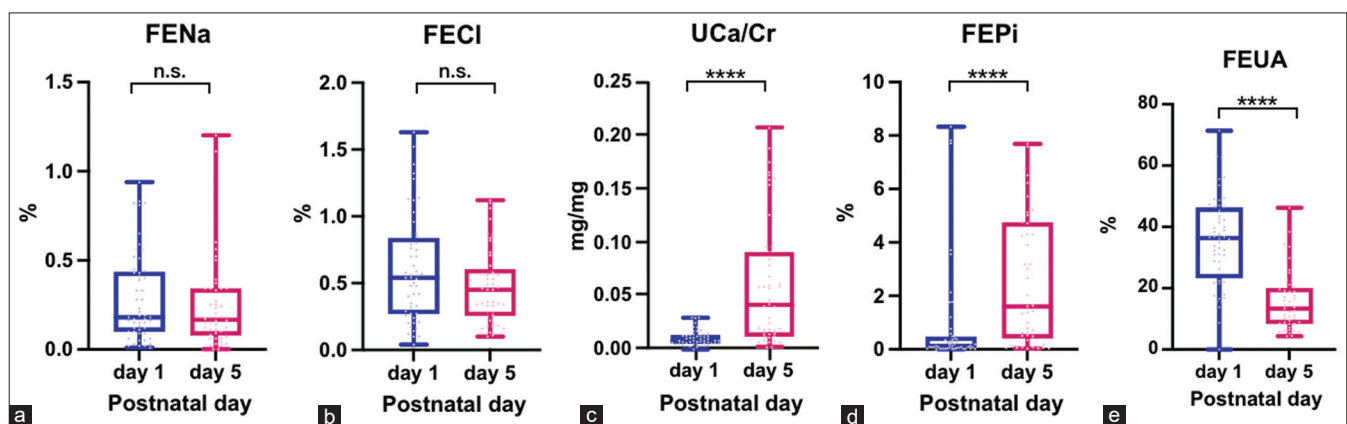


Figure 2: (a-e) Box plots of urine electrolyte excretion in healthy term neonates on the 1st and 5th days after birth. Comparisons of urine electrolyte excretion levels and biochemistries between the 1st and 5th postnatal days were made using the Wilcoxon signed-rank test. Significance levels are indicated as * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, **** $P < 0.0001$. FE = Fractional excretion; Na⁺ = Sodium; K⁺ = Potassium; Cl⁻ = Chloride; Ca = Calcium; Pi = Phosphate; UA = Uric acid; UCa/Cr = Urine calcium-to-creatinine ratio; TmP/GFR = Tubular maximum phosphate reabsorption per glomerular filtration rate

healthy term neonates. It boasts the largest cohort of neonates analyzed for urine electrolytes to date, filling a crucial knowledge gap by focusing on term neonates, a demographic often overlooked in previous research, which predominantly targeted preterm infants.

In the immediate 24–48 h after delivery, oral nutrition may be insufficient, yet postpartum increases in oxygenation and vasoactive hormones facilitate the return of interstitial fluid to the vasculature to maintain intravascular volume. This process, which stimulates the heart to release atrial natriuretic peptide, enhances Na^+ and water excretion by the kidneys, leading to a reduction in total body water and accompanying weight loss.⁹ The minimal decrease in serum Na^+ levels with stable FENa within the clinically normal range suggests effective renal and systemic regulation of sodium balance during this transition. The neonate's capacity to maintain Na^+ within a tight range, despite significant extracellular fluid (ECF) changes, highlights the renal system's maturity and the body's homeostatic mechanisms' efficiency in adapting to postnatal life. Conversely, we noted that the FEUA level, considered a fluid status marker in children and adults, was exceptionally high initially and decreased markedly over the 1st week. While ECF volume changes may contribute to this trend, the decline is more indicative of renal tubule maturation and oxidative stress impact during this period, making FEUA a less straightforward tool for analyzing ECF volume changes.^{10,11}

We found neonates consistently had blood K^+ levels within the normal to high range, with Day 5 values higher than Day 1. This underscores the unique physiological adaptations neonates undergo to support their rapid growth and development. Initially, the active transplacental transfer and renal immaturity create a high potassium environment critical for cellular functions and growth.¹ As neonates transition to postnatal life, retaining ingested potassium becomes essential, supporting ongoing cellular activity.¹² The aldosterone-sensing distal nephron plays a vital role in this process, showing a reduced response to aldosterone, which diminishes potassium excretion.¹³ Furthermore, physiological dehydration stimulates angiotensin II production, enhancing electroneutral sodium reabsorption through the renal thiazide-sensitive NaCl cotransporter. This mechanism not only conserves sodium but also reduces the tubular lumen's negative electrical potential, thereby inhibiting potassium secretion and maintaining higher serum potassium levels during the neonatal period.¹⁴

After birth, neonates experience a sharp cessation of maternal calcium supply, leading to a decline in serum Ca levels.¹⁵ However, in the first 2–3 days of life, plasma parathyroid hormone (PTH) levels remain low with minimal responsiveness to hypocalcemia, resulting in transient neonatal hypocalcemia.^{16,17} This pattern was observed in our subjects, with initial low adjusted serum total Ca levels that

normalized as feeding increased and PTH activity began, keeping FECa persistently low. Meanwhile, serum Pi levels gradually increase after birth due to increased phosphorus intake, endogenous mobilization, enhanced renal reabsorption, and a subdued PTH response.^{17–19} This corresponds with our findings of increasing TmP/GFR from Day 1 to Day 5.²⁰ During this early period, the gastrointestinal response to 1,25-dihydroxyvitamin D and the renal response to fibroblast growth factor 23 are immature, minimally affecting Ca and Pi homeostasis.¹⁸ The dietary regimen, complying with the WHO guidelines and excluding additional fortifiers or supplements, did not alter the typical body weight changes in our cohort. Although not extensively adjusted for these parameters, the serum Ca and Pi changes reflect typical trends in standard care, offering a reference range for clinicians.

Despite its breadth, our study is limited by its relatively small, predominantly male cohort and the absence of specific feeding volume data. Nevertheless, the feeding approach – adhering to international standards for both breastmilk and formula – mirrors real-world caregiving settings. Future research should expand the sample size, ensure gender diversity, and detail feeding practices to enhance insights into neonatal electrolyte management.

CONCLUSION

Our study has successfully established reference levels for electrolytes in the urine of healthy newborns. Recognizing the postnatal dynamic changes in electrolyte levels, our findings provide crucial insights into the alterations of urine electrolyte levels in healthy-term newborns. This knowledge significantly advances our current understanding and offers substantial benefits for improving clinical practice in newborn care.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, JJ Ding, upon reasonable request.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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