

Fellow's Column: The Blood Urea Nitrogen/Creatinine Ratio in Preterm Infants with Patent Ductus Arteriosus

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Summary:

Elevated blood urea nitrogen (BUN) and serum creatinine (SCr) ratio has been associated with acute kidney injury (AKI). Preterm infants with patent ductus arteriosus (PDA) have unique fluid-electrolyte balance in the first few days of life and are at risk of pre-renal azotemia and AKI. We studied trends in BUN/SCr ratios within the first two weeks of life of four preterm infants (one 23-week GA, two 24-week GA, and one 25-week GA) with PDA. We found a significant correlation between the BUN and SCr level, $r = 0.59$, $p = <0.001$. The BUN/SCr ratio was noted to be higher in the first week of life, which trended down in the second week. We concluded that BUN/SCr ratios could be used as an adjunct in monitoring patients' kidney function within the first two weeks of life in the extremely preterm infant with PDA. Further studies are needed to look at the normal BUN/SCr ratio ranges in extremely premature infants.

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Introduction:

Patent ductus arteriosus (PDA) is common in preterm infants. The incidence is inversely proportional to the gestational age (GA). PDA causes significant steal in the blood flow (BF) during diastole, resulting in decreased BF in the descending aorta, compromising renal perfusion. This reduction in glomerular blood flow decreases the excretion of urea and creatinine, resulting in increased blood urea nitrogen (BUN) and serum creatinine (SCr). In addition, medications used to treat PDA inhibit prostaglandin, resulting in decreased urine output and further elevation of the BUN/Cr ratio. (1) High BUN/SCr ratio has been associated with acute kidney injury (AKI) in critically ill children using nephrotoxic medications. (2) Preterm infants with PDA have unique fluid-electrolyte balance profiles within the first few days of life. They are at risk of pre-renal azotemia and AKI. We studied BUN/SCr ratios trends within the first 2 weeks of life of four preterm infants (one 23-week GA, two 24-week GA, and one 25-week GA) with PDA.

Case 1:

The patient was a Preterm infant with a gestational age of 23 2/7 weeks. The mother did not receive any steroids. Apgar scores were 0, 6, and 7 at 1, 5, and 10 minutes, respectively. The infant was intubated in the delivery room. One umbilical venous and two

arterial catheters were inserted on admission to the NICU. The infant was placed on a high-frequency oscillator ventilator and was started on total parental nutrition. Serum electrolytes were monitored daily while on TPN. An echocardiogram was obtained on day 3 of life.

Case 2:

The patient was a preterm infant with a gestational age of 25 3/7 weeks. The pregnancy was complicated by no prenatal care, uncontrolled hypertension, and vaginal bleeding. Apgar scores were 3, 6, and 7 at 1, 5, and 10 minutes, respectively. The infant was intubated in the delivery room. One umbilical venous and two arterial catheters were inserted on admission to the NICU. The infant was placed on a high-frequency oscillator ventilator and was started on total parental nutrition. Serum electrolytes were monitored daily while on TPN. An echocardiogram was obtained on day 3 of life.

Case 3:

The patient was a Preterm infant with a gestational age of 24 2/7 weeks. The pregnancy was complicated by premature prolonged rupture of membranes. Apgar scores were 2 and 7, at 1 and 5 minutes, respectively. The infant was intubated in the delivery room. On admission to the NICU, one umbilical venous and two arterial catheters were inserted. The infant was placed on a high-frequency oscillator ventilator and was started on total parental nutrition. Serum electrolytes were monitored daily while on TPN. An echocardiogram was obtained on day 3 of life.

