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Glomerular Filtration Rate Estimation by Serum Creatinine or Serum Cystatin C in Preterm (<31 Weeks) Neonates

Glomerular filtration rate (GFR) was estimated by serum creatinine (Schwartz's equation) and serum cystatin C (Filler's equation) in preterm neonates (24-31 weeks of gestation) in a prospective cohort study. Serum creatinine and cystatin C was obtained at birth and then every two weeks during the first month. We found a poor fit between two methods, and a steadier GFR assessment by cystatin C.

Keywords: *Acute kidney injury, Diagnosis, Infants, Renal function tests.*

Accurate measurement of glomerular filtration rate (GFR) in preterm infants is difficult and frequently imprecise. Serum creatinine (SCr) based GFR is erratic due to its tubular secretion and reabsorption, changing muscle mass, bilirubin and fluid variations [1]. Serum Cystatin C is independent of muscle mass, bilirubin, age, sex, weight, or diet, and can be used to estimate GFR [2]. Cystatin C has been described as a better maker to estimate GFR than serum creatinine. However, very few studies have been conducted in preterm neonates <31 weeks [3,4]. To help us guide clinical decisions, we aimed to determine estimated GFR (GFR) by both methods.

This prospective cohort study was done at Vidant medical center Greenville, North Carolina after Institutional Review Board approval. We included neonates (24 to 31 weeks' gestational age) within 48 h of birth. We excluded neonates with confirmed sepsis, renal failure and prenatal congenital renal abnormalities. We estimated GFR at 48 hours of life, and on day 14 and day 28 of life. Cystatin C GFR was estimated by Filler's equation [log GFR=1.962+ [1.123xlog (1/cystatin C)], and creatinine based CGFR by schwartz equation [GFR=k × height/cr, k=0.33] [5]. Serum Creatinine was IDMS traceable and Cystatin C was measured by nephelometric immunoassay method using international reference materials. Both methods were compared by Bland Altman plots. Post-conceptional age was plotted against serum cystatin C- and creatinine-based eGFR.

Serum creatinine and Cystatin C was measured in 37 samples taken from 14 infants mostly (12/14) delivered by Caesarian-section. Out of 14 patients, 11 had received gentamicin for suspected sepsis in first 48 hours, and all had respiratory distress syndrome. Four patients had required dopamine for hypotension, and one patient had received indomethacin for hemodynamically- significant patient ductus arteriosus. Mean serum creatinine levels decreased steadily (P=0.007), and mean eGFR using creatinine increased (P=0.001) during first month (***Table* I, *Web Fig.* 1a**). Mean Serum cystatin C decreased from 1.39 mg/dL to 1.30 mg/dL (P=0.42). GFR estimated by cystatin C was significantly higher, and did not show much variability over time until the end of our observations (***Web Fig*. 1b,1c**). The poor fit was seen in the Bland Altman plot with the mean difference (Filler - Schwarz) around 25 with nearly all differences greater than 25 when the mean of the two measure was 50 or less and nearly all differences less than 25 when the mean was greater than 50 (***Web Fig*. 1d**).

In our study, serum creatinine and serum cystatin C levels decreased and eGFR increased with advanced postnatal age, possibly due to renal maturation [6]. This

TABLE I SERUM CREATININE AND CYSTATIN C VALUE AND CORRESPONDING GLOMERULAR FILTRATION RATE

Parameter	*Day of Life*		
	0-2 (n=14)	*14-16 (n=11)*	*28-30 (n=7)*
Cystatin C (Mean)	1.38	1.39	1.30
Cystatin C; Median (range)	1.38 (1.27-1.48)	1.35 (1.28-1.47)	1.34 (1.25-1.36)
GFR cystatin C	64.4	64.3	68.7
Serum Creatinine (Mean)[#]	0.63	0.43	0.29
Serum Creatinine (Median)	0.62	0.41	0.21
GFR creatinine (Mean)[#]	21.3	39.3	62.8

[#]P value significant (<0.05) between three recordings.

study shows that in preterm infants below 31 weeks, both methods for eGFR are poor fit to each other. They are especially different between 24-27 weeks of post conceptional age. This may, at least in part, be explained due to placental transfer of creatinine.

The limitations of the study are small sample size, influence of typical neonatal drugs and no gold standard measurement. As shown in (***Table* I**), infants had different degrees of severity of illness that could have an impact on serum creatinine and CysC levels. Currently, there is no international calibration for CysC.

In conclusion, this study shows that Cystatin C and serum creatinine estimate GFR differently in preterm infants below 31 weeks.

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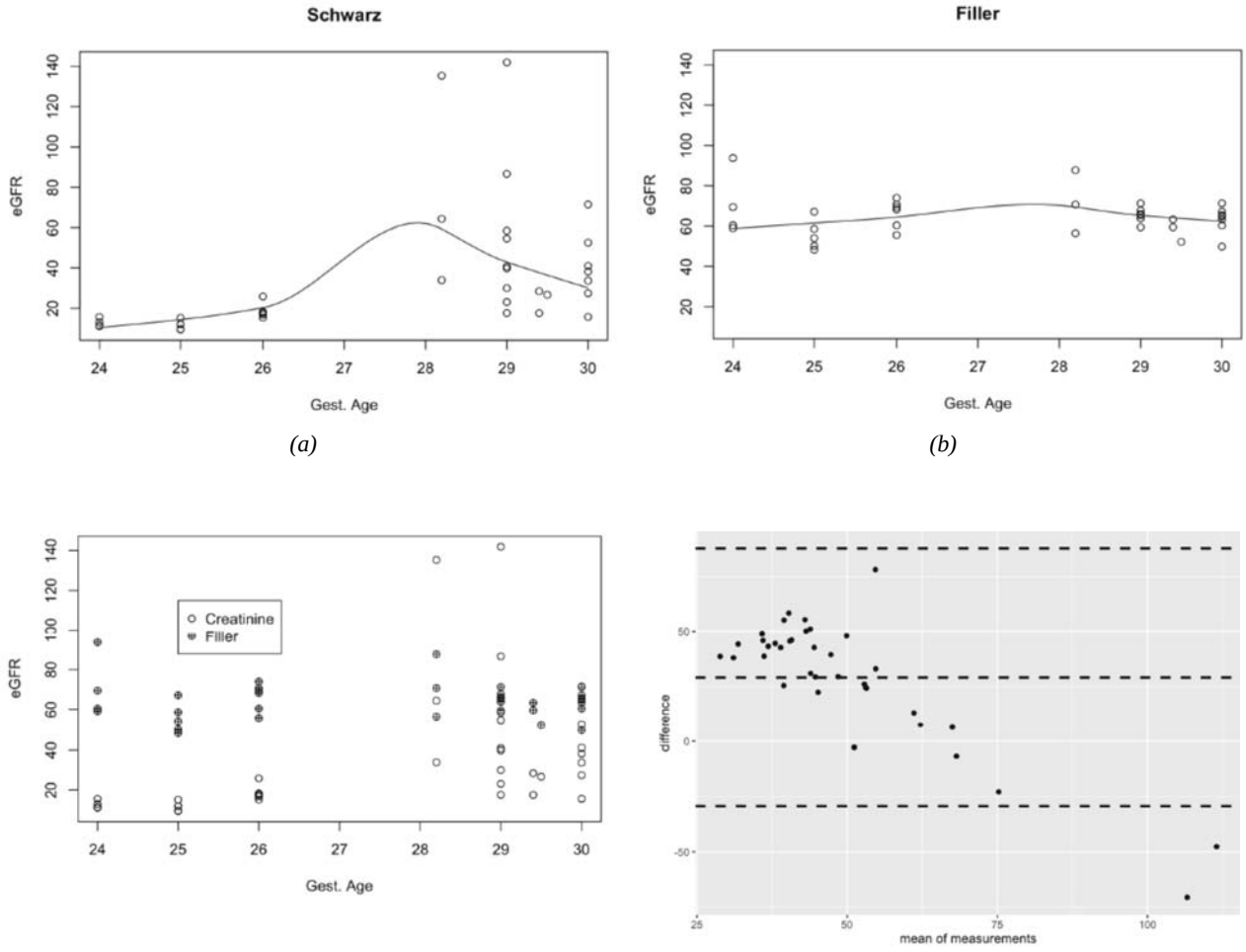

WEB FIG. 1 *Estimation of Glomerular filtration rate by (a) Serum Creatinine (Schwartz Method); (b) Serum Cystatin C (Filler Method); (c) both methods; and (d) Bland Altman Plots of comparison.*