Published in final edited form as:

Hypertens Pregnancy. 2009 ; 28(3): . doi:10.1080/10641950801986720.

A Comparison of Prediction Equations for Estimating Glomerular Filtration Rate in Pregnancy

Sofia B. Ahmed^{1,†}, Rhonda Bentley-Lewis^{2,†}, Norman K. Hollenberg^{2,3}, Steven W. Graves⁴, and Ellen W. Seely²

¹Division of Nephrology, Department of Medicine, Foothills Medical Centre, University of Calgary, Calgary, Alberta, Canada

²Divisions of Endocrinology, Diabetes and Hypertension, Department of Medicine, Boston, Massachusetts

³Radiology, Brigham and Women's Hospital, Boston, Massachusetts

⁴Department of Chemistry and Biochemistry, Brigham Young University, Provo, Utah

Abstract

Objective—To compare existing glomerular filtration rate (GFR) prediction equations with the gold standard, inulin clearance, in pregnancy.

Methods—Five equations were assessed for precision, bias, and accuracy in prediction of true GFR, measured by inulin clearance in 12 healthy, pregnant women during the second (T2) and third (T3) trimesters and in postpartum (PP).

Results—Precision was greatest with 24-hour creatinine clearance estimation of GFR ($R^2 = 13\%$ (T2), $R^2 = 26\%$ (T3)). Other than 100/SCr, all equations underestimated true GFR. 30% accuracy was greatest in 100/SCr (83% (T2), 92% (T3)).

Conclusions—Current GFR prediction formulae do not appear to be sufficient for estimating GFR in the gravid state.

Keywords

Pregnancy; Glomerular filtration rate; Prediction equation; Inulin clearance; Kidney

INTRODUCTION

One of the most striking changes in pregnancy is the dramatic increase in renal hemodynamics. Glomerular filtration rate (GFR) increases by approximately 50%, and renal plasma flow (RPF) reaches levels 50% to 80% above prepregnancy RPF, although renal hemodynamics return to normal levels in the postpartum period (PP) (1).

2009 Copyright © Informa Healthcare USA, Inc.

Address correspondence to Sofia B. Ahmed MD, MMSc, FRCPC, Foothills Medical Centre, Room C201D, 1403-29th St. NW, Calgary, Alberta, Canada, T2N 2T9. sofia.ahmed@calgaryhealthregion.ca.

[†]These authors contributed equally to the work.

CONFLICT OF INTEREST STATEMENT

The results presented in this paper have not been published previously in whole or part, except in abstract format at the 2006 International Society for the Study of Hypertension in Pregnancy World Congress in Lisbon, Portugal and there are no potential conflicts of interest.

A noninvasive and accurate estimate of GFR is one of the most coveted goals in nephrology. This is particularly relevant in pregnancy, where bedside evaluation of GFR can prove especially difficult, given the changing renal hemodynamics associated with gestation. Traditionally, the gold standard for GFR determination requires administration of inulin or radioisotopes, both of which are cumbersome and expensive. Additionally, ^{125}I -iothalamate and $^{99\text{m}}\text{Tc}$ -diethylenetriamine-pentaanetic acid renal clearance studies are relatively contraindicated in pregnant women. Serum creatinine (SCr) routinely decreases during pregnancy due to the hyperfiltration state of the kidney, resulting in an increase in the calculated GFR (1). Clinicians rely on GFR prediction equations to guide their medical decision-making; this is especially true in the case of kidney disease present pre-pregnancy, where a significant decrease in renal clearance can prompt early delivery of the fetus (2), in order to avoid potential maternal or fetal morbidity or mortality.

While there are studies evaluating the accuracy of some GFR prediction equations compared to measured GFR in healthy adult humans (3–5), there are limited data on the utility of these equations as compared to the gold standard, inulin clearance, in the setting of a normal pregnancy. Twenty-four hour creatinine clearance (CrCl) is currently the standard of care in terms of evaluating renal function in pregnancy (6).

