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Outcome and risk factors associated with perirenal subcapsular fluid collections in extremely preterm infants with acute kidney injury

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Abstract

Objectives To investigate the incidence of, clinical outcome of, and risk factors for perirenal subcapsular fluid collections in extremely preterm infants with acute kidney injury (AKI).

Methods Extremely preterm infants with AKI who underwent renal ultrasonography (US) during neonatal intensive care unit stay were classified into two groups according to the presence of a perirenal subcapsular fluid collection at US. Clinical outcome was compared, and relevant data were analysed, including demographics and comorbidities of the infants, as well as maternal demographics. The risk factor of perirenal subcapsular fluid in infants with AKI was tested with univariate and multivariate logistic regression analysis.

Results A perirenal subcapsular fluid collection was detected in 7 of 56 (13%) extremely preterm infants with AKI (male to female ratio, 5:2; mean gestational age, 23.6 ± 1.4 weeks) and it appeared bilaterally in most cases (86%, 6/7). The mortality rate was higher in infants with perirenal subcapsular fluid collections and AKI (86%, 6/7) than with AKI alone (35%, 17/49) ($p = 0.015$). Infants with perirenal subcapsular fluid collections and AKI were of a lower gestational age, and more frequently showed episodes of intestinal perforation, use of medication having potential to impair renal function, and a history of maternal chorioamnionitis ($p < 0.05$). Multivariate analysis revealed a significantly higher risk for perirenal subcapsular fluid collections in extremely preterm infants who were treated with anti-fungal agents (OR, 13.2 (95% CI: 1.5, 119.4); $p = 0.022$).

Conclusions Although a perirenal subcapsular fluid collection occurred in a small proportion of extremely preterm infants with AKI, its presence was associated with high mortality. The use of anti-fungal agents was an independent risk factor for a perirenal subcapsular fluid collection.

Key Points

- *A perirenal subcapsular fluid collection may occur in association with acute kidney injury.*
- *A perirenal subcapsular fluid collection has a grave prognostic implication in extremely preterm infants.*
- *The use of anti-fungal agent might be associated with perirenal subscapular fluid collections in critically ill extremely preterm infants with AKI.*

Keywords Acute kidney injury · Transudate · Infant, extremely premature · Ultrasonography

Abbreviations

AKI	Acute kidney injury
CRRT	Continuous renal replacement therapy
IVH	Intraventricular haemorrhage
NEC	Necrotizing enterocolitis
NICU	Neonatal intensive care units
PD	Peritoneal dialysis
US	Ultrasonography

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Introduction

Acute kidney injury (AKI), previously referred to as acute renal failure, is common in critically ill neonates hospitalised in neonatal intensive care units (NICU), particularly in infants

with preterm birth and growth restriction [1–4]. Multiple factors likely contribute to the development of AKI, including perinatal foetal distress and multiple postnatal exposures such as hypotension, sepsis, and administration of potentially nephrotoxic medications [1, 2, 4, 5]. Neonatal AKI is associated with higher mortality and longer hospital stays, as well as an increased risk for chronic kidney disease, which occurs to a greater degree in preterm infants in the context of incomplete nephrogenesis [1, 3].

A perirenal subcapsular fluid collection is rarely encountered in clinical practice and results from various clinical conditions including urinary obstruction, trauma, renal tumour, and, parenchymal kidney disease with or without AKI [6]. Distension of the renal capsule due to massive fluid accumulation may compress the kidney parenchyma, resulting in deterioration of renal function [7, 8]. The pathophysiology of this fluid is unclear, and its aetiology has been ascribed to veno-occlusive state and sodium retention [9–11]. To date, eight publications involving a total of 62 cases (mean age, 36.7 years; range, 16–71 years, based on available data) have appeared in the PubMed online database regarding perirenal subcapsular fluid collections related to renal parenchymal disease or AKI [8–15]. To our knowledge, no reports have yet been published regarding the finding of perirenal subcapsular fluid collections related to AKI in preterm infants using renal ultrasonography (US).

For this reason, this study investigated the incidence of, clinical outcome of, and risk factors for perirenal subcapsular fluid collections in extremely preterm infants with AKI.

Materials and methods

Study population

This retrospective study was approved by our institutional review board. The need to obtain informed consent was waived, and patient information was anonymised prior to analysis. From January 2012 to June 2017, we retrospectively reviewed all infants born prematurely before 28 completed weeks of gestation and admitted to the NICU in our tertiary academic centre. Infants who died within the first few days of life were excluded because there were often insufficient numbers of serum creatinine measurements to classify these infants as having AKI [3]. AKI was defined as a decrease in urine output less than 0.5 mg/kg/h after the first 24 h of life and/or a rise in serum creatinine level more than 1.5 mg/dL that developed 48–72 h after birth [5, 16]. A perirenal subcapsular fluid collection was defined as fluid superficial to the renal parenchyma without rupture into the retroperitoneum and it consisted of a perirenal fluid collection, partly or completely surrounding the kidney with indentations of the renal parenchyma [10]. The case group consisted of infants diagnosed with AKI and having a perirenal subcapsular fluid collection at US. The control group consisted of infants diagnosed with AKI but with no perirenal subcapsular fluid collection.

Clinical data collection

The medical records of eligible infants were reviewed to collect demographic data, clinical characteristics, and outcomes. The infants' demographic data included gender, gestational age at birth, birth weight, and Apgar scores at 1 and 5 min. When present, the following comorbid conditions were documented: sepsis, necrotizing enterocolitis (NEC, modified Bell's stage IIA–IIIA) [17], intestinal perforation, patent ductus arteriosus, high-grade intraventricular haemorrhage (IVH), and respiratory distress syndrome. Exposures to the following potentially nephrotoxic drugs were also documented: antibiotics (aminoglycosides (gentamicin and amikacin), vancomycin, and cefotaxime), inotropics (dopamine, dobutamine, and epinephrine), and anti-fungal agents (amphotericin B and ambisome). Maternal clinical data were also collected, including maternal infection, premature rupture of membranes, the use of prenatal steroid, and pregnancy-induced hypertension. Neonatal sepsis was divided into two subtypes depending on whether the onset of symptoms was before 72 h of life (early-onset) or later (later-onset) [18]. High-grade intraventricular haemorrhage (IVH) was defined as grades 3 and 4 IVH of Papile classification [19]. Survival up to 36 weeks of corrected gestational age or hospital discharge before 36 weeks of corrected gestational age was regarded as survival.

US examinations

All infants underwent detailed renal US examinations, which were conducted by one of two paediatric radiologists (S.Y.Y. and T.Y.J. with 10 and 4 years of experience in paediatric US, respectively, at the time each first evaluated the study subjects). In our NICU, renal US examinations were performed when infants had oliguria or increased serum creatinine levels, and follow-up US studies were done when infants had persistent or aggravated renal insufficiency. The US system consisted of LOGIQ E9 instrument (GE Healthcare) or Acuson S2000 instrument (Siemens Healthineers), each equipped with high-frequency linear-array transducers (9 MHz or 6–15 MHz). Fasting was not required before the US examinations, and no infant was sedated. The same two radiologists (S.Y.Y. and T.Y.J., now with 15 and 9 years of paediatric imaging interpretation experience) retrospectively reviewed all images in consensus. Although the reviewers knew that all the infants had been referred with a chief complaint of oliguria or increased creatinine level, they were unaware of any other clinical information.

The parameters assessed by US included renal cortical echogenicity, length of the kidney, and the presence of hydronephrosis. The renal cortical echogenicity was compared with that of the liver on grey scale images. A perirenal subcapsular fluid collection was assessed with an emphasis on the internal characteristics, pattern (focal vs. diffuse), and thickness of a fluid collection. Regarding internal characteristics, simple fluid was defined as anechoic, whereas complicated fluid was defined as fluid containing low-level internal echoes with or without strands. Focal pattern was defined as a fluid collection partly surrounding the kidney, and diffuse pattern was defined as a fluid collection completely surrounding the kidney in a circumferential appearance. The thickness of the fluid was measured at the greatest dimension of the fluid collection. Measurements of a fluid collection in three orthogonal planes were also made to calculate the volume of a fluid collection. For spherical- or ellipsoidal-shaped fluid collection, the ellipsoid formula (0.52 × length × width × height) was applied. When the fluid collection was crescent-shaped, the volume of fluid collection was calculated by subtracting the smaller ellipsoid from the larger one.

Renal Doppler examination included colour Doppler imaging of main renal arteries and main renal veins, and spectral Doppler with resistive index (RI) measurements of the main renal arteries, intrarenal arcuate arteries, and main renal veins.

Statistical analysis

Differences in continuous variables were presented as means and standard deviations (SD) and were analysed with the Student *t* test or Wilcoxon rank sum test as appropriate. Differences in categorical variables were tested with Fisher's exact test and expressed as counts and percentages. Univariate and multivariate logistic regression analyses were used to analyse the demographic and clinical parameters as possible risk factors for the presence of a perirenal subcapsular fluid collection in these extremely preterm infants with AKI. The variables with *p* values less than 0.05 in the univariate analyses were entered into the final multivariate model to identify significant risk factors for a perirenal subcapsular fluid collection after adjustment for other risk factors. Results were provided as odd ratios (OR) with 95% confidence intervals (CI). All *p* values lower than 0.05 were considered statistically significant. All statistical analyses were performed with software (SAS, version 9.4 (SAS Institute) and R 3.4.0 (http://www.R-project.org/)).

Results

Incidence and clinical outcome

A total of 311 extremely preterm infants were admitted to the NICU during the study period, and two infants died within the first 3 days of life. Of the 309 infants, 60 (19%) had AKI during their NICU stay. Infants ($n = 4$) who did not undergo renal US at the time of AKI were excluded. Ultimately, the data for 56 extremely preterm infants (male to female ratio, 32:24; mean gestational age at birth, 24.6 ± 1.4 weeks; mean birth weight, 673.8 g ± 164.8) were analysed. On the renal US images for assessing AKI, 7 of 56 infants (13%) had perirenal subcapsular fluid collections. A perirenal subcapsular fluid collection was detected at 28 (24–29) days of life (median and interquartile range) and at 7 days (5–11) (median and interquartile range) after the diagnosis of AKI. The remaining 49 infants who had no perirenal subcapsular fluid collection comprised the control group. Demographic data and clinical characteristics are listed in Table 1 for both groups. Infants with perirenal subcapsular fluid collections and AKI were born at a significantly earlier mean gestational age (23.6 ± 1.4 weeks vs. 24.7 ± 1.3 weeks) ($p = 0.046$).

Mortality was higher in infants with perirenal subcapsular fluid collections and AKI (86%, 6/7) than with AKI alone (35%, 17/49) ($p = 0.015$). All six deceased infants with perirenal subcapsular fluid collections had AKI at the time of death. Among the infants with AKI alone who died, 76% (13/17) had AKI at the time of death, and 24% (4/17) had a resolution of their AKI at the time of their death. Among the deceased infants, mean survival time after AKI diagnosis was 16.0 ± 3.8 days (range, 9–20 days) in case group and 21.0 ± 15.5 days (range, 1–59 days) in control group ($p = 0.523$). The mean survival time after detection of a perirenal subcapsular fluid collection at US was 9.0 ± 4.9 days (range, 2–15 days). The single surviving infant was discharged from the NICU 112 days after sonographic detection of perirenal subcapsular fluid.

No infants with perirenal subcapsular fluid collections and AKI showed hypertension.

Risk factors

The risk factors for the appearance of a perirenal subcapsular fluid collection in preterm infants with AKI are summarised in Table 2. Univariate analysis showed intestinal perforation (OR 8.4, 95% CI 1.4–51.7; $p = 0.021$) and anti-fungal agents (OR 17.6, 95% CI 2.2–138.3; $p = 0.006$) were associated with the increased risk of a perirenal subcapsular fluid collection. Multivariate analysis showed a significantly higher risk of a perirenal subcapsular fluid collection in extremely preterm infants treated with anti-fungal agents (OR 13.2, 95% CI 1.5–119.4; $p = 0.022$).

Management

Of seven infants with perirenal subcapsular fluid collections and AKI, two (29%) were managed with percutaneous fluid drainage by placement of draining catheters in case 3 (Fig. 1) and by fluid aspiration under US guidance in case 4 (Fig. 2).

Table 1 Baseline clinical characteristics of study patients

Variables	Total ($n = 56$)	Case group ($n = 7$)	Control group ($n = 49$)	p value
Infants' demographic data				
Male	32/56 (57%)	5/7 (71%)	27/49 (55%)	0.686[b]
Gestational age at birth (weeks)[a]	24.6 ± 1.4	23.6 ± 1.5	24.7 ± 1.3	0.046[c]
Birth weight (g)[a]	673.8 ± 164.8	630 ± 157.9	675.9 ± 166.4	0.458[c]
Small for gestational age	7/56 (13%)	0/7 (0%)	7/49 (14%)	0.578[b]
Apgar score at 1 min[a]	4.5 ± 1.6	5.1 ± 1.6	4.5 ± 1.6	0.296[c]
Apgar score at 5 min[a]	6.9 ± 1.5	7.4 ± 1.5	6.8 ± 1.5	0.304[c]
Postnatal age of AKI diagnosis (days)[a]	17.5 ± 9.3	21.7 ± 11.5	16.9 ± 8.9	0.198[c]
Mortality	23/56 (41%)	6/7 (86%)	17/49 (35%)	0.015[b]
Comorbidities				
Sepsis	33/56 (59%)	4/7 (57%)	29/49 (59%)	1.000[b]
Early-onset sepsis	20/56 (36%)	3/7 (43%)	17/49 (35%)	0.691[b]
Late-onset sepsis	13/56 (23%)	1/7 (14%)	12/49 (24%)	1.000[b]
Necrotizing enterocolitis	16/56 (29%)	4/7 (57%)	12/49 (24%)	0.094[b]
Intestinal perforation	7/56 (13%)	3/7 (43%)	4/49 (8%)	0.035[b]
Patent ductus arteriosus	53/56 (95%)	7/7 (100%)	46/49 (94%)	1.000[b]
High-grade IVH	7/56 (13%)	2/7 (29%)	5/49 (10%)	0.208[b]
Respiratory distress syndrome	54/56 (96%)	7/7 (100%)	47/49 (96%)	1.000[b]
Administered drugs	43/56 (77%)	7/7 (100%)	36/49 (73%)	0.182[b]
Antibiotics	39/56 (70%)	7/7 (100%)	32/49 (65%)	0.088[b]
Inotropics	22/56 (39%)	5/7 (71%)	17/49 (35%)	0.099[b]
Anti-fungal agents	5/56 (9%)	3/7 (43%)	2/49 (4%)	0.011[b]
Maternal exposures				
Chorioamnionitis	27/56 (48%)	6/7 (86%)	21/49 (43%)	0.048[b]
Premature rupture of membranes	23/56 (41%)	2/7 (29%)	21/49 (43%)	0.688[b]
Prenatal steroid	50/56 (89%)	7/7 (100%)	43/49 (88%)	1.000[b]
Pregnancy-induced hypertension	6/56 (10%)	0/7 (0%)	6/49 (12%)	1.000[b]

Unless otherwise indicated, data are numbers of patients with percentages in parentheses

AKI acute kidney injury, *IVH* intraventricular haemorrhage

[a] Data are means ± standard deviation

[b] The p values are from Fisher's exact test

[c] The p values are from the Student t test or Wilcoxon rank sum test as appropriate

Fluid analysis was performed in only one infant (case 3), and the fluid was clear and compatible with transudation (pH, 8.0; fluid/serum protein ratio, 0.2; glucose, 50 mg/dL; creatinine, 1.4 mg/dL; gram stain and culture results, negative). Another three infants (43%) were treated with peritoneal dialysis (PD) and continuous renal replacement therapy (CRRT). In control group, 5 of 49 (10%) infants with AKI alone were treated with PD ($n = 4$, 8%) or CRRT ($n = 1$, 2%).

Table 2 Risk factor analysis for perirenal subcapsular fluid collections in extremely preterm infants with acute kidney injury

Variables	Univariate analysis[a] Odds ratio	p value	Multivariate analysis[a] Odds ratio	p value
Gestational age at birth (weeks)	0.911 (0.828–1.002)	0.055		
Birth weight (g)	0.998 (0.993–1.003)	0.451		
Sepsis	0.920 (0.185–4.562)	0.918		
Necrotizing enterocolitis	4.111 (0.803–21.035)	0.090		
Intestinal perforation	8.438 (1.377–51.713)	0.021	5.984 (0.767–46.674)	0.088
High-grade IVH	3.520 (0.536–23.133)	0.190		
Administered drugs				
Antibiotics	NA			
Inotropics	4.706 (0.824–26.871)	0.081		
Anti-fungal agents	17.625 (2.246–138.277)	0.006	13.202 (1.460–119.398)	0.022
Chorioamnionitis	7.997 (0.894–71.542)	0.063		
Premature rupture of membranes	0.533 (0.094–3.023)	0.478		

Multivariate analysis was performed by using the variables showing $p < 0.05$ at univariate analysis

NA not applicable, *IVH* intraventricular haemorrhage

[a] Numbers in parentheses are 95% confidence intervals

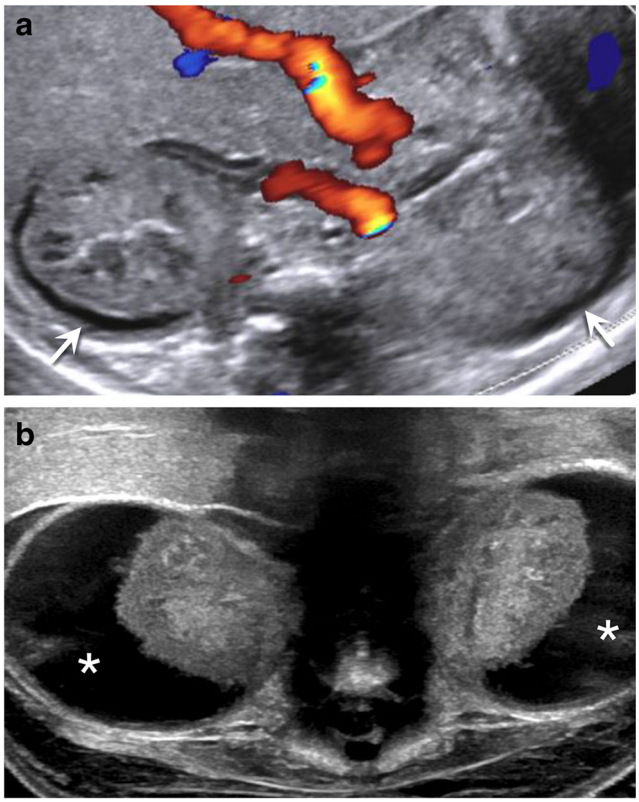

Fig. 1 Case 3: Extremely preterm female infant (born at gestational age of 22 weeks and 6 days) with perirenal subcapsular fluid collections and acute kidney injury; this infant deceased at corrected gestational age of 28 weeks and 5 days. **a** US image at 35 days of life shows thin layer of perirenal subcapsular fluid (arrows), surrounding the kidney in a diffuse pattern. **b** Follow-up US image after 5 days shows increased amount of fluid (asterisks), ranging from 1.1 to 1.3 cm in thickness with indentations of the renal parenchyma. Percutaneous draining catheters were placed, and negligible amounts of fluid were drained for 5 days (not shown here)

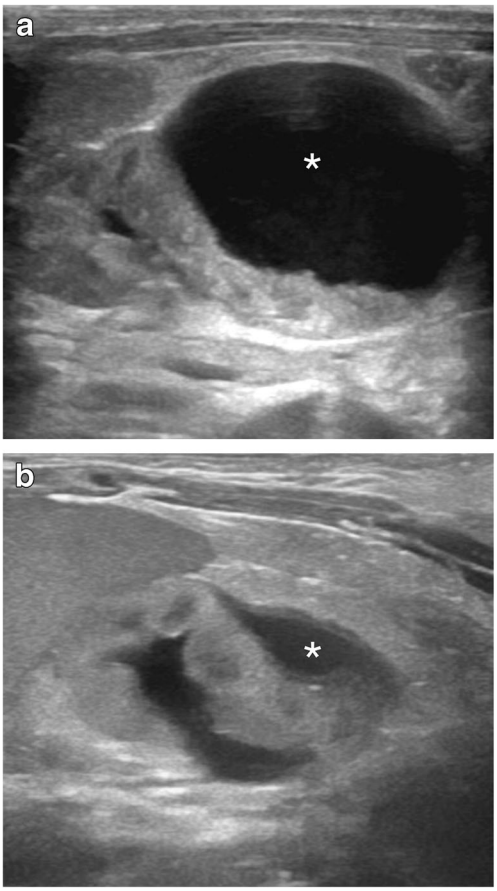

Fig. 2 Case 4: Extremely preterm male infant (born at gestational age of 24 weeks and 1 day) with perirenal subcapsular fluid collections and acute kidney injury; this infant survived. **a** US image at 57 days of life shows a perirenal subcapsular fluid collection (asterisk), measuring 1.9 cm in thickness, in a focal pattern. **b** US image immediate after fluid aspiration under US guidance shows decrease in amount of fluid collection (asterisk), measuring 0.4 cm in thickness. Although re-accumulation of fluid, measuring 1.0 cm in thickness, occurred on 4 days after fluid aspiration, perirenal subcapsular fluid collections disappeared gradually and the kidneys appeared to be shrunken on 7 months later (not shown here)

US findings

During their NICU stay, the mean number of renal US studies per patient after AKI diagnosis was 4.1 ± 2.8 (range, 2–9) in case group and 3.5 ± 2.4 (range, 1–14) in control group. Kidneys showed increased cortical echogenicity in 71% (5/7) of case group and in 67% (33/49) of control group ($p = 1.000$). The mean length of the kidneys was 3.1 ± 0.4 cm in the case group and 3.2 ± 0.4 cm in the control group ($p = 0.660$). No infant showed hydronephrosis in either group.

Seven infants in the case group had 13 subcapsular fluid collections (Table 3): six (86%) were bilateral and one (14%) was unilateral. All 13 perirenal subcapsular fluid collections were simple fluid. The perirenal subcapsular fluid collection usually had a diffuse pattern (69%, 9/13). The thickness of the fluid collection ranged from 0.3 to 1.9 cm with a mean of 1.1 cm. The sonographically determined volume of the perirenal subcapsular fluid collection averaged 3.2 mL (range, 0.1–6.4 mL). Spectral Doppler US examinations were performed in five of seven infants (71%). Among them, the average RI values of intrarenal arteries were 0.9 (range, 0.8–1), and the average velocities were 47.4 cm/s (range, 5.4–66.9 cm/s) in the main renal arteries and 29.8 cm/s (range, 26.1–37.2 cm/s) in the intrarenal arteries. There were no cases of renal vein thrombosis. Subsequent follow-up US examinations were performed in six infants with a mean interval time of 5.5 ± 2.2 days. Overall, 82% (9/11) of the subcapsular fluid collections showed an increase in amount and 18% (2/11) of the subcapsular fluid collections remained unchanged at the follow-up US.

Discussion

Our study revealed an incidence of AKI in extremely preterm infants of 19% (60/309) during their NICU stay, which is similar to the values reported in previous studies for very

Table 3 Clinical characteristics and US findings in extremely preterm infants with perirenal subcapsular fluid collections and AKI

No.	Sex	GA at birth (weeks)	cGA at AKI (weeks)[a]	cGA at fluid (weeks)[b]	Fluid pattern (right–left)	Fluid thickness, cm/Vol (mL) (right–left)	Outcome	Management
1	M	21 + 0	22 + 1	23 + 0	Diffuse - diffuse	0.5/1.4–0.4/0.7	Deceased	(−)
2	M	22 + 5	26 + 3	27 + 0	Focal - (−)	1.2/2.7–(−)	Deceased	(−)
3	F	22 + 6	26 + 2	27 + 5	Diffuse - diffuse	1.3/3.3–1.1/3.5	Deceased	PCD
4	M	24 + 1	30 + 2	32 + 1	Focal - focal	1.7/4.5–1.9/5.0	Survived	Fluid aspiration
5	F	24 + 5	28 + 0	29 + 1	Focal - focal	0.3/0.1–1.0/1.9	Deceased	CRRT
6	M	24 + 6	27 + 0	29 + 0	Diffuse - diffuse	1.4/6.4–0.6/2.4	Deceased	CRRT
7	M	25 + 0	26 + 6	28 + 3	Diffuse - diffuse	1.0/3.5–1.3/6.2	Deceased	PD

US ultrasound, *AKI* acute kidney injury, *GA* gestational age, *cGA* corrected gestational age, *Vol* volume, *PCD* percutaneous catheter drainage, *CRRT* continuous renal replacement therapy, *PD* peritoneal dialysis

[a] Corrected gestational age (weeks) at the time of AKI diagnosis

[b] Corrected gestational age (weeks) at the time of perirenal subcapsular fluid seen at US

low birth weight infants (18–40%) [1, 3]. Preterm infants with growth restriction are more vulnerable to AKI than are term-born infants, due to their functionally immature kidneys and significantly delayed adaptation of the renal system to the extra-uterine environment [20]. The most common type (more than 80%) of AKI in preterm infants is due to pre-renal causes including hypovolemia, hypotension, and nephrotoxic medications. Intrinsic renal and post-renal AKI rarely occur, with an incidence of 11% and 3%, respectively [21].

The subcapsular space is a potential area beneath the renal capsule where various fluids can accumulate and result in compression of renal parenchyma [10]. The causes of a perirenal subcapsular fluid collection include urinary obstruction, trauma, renal tumour, and renal vascular disease [6]. In addition, a perirenal subcapsular fluid collection has been described as a rare complication of renal parenchymal disease with or without AKI [8–13, 15]. Orofino et al [11] first identified the unilateral subcapsular fluid collection in an adult patient with membranous nephropathy and renal vein thrombosis. They ascribed its aetiology to veno-occlusive disease with thrombosis in the main or small intrarenal veins and alteration of the intravascular hydrostatic capillary and oncotic pressure. Conversely, Haddad et al [10] reported two cases of subcapsular fluid collections without intrarenal vein thrombosis based on histopathological analysis of the renal biopsy specimens. They attributed the development of a perirenal subcapsular fluid collection to a sodium retention state which could have led to fluid extravasation and a resulting transudate accumulation. Similar to previous studies, the biochemical analysis of the fluid in our patient (case 3) revealed transudation.

Yassa et al [9] described perirenal subcapsular fluid collections in adult patients with AKI and termed it 'kidney sweat', a new sign of AKI found in 14% (47/330) of their patients with AKI, which is comparable to the percentage found in our study (13%, 7/56). However, Haddad et al [10] reported the presence of perirenal subcapsular fluid collections in nine adolescent and adult patients with renal parenchymal disease without AKI, and they concluded that the presence of AKI was not mandatory for the development of a perirenal subcapsular fluid collection. In our opinion, the presence of a perirenal subcapsular fluid collection may reflect renal impairment, regardless of the severity of kidney disease, and it may further exacerbate renal damage by compressing renal parenchyma, creating a vicious cycle.

To our knowledge, ours is the first study evaluating the clinical significance of and risk factors for perirenal subcapsular fluid collections in extremely preterm infants. Contrary to previous reports in older age [8, 10–15], extremely preterm infants with perirenal subcapsular fluid collections and AKI showed high mortality rate (86%, 6/7) in our study. Extremely preterm infants with perirenal subcapsular fluid collections and AKI were more likely to be of an earlier gestational age and have intestinal perforation and a history of maternal chorioamnionitis, in addition to being exposed to anti-fungal agents, when compared to the infants with AKI alone. Based on our results, we can infer that perirenal subcapsular fluid collection may develop in critically ill, extremely preterm infants in association with AKI. The bilaterality (86%, 6/7) and transudative nature of the perirenal subcapsular fluid may support this inference. Although multivariate analysis identified the use of nephrotoxic anti-fungal agents as a significant risk factor for perirenal subcapsular fluid in our study, the critical condition of the infants who required an empirical anti-fungal therapy may also contribute to the development of a perirenal subcapsular fluid collection. According to the literature, AKI per se was associated with poor outcomes in preterm infants. Koralkar et al [1] evaluated 229 very low birth weight infants and found that mortality was significantly higher in infants with AKI than in those without AKI (42% vs. 5%, $p < 0.001$). Carmody et al [3] evaluated similar findings in a large retrospective study of 455 very low birth weight infants, where AKI was independently associated with increased mortality (OR 4.0, 95% CI 1.4–11.5) and long hospital stays (11.7 days, 95% CI 5.1–18.4). In addition to this knowledge, we found that the presence of the perirenal subcapsular fluid may be an indicator of poorer outcome in preterm infants with AKI.

A massive subcapsular fluid collection associated with renal parenchymal disease and/or AKI was treated successfully

by percutaneous or surgical drainage in adolescent and adult patients [8–10, 12–15]. Similarly, we have performed percutaneous fluid drainage in two neonates, and one of them survived. However, further investigation in a larger sample size is needed before recommending percutaneous fluid drainage as a therapeutic modality in preterm infants with perirenal subcapsular fluid collections and AKI.

The main limitations of the present study were the potential bias of inclusion and exclusion criteria due to the retrospective design and the small study population of the case group. The incidence of AKI in extremely preterm infants might be underestimated because the most critical infants (who did not survive beyond the few first postnatal days) were excluded. Lastly, the lack of biochemical analysis of the stagnant fluid may limit our capability to verify the mechanism of a perirenal subcapsular fluid collection.

In conclusion, a perirenal subcapsular fluid, in the setting of extreme prematurity and AKI, was associated with a high mortality rate. Critically ill extremely preterm infants with AKI who were treated with anti-fungal agents have a risk of a perirenal subcapsular fluid collection. Further research is needed to identify the mechanism, clinical implications, and management of perirenal subcapsular fluid collections in preterm infants with AKI.

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Compliance with ethical standards

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Informed consent Written informed consent was waived by the Institutional Review Board.

Ethical approval Institutional Review Board approval was obtained.

Methodology
- Retrospective
- Observational study
- Performed at one institution

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