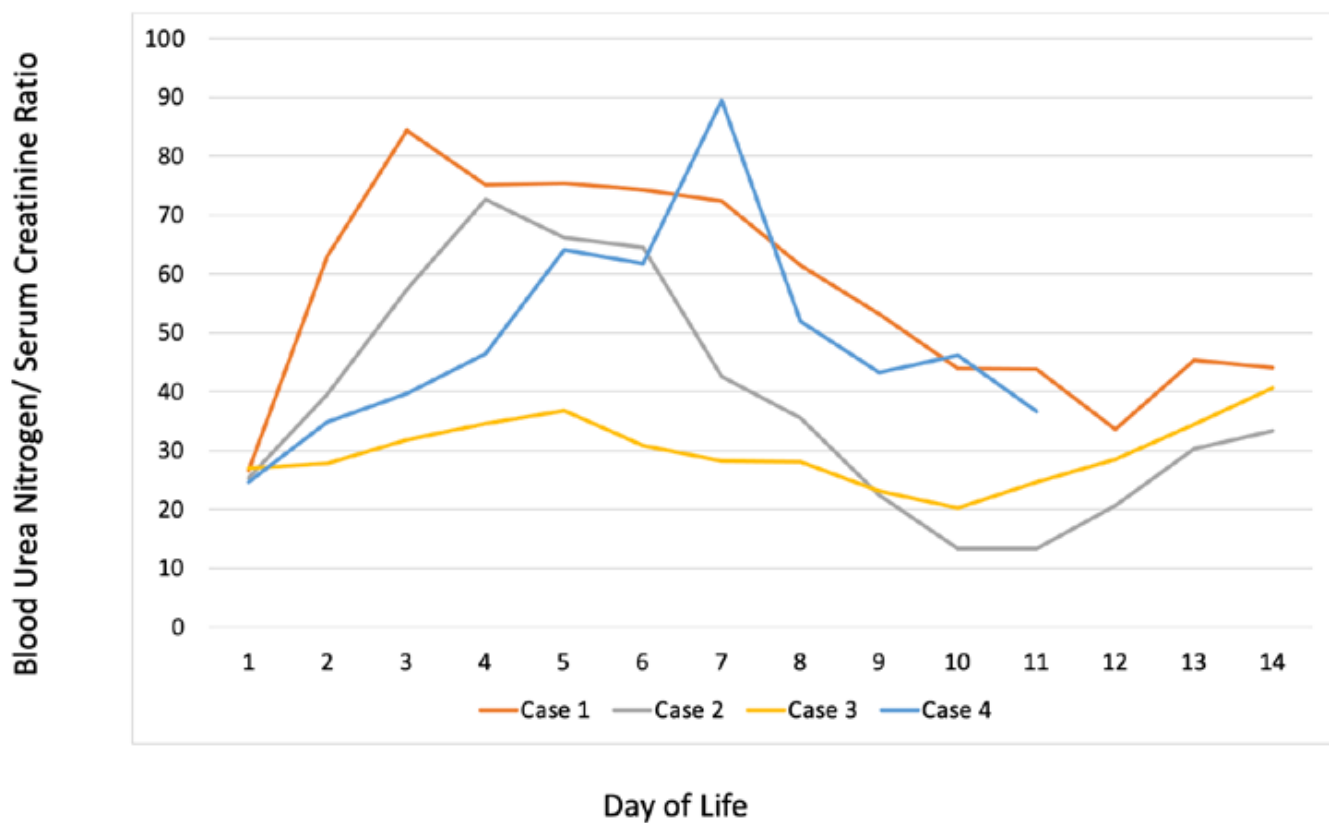
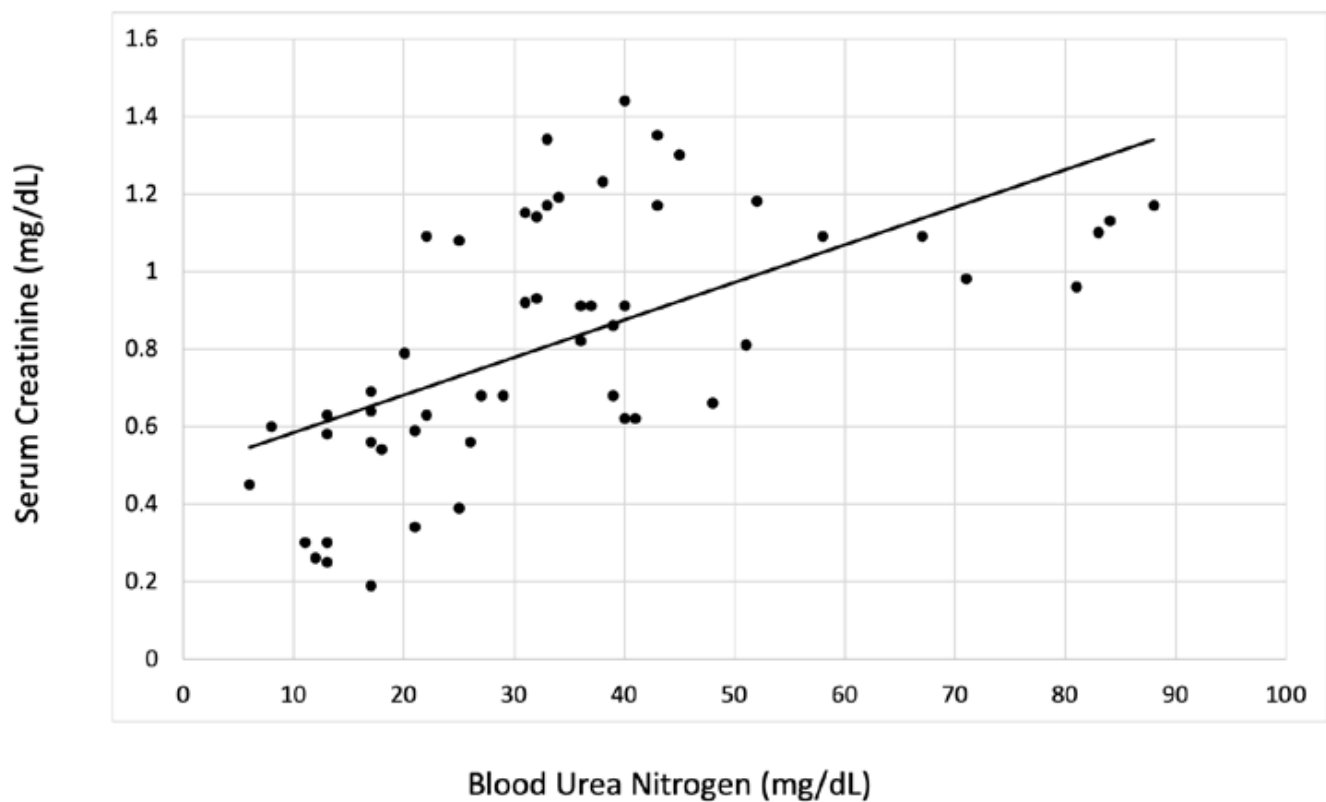
Case 4:

The patient was a preterm infant with a gestational age of 24 5/7 weeks. The pregnancy was complicated by concern for placental abruption. The infant was intubated in the delivery room. On admission to the NICU, one umbilical venous and two arterial catheters were inserted. The infant was placed on a high-frequency oscillator ventilator and was started on total parental nutrition. Serum electrolytes were monitored daily while on TPN. An echocardiogram was obtained on day 3 of life.

"We found a significant correlation between the BUN and SCr levels, $r = 0.59$, $p < 0.001$ (Figure 1). The BUN/SCr ratios were higher in the first week of life and trended down within the second week (Figure 2)."

Methods/Results:

The laboratory details were collected from the electronic chart. The BUN/SCr ratio (mg/mg) is represented in the metric system (the link <http://www.scymed.com/en/smnxps/pspg152.htm> could be used to convert to the SI system). A total of 53 samples were reviewed; 14 consecutive days were trended for cases 1, 2, and 3, while 11 days were trended for case 4 (Table 1). We found a significant correlation between the BUN and SCr levels, $r = 0.59$, $p < 0.001$ (Figure 1). The BUN/SCr ratios were higher in the first week of life and trended down within the second week (Figure 2).



Legend to Figures: Figure 1: Correlation Between Blood Urea Nitrogen and Serum Creatinine Levels. Figure 2: Blood Urea Nitrogen / Creatinine Ratio Trends in Preterm Infants within the First Two Weeks of Life

“All infants studied had a PDA during the first two weeks of life, which was managed conservatively. In these infants, we observed high BUN/ SCr ratios within the first week of life, which trended down within the second week.”

Discussion:

All infants studied had a PDA during the first two weeks of life, which was managed conservatively. In these infants, we observed high BUN/ SCr ratios within the first week of life, which trended down within the second week. The combined mean BUN was 34 ± 22 mg/dL, and the combined mean SCr was 0.82 ± 0.32 mg/dL, which were higher than reports from previous studies regarding the same gestational age (GA). (3,4) Zhang and Zeng (3) reported a mean SCr of $69.7 \mu\text{mol/L}$ (0.79 mg/dL) within the first 24 hours of life in healthy control groups, whereas infants born with a history of perinatal events had a mean SCr of $85 \mu\text{mol/L}$ (0.96 mg/dL) within the first 24 hours of life. The mean BUN levels reported were 5.26 mmol/L (14.73 mg/dL) and 5 mmol/L (14 mg/dL), respectively. Similarly, Cuzzolin et al. (4) studied SCr values within the first 28 days of life in preterm infants. In their study cohort, group A consisted of infants born between 22-25 weeks GA. The SCr values within the first two weeks of life among group A were $78.7 \pm 19.4 \mu\text{mol/L}$ (0.89 ± 0.22 mg/dl) on day 1 and 84.9 ± 31.8 micro $\mu\text{mol/L}$ (0.96 ± 0.36 mg/dl) at day 14, which were comparable to the values observed in our four cases.

“ In our pursuit of a conservative approach, we noted improvement in patients’ renal function over time. This ultimately concluded that observed AKI among preterm infants with PDA might reflect renal immaturity rather than pathologic conditions.”

Based on the mean SCr levels of 0.82 mg/dL, none of the preterm infants would have qualified as having AKI based on the pRIFLE (pediatrics -risk, injury, failure, loss, end-stage) and KDIGO (Kidney Disease: Improving Global Outcomes) definition. (5,6) Gallo et al. (7) reported 27 % of AKI among preterm infants was associated with medical treatment for a hemodynamically significant PDA. Seo et al. (8) also noted a high prevalence of AKI without any adverse outcome among preterm infants whose PDAs were managed conservatively. In our pursuit of a conservative approach, we noted improvement in patients’ renal function over time. This ultimately concluded that observed AKI among preterm infants with PDA might reflect renal immaturity rather than pathologic conditions.

In conclusion, BUN/SCr ratio could be used as an adjunct in monitoring kidney function in the extremely preterm infant with PDA within the first two weeks of life. Further studies are needed to define normal BUN/SCr ratio ranges in extremely premature infants.

Table 1: BUN, SCr and BUN/SCr Ratios Among the Preterm Infants

Case 1

Day	BUN	Creatinine	BUN: Creatinine Ratio
1	17	0.64	26.56
2	51	0.81	62.96
3	81	0.96	84.37
4	88	1.17	75.21
5	83	1.1	75.45
6	84	1.13	74.33
7	71	0.98	72.44
8	67	1.09	61.46
9	58	1.09	53.21
10	40	0.91	43.95
11	36	0.82	43.90
12	31	0.92	33.69
13	39	0.86	45.34
14	52	1.18	44.06

Case 2

Day	BUN	Creatinine	BUN SCr Ratio
1	20	0.79	25.31
2	36	0.91	39.56
3	39	0.68	57.35
4	48	0.66	72.77
5	41	0.62	66.12
6	40	0.62	64.51
7	29	0.68	42.64
8	21	0.59	35.59
9	13	0.58	22.41
10	8	0.6	13.33
11	6	0.45	13.33
12	13	0.63	20.63
13	17	0.56	30.35
14	18	0.54	33.33

Case 3

Day	BUN	Creatinine	BUN SCr Ratio
1	31	1.15	26.95
2	40	1.44	27.77
3	43	1.35	31.85
4	45	1.3	34.61
5	43	1.17	36.75
6	38	1.23	30.89
7	33	1.17	28.20
8	32	1.14	28.07
9	25	1.08	23.14
10	22	1.09	20.18
11	33	1.34	24.62
12	34	1.19	28.57
13	32	0.93	34.40
14	37	0.91	40.65

Case 4

Day	BUN	Creatinine	BUN SCr ratio
1	17	0.69	24.63
2	22	0.63	34.92
3	27	0.68	39.70
4	26	0.56	46.42
5	25	0.39	64.10
6	21	0.34	61.76
7	17	0.19	89.47
8	13	0.25	52
9	13	0.3	43.33
10	12	0.26	46.15
11	11	0.3	36.66

BUN: Blood Urea Nitrogen, mg/dL

Creatinine, mg/dL

SCr: Serum Creatinine

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