International Journal of Science and Research Methodology (IJSRM)
Volume 27, Issue 10, October 2024 ijsrm.humanjournals.com ISSN: 2454-2008

Evolution of Creatinine and Serum Cystatin C in Premature: A Cohort Study

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Received: 2024-10-05 Revised: 2024-10-14 Accepted: 2024-10-19

ABSTRACT

Background: Premature birth is a potential risk factor for kidney disease and the diagnosis of this disease among newborns, although challenging, can be performed early in childhood. **Purpose:** The purpose of this study was evaluate the evolution of creatinine and serum cystatin C among children born with gestational age ≤34 weeks. **Methods:** Cohort study with assessment of renal function at birth and follow-up: < 3, 4-6 7-24, 25-36 months. Clinical and anthropometric characteristics were considered. Estimates of glomerular filtration rate (GFR) were obtained using equations. **Results:** Of the 105 children evaluated at birth, 54.3% were boys, with mean creatinine values of 0.71±0.32 and cystatin values of 1.52±0.32. Regardless of the period of renal function evaluation, the children had elevated serum cystatin C and reduced GFR. Serum creatinine and respective GFR were normal. When comparing the GFR at birth with those at follow-up, a significant difference was found in that estimated by cystatin in children aged 7-24 months. **Conclusion:** Cystatin C may be more reliable than serum creatinine for detection of altered renal function in preterm infants.

KEYWORDS: Preterm. Creatinine. Cystatin C. Glomerular filtration rate. Renal function.

INTRODUCTION

Alterations in renal function among preterm neonates have been increasingly reported[1]. Evidence suggests that renal dysfunction in this population can be identified early in childhood[2]. However, the diagnosis of kidney disease among neonates remains challenging[3].

Globally 10% to 11% of all births are preterm[4] and Brazil is the 9th country in the world in number of preterm live births[5]. Estimates of kidney disease in this population are isolated and range from 12% to 60%[6].

Preterm neonates have a higher risk of nephron deficit, as most nephrons form between 20 and 34-36 weeks of gestation[7]. Some nephrogenesis continues for up to 4-6 weeks after preterm birth, however it is reduced and the resulting glomeruli are not normal[8]. Because of the adverse effect of this process, preterm birth is a potential risk condition for kidney disease and, associated with other factors increase the chance of developing it in adulthood[9].

Thus, early assessment and detection of kidney dysfunction in this vulnerable population is of paramount importance to enable monitoring and development of preventive actions aimed at preserving kidney function throughout life[10], as well as interventions that delay progression to chronic kidney disease[11].

Among the biomarkers of renal function, creatinine is the most widely used[12-14] however, it may not be the most suitable for neonates[13,15] because it has important limitations[16,17]. Despite being considered the gold standard, the use of inulin has been restricted to scientific research given the complexity of its management, especially among children[18]. Serum beta-trace protein has also been touted as reliable for detecting renal function among neonates, but more studies are still needed[19].

Cystatin C, in turn, is seen as a promising and possibly, the most suitable biomarker for assessment of neonatal renal function[20]. However, there is discussion about its prognostic value[21] and its availability is more costly and limited[22].

Although many studies assess renal function among preterm neonates, there is a wide variety of biomarkers used[19,21]. Furthermore, few focus on comparing those considered most clinically useful for clinical practice[12,23] and present divergent results.

Thus, the objective of this study was to evaluate the evolution of serum creatinine and cystatin C among children born with gestational age less than or equal to 34 weeks, in order to contribute to the early diagnosis of kidney disease in this population at risk, enabling timely interventions and better outcomes.

MATERIAL AND METHODS

Design

Prospective cohort study conducted with children born prematurely admitted to the Neonatal Unit of a University Hospital in Northeastern Brazil, from June 1st, 2017, to May 31st, 2018.

Participants/ Sample

Considering the size of the study population (152 eligible preterm neonates), the sample size calculation was obtained adopting prevalence of renal function alteration of 12%[29], sampling error of 4% and confidence level of 95%. Thus, the minimum sample size was 94. Providing for possible losses (10%), the final required sample size was 104 preterm neonates.

Procedures

In the study, neonates with gestational age less than or equal to 34 weeks, admitted to the Neonatal Unit of the University Hospital in question, during the period of interest for this study, were included. Neonates with complex congenital malformations and/or with congenital anomalies of the kidney or urinary tract were not included.

Gestational age was obtained by the records in the pregnant woman's card considering primarily the first trimester ultrasound. When not available, the date of the last menstrual period was used and, when absent, estimates were calculated by the New Ballard Method[25].

In the initial survey, 152 eligible preterm neonates were identified and evaluated in the first stage. Before discharge, 18 died and 29 did not return for evaluation or were not located, leaving a total of 105 preterm neonates in this study.

Data collection occurred at two distinct moments, at birth and at follow-up, when children returned for routine consultations. In the first stage, 3 days after birth, were evaluated the clinical and laboratory conditions related to preterm neonates. Data were obtained through electronic medical records and pediatric consultation, and the following variables of the newborn were considered: sex; gestational age, in weeks; birth weight, in grams, measured by two people using Filizola® electronic scales; length at birth, performed by two people using an acrylic Sanny® stadiometer, graduated in tenths of centimeters, with the child in the supine

position and lower limbs extended, with the head positioned on the fixed portion of the stadiometer and the feet on the movable portion; Apgar score on the fifth minute (ranging from 0 to 10 where values below 7 may reflect perinatal asphyxia); type of delivery (normal or cesarean), need for resuscitation, weight/gestational age adequacy[31] and serum creatinine and cystatin dosages.

After discharge, at follow-up, the preterm neonates returned to the hospital outpatient clinic for routine assessments, when anthropometric and laboratory evaluations were also performed. The variables of interest were height (cm) and serum creatinine (mg/dL) and cystatin C (mg/L) levels. Considering that the children in the study had different ages at follow-up, the sample was divided into four groups for evaluation of renal function: Group 1 - return at 3 months of age; Group 2 - return between 4 and 6 months of age; Group 3 - return between 7 and 24 months of age; and Group 4 - return between 25 and 36 months of age.

The height obtained in this stage was measured in centimeters using a Sanny® acrylic stadiometer, graduated in tenths of centimeters, with the child in the supine position and lower limbs extended, with the head positioned on the fixed portion of the stadiometer and the feet on the movable portion.

For the evaluation of serum creatinine and cystatin dosages, venous or arterial blood samples were collected, using 1 ml of serum, along with the routine collections performed by professionals from the Neonatal Unit in the first stage and by technicians from the clinical analysis laboratory in the follow-up. They were then sent for processing in the Clinical Analysis Laboratory.

The dosage of plasma creatinine was determined by the modified Jaffé colorimetric method, which has as its principle the reaction, in alkaline solution, of creatinine with picric acid. The spectrophotometric reading was measured at a wavelength of 512 nm. Serum cystatin C dosage was obtained from the Nephelometry technique, using immunoturbidimetric assay with reaction intensification by latex particles, internationally standardized[27]. Aggregate is determined turbidimetrically at 700/546 nm. Cystatin C was measured using the Roche/Hitachi cobas c systems, with cobas c 311/501 automated analyzers (PENIA) using the Roche/Hitachi CYSC2 reagent. The frequency of calibrations occurred after reagent lot changes or every 90 days.

The trials were internationally standardized, enabling IDMS (isotope dilution mass spectrometry) screening, as proposed by Anders Grubb and used by most commercial suppliers of cystatin C[28]. For collection and preparation of blood samples, tubes with serum separation gel were used, centrifuged and stored at - 10ºC, and the assay was performed according to the manufacturer's protocol.

The reference values used for serum creatinine and cystatin C followed the definitions of Mazzachi et al.[29] and Erlandsen et al.[30], respectively.

Data Analysis

Statistical analyses were performed using the Stata software, version 14.0. Categorical variables were presented as medians, minimum values, maximum values, interquartile range, frequencies and percentages and numerical variables as median, mean and standard deviation (mean ± SD). The normality of the variables was assessed by the Shapiro-Wilk test.

To evaluate renal function, serum creatinine and cystatin C levels were used in addition to the respective GFR estimates. The Wilcoxon nonparametric test was used to compare the means of the clinical variables at the different times, with a significance level of 5%.

Creatinine-based GFR (mL/min/1.73m^2) was calculated using the Schwartz formula: constant value multiplied by the height in centimeters divided by the serum creatinine value, with 0.33 as the constant value, indicated for preterm infants[31]. For estimation of GFR based on cystatin C (mL/min/1.73m ^{2}) the formula was used: log (GFR) ¼ 1.962 þ [1.123 log (1 /cystatin C)][32].

This study obtained approval from the Research Ethics Committee (CAAE 68451117.0.0000.5086).

RESULTS

A total of 105 preterm neonates were evaluated, most of them male (54.3%), born by cesarean section (58.1%) and who did not need to undergo resuscitation procedure (53.3%). The mean birth weight of the study population was 1,414±352 grams and the mean birth length was 38.7±3.28 cm. The other clinical characteristics of these children are shown in Table 1.

Table 1. Clinical characteristics of children born with gestational age ≤34 weeks. São Luís-MA, 2017-2018.

Variables	n (%)	Md (Min-Max)	Mean ± SD	IQR
Sex				
Female	48 (45,71)			
Male	57 (54,29)			
Type of delivery				
Vaginal	44 (41,90)			
Cesarean section	61 (58,10)			
Resuscitation				
Yes	49 (46,67)			
No	56 (53,33)			
Gestational Age		31,4 (24,3 - 34)	31,2 ± 2,02	2,6
Birth Weight (grams)		1.400 (665 - 2240)	1.414 ± 352	515
Gestational weight/age adequacy				
PIG	29 (27,62)			
AIG	74 (70,48)			
GIG	2 (1,90)			
Apgar 5th minute		8 (3 -10)	8,1 ± 1,17	1
Length at birth (centimeters)		39,4 (30,5 -48,5)	38,7 ± 3,28	4,5
Return Length/Stature (centimeters)		78 (41 - 97)	76,8 ± 12,30	12

SGA - small for gestational age. AGA - appropriate for gestational age. LGA - large for gestational age. Md - median. Min - minimum values. Max - maximum values. SD - standard deviation. IQR - interquartile range.

Table 2 presents data on renal function according to age at return of the children. Mean serum creatinine values were within the normal range and decreased when evaluated at birth and at the different return ages: at 3 months (0.68±0.15 versus 0.40±0.15; p-value=0.0117), between 4 and 6 months (0.62±0.22 versus *0.*30±0.97; p-value=0.0180), between 7 and 24 months of age (0.61±0.21 versus *0.*37±0.33; p-value<0.001) and between 25 and 36 months of age (0.68±0.55 versus *0.*46±0.39; p-value=0.0303).

When the rates of serum cystatin C were evaluated, it was found that children aged between 7 and 24 months showed mean values higher than those considered normal and an increase from the first to the second moment (1.50±0.34 versus 1.71±0.37; p-value=0.0012). Similar behavior was observed in group 4, but without statistical significance (Table 2).

At birth, the estimated creatinine-based GFR was below the cut-off point considered normal and increased at the second time point of assessment, remaining within normal ranges, while the cystatin C-based GFR was shown to be above the reference value among all groups at the first time point of assessment with a reduction in the different return ranges, being significant among children returning between 7 and 24 months of age (62.09±17.81/53.67±16.83; p- value=0.0033) (Table 2).

Table 2. Renal function of children born with gestational age ≤34 weeks, according to age at return. São Luís-MA, 2017-2018.

Groups	Birth			Follow-up			
	Md (Min-Max)	Mean ± SD	Reference value at birth	Md (Min-Max)	Mean ± SD	Reference value by age of return	p-value
Serum Creatinine (mg/dL)							
Group 1	0,69 (0,38-0,88)	0,68 ± 0,15	0,4 -1,4	0,40 (0,15-0,69)	0,40 ± 0,15	0,4 -1,4	0,0117
Group 2	0,59 (0,30-0,97)	0,62 ± 0,22		0,30 (0,20-0,44)	0,30 ± 0,96		0,0180
Group 3	0,59 (0,10-1,34)	0,61 ± 0,21		0,30 (0,10-2,85)	0,37 ± 0,33		<0,001
Group 4	0,55 (0,10-2,82)	0,68 ± 0,55		0,33 (0,10-1,81)	0,46 ± 0,39		0,0303
Serum cystatin (mg/L)							
Group 1	1,84 (1,52-1,97)	1,80 ± 0,14	0,8	1,62 (0,96-2,20)	1,64 ± 0,48	0,8	0,2076
Group 2	1,76 (1,08-2,01)	1,71 ± 0,31		1,64 (1,12-2,44)	1,63 ± 0,47		0,4990
Group 3	1,49 (0,76-2,75)	1,50 ± 0,34		1,74 (0,85-2,53)	1,71 ± 0,37		0,0012
Group 4	1,32 (0,80-2,75)	1,43 ± 0,45		1,69 (0,97-2,35)	1,68 ± 0,37		0,0620
GFR - Serum Creatinine (mL/min/1.73m ^{2})							
Group 1	23,32 (14,27-37,76)	23,90 ± 6,91	47	60,22 (29,78-118,08)	64,05 ± 27,43	60	0,0117
Group 2	27,85 (15,85-53,98)	29,20 ± 12,09		83,37 (52,18-127,10)	83,15 ± 25,44	80	0,0180
Group 3	28,11 (10,97-198,85)	30,70 ± 22,31		107,54 (12,56-377,20)	115,92 ±60,95	100	<0,001
Group 4	28,28 (6,25-149,65)	33,93 ± 29,17		108,73 (14,29-352,60)	113,50 ±70,78	120	0,0004
GFR - Serum Cystatin (mL/min/1.73m ^{2})							
Group 1	46,07 (42,79-57,25)	47,51 ± 4,66	47	55,26 (37,80-95,92)	57,99 ± 20,72	60	0,2076
Group 2	48,56 (41,83-84,03)	52,48 ± 14,47		52,57 (33,65-80,67)	57,31 ± 17,14	80	0,3105
Group 3	58,55 (29,42-124,70)	62,09 ± 17,81		49,20 (32,31-109,97)	53,67 ± 16,83	100	0,0033
Group 4	67,08 (29,42-117,71)	67,46 ± 22,17		50,88 (35,10-94,81)	54,70 ± 16,87	120	0,0793

Group 1- return at 3 months of age. Group 2- return between 4 and 6 months of age. Group 3 - return between 7 and 24 months of age. Group 4 - returns between 25 and 36 months of age. Moment 1 - data obtained at birth. Moment 2 - data obtained at the follow-up. Md - median. Min - minimum values. Max - maximum values. SD - standard deviation.

DISCUSSION

In this study, children with gestational age less than or equal to 34 weeks had elevated cystatin levels at birth and follow-up, when observed the reference values used[29,30]. Mean serum creatinine values were also higher at birth compared to the different return ages, but within the ranges considered normal. When comparing the GFR at birth and follow-up, a significant difference was found in cystatin estimation at the age range of 7 to 24 months of age.

Kandasamy et al.[20] conducted a cohort of 45 neonates under 28 weeks gestational age and followed up to 24 months of life, assessing creatinine and cystatin C levels at three time points (6, 12, and 24 months). In that study, serum creatinine levels showed a negative

correlation with gestational age and the mean cystatin C level was highest in the neonatal period, showing decline, followed by stabilization at 24 months. Another longitudinal study developed by Nakashima et al.[13] with 261 preterm neonates during the first year of life assessed serum creatinine and cystatin C levels in addition to their respective GFR at 4 different times: 6-30 days, 3-5 months, 7-9 months, and 12-14 months after birth. Their results showed a decrease in cystatin C levels throughout the first year of life, while serum creatinine levels decreased rapidly by 3-5 months and their GFR rate increased significantly with increasing age until approximately 1 year after birth.

In both studies, the behavior of serum creatinine was similar to that demonstrated in this research. The levels of cystatin C, however, were divergent, as they remained elevated in both moments evaluated in this study, pointing to changes in renal function and reinforcing the idea that it may be the most appropriate biomarker for evaluation of neonatal renal function.

Higher serum creatinine values at birth are commonly portrayed in neonates[23], due to the influence of maternal levels, regardless of gestational age[3,33], which gradually returns to normal values, as per the results found in this study. The initial increase is considered secondary to its tubular reabsorption by the immature kidney so that, even among relatively healthy preterm, stabilization of creatinine levels can take 3 to 8 weeks[34].

In addition, creatinine is a metabolic product of muscle tissue, and its rate of production can change depending on muscle mass[35]. Thus, although it is widely used to determine GFR[12] and detect changes in renal function, it is possible for creatinine levels to be overestimated[34] and cause delay in the diagnosis of renal change[15].

Compared to serum creatinine, cystatin C does not cross the placental barrier, and therefore there is no correlation between maternal and cord blood cystatin C concentrations[36]. Furthermore, cystatin C has constant production, its levels are not influenced by muscle mass or sex[37], and it can pass freely through the glomerulus[38].

Different studies point to cystatin C as a more sensitive alternative than creatinine for GFR assessment in preterm neonates[20,22,39] however creatinine remains important for estimating GFR[12], congruent to the findings of this study where serum cystatin C and its GFR were able to point to impaired renal function in the 7-24 month age group while creatinine levels were within ranges considered normal.

Through a prospective case-control study, when evaluating 53 preterm neonates and 31 full-term neonates to determine the impact of prematurity on renal development, Kandasamy et al.[2] identified that despite smaller renal volume and evidence of glomerular injury in the early neonatal period, there were no major differences between the GFRs of the two groups. However, these are studies with weaknesses related to relatively small sample size[2,20], heterogeneity of the population[3], and infeasibility of using serum creatinine[20].

The strengths of this study were that it was a cohort study that followed a relevant number of preterm neonates and used cystatin C to estimate GFR, which is indicated as a sensitive biomarker for such[39]. The gold standard for determining GFR estimates was not used and may have been a limitation, however its use is complex in this population[3].

CONCLUSIONS

In this study, the evolution of the biomarkers evaluated revealed that in infants with premature birth, cystatin C may be superior to creatinine in that it detected changes in renal function in preterm neonates and can be used from birth.

These results shed light on the importance of early and long-term monitoring of kidney function in this at-risk population.

Further studies should be conducted to continue the follow-up of this at-risk.

population to assess the prevalence of renal failure at older ages.

ACKNOWLEDGMENTS

We thank the patients and their families for their willingness to participate in this research with the goal of optimizing the care of children at risk of developing kidney disease.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

REFERENCES

1. Heo JS, Lee JM. The Long-Term Effect of Preterm Birth on Renal Function: A Meta-Analysis. International Journal of Environmental Research and Public Health. 2021;18(6):1-17.
2. Kandasamy Y, Rudd D, Smith R, Lumbers ER, Wright IM. Extra uterine development of preterm kidneys. Pediatr Nephrol. 2018;33(6):1007-1012.
3. Filler G, Yasin A, Medeiros M. Methods of assessing renal function. Pediatr Nephrol. 2014;29(2):183-192.
4. Lee AC, Blencowe H, Lawn JE. Small babies, big numbers: global estimates of preterm birth. Lancet Glob Health. 2019;7(1):2-3.
5. Chawanpaiboon S, Vogel JP, Moller AB, Lumbiganon P, Petzold M, Hogan D et al. Global, regional, and national estimates of levels of preterm birth in 2014: a systematic review and modelling analysis. Lancet Glob Health. 2019;7:37-46.
6. Pulju M, Pruitt C, Reid-Adam J, Spear E, Stroustrup A, Green RS et al. Renal insufficiency in children born preterm: examining the role of neonatal acute kidney injury. J Perinatol. 2021;41(6):1432-1440.
7. Moritz KM, Wintour EM, Black MJ, Bertram JF, Caruana G. Factors influencing mammalian kidney development: implications for health in adult life. Adv Anat Embryol Cell Biol. 2008;196:1-78.
8. Black MJ, Sutherland MR, Gubhaju L, Kent AL, Dahlstrom JE, Moore L. When birth comes early: effects on nephrogenesis. Nephrology. 2013;18(3):180-182.
9. Uemura O, Ishikura K, Kaneko T, Hirano D, Hamasaki Y, Ogura M et al. Perinatal factors contributing to chronic kidney disease in a cohort of Japanese children with very low birth weight. Pediatr Nephrol. 2021;36(4):953-960.
10. Crump C, Sundquist J, Winkleby M A, Sundquist K. Preterm birth and risk of chronic kidney disease from childhood into mid-adulthood: national cohort study. BMJ. 2019;365:1346.
11. Starr MC, Hingorani SR. Prematurity and future kidney health: the growing risk of chronic kidney disease. Curr Opin Pediatr. 2018;30(2):228-235.
12. Kastl JT. Renal function in the fetus and neonate - the creatinine enigma. Semin Fetal Neonatal Med. 2017;22(2):83-89.
13. Nakashima T, Inoue H, Fujiyoshi J, Matsumoto N. Longitudinal analysis of serum cystatin C for estimating the glomerular filtration rate in preterm infants. Pediatr Nephrol. 2016;31(6):983-989.
14. Bateman DA, Thomas W, Parravicini E, Polesana E, Locatelli C, Lorenz JM. Serum creatinine concentration in very-low-birth-weight infants from birth to 34-36 wk postmenstrual age. Pediatr Res. 2015;77(5):696-702.
15. Kandasamy Y, Rudd D, Smith R. The relationship between body weight, cystatin C and serum creatinine in neonates. J Neonatal Perinatal Med. 2017;10(4):419-423.
16. Filler G, Guerrero-Kanan R, Alvarez-Elías AC. Assessment of glomerular filtration rate in the neonate: is creatinine the best tool? Curr Opin Pediatr. 2016;28(2):173-179.
17. Finney H, Newman DJ, Thakkar H, Fell JM, Price CP. Reference ranges for plasma cystatin C and creatinine measurements in premature infants, neonates, and older children. Arch Dis Child. 2000;82(1):71-75.
18. Filler G, Yasin A, Medeiros M. Methods of assessing renal function. Pediatr Nephrol. 2014;29(2):183-192.
19. Khosravi N, Asgari M, Khalessi N, Hoseini R, Khosravi N. Serum Beta-Trace Protein for Assessment of Kidney Function in Neonates. Iran J Kidney Dis. 2018;12(1):11-13.
20. Kandasamy Y, Rudd D. Cystatin C: A more reliable biomarker of renal function in young infants? A longitudinal cohort study. Acta Paediatr. 2021;110(4):1341-1345.
21. Unal ET, Ozer EA, Kahramaner Z, Erdemir A, Cosar H, Sutcuoglu S. Value of urinary kidney injury molecule-1 levels in predicting acute kidney injury in very low birth weight preterm infants. J Int Med Res. 2020;48(12):300060520977442.
22. Renganathan A, Warner BB, Tarr PI, Dharnidharka VR. The progression of serum cystatin C concentrations within the first month of life after preterm birth-a worldwide systematic review. Pediatr Nephrol. 2021;36(7):1709-1718.
23. Pasala S, Carmody JB. How to use… serum creatinine, cystatin C and GFR. Arch Dis Child Educ Pract Ed. 2017;102(1):37-43.
24. Nagaraj N, Berwal PK, Srinivas A, Berwal A. A study of acute kidney injury in hospitalized preterm neonates in NICU. J Neonatal Perinatal Med. 2016;9(4):417-421.
25. Ballard JL, Khoury JC, Wedig K, Wang L, Eilers-Walsman BL, Lipp R. New Ballard Score, expanded to include extremely premature infants. J Pediatr. 1991;119(3):417-23.
26. Villar J, Cheikh Ismail L, Victora CG, Ohuma EO, Bertino E, Altman DG, et al. International standards for newborn weight, length, and head circumference by gestational age and sex: the Newborn Cross-Sectional Study of the NTERGROWTH-21st Project. Lancet. 2014;384(9946):857-868.
27. Voskoboev NV, Larson TS, Rule AD, Lieske JC. Analytic and clinical validation of a standardized cystatin C particle enhanced turbidimetric assay (PETIA) to estimate glomerular filtration rate. Clin Chem Lab Med. 2012;50(9):1591-1596.
28. Grubb A, Blirup-Jensen S, Lindström V, Schmidt C, Althaus H, Zegers I; IFCC Working Group on Standardisation of Cystatin C (WG-SCC). First certified reference material for cystatin C in human serum ERM-DA471/IFCC. Clin Chem Lab Med. 2010;48(11):1619-1621.
29. Mazzachi BC, Peake MJ, Ehrhardt V. Reference Range and Method Comparison Studies for Enzymatic and Jaffé Creatinina Assays in Plasma and Serum and Early Morning Urine. Clin. Lab. 2000;46:53-55.
30. Erlandsen EJ, Randers E, Kristensen JH. Evaluation of the Dade Behring N Latex Cystatin C assay on the Dade Behring Nephelometer II System. Scand J Clin Lab Invest. 1999;59(1):1-8.

31. Schwartz GJ, Muñoz A, Schneider MF, Mak RH, Kaskel F, Warady BA, Furth SL. New equations to estimate GFR in children with CKD. J Am Soc Nephrol. 2009;20(3):629-637.
32. Filler G, Lepage N. Should the Schwartz formula for estimation of GFR be replaced by cystatin C formula? Pediatr Nephrol. 2003;18(10):981-985.
33. Bariciak E, Yasin A, Harrold J, Walker M, Lepage N, Filler G. Preliminary reference intervals for cystatin C and beta-trace protein in preterm and term neonates. Clin Biochem. 2011;44(13):1156-1159.
34. Askenazi DJ, Griffin R, McGwin G, Carlo W, Ambalavanan N. Acute kidney injury is independently associated with mortality in very low birthweight infants: a matched case-control analysis. Pediatr Nephrol. 2009;24(5):991-997.
35. Muhari-Stark E, Burckart GJ. Glomerular filtration rate estimation formulas for pediatric and neonatal use. J Pediatr Pharmaco Therap. 2018;23(6):424-431.
36. Abitbol CL, Seeherunvong W, Galarza MG, Katsoufis C, Francoeur D, Defreitas M et al. Neonatal kidney size and function in preterm infants: what is a true estimate of glomerular filtration rate? J Pediatr. 2014;164(5):1026-1031.
37. Bokenkamp A, Domanetzki M, Zinck R, Schumann G, Byrd D, Brodehl J. Cystatin C - a new marker of glomerular filtration rate in children independent of age and height. Pediatrics. 1998;101:875-881.
38. Elmas AT, Tabel Y, Elmas ON. Serum cystatin C predicts acute kidney injury in preterm neonates with respiratory distress syndrome. Pediatr Nephrol. 2013;28(3):477-484.
39. Filler G, Bhayana V, Schott C, Díaz-González de Ferris ME. How should we assess renal function in neonates and infants? Acta Paediatr. 2021;110:773-780.

How to cite this article:
Patrícia Franco Marques et al. Ijsrm.Human, 2024; Vol. 27 (10): 33-40.

Conflict of Interest Statement: All authors have nothing else to disclose.