The importance of accurately diagnosing a change in renal function during gestation raised the question of how well existing GFR prediction equations predicted the true value determined by inulin clearance. We compared GFR measured by inulin clearance to GFR calculated by several published GFR prediction equations, including 24-hour and 6-hour CrCl, Cockcroft-Gault CrCl, Modification of Diet in Renal Disease GFR (MDRD2), 100/SCr, and the Diabetes and Complications Control Trial (DCCT) GFR. We examined these equations in healthy women on a fixed salt intake during the second (T2) and third (T3) trimesters of pregnancy, as well as during the PP period.

MATERIALS AND METHODS

Subjects

Twelve normotensive women were recruited at random from the antenatal clinic at the Brigham and Women's Hospital (BWH). They were enrolled in the study prior to 20 weeks gestational age (GA) and fulfilled the entry criteria of an uncomplicated pregnancy at the initiation of study, no medication use except prenatal vitamins, and no current medical illness, including hypertension, diabetes, or nephropathy. All of these women had uncomplicated singleton pregnancies. At the time of each evaluation, each subject was normotensive, normoglycemic, and had normal levels of SCr and urinary protein.

The study protocol was approved by the BWH Institutional Review Board and conducted in accordance with institutional guidelines. All subjects provided written informed consent prior to study participation. Pre-pregnancy weight, height, and normal blood pressure measurements were confirmed by investigator review of prenatal medical records. The subjects underwent the study protocol in the second trimester (T2) between 19 and 23 weeks GA and in the third trimester (T3) between 32 and 37 weeks GA. The PP studies were performed between 6 weeks and one year after delivery and none of the subjects was pregnant at the time of the PP study. One subject was unable to return for the PP studies and thus was not included in the PP analysis.

Protocol

Prior to each study day, subjects were placed on a standardized diet for 2 days containing 100 mEq of sodium and 100 mEq of potassium. An ambulatory 24-hour urine collection was obtained and analyzed for volume, sodium, and creatinine on the second of these days. On

the morning of the third day, the subjects presented to the BWH General Clinical Research Center (GCRC) and were provided with a breakfast standardized for sodium, potassium, and protein. An intravenous catheter was placed in each arm—one for blood drawing and the second for infusion. Subjects were studied in the left lateral decubitus (LLD) position and blood pressures was measured twice and averaged every 15 minutes using a DinamapTM automated blood pressure monitor (Critikon, Inc., Tampa, FL). Mean arterial pressure (MAP) was calculated as $MAP = DBP + (1/3 * [systolic\ blood\ pressure - diastolic\ blood\ pressure])$. Each subject was given loading doses of 8 mg/kg of para-aminohippurate (PAH) and 50 mg/kg of inulin, followed by constant infusions of PAH at 12 mg/min and inulin at 30 mg/min for 60 minutes, after which time renal hemodynamic measurements were obtained. After completion of the inulin study, a 6-hour urine collection acquired between 9 a.m. and 3 p.m. on the study day was analyzed for volume, sodium, and creatinine. Every attempt was made to ensure that the first and final voids of the urine collection were performed in the LLD position.

Analytical Methods

Renal clearance studies were assessed with inulin (Inutest Polyfructosan, Fresenius Pharma, Linz, Austria) and para-aminohippurate (PAH, Clinalfa, Läufelfingen, Switzerland) as previously described (7). Serum PAH and inulin were measured by autoanalyser. Serum and urine creatinine (UCr) levels were measured by alkaline picrate reactions with a DAX96 (Bayer) machine.

Statistical Analysis

Descriptive Statistics—All results are presented as mean $\pm$ SE. Differences in weight, laboratory values, and renal hemodynamics over the course of pregnancy or the postpartum period in each subject were determined by a repeated measures design.

Methods for Comparing Equations to Predict GFR—The mean and median absolute differences were calculated as absolute difference = predicted value – measured value. The percent (%) absolute difference was calculated as % absolute difference = (predicted value – measured value) $\times$ 100/measured value. Bias, a measure of systematic error, was defined by the mean prediction error (ME):

$$ME = \sum_{i=1}^N (pe_i) / N$$

where pe_i = predicted value – true value and N = sample size.

Predicted GFR was compared with true GFR (as measured by inulin clearance) by the Bland and Altman method (8). The overall agreement between the predicted GFR and the measured GFR on a continuous scale was evaluated using Lin's concordance correlation coefficient (CCC) (9). The R^2 statistic was derived by simple linear regression and reflects the predictive ability of the model. Associations were analyzed by univariate regression analysis (Pearson). Statistical analyses were performed using Stata (version 9.0; Stata Corp, College Station, TX) with two-tailed significance levels of 0.05.

Associations between measured GFR by inulin clearance and calculated CrCl/GFR, based on commonly used prediction formulae recommended by the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines for estimation of GFR (10) were evaluated. The prediction equations used are listed as follows:

1. 24h CrCl [11,12]: $[\text{UCr (mg/dL)} \times \text{Total Volume (mL)}]/(\text{SCr} \times 1440 \text{ min})$
2. 6h CrCl: $[\text{UCr (mg/dL)} \times \text{Total Volume (mL)}]/(\text{SCr} \times 360 \text{ min})$
3. Cockcroft-Gault [13]: $\text{CrCl} = ((140 - \text{Age}) \times \text{Weight (kg)})/(\text{SCr} \times 72) \times 0.85$
4. MDRD2 [14]: $\text{GFR} = 186 \times [\text{SCr}]^{-1.154} \times [\text{Age}]^{-0.203} \times [0.742]$
5. $100/\text{SCr}$
6. DCCT [15]: $\exp[5.270 - 0.3739 \times \log(\text{SCr}) - 0.1472 \times \log(\text{age}) - 0.066]$

Of note, only nonindexed measurements and estimations of GFR have been reported due to both body mass index (BMI) and body surface area (BSA) change during pregnancy. Because the estimated GFR from the MDRD2 and DCCT equations is expressed as corrected to body surface area (BSA), these results were multiplied by the BSA calculated as $(0.007184 \times \text{Height (cm)}^{0.725} \times \text{Weight (kg)}^{0.425})$ (16) and divided by 1.73 in order to express the GFR as ml/min.

RESULTS

Clinical and laboratory characteristics of this study population are summarized in Table 1. All study subjects were Caucasian, between the ages of 19 and 37 years, with normal renal function, and in sodium balance at each study time point (mean 24-hour urinary sodium excretion vs. sodium intake of 100 mEq, $p = 0.3$). Several of the women were multigravid (gravida range, 0 to 4) and multiparous (parity range, 0 to 2). As expected, the MAP was lower during pregnancy than PP and mean weight increased over the course of the study, although neither of these changes achieved statistical significance. The SCr was lower during pregnancy than PP (T2 vs. PP, $p = 0.005$; T3 vs. PP, $p = 0.02$), although no differences were seen in UCr levels (T2 vs. PP, $p = 0.9$; T3 vs. PP, $p = 0.9$). The renal plasma flow was greater in pregnancy compared with PP, but did not differ significantly between trimesters (T2 vs. T3, $p = 0.5$; T2 vs. PP, $p = 0.007$; T3 vs. PP, $p = 0.03$); the GFR followed a similar pattern (T2 vs. T3, $p = 0.7$; T2 vs. PP, $p = 0.004$; T3 vs. PP, $p = 0.001$).

Performance assessments of the prediction equations evaluated for GFR estimation (10) as compared to GFR determined by inulin clearance are presented in Table 2 and Figure 1. Most published equations underestimated the true GFR of pregnancy, as indicated by the bias or mean prediction error. The Cockcroft-Gault and $100/\text{SCr}$ equations were the least biased, in that these equations under- or overestimated the true GFR in the T2 and T3 the least compared to the other published formulae. The most accurate results during pregnancy were obtained with the $100/\text{SCr}$ and DCCT equations, which were both within 30% and 50% of the inulin-derived GFR 83% and 92% of the time, respectively. However, the CCC in the case of each GFR prediction formula was very poor.

Precision, reflected by the R^2 statistic, was greatest overall in the CrCl estimated by both the 24-hour and 6-hour urine collections. There was good correlation between the 24-hour and 6-hour urine collections at all time points (T2: $R = 0.70$, $p = 0.01$ and CCC 0.907 [95% CI 0.798, 1.016]; T3: $R = 0.69$, $p = 0.01$ and CCC 0.791 [95% CI 0.583, 0.998]; PP: $R = 0.84$, $p = 0.002$ and CCC 0.887 [95% CI 0.750, 1.024]). In the PP phase of the study, the $100/\text{SCr}$ equation performed most accurately at 73% (within 30% of measured value) and 100% (within 50% of measured value), and the DCCT formula was the least biased (-4 mean prediction error) of all of the formulae.

DISCUSSION

The systematic evaluation of healthy pregnant women during the two latter trimesters and in the postpartum period allowed us to evaluate the capabilities of published GFR prediction equations compared to true GFR measured by inulin clearance. While all of the standard GFR prediction equations showed poor correlation with the measured GFR, it is reassuring to note that the current recommendation of calculating CrCl from the 24-hour urine collection (10) is the most precise of all published methods of predicting GFR in pregnancy, although only 58% to 67% of patients in our study had a GFR estimate within 30% of the true value. Of note, we found that the results of the 6-hour urine collection were reasonably well correlated to those of the 24-hour urine collection. In clinical practice, the 6-hour collection may be more reliable given the ease with which this test is done relative to the more cumbersome and potentially inaccurately performed 24-hour collection (17,18). It is important to note, however, that the 24-hour urine collection results reported here were performed in a tightly controlled research setting, and that timed CrCl studies might not be as accurate outside of a clinical research unit.

There are several factors that can influence the estimation of 24-hour CrCl. Physiological ureteral dilation in pregnancy (19) can result in substantial retention of urine: urine may have entered the ureters prior to the collection period, which if included in the final measurement, would result in overestimation of GFR by the 24-hour CrCl. Alternatively, if there is incomplete ureteral emptying at the end of the 24-hour period, then this would result in an underestimation of the true GFR. In addition, there is evidence that there is significant variability in daily urinary creatinine excretion (20). However, we aimed to minimize these potential biases by controlling dietary intake and careful monitoring and standardization of the 24-hour urinary collection procedure. Furthermore, creatinine secretion is affected by several drugs which have been reported to increase SCr without influencing its glomerular filtration (21), but none of our subjects were ingesting any medications other than prenatal vitamins.

Other investigators have previously evaluated the accuracy of GFR prediction formulae in pregnancy. Davison and Hytten previously found that 24-hour CrCl systematically underestimated inulin clearance during gestation (22). Smith et al more recently demonstrated that the MDRD2 formula also underestimated measured GFR in both healthy and preeclamptic pregnancies (23). The agreement between the Cockcroft-Gault, MDRD2 and 24-hour CrCl in women with a hypertensive disorder of pregnancy has also been found to be suboptimal[24]. While endogenous markers of GFR, such as cystatin-C or beta trace protein, have been studied in pregnancy, they do not appear to reliably reflect renal function in this population (25,26). To the best of our knowledge, the evaluation of six commonly used GFR prediction equations compared to the gold standard, inulin clearance, in both the second and third trimesters and postpartum in women on a fixed salt intake has not been previously described; thus, we believe our study is unique.

It is not surprising that neither the Cockcroft-Gault nor the MDRD2 formulae, the most commonly used GFR prediction equations, accurately predict the true GFR measured during pregnancy. Both equations were designed for patients in a steady state of creatinine balance, which pregnancy is not. GFR increases progressively during the first half of pregnancy before reaching a peak level in T2 that exceeds nongravid levels by 40% to 60%, after which it remains relatively constant until the end of pregnancy (1). The Cockcroft-Gault equation predicts CrCl rather than GFR and was derived from 249 healthy Caucasian men; the equation was subsequently adjusted for use in the female population using a 0.85 correction factor to account for the decreased muscle mass of women (13). The MDRD2 equation provides a clinically useful estimate of GFR only up to approximately 60 ml/min/1.73m²,

because it was derived from a large sample of nonpregnant individuals, which included only 40% women with a wide range of kidney diseases (14). In this study population, the authors found the variability of the difference between the observed and predicted values was greater for higher GFR values.

Few reports exist comparing prediction formulae to measured GFR in a nongravid population with renal hyperfiltration similar to that observed in pregnancy. Vervoort et al. (27) reported no advantage of the MDRD2 equation over the Cockcroft-Gault formula compared to inulin clearance in either healthy subjects or normoalbuminuric type 1 diabetic patients, who have supranormal inulin clearance similar to a pregnant subject. More recently, Ibrahim et al. demonstrated that the abbreviated MDRD2 formula underestimated and the Cockcroft-Gault formula overestimated GFR in type 1 diabetic, normoalbuminuric patients with preserved kidney function (15). Of note, however, the equation derived in this study, while based on a hyperfiltering population, did not perform better in our pregnant subjects than the currently recommended 24-hour CrCl. Similarly, hypertensive African-American patients, despite similar Scr concentrations (within normal limits) compared to hypertensive Caucasians, have GFR levels in the hyperfiltration range (28), suggesting that traditional prediction equations do not work well in all populations.

Our study is limited because only 12 healthy Caucasian women were included, which restricts the generalizability of our results. However, our study strengths include that all of these women were studied in sodium balance, left lateral recumbency, and under rigorous GCRC conditions. Moreover, the GFR and RPF values reported in our study were similar to those previously measured by inulin clearance, both in normal pregnancy (22,29–35) and in the healthy non-gravid state (36–38). Additionally, all determinations of true GFR were done by inulin clearance, rather than a combination of measurement techniques; thus, we avoided the interassay variability that has constrained other previously published reports (3). Because both BMI and BSA change during pregnancy, we reported nonindexed measurements and estimations of GFR, as has been done in previous studies (35,36,39).

Precise knowledge of GFR during pregnancy has implications for the evaluation of glomerular disease. For example, patients with preeclampsia often have SCr levels in the normal range, both because of pregnancy (1) and the limited sensitivity of SCr levels to detect subtle changes in GFR (40). Prompt identification of pregnant women at risk of worsening kidney disease is crucial because any change in renal function may have implications for both the mother and fetus (2). Physicians are therefore required to base their assessments on the calculated CrCl, typically from a 24-hour urine collection, which we have shown to be an inaccurate predictor of GFR, even in a research setting. However, it must be emphasized that our study did not include subjects with renal dysfunction or racial diversity, and thus our findings may not necessarily be extrapolated to these populations.

In summary, we have demonstrated that the predictive capabilities of the published formulae evaluated in our study are suboptimal for patient care, thereby indicating the need for an accurate GFR prediction equation in pregnancy. Nonetheless, further study in larger and more diverse patient populations is necessary.

Acknowledgments

This work was, in part, supported by funding from the Kidney Foundation of Canada (Dr. Ahmed) and the National Institutes of Health: K23 RR023333 (Dr. Bentley-Lewis); T32 HL-07609, P01AC00059916 and 1P50ML53000-01 (Dr. Hollenberg); K24 RR018613, RO1 HL67332, and SCOR P50-HL55000 (Dr. Seely); and GCRC M01-RR02635.

References

1. Lindheimer MD, Davison JM, Katz AI. The kidney and hypertension in pregnancy: Twenty exciting years. *Semin Nephrol.* 2001; 21:173–189. [PubMed: 11245779]
2. Jones DC, Hayslett JP. Outcome of pregnancy in women with moderate or severe renal insufficiency. *N Engl J Med.* 1996; 335:226–232. [PubMed: 8657238]
3. Lin J, Knight EL, Hogan ML, Singh AK. A comparison of prediction equations for estimating glomerular filtration rate in adults without kidney disease. *J Am Soc Nephrol.* 2003; 14:2573–2580. [PubMed: 14514734]
4. Rule AD, Larson TS, Bergstralh EJ, Slezak JM, Jacobsen SJ, Cosio FG. Using serum creatinine to estimate glomerular filtration rate: Accuracy in good health and in chronic kidney disease. *Ann Intern Med.* 2004; 141:929–937. [PubMed: 15611490]
5. Poggio ED, Wang X, Greene T, Van Lente F, Hall PM. Performance of the modification of diet in renal disease and cockcroft-gault equations in the estimation of gfr in health and in chronic kidney disease. *J Am Soc Nephrol.* 2005; 16:459–466. [PubMed: 15615823]
6. Quadri KH, Bernardini J, Greenberg A, Laifer S, Syed A, Holley JL. Assessment of renal function during pregnancy using a random urine protein to creatinine ratio and Cockcroft-Gault formula. *Am J Kidney Dis.* 1994; 24:416–420. [PubMed: 8079966]
7. Smith HW, Goldring W, Chasis H. The measurement of the tubular excretory mass, effective blood flow and filtration rate in the normal human kidney. *JCI.* 1938; 17:263. [PubMed: 16694570]
8. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet.* 1986; 1:307–310. [PubMed: 2868172]
9. Lin LI. A concordance correlation coefficient to evaluate reproducibility. *Biometrics.* 1989; 45:255–268. [PubMed: 2720055]
10. K/DOQI clinical practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. *Am J Kidney Dis.* 2002; 39:S1–266. [PubMed: 11904577]
11. Lubowitz H, Slatopolsky E, Shankel S, Rieselbach RE, Bricker NS. Glomerular filtration rate. Determination in patients with chronic renal disease. *Jama.* 1967; 199:252–256. [PubMed: 6071183]
12. Lavender S, Hilton PJ, Jones NF. The measurement of glomerular filtration-rate in renal disease. *Lancet.* 1969; 2:1216–1218. [PubMed: 4187812]
13. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron.* 1976; 16:31–41. [PubMed: 1244564]
14. Levey AS, Greene T, Kusek J, Beck GJ, Group MS. A simplified equation to predict glomerular filtration rate from serum creatinine [abstract]. *J Am Soc Nephrol.* 2000; 11:A0828.
15. Ibrahim H, Mondress M, Tello A, Fan Y, Koopmeiners J, Thomas W. An alternative formula to the cockcroft-gault and the modification of diet in renal diseases formulas in predicting gfr in individuals with type 1 diabetes. *J Am Soc Nephrol.* 2005; 16:1051–1060. [PubMed: 15716336]
16. Wang Y, Moss J, Thisted R. Predictors of body surface area. *J Clin Anesth.* 1992; 4:4–10. [PubMed: 1540367]
17. Ginsberg JM, Chang BS, Matarese RA, Garella S. Use of single voided urine samples to estimate quantitative proteinuria. *N Engl J Med.* 1983; 309:1543–1546. [PubMed: 6656849]
18. Côté AM, Lam E, Von Dadelszen P, Magee LA. Accuracy of the 24h urine collection in hypertensive women. *Hypertens Pregnancy.* 2006; 25(Suppl):230.
19. Brown MA. Urinary tract dilatation in pregnancy. *Am J Obstet Gynecol.* 1991; 164:642–643. [PubMed: 1992717]
20. Lindow SW, Davey DA. The variability of urinary protein and creatinine excretion in patients with gestational proteinuric hypertension. *Br J Obstet Gynaecol.* 1992; 99:869–872. [PubMed: 1450132]
21. Andreev E, Koopman M, Arisz L. A rise in plasma creatinine that is not a sign of renal failure: Which drugs can be responsible? *J Intern Med.* 1999; 246:247–252. [PubMed: 10475992]
22. Davison JM, Hytten FE. Glomerular filtration during and after pregnancy. *J Obstet Gynaecol Br Commonw.* 1974; 81:588–595. [PubMed: 4420303]

23. Smith MC, Moran P, Ward MK, Davison JM. Assessment of glomerular filtration rate during pregnancy using the mdrd formula. *Bjog*. 2008; 115:109–112. [PubMed: 17970797]
24. Côté AM, Lam E, Von Dadelszen P, Magee LA. Agreement between mdrd/cockcroft-gault formulae and creatinine clearance in hypertensive pregnant women. *Hypertension in Pregnancy*. 2006; 25:229. [PubMed: 17065043]
25. Strevens H, Wide-Swensson D, Torffvit O, Grubb A. Serum cystatin c for assessment of glomerular filtration rate in pregnant and non-pregnant women. Indications of altered filtration process in pregnancy. *Scand J Clin Lab Invest*. 2002; 62:141–147. [PubMed: 12004930]
26. Akbari A, Lepage N, Keely E, Clark HD, Jaffey J, MacKinnon M, Filler G. Cystatin-c and beta trace protein as markers of renal function in pregnancy. *Bjog*. 2005; 112:575–578. [PubMed: 15842279]
27. Vervoort G, Willems HL, Wetzels JF. Assessment of glomerular filtration rate in healthy subjects and normoalbuminuric diabetic patients: Validity of a new (mdrd) prediction equation. *Nephrol Dial Transplant*. 2002; 17:1909–1913. [PubMed: 12401845]
28. Kotchen TA, Piering AW, Cowley AW, Grim CE, Gaudet D, Hamet P, Kaldunski ML, Kotchen JM, Roman RJ. Glomerular hyperfiltration in hypertensive african americans. *Hypertension*. 2000; 35:822–826. [PubMed: 10720601]
29. De Alvarez RR. Renal glomerulotubular mechanisms during normal pregnancy. I. Glomerular filtration rate, renal plasma flow, and creatinine clearance. *Am J Obstet Gynecol*. 1958; 75:931–944. [PubMed: 13520812]
30. Dignam WJ, Titus P, Assali NS. Renal function in human pregnancy. I. Changes in glomerular filtration rate and renal plasma flow. *Proc Soc Exp Biol Med*. 1958; 97:512–514. [PubMed: 13518320]
31. Davison JM, Dunlop W, Ezimokhai M. 24-hour creatinine clearance during the third trimester of normal pregnancy. *Br J Obstet Gynaecol*. 1980; 87:106–109. [PubMed: 7362796]
32. Davison JM, Dunlop W. Renal hemodynamics and tubular function normal human pregnancy. *Kidney Int*. 1980; 18:152–161. [PubMed: 7003196]
33. Ezimokhai M, Davison JM, Philips PR, Dunlop W. Non-postural serial changes in renal function during the third trimester of normal human pregnancy. *Br J Obstet Gynaecol*. 1981; 88:465–471. [PubMed: 7236549]
34. Sims EA, Krantz KE. Serial studies of renal function during pregnancy and the puerperium in normal women. *J Clin Invest*. 1958; 37:1764–1774. [PubMed: 13611044]
35. Moran P, Baylis PH, Lindheimer MD, Davison JM. Glomerular ultrafiltration in normal and preeclamptic pregnancy. *J Am Soc Nephrol*. 2003; 14:648–652. [PubMed: 12595500]
36. Krutzen E, Olofsson P, Back SE, Nilsson-Ehle P. Glomerular filtration rate in pregnancy: A study in normal subjects and in patients with hypertension, preeclampsia and diabetes. *Scand J Clin Lab Invest*. 1992; 52:387–392. [PubMed: 1514017]
37. Lafayette RA, Malik T, Druzin M, Derby G, Myers BD. The dynamics of glomerular filtration after caesarean section. *J Am Soc Nephrol*. 1999; 10:1561–1565. [PubMed: 10405212]
38. Hladunewich MA, Lafayette RA, Derby GC, Blouch KL, Bialek JW, Druzin ML, Deen WM, Myers BD. The dynamics of glomerular filtration in the puerperium. *Am J Physiol Renal Physiol*. 2004; 286:F496–503. [PubMed: 14612381]
39. Milne JE, Lindheimer MD, Davison JM. Glomerular heteroporous membrane modeling in third trimester and postpartum before and during amino acid infusion. *Am J Physiol Renal Physiol*. 2002; 282:F170–175. [PubMed: 11739125]
40. Shemesh O, Golbetz H, Kriss JP, Myers BD. Limitations of creatinine as a filtration marker in glomerulopathic patients. *Kidney Int*. 1985; 28:830–838. [PubMed: 2418254]

T2 R^2 :	13%	17%	11%	7%	9%	11%
T3 R^2 :	26%	8%	2%	9%	0.1%	6%
PP R^2 :	22%	21%	2%	0.2%	12%	0.02%

Figure 1.

Comparison of equations to predict GFR. The values of R^2 indicate the percentage of variance of GFR accounted for by the equation. Abbreviations: T2, 2nd trimester; T3, 3rd trimester; PP, Postpartum.

Table 1

Baseline Characteristics

	Pre-Pregnancy	2 nd Trimester	3 rd Trimester	Postpartum
Age (years)	29 ± 1			
Caucasian (%)	100			
Gravida	1.3 ± 0.4			
Parity	0.4 ± 0.2			
Height (cm)	164 ± 2			
Weight (kg)	65 ± 5	69 ± 3	75 ± 3	71 ± 5
BMI (kg/m ²)	24.1 ± 1.5	25.4 ± 1.0	27.1 ± 1.1	26.1 ± 1.8
Study Date (weeks)		21.3 ± 0.2	34.0 ± 0.2	15.2 ± 1.7
Serum Cr (mg/dl) (μmol/L)		0.63 ± 0.04 [*] (56 ± 4 [*])	0.67 ± 0.03 [*] (59 ± 3 [*])	0.79 ± 0.03 (70 ± 3)
Urine Cr (mg/24h)		1110 ± 51	1129 ± 54	1117 ± 63
Urine Na (mmol/24h)		87 ± 6	98 ± 12	95 ± 12
MAP (mm Hg) [†]		61 ± 2	60 ± 2	64 ± 2
RPF (ml/min) [†]		882 ± 49 [*]	841 ± 54 [*]	682 ± 34
GFR (ml/min) [†]		154 ± 6 [*]	157 ± 4 [*]	128 ± 7

Data are mean ± SE.

^{*} p < 0.05 compared to Postpartum

[†] Median of readings at † = 0 min, 5 min and 10 min

Abbreviations: BMI, body mass index; BSA, body surface area; Cr, creatinine; Na, Sodium; MAP, mean arterial pressure; RPF, renal plasma flow; GFR, glomerular filtration rate.

Mean calculated CrCl or GFR, bias, accuracy, and concordance correlation coefficient of GFR prediction equations compared with GFR measurements

Table 2

	Mean CrCl/GFR (ml/min) ± SE	Bias (95% Limits of Agreement)	Accuracy% within		Concordance Correlation Coefficient (95% CI)
			30%	50%	
2 nd Trimester					
Measured GFR *	154 ± 6	N/A	N/A	N/A	1
24h CrCl	129 ± 11	-24 (-95 to 47)	67	92	0.219 (-0.121 to 0.560)
6h CrCl	134 ± 11	-20 (-90 to 51)	67	92	0.256 (-0.104 to 0.615)
MDRD2	129 ± 10	-24 (-87 to -39)	67	83	0.201 (-0.183 to 0.586)
Cockcroft-Gault	151 ± 12	-2 (-78 to 75)	67	92	0.205 (-0.280 to 0.689)
100/SCr	165 ± 9	11 (-52 to 75)	83	92	0.228 (-0.228 to 0.683)
DCCT	136 ± 5	-17 (-59 to 24)	83	92	0.228 (-0.197 to 0.652)
3 rd Trimester					
Measured GFR *	157 ± 4	N/A	N/A	N/A	1
24h CrCl	120 ± 8	-37 (-89 to -15)	58	100	0.139 (-0.068 to 0.345)
6h CrCl	124 ± 6	-33 (-78 to -12)	83	100	0.095 (-0.117 to 0.307)
MDRD2	122 ± 7	-35 (-84 to 15)	67	92	0.051 (-0.163 to 0.265)
Cockcroft-Gault	151 ± 9	-6 (-62 to 51)	83	92	0.230 (-0.243 to 0.703)
100/SCr	153 ± 7	-4 (-56 to 48)	92	100	0.033 (-0.508 to 0.574)
DCCT	138 ± 4	-19 (-52 to 14)	83	92	0.120 (-0.190 to 0.430)
Postpartum					
Measured GFR *	128 ± 7	N/A	N/A	N/A	1
24h CrCl	100 ± 7	-28 (-113 to 57)	45	91	-0.326 (-0.744 to 0.093)
6h CrCl	105 ± 7	-24 (-102 to 55)	64	82	-0.286 (-0.735 to 0.162)
MDRD2	96 ± 8	-33 (-108 to 42)	45	82	-0.070 (-0.426 to 0.285)
Cockcroft-Gault	121 ± 15	-8 (-113 to 97)	55	73	-0.040 (-0.611 to 0.531)
100/SCr	129 ± 6	1 (-68 to 71)	73	100	-0.340 (-0.897 to 0.216)
DCCT	125 ± 6	-4 (-66 to 57)	73	91	-0.013 (-0.654 to 0.628)

Abbreviations: CrCl, creatinine clearance; GFR, glomerular filtration rate; SE, standard error; CI, confidence interval; MDRD2, Modification of Diet in Renal Disease 2; SCr, serum creatinine; DCCT; Diabetes and Complications Control Trial.

* Median of readings at t = 0 min, 5 min and 10 min.