Scientific Foundation SPIROSKI, Skopje, Republic of Macedonia
Open Access Macedonian Journal of Medical Sciences. 2020 Dec 15; 8(B):1256-1261.
https://doi.org/10.3889/oamjms.2020.5005
eISSN: 1857-9655
Category: *B - Clinical Sciences*
Section: *Gynecology and Obstetrics*

Preterm Small Gestational Age Newborns: Impact on Renal Size and Function

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Edited by: Ksenija Bogoeva-Kostovska
Citation: El-Sharkawy M, Badawy M, Abd El Dayem SM, Badr A, Salama H, Inji Galal El-Dine Abdou El-Sherbini IGE-DA, Abd El-Momeim S. Preterm Small Gestational Age Newborns: Impact on Renal Size and Function. Open Access Maced J Med Sci. 2020 Dec 15; 8(B):1256-1261. https://doi.org/10.3889/oamjms.2020.5005
Keywords: Cystatin C; Estimation of glomerular filtration rate; Premature small gestational age; Renal size and function
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Received: 26-May-2020
Revised: 10-Nov-2020
Accepted: 29-Nov-2020

Funding: This research did not receive any financial support
Competing Interest: The authors have declared that no competing interest exists

Abstract

OBJECTIVE: The objective of the study was to evaluate the size and function of the kidney in high-risk premature small gestational age (PT/SGA) newborns. Furthermore, estimation of the glomerular filtration rate (GFR) was done by comparing Cystatin C-based method with the creatinine –based method in those preterm newborns.

PATIENTS AND METHODS: The study included 20 PT/SGA and controls (20 preterm appropriate for gestational age [PT/AGA] and 20 full-term [FT] newborns). Serum creatinine, blood urea nitrogen, and cystatin C were determined on days 3 and 7 of the study for all newborn infants. GFR was assessed by cystatin C-based method and creatinine-based method. Evaluation of the renal size by ultrasound was done on day 7 of neonatal life.

RESULTS: A significant difference was found in the length and transverse diameter of both kidneys, comparing PT/SGA group with PT/AGA and FT group. Cystatin C on day 3 of PT/SGA group had a significant difference than PT/AGA and FT group. Estimation of GFR (eGFR) calculated by filler Zappitelli, Grubb, Larsson, and Dorum formulae of PT/SGA group had a significant difference comparing with PT/AGA and FT group on days 3 and 7.

CONCLUSION: PT/SGA newborns have reduced renal size and immature renal function. Cystatin C is a marker for renal function superior to creatinine as it is not affected by body mass index, gestational age, and birth weight. Cystatin C-based eGFR is more accurate and more sensitive to minor changes in GFR than creatinine-based equation.

Introduction

Infants with small gestational age (SGA) are liable to renal problems, increase albumin/creatinine ratio, decrease in glomerular filtration rate (GFR), hypertension, and lastly end-stage renal failure [1].

Impaired nephrogenesis leads to fetal growth restriction, adult hypertension, and decrease in renal functional. Hyperfiltration resulted from a reduced number of glomeruli, leads to hypertension, sclerosis of the glomeruli, and impairment of renal function [2].

Preterm with appropriate gestational age (premature [PT]/AGA) is at risk of impairment of renal growth in the 2nd year of life (by ultrasound), decreased in GFR at school-age, hypertension in young adulthood, and later on glomerular sclerosis [3].

Plasma cystatin C is a low-molecular-weight protein, functions as an extracellular inhibitor of cysteine protease, and can be used as a marker of GFR [4].

We assessed renal size and function in premature SGA (PT/SGA) newborns who are at high risk for renal insufficiency in the neonatal period and later on in life. Furthermore, we compared creatinine-based method with cystatin C-based method in the estimation of GFR among PT/SGA newborns.

Patients and Methods

It is a prospective, randomized, and case-control study conducted in the neonatal intensive care unit, Abu El Rish Hospital, Cairo University. Approval of the ethical committee of National Research Center was taken and written informed consent of parents of the neonates.

The study was carried out on three groups: First group included 20 preterm SGA (gestational age <37 weeks) newborns with postnatal age <28 days and birth weight or birth crown-heel length less than 10th percentile for gestational age. The 2nd group included 20 preterm AGA (gestational age <37 weeks) newborns were enrolled in this study as a control group. They were matched for sex, gestational age, mode of

delivery, and 5 min Apgar score and birth weight or birth crown-heel length was between the 10th and 90th percentile for gestational age. The 3rd group included 20 full-term (FT) newborns, they were also enrolled as a control group. They were matched for sex, gestational age (≥37 weeks), mode of delivery, and 5 min Apgar score. The 3rd group was divided as 3 neonates FT small for gestational age and the remaining 17 neonates as FT AGA. On the other hand, any newborn infant in the three groups had congenital anomalies especially renal were excluded from the study.

We recorded any postnatal complications/ outcomes during hospitalization in the form of abnormality in blood pressure (hypertension requiring antihypertensive therapy or hypotension requiring inotropic), nephrotoxic drugs (e.g., vancomycin or aminoglycosides), blood, and/or blood products transfusion.

Clinical examination for neonates

Assessment of gestational age was done through analysis of maternal dates, and modified Ballard score. Complete examination including cardiac, chest, abdominal, and neurological. Weight, body length (BL), and head circumference measures were recorded at birth; weight was recorded also at days 3 and 7 of life. Urine output: Diaper weight was recorded on days 3 and 7 of life by digital weighing scale to the nearest 0.005 kg. Diaper weight was divided by (hours of urine collection × weight of the newborns). Blood pressure: Blood pressure was recorded on days 3 and 7 of life measured by the digital apparatus. It was recorded every 3 h and mean reading is calculated and recorded then it was plotted on curve of blood pressure for gestational age.

$$\text{Ponderal index} = \frac{\text{Defined as weight (grams)}}{\text{Length (cm)}^3}$$

and it was calculated for those newborns identified as SGA.

Laboratory investigations to assess renal functions

Blood sample (0.5 ml) was collected, separated by centrifugation at 4000 cycles for 8 min, and stored at −25°C in Eppendorf tubes.

Serum creatinine (S. Cr), blood urea nitrogen (BUN), and cystatin C were determined on days 3 and 7 of the study for all newborns included in the study. They were performed on Hitachi 911 analyzer (Boehringer, Germany) using Rouchi/Hitachi kits.

Estimation of eGFR (eGFR)

1. GFR based on creatinine level was estimated using Schwartz formula
   - Schwartz: eGFR= 0.413×BL(cm)/Cr(mg/dl) or 36.5 × BL(cm)/ Cr(μmol/l) (5)
2. GFR-based cystatin C was estimating using:
   - Filler (5): $eGFR=91.62\times (CysC)^{-1.123}$
   - Zappitelli(5): $eGFR=75.94\times(CysC)^{-1.170}$
   - Grubb(5): $eGFR= 83.93 \times (CysC)^{-1.676}$
   - Larsson(5): $eGFR= 77.24 \times (CysC)^{-1.2623}$
3. In addition, we used combined formulas based on CysC, Cr levels, and BUN:
   - Schwartz CKiDs (5)

$9.1 \times (HT/S.\ Cr)^{0.516} \times (1.8/Cyst\ C)^{0.294} \times (30/BUN)^{0.169} \times (1.099)^{Male} \times (HT/1.4)^{0.188}$

Abdominal sonography

It was performed to assess renal size on day 7 of neonatal life. A 5–10 MHz linear array transducer was used in the trapezoid mode (z.one, Zonare Medical System, Calif., USA). Newborns were scanned in prone and lateral positions, usually 1 h after taking a feed so that they were soothed. To avoid inter-observer variability, all sonography was performed by one pediatrician with experience in pediatric sonography.

Statistical analysis

PASW statistical software package (V. 18.0, IBM Corp., USA, 2010) was used for data analysis. Data were expressed as mean ± SD for quantitative measures and both number and percentage for categorized data. One-way ANOVA and Kruskal–Wallis test were used for comparison of more than two groups followed by *post hoc* test for detection of significance. Chi-square was done for comparison of qualitative data.

Results

There was a highly significant difference between the three groups as regards weight, length, and head circumferences on days 1, 3, and 7 of life ($p < 0.01$). On the other hand, there were no significant differences between the three groups regarding sex, Apgar score at 1 and 5 min ($p > 0.05$) (data not presented).

A significant difference was found in the length and transverse diameter of the right and left kidney, comparing PT/SGA group with PT/AGA group and FT group ($p < 0.05$) (Table 1).

A highly significant difference was found as regards cystatin C on day 3 of life when PT/SGA group was compared with PT/AGA Group II and FT group ($p < 0.01$). No significant difference was found between the three groups as regards serum creatinine, serum urea, and serum BUN on day 3 of life ($p < 0.05$) (data not shown).

Table 1: Comparison between Group I (PT/SGA), Group II (PT/AGA), and Group III (FT) as regards renal dimensions

Renal dimensions	PT/SGA (Group I)	PT/AGA (Group II)	FT (Group III)	One-way ANOVA test			*Post hoc* analysis		
	n=20	n=20	n = 20	F	p-value	Sig	P1	P2	P3
Right kidney									
Length (mm)									
Mean ± SD	3.3 ± 0.35	3.81 ± 0.53	3.83 ± 0.87	4.750	0.012	HS	0.011	0.009	0.933
Range	3–4.2	2.3–4.6	2–4.9						
Transverse diameter (mm)									
Mean ± SD	1.55 ± 0.1	1.72 ± 0.22	1.77 ± 0.39	3.849	0.027	HS	0.042	0.011	0.608
Range	1.4–1.7	1.1–2.2	0.9–2.2						
Left kidney									
Length (mm)									
Mean ± SD	3.28 ± 0.32	3.6 ± 0.76	3.92 ± 0.84	4.314	0.018	S	0.044	0.005	0.151
Range	1.4–1.7	1.1–2.2	0.9–2.2						
Transverse diameter (mm)									
Mean ± SD	1.66 ± 0.1	1.84 ± 0.27	1.85 ± 0.36	3.271	0.045	S	0.036	0.027	0.908
Range	1.6–1.8	1.3–2.3	1.1–2.3						

P: Probability, P1: Group I versus Group II, P2: Group I versus Group III, P3: Group II versus Group III, p>0.05, Non-significant. p<0.05, Significant, p<0.01, Highly significant. N: number. Sig: Significance. HS: Highly significant, S: Significant, SD: Standard deviation, SGA: Small for gestational age, AGA: Appropriate for gestational age, PT: Preterm, FT: Full term.

Table 2: Comparison between Group I (PT/SGA), Group II (PT/AGA), and Group III (FT) as regards estimated GFR calculated by various formulae on day 3 of life

Day 3/1st author	PT/SGA (Group I)	PT/AGA (Group II)	FT (Group III)	One-way ANOVA			Post hoc analysis		
				F	P-value	Sig	P1	P2	P3
Schwartz									
Mean ± SD	26.49 ± 11.85	23.06 ± 7.38	24.55 ± 13.74	0.425	0.656	NS	0.361	0.603	0.679
Range	13.66–55.54	11.36–37.61	5.83–51.63						
Filler									
Mean ± SD	98.41 ± 23.59	140.86 ± 27.10	135.56 ± 26.72	16.013	0.000	HS	0.000	0.000	0.519
Range	44.67–138.98	92.35–179.29	96.94–176.41	44.67–138.98					
Zappitelli									
Mean ± SD	81.92 ± 20.32	118.97 ± 23.78	114.31 ± 23.44	15.992	0.000	HS	0.000	0.000	0.516
Range	35.93–117.22	76.57–152.84	80.54–150.28						
Grubb									
Mean ± SD	95.34 ± 31.74	161.58 ± 44.94	152.65 ± 44.19	15.563	0.000	HS	0.000	0.000	0.491
Range	28.73–156.32	84.92–228.6	91.3–223.13						
Larsson									
Mean ± SD	84.05 ± 22.20	125.58 ± 26.93	120.28 ± 26.54	15.940	0.000	HS	0.000	0.000	0.511
Range	34.45–123.39	77.93–164.28	82.3–161.31						
CKID									
Mean ± SD	34.04 ± 7.54	38.12 ± 14.81	36.52 ± 12.23	0.520	0.598	NS	0.315	0.535	0.680
Range	22.47–48.44	23.56–90.82	18.89–58.2						
Dorum									
Mean ± SD	82.00 ± 22.66	125.21 ± 28.25	119.64 ± 27.83	15.892	0.000	HS	0.000	0.000	0.507
Range	31.89–122.73	75.54–166.07	80.02–162.9						

Data are presented as the mean ± SD (in ml/min/1.73 m^2). Sig: Significance, HS: Highly significant, NS: Non-significant. p: probability. P1: Group I versus Group II, P2: Group I versus Group III, P3: Group II versus Group III, p>0.05, Non-significant, p<0.01, Highly significant, SD: Standard deviation, SGA: Small for gestational age, AGA: Appropriate for gestational age, PT: Preterm, FT: Full term, eGFR: Estimated glomerular filtration rate.

Table 3: Comparison between Group I (PT/SGA), Group II (PT/AGA), and Group III (FT) as regards estimated GFR calculated by various formulae on day 7 of life

Day 7	PT/SGA (Group I)	PT/AGA (Group II)	FT (Group III)	One-way ANOVA			*Post hoc* analysis		
				F	p-value	Sig	P1	P2	P3
Schwartz									
Mean ± SD	32.39 ± 19.48	25.31 ± 13.51	22.70 ± 11.56	1.878	0.163	NS	0.162	0.074	0.630
Range	15.54 – 83.63	0.48 – 48.81	7.62 – 41.3						
Filler									
Mean ± SD	114.03 ± 35.12	134.05 ± 20.45	145.17 ± 14.33	8.046	0.001	HS	0.004	0.000	0.163
Range	55.37–163.52	106.72–188.91	124.32–176.41						
Zappitelli									
Mean ± SD	95.58 ± 30.50	112.94 ± 17.98	122.69 ± 12.61	8.008	0.001	HS	0.014	0.000	0.161
Range	44.93–138.86	89.02–161.39	104.37–150.28						
Grubb									
Mean ± SD	120.32 ± 51.84	149.29 ± 34.62	167.39 ± 24.58	7.533	0.001	HS	0.021	0.000	0.144
Range	39.58–199.24	105.38–247.13	132.36–223.13						
CKID									
Mean ± SD	42.39 ± 14.81	38.05 ± 13.45	35.28 ± 11.93	1.226	0.302	NS	0.330	0.132	0.563
Range	28.87–74.84	5.8–65.79	18.98–48.83						
Dorum									
Mean ± SD	98.06 ± 34.98	117.86 ± 21.49	129.38 ± 15.14	7.864	0.001	HS	0.016	0.000	0.155
Range	41.15–148.87	89.69–176.69	107.52–162.9						

Data are presented as the mean ± SD (in ml/min/1.73 m^2). Sig: Significance, HS: Highly significant, NS: Non-significant. p: Probability. P1: Group I versus Group II, P2: Group II versus Group III, P3: Group II versus Group III, p>0.05, Non-significant, p<0.01, Highly significant, SD: Standard deviation, SGA: Small for gestational age, AGA: Appropriate for gestational age, PT: Preterm, FT: Full term, GFR: Glomerular filtration rate.

Table 4: Comparison between preterm small gestational age, preterm appropriate gestational age, and full-term group as regards the presence of renal insufficiency as defined by AKI network

Renal insufficiency as defined by AKI network	PT/SGA		PT/AGA		OR	95% CI	p-value	Sig
	n	**%**	**n**	**%**				
Increase in creatinine 0.3 mg/dL in 48 h (%)	9	45.0	2	10.0	7.364	1.337 - 40.548	0.013	S
Increase in creatinine by 50% in 48 h (%)	8	40.0	2	10.0	6	1.082 - 33.274	0.028	S
	PT/SGA		FT		OR	95% CI	p-value	Sig
	n	%	n	%				
Increase in creatinine 0.3 mg/dL in 48 h (%)	9	45.0	1	5.0	15.545	1.730 - 139.591	0.003	S
Increase in creatinine by 50% in 48 h (%)	8	40.0	0	0.0	-	-	-	-
	PT/AGA		FT		OR	95% CI	p-value	Sig
	n	%	n	%				
Increase in creatinine 0.3 mg/dL in 48 h (%)	2	10.0	1	5.0	2.111	0.176 - 25.349	0.548	NS
Increase in creatinine by 50% in 48 h (%)	2	10.0	0	0.0		-	0.311	NS

OR: Odds ratio, CI: Confidence interval, n: Number. %: Percentage. p: Probability. Sig: Significance. S: Significant, SGA: Small for gestational age, AGA: Appropriate for gestational age. PT: Preterm.

Table 5: Correlation between the mean length of the right kidney with demographic and laboratory parameters among the three groups

V1	V2		PT/SGA (Group I)		PT/AGA (Group II)		FT (Group III)	
			r	p-value	r	p-value	r	p-value
Mean length of right and left kidney (cm)	Weight (day 1)		0.942**	0.000	0.768**	0.000	0.941**	0.000
	Weight (day 3)		0.970**	0.000	0.789**	0.000	0.978**	0.000
	Weight (day 7)		0.796**	0.000	0.797**	0.000	0.958**	0.000
	Length (cm)		0.620**	0.003	0.623**	0.003	0.458*	0.042
	GA (weeks)		0.975**	0.000	0.576**	0.008	0.460**	0.041
	Urine output Cc/kg/h (day 3)		−0.002	0.992	−0.093	0.705	0.051	0.832
	Urine output Cc/kg/h (day 7)		0.371	0.108	−0.194	0.426	−0.476	0.054
	Creatinine (mg/dl) (day 3)		0.239	0.355	−0.032	0.893	0.149	0.532
	Creatinine (mg/dl) (day 7)		0.470	0.056	0.367	0.122	0.118	0.674
	Urea (mg/dl) (day 3)		0.605	0.051	−0.252	0.299	−0.030	0.900
	Urea (mg/dl) (day 7)		0.674	0.058	−0.258	0.301	0.391	0.135
V1	V2		Independent t-test					
Mean length of right and left kidney (cm)	Sex	Females Males	0.684	0.503	−0.127	0.900	1.145	0.267
	Ponderal index	Normal low	−0.199	0.845	0.006	0.995	3.874	0.001
	Blood pressure	High normal	0.985	0.338	0.311	0.756	0.850	0.407

r: Correlation coefficient. p: Probability. p>0.05, Non-significant, p<0.01, Highly significant. p<0.05, significant, SGA: Small for gestational age, AGA: Appropriate for gestational age, PT: Preterm, FT: Full term, GA: Gestational age.

A highly significant difference of eGFR calculated by filler Zappitelli, Grubb, Larsson, and Dorum formulae was reported in PT/SGA group comparing with PT/AGA group and FT group on days 3 and 7 of life (Tables 2 and 3). PT/SGA group had a significantly higher incidence of increase serum creatinine during a 48 h period by 0.3 mg/dl and also a higher incidence of increase in serum creatinine by 50% during a 48 h period when compared with PT/AGA group and FT group. On the other hand, no significant difference was found when P/T AGA was compared with FT group (Table 4).

A significant negative correlation was detected between cystatin C and urine output on day 3 and 7 of life in PT/SGA group ($p < 0.05$). A significant positive correlation was found between serum creatinine on day 3 of life with birth weight in PT/ SGA group. Furthermore, serum creatinine had a significant positive correlation with length, gestational age, and ponderal index in FT group on day 3 of life and with gestational age on day 7 of life ($p < 0.05$) (data not shown).

Table 5 showed a significant positive correlation between mean renal length with gestational age, length, birth weight on days 1, 3, and 7 of life among the three groups ($p < 0.05$) (Table 5).

Discussion

In the view of the baseline demographic characteristic, a highly significant difference was found between the three groups as regards weight, length, and head circumference on days 1, 3, and 7 of life. On the other hand, there was no significant difference between the three groups with respect to sex, mode of delivery, and Apgar score at 1 and 5 min.

In the literature, there are few detailed studies to interpret the renal dimensions in PT/SGA and PT/AGA newborns. However, sonography is one of the most common imaging methods used in routine practice. In our study, when assessing renal size on day 7 of life, we found that PT/ SGA group had significantly lower renal dimensions (length and transverse diameter) on both right and left kidney when compared with PT/AGA group and also when compared with FT group.

Our results are consistent with that of Mishra *et al*. [5], who reported that the mean combined kidney volume (CKV) was significantly lower among SGA newborns compared to that of AGA and LGA subjects, but in this study, both preterm and FT newborns were included in SGA group. Similarly, Marsoosi *et al*. [6] reported that average renal size was significantly smaller in newborns with intrauterine growth retardation (IUGR) compared with AGA ones. Furthermore, this study differs from our study in the inclusion of both preterm and FT newborns in the IUGR group.

In the view of the assessment of renal function in the studied groups, we found that PT/SGA group on day 3 of life had significantly higher serum cystatin C level than the other two groups. However, no significant difference was found between the three groups as regards the serum level of creatinine and urea. Similarly, Giapros *et al*. [7] reported no difference between PT/SGA and PT/AGA (receiving aminoglycoside) as regard serum creatinine on day 3 of life. In the contrary, Aly *et al*. [3] demonstrated that PT/SGA group had significantly higher creatinine levels on day 3 of life when compared with PT/AGA group. The discrepancy between studies may be due to affection of serum creatinine level by many factors as hydration and other co-morbid conditions as sepsis, respiratory distress, and NEC, which are not the same in the two studies.

In contrast to our study, Treiber and Balon [8] demonstrated that SGA newborns have comparable serum cystatin C level with their counterpart AGA newborns. The discrepancy between this study and our study may be due to that in Treiber and Balon study, either preterm or full-term newborns were included in the SGA group.

On the attempt to follow-up renal function on day 7 of life, we found no significant difference between the three groups regarding serum creatinine,

urea, and cystatin C. These findings were similar to Aly *et al*. [3] study who reported that serum creatinine was comparable between PT/SGA and PT/AGA groups on day 7 of life. Moreover, Giapros *et al*. [7] demonstrated that there was no significant difference in serum creatinine level when comparing PT/SGA group with PT/AGA group on day 7 of life.

In the present study, evaluation of GFR in the studied groups, we found that eGFR using cystatin C serum level alone was significantly lower in PT/SGA group when compared with PT/AGA and FT group on both day 3 and 7 of life. However, eGFR using creatinine serum level (Schwartz equation) had no consistent difference between the three groups on both days 3 and 7 of life. Furthermore, eGFR using both creatinine and cystatin C serum level (CKID equation) had no significant difference between the three groups on days 3 and 7 of life.

Our findings are consistent with that of Marsoosi *et al*. [6], who demonstrated that cystatin C-based GFR was significantly lower in SGA compared to AGA ones, but in their study, both FT and PT newborns were included either in SGA or AGA group. Moreover, Lyengar *et al*. [9] declared that SGA group has significantly lower cystatin C-based GFR than AGA group at birth and at 6 months, but in their study, both PT and FT were included in either SGA or AGA group. Similarly, Bilge *et al*. [10] documented in their retrospective study that eGFR using creatinine serum level showed no significant difference between FT/SGA and FT/AGA group.

In our study, we used the acute kidney injury (AKI) network criteria for newborns, which were proposed to represent acute renal failure across population, locations, and scenarios. We compared the absolute levels of creatinine between groups in addition to determining odds ratios of meeting defined AKI criteria and found that PT/SGA group had significantly lower ratios than either PT/AGA group or FT group. The previous observations were consistent with the previous reports of Aly *et al*. [3], who documented that PT/SGA group had significantly lower ratios of meeting defined AKI criteria than PT/AGA group.

Upon evaluating the correlation between cystatin C and creatinine with other parameters, we found that cystatin C on days 3 and 7 of life was not correlated with gender, length, gestational age, birth weight, and ponderal index in all groups. On the other hand, creatinine on day 3 of life was positively correlated with birth weight in PT/ SGA group, with ponderal index in FT group, and on day 7 of life with gestational age in FT group. These findings reflect that in contrast to creatinine, cystatin C values were not affected by other factors such as body mass and age; therefore, cystatin C is a more reliable marker for renal functions than creatinine. Similarly, Elmas *et al*. [11] demonstrated that cystatin C values did not exhibit any significant difference according to gestational age, birth weight, and gender.

Our results showed no correlation between cystatin C and creatinine on the 3rd and the 7th day of life. This finding is consistent with that of Armangil *et al*. [12], who observed no significant correlation between cystatin C and creatinine on the 3rd day of life. Moreover, Elmas *et al*. [11] demonstrated that there were no significant correlations between cystatin C and creatinine on the 3rd day of life.

Upon evaluating the correlation between renal dimensions with other parameters, we choose to make a correlation between mean renal lengths versus other parameters as no significant difference was seen between right and left renal length. We found a significant positive correlation between mean renal length with neonatal length, neonatal birth weight on 1st, 3rd, and 7th day of life, gestational age, and ponderal index among the three groups.

These findings are consistent with Mishra *et al*. [5], who found that weight for gestational age, birth weight, gestational age, gender, postnatal age, crown heel, and crown-rump length was found to have a significant association with mean CKV, but in their study, both FT and preterm newborns were included in both SGA group and AGA group.

Moreover, in our study, there was no significant correlation between mean renal length and ponderal index being low (i.e., asymmetrical SGA) or normal (i.e., symmetrical SGA) in PT/SGA group, indicating that all PT/SGA newborns have low renal length irrespective of the time of intrauterine insult. Similarly, Mishra *et al*. [5] documented that there was no significant difference in kidney volumes between those with a low ponderal index or asymmetrical IUGR versus those with the appropriate ponderal index or symmetrical IUGR.

We concluded that PT/SGA newborns have reduced renal size and immature renal function as they have significantly higher serum cystatin C and lower cystatin C-based eGFR. PT/SGA is more susceptible for acute renal failure and has lower ratios of meeting defined AKI criteria than PT/AGA group. Cystatin C is a marker for renal function superior to creatinine as it is not affected by body mass index, gestational age, and birth weight. Cystatin C-based eGFR is more accurate and more sensitive to minor changes in GFR than creatinine-based equation.

We recommend that implication of new strategies in the clinical management of PT/SGA newborns as renal dosing of drugs based on cystatin C clearance or empiric avoidance of nephrotoxic drugs. The long-term follow-up of PT/SGA is emphasized as they have catch up in GFR despite having small kidney size. Cystatin C-based GFR is an important strength in that it reduces potential confounders introduced by serum creatinine and is a useful tool to predict renal impairment in high-risk newborns. GFR changes daily after birth due to postnatal adaptation of renal functions;

so, several studies are needed to find an accurate assessment of GFR in newborns.

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