A simplified bedside method for estimating glomerular filtration rate in term neonates

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An accurate estimation of renal function in neonates is very essential as many management decisions including fluid and electrolyte administration and the use of therapeutic agents are based on it. An overall estimate of renal function can be made by measuring the glomerular filtration rate (GFR). The classic technique used for GFR requires the use of substances as inulin, Cr-EDTA ^{99}mTc-DTPA, ^{125}I-iothalamate and polyfructosan with multiple timed collections of urine.[1] These methods are expensive, labor intensive and require administration of chemical substances and therefore, are inappropriate in a sick baby. Another novel method described recently for monitoring GFR is the measurement of plasma cystatin C, which requires immunoassay technique and may not be readily available.[2] Schwartz and Brion,[3] in a series of studies described a much more simpler and rapid way of estimating the GFR in neonates by a formula using plasma creatinine.[3] This formula has been adopted by clinicians and has already been used in research.[4] The formula by Schwartz for calculating GFR is kL/Pcr, where k is a constant, L is the length of the infant in centimeters and Pcr is the plasma creatinine value expressed in mg/dl. The value of 'k' was calculated by regression analysis and was found to be 0.45 for term neonates.

We propose further modification in this formula. The reason behind this proposal is that in term infants, variation in length is not much. We have shown in a previous study that the length of the term infants does not deviate much from a mean of 50 centimeters.[5] Thus, we rounded off the length parameter in the Schwartz's formula to 50 cm. We also altered the unit of expression of plasma creatinine from mg/dl to mmol/L, the International System of units or System Internationalé (SI), which is followed extensively and also used in the literature. To convert plasