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Original Article

Assessing Cranio-Caudal Renal Length and Kidney Functions in Newborns: Correlation with Gestational Age, Neonatal Weight, and Length in Indian Newborns

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Abstract
Background: Kidney development in humans initiates around the 5th week of gestation and continues until the 36th week. Premature infants often have fewer nephrons, leading to compensatory hyperfiltration and potential kidney function impairments. Accurate reference ranges for neonatal kidney dimensions are crucial for diagnosing and managing renal disorders. This study evaluates the correlation between renal length, gestational age, neonatal weight, and length in Indian newborns, and examines the relationship between gestational age, serum creatinine, and estimated glomerular filtration rate (eGFR).
Methods: The study was conducted among 150 newborns at Mahatma Gandhi Medical College, Jaipur, India. Inclusion criteria included gestational ages of 30-40 weeks, birth weights above 1.5 kg, and normal maternal serum creatinine levels. Newborns with congenital anomalies of the kidney and urinary tract or those requiring NICU support were excluded. Cord blood samples were collected for serum creatinine analysis, and renal lengths were measured using ultrasonography on the second day of life. eGFR was calculated using the modified Schwartz formula. Data was analysed using correlation and regression analyses.
Results: The study found significant positive correlations between renal length and gestational age (r=0.411), birth weight (r=0.507), and neonatal length (r=0.495). Simple linear regression revealed that gestational age, birth weight followed by neonatal length were the significant Predictor. Multiple regression analysis confirmed birth weight and neonatal length as significant predictors of renal length. Cord blood creatinine levels showed no significant correlation with gestational age, while eGFR correlated positively (r=0.216).
Conclusion: Birth weight and neonatal length are reliable predictors of renal length in Indian neonates, while gestational age correlates better with eGFR than with serum creatinine.
Keywords: Renal length, Gestational age, Neonatal weight, Neonatal length, Serum creatinine, Estimated glomerular filtration rate (eGFR)

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Introduction:
kidney development occurs due to precise interactions between embryonic tissues during intrauterine life. As mentioned by Hoy WE et al[1] kidney development in humans begins as early as the 5th week of gestation and continues up to the 36th week. It has been stated by Srivastav RN et al[2] that the development of a nephron is initiated by the 10th week of gestation, but the most active period of nephron development is between 20 and 36 weeks of intrauterine life. No new nephrons are formed after this period. As noted by Starzec K, Luyckx VA et al[3,4] that children born prematurelyhave decreased establishment of nephrons, which in turn is compensated by hyperfiltration of the remaining nephrons; this kind of compensation in early life may predispose to variable

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degrees of impairments in kidney functions. As per the report of Malshe et al[5] kidney dimensions are influenced by various clinical variables, including gestational age, neonatal weight, and neonatal length. Study conducted by Iyengar A et al[6]have emphasized that the kidney dimensions vary with the level of prematurity. Currently, very few studies have been done to find out the factors which influence the dimensions of kidneys at birth. Similarly, whether different kidney dimensions at birth also affect kidney functions or not, hasn't been studied much till date.

Therefore, assessment of kidney functions that is, serum creatinine and eGFR (estimated glomerular filtration rate) is also quite inconclusive in newborns as kidneys are immature, and there are no reference values of serum creatinine in the neonatal age group. Nor there is data whether kidney dimensions affect kidney functions.

The present study assesses the correlation between newborns' kidney length (most important dimension used to label the diagnosis of normal sized or enlarged or contracted kidney) and gestational age, neonatal weight, and neonatal length. The study also seeks to develop a predictive model for renal length based on these parameters. We also assessed the correlation of serum creatinine and eGFR with gestational age, thus trying to analyse the best correlates of kidney length and kidney functions in newborns.

Hence, the present study was undertaken to find the relationships between gestational age and anthropometric parameters of neonate and kidney length and functions. If such relationship is established through further research with large sample size and multicentric population, then it can be helpful in assessing various kidney disorders like birth asphyxia, congenital anomalies of kidneys, neonatal acute kidney injury, etc which can cause an increase or decrease in the dimensions of kidneys. The correct and reliable reference range of kidney dimensions in such cases will be quite helpful for clinical evaluation and management.

Materials and Method:

This observational study was conducted from August 2022 to February 2024 among 150 newborns delivered either by spontaneous vaginal delivery (SVD) or lower segment caesarean section (LSCS) and admitted for observation in the Postnatal Ward of the Department of Paediatrics at Mahatma Gandhi Medical College, Jaipur, Rajasthan, India. The necessary approval from the Institutional Ethics Committee was taken before conducting the study. Normal infants born between 30 and 40 weeks of gestation with a birth weight above 1.5 kg were enrolled in the study, adhering to specific inclusion and exclusion criteria for infants and their mothers. Included newborns had cord blood serum creatinine levels below 1 mg/dL and were free from any medical conditions requiring NICU (Neonatal Intensive care Unit) support. Their mothers had serum creatinine levels below 1 mg/dL in the third trimester. They did not suffer from any antenatal illnesses such as pregnancy-induced hypertension (PIH), diabetes, hypothyroidism, or hyperthyroidism, regardless of their gravid status. Excluded newborns were those diagnosed with congenital anomalies of the kidney and urinary tract (CAKUT), very low birth weight (VLBW), or large for gestational age (LGA). Newborns, whose mothers had serum creatinine levels above 1 mg/dL or suffered from any antenatal illness were also excluded.

Written consent for recruited newborns was obtained from the mothers for the cord blood sample collection and the ultrasound sonography (USG) assessment of kidney size. The cord blood serum creatinine sample was collected immediately after delivery in the labour room and sent to the laboratory for analysis. eGFR (estimated glomerular filtration rate) was calculated using modified Schwartz formula. Selected newborns were screened by USG in a prone position on an attendant’s lap to measure the kidney length (maximum cranio-caudal dimension) of both the right and left kidneys on the second day of life using a SIEMENS Acuson X300 PE Ultrasonography Machine, Model S.NO. 350778. The neonate's birth weight and crown heel length were measured using a digital neonatal weighing scale and infantometer, respectively.

Statistical Analysis:

All the statistical analysis was performed with SPSS version 29.0.2.0 (20). All the quantitative measurements were expressed as mean with standard deviation or median with interquartile range depending upon the normality condition of the data. The Karl Pearson coefficient of correlations of gestational age, baby birth weight, baby length with cranio-caudal renal length, as well as cord blood creatinine level, estimated glomerular filtration rate (eGFR) with weeks of gestation was calculated. After establishing the correlation, simple and multiple linear regression was performed to generate the equation and to predict cranio-caudal renal length with gestational age, birth weight, and baby length. The scatter plot was used to inspect the correlation structure between the correlated variables visually. All the statistical tests were performed at a 5 % significance level, and a p-value < 0.05 was considered statistically significant.

Results:

The study included 150 newborns with a mean gestational week of 37.32 weeks (SD = 2.63). The babies had a mean weight of 2.56 kg (SD = 0.54) and a mean length of 46.96 cm (SD = 2.93) at birth. The cord blood creatine level of the newborns averaged 0.60 mg/dl (SD = 0.28), while the estimated glomerular filtration rate averaged 35.36 mL/min (SD = 7.86). Additionally, the average renal length of the newborns was 36.75 mm (SD = 3.75), as shown below in **Table 1**.

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Table 1. Baseline Clinical Characteristics of Newborn Babies

Variables	Mean (SD) (n=150)
Gestational week (week)	37.32 (2.63)
Baby Weight (kg)	2.56 (0.54)
Baby Length (cm)	46.96 (2.93)
Cord blood Creatine level (mg/dl)	0.60 (0.28)
Estimated glomerular filtration rate (mL/min)	35.36 (7.86)
Average Renal Length (mm)	36.75 (3.75)

The Cranio-caudal renal length of both kidneys in each patient was measured, resulting in 300 kidney measurements from the 150 patients. Subsequently, the Karl Pearson coefficient of correlation and regression analyses were performed using linear and multiple regression models. This comprehensive approach allowed us to thoroughly investigate the relationships and predictive factors associated with the renal length of a baby. The scatter plots illustrate the linear relationship between gestational age, birth weight, and neonatal length with cranio-caudal renal length, as shown in **Figures 1-3**. The correlation analysis was carried using average of the right and left renal lengths for each patient.This method enabled us to ascertain the strength and direction of relationships of cranio-caudal renal length with gestational age, baby weight, and baby length. The correlation coefficients of renal length with gestational age were 0.411, with baby birth weight was 0.507, and with baby length was 0.495 respectively. Notably, all coefficients exhibited statistical significance at the 0.01 level (2-tailed), indicating a positive relationship. Consequently, it is reasonable to infer that as gestational age, baby weight, and baby length increase, there is a corresponding increase in cranio-caudal kidney length. Moreover, among the variables examined, baby weight demonstrated the strongest correlation with renal length, as illustrated in **Table 2.**

Table 2. Correlation coefficient of Gestational Age, Baby Birth Weight, Baby length with Cranial caudal renal length

Variables	Average renal length (cms)
Gestational Age (week)	($r=0.411^{**}$)
Baby Weight (kg)	($r=0.507^{**}$)
Baby length (cms)	($r=0.495^{**}$)

Correlation is significant at the 0.01 level (2-tailed).

Simple linear regression analysis was done to explore these relationships further to assess the impact of each predictor on craniocaudal renal length and was quantified by coefficients of determination (R^2). The regression coefficient (β) for gestational age obtained was 0.59 (95% CI: 0.37, 0.80), with a significant p-value (<0.001); the coefficient of determination was ($R^2 = 0.17$), meaning thereby that approximately 17% of the variability observed in cranio-caudal renal length can be accounted for by gestational age. Conversely, for baby length, the β was 0.63 (95% CI:0.45, 0.81), with a significant p-value (<0.001), explaining 25% of the variability ($R^2 = 0.25$). While the regression coefficient (β) for baby birth weight was found to be 3.54 (95% CI: 2.56, 4.51), accompanied by a significant p-value (<0.001), and elucidating 26% of the variability ($R^2 = 0.26$). The analysis showed that birth weight exerted the most substantial impact on cranial-caudal renal length, followed closely by baby length. Conversely, gestational age emerged as the least influential predictor in the model, as shown in**Table 3.**

Table 3: Simple Linear Regression for Predicting Cranial Caudal Renal Length using Gestational Age, Baby Weight, and Baby Length

Univariate Regression Equations	Variables	Regression Coefficient (β) with 95% CI	t value	P value
14.89+0.59*Gestational Age	Gestational Age	0.59 (0.37, 0.80)	5.48	<0.001
27.69+3.54*Baby weight	Baby weight	3.54 (2.56, 4.51)	7.16	<0.001
6.99+0.63* Baby length	Baby length	0.63 (0.45, 0.81)	6.93	<0.001

CI: Confidence interval

Later, the multiple regression analysis was carried out to ascertain the impact of birth weight and baby length on cranial-caudal renal length. The gestational age was not included as it is closely associated with the baby's birth weight and length. The analysis revealed that both birth weight and length emerged as significant predictors for cranial-caudal renal length. The coefficient of regression (β) for baby weight was estimated at 2.15 (95% CI: 0.57, 3.73), yielding a statistically significant p-value of 0.008. Similarly, the coefficient of regression (β) for baby length was determined to be 0.32 (95% CI: 0.03, 0.61),

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accompanied by a significant p-value of 0.031, as illustrated in **Table 4**

Table 4: Multiple Liner Regression for Predicting Cranial Caudal Renal Length

Variables	Regression Coefficient (β) with 95% CI	t value	P value
(Constant)	16.18 (5.47, 26.90)	2.98	0.003
Baby weight (kg)	2.15 (0.57, 3.73)	2.69	0.008
Baby length (cms)	0.32 (0.03, 0.61)	2.18	0.031

The correlation of cord blood creatinine level and eGFR with gestational age was examined, as shown in **Table 5**. The correlation coefficient of gestational age with cord blood creatinine level was statistically insignificant. Conversely, the correlation coefficient of gestational age with eGFR was positive (0.216), though, poor but significant at 0.01 level of significance.

Table 5. The correlation coefficient of Cord blood Creatinine level, eGFR, with Gestational Age (week)

Variables	Gestational Age (week)
Cord blood creatinine level (mg/dl)	(r= -0.083)
eGFR	(r= 0.216**)

**Correlation is significant at the 0.01 level (2-tailed)

Figure 1. Scatter Plot showing the correlation of Renal Length with Gestational Week

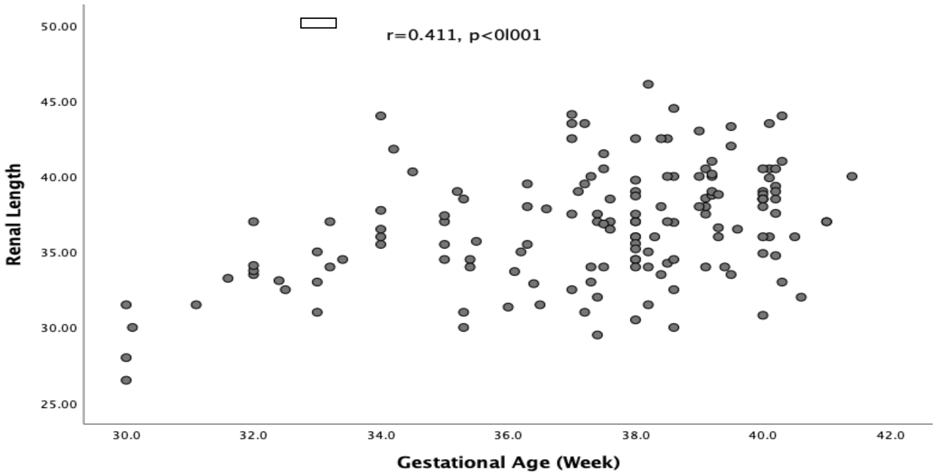

Figure 2. Scatter Plot showing the correlation of Renal Length with Baby Weight

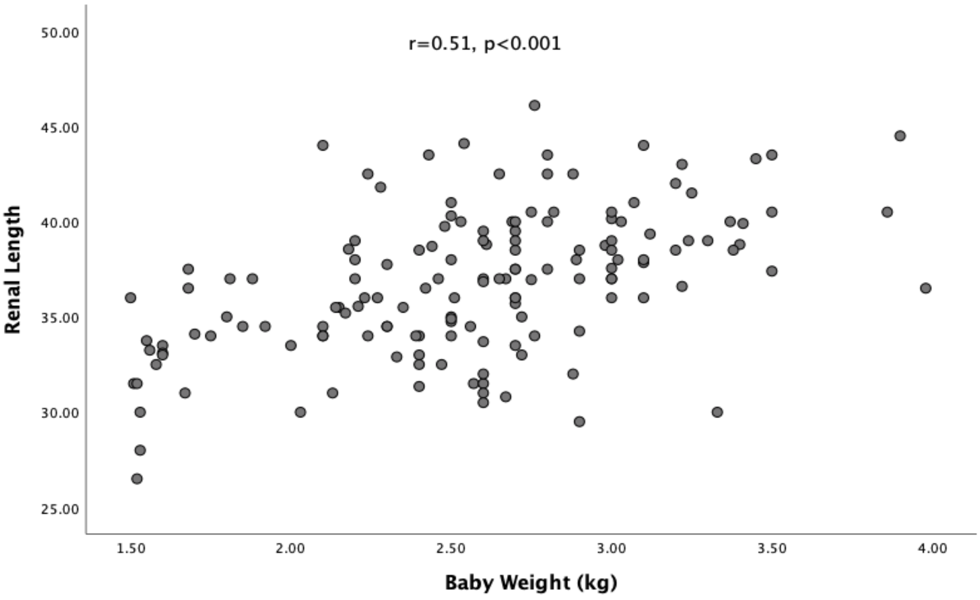

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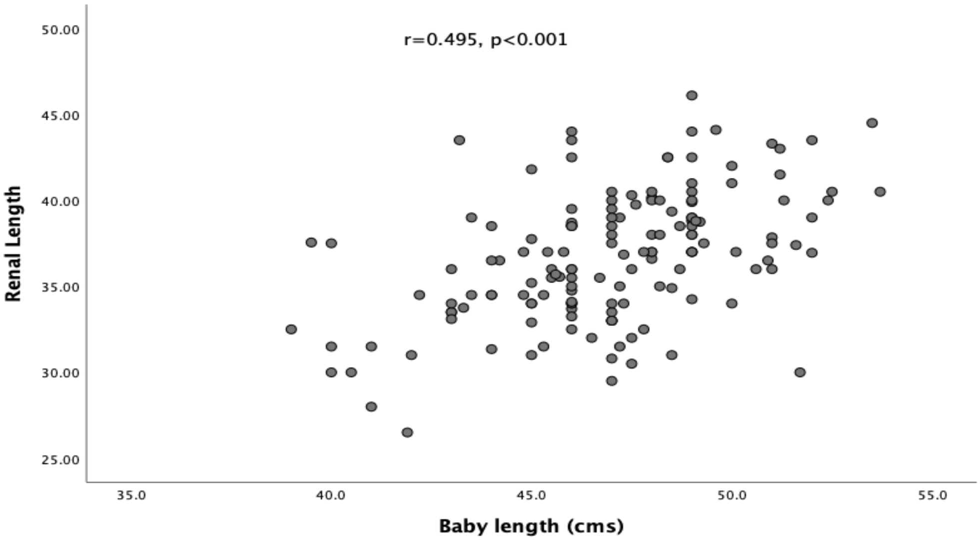
Figure 3. Scatter Plot showing the correlation of Renal Length with Baby Length



Discussion:

Kidneys are vital organs that play an essential role in the survival of an individual. Every organ in the human body has set dimensions based on the individual's age. Any alteration in these dimensions can help in predicting the various abnormalities in the human body. Similarly, in the case of kidney dimensions, the increase or decrease in kidney size can help both in the diagnosis and prognosis of the presenting pathology. This particularly becomes important in the neonatal age when kidney size varies with baby's anthropometric variables. Since there are no established cut-off values of kidney size in the neonatal period, it is difficult to assess and comment upon nephromegaly or contracted kidneys in various acute and chronic medical conditions affecting kidneys in the neonatal period. Similarly, there are no established serum creatinine values as per the neonate's gestational age at the time of birth.

Thus, kidney size and kidney function parameters (cord blood creatinine and eGFR), which play an essential role in managing and monitoring kidney disorders, have no established values in newborns. In the opinion of El Sadek AE et al[7]. Serum creatinine is not a promising biomarker in assessing AKI as the values reflect maternal values initially for the first week of life. But Bhowmick R etal[8] noticed that when eGFR is calculated using modified Schwartz formula then its values correlate well with other standard quantitative GFR estimation techniques like DTPA GFR.

As per the report of LaRosa DA etal[9] conditions like birth asphyxia, neonatal sepsis, and dehydration affect kidneys in significant proportion, these neonates require both kidney size and kidney function monitoring for prolonged periods. Similar condition holds true for various congenital anomalies of Kidney and Urinary Tract (CAKUT)

Therefore, we conducted the present study where we estimated kidney length, cord blood serum creatinine, and eGFR of 150 normal newborns between the gestational age of 30-40 weeks and weighing more than 1.5 kg. We studied the effect of anthropometric parameters of newborns, that is, baby birth weight, baby length, and gestational age, on cranio-caudal renal length and gestational age on cord blood serum creatinine and eGFR in the above-mentioned newborn population.

We observed that each anthropometric parameter, gestational age, baby weight, and baby length, showed a statistically significant correlation with the baby's cranio-caudal renal length. Interestingly, all coefficients exhibited statistical significance at the 0.01 level (2-tailed), indicating a positive relationship with baby birth weight having the highest correlation. The baby's gestational age showed a significant correlation but emerged as a weak predictor of cranio-caudal renal length. On simple regression analysis, baby birth weight has the most significant impact on cranio-caudal renal length with 26% variability, followed closely by baby length in succession that explained 25% variability. A similar outcome was seen in a study performed in Jos, Nigeria, by Ocheke IE et al[10] (2018), where a correlation of baby parameters was seen with renal length. Their study concluded that baby weight had the strongest correlation with renal length. An Indian research study in Pune, Maharashtra, by Malshe et al[5] (2018), found that renal length correlated best with baby weight. On multiple regression, birth weight and length emerged as the strongest and most positive predictors of cranio-caudal kidney length. It was also stated by Giapros V et al [11](2006) that gestational age has positive impact on kidney length, but after 41st week of gestation kidney length becomes independent of gestational age, in both small for gestational age and appropriate for gestational age infants. Simultaneously Obrycki L et al [12](2023) stated that it is important to emphasise that unlike neonates, the

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kidney length in pediatric population correlates very well with age and body surface area.

Simultaneously, we also tried to find a correlation between gestational age with cord blood creatinine and eGFR. It was also reported by Salem et al[13] 2021 and Abitbol et al[14] 2014, that there was a positive and significant correlation of eGFR with gestational age, which means that as gestational age increases, the eGFR also increases. On the contrast, it was observed that cord blood creatinine correlated insignificantly with gestational age. Similar findings were clearly stated by Allegaert K et al [15] (2021) that serum creatinine patterns are complex in neonatal age group and it is important to study role of serum creatinine as AKI biomarker in neonates.Since eGFR is calculated using serum creatinine and the length of the subject, the positive correlation between eGFR and gestational age is due to length of baby used in calculation of eGFR and not due to serum creatinine. Hence, eGFR seems to be a superior marker for evaluating kidney functions in neonates compared to cord blood creatinine.

Thus, we observed that, baby weight best affects the cranio-caudal kidney length, whereas eGFR is better influenced by gestational age in comparison to cord blood creatinine, which remains nearly similar throughout from 32 to 40 weeks of gestation.

Conclusion:

In the absence of established average reference values for cranio-caudal kidney length and cord blood creatinine levels in neonates across different gestational ages, this study found that among Indian neonates, birth weight and baby length was the most reliable predictor of kidney length, whereas gestational age best correlates with the estimated glomerular filtration rate (eGFR) than serum creatinine. Thus, we recommend conducting more extensive studies to identify additional predictors, potentially including maternal factors, to more accurately predict cranio-caudal kidney length. Additionally, we suggest monitoring estimated glomerular filtration rate (eGFR) instead of serum creatinine for evaluating kidney function.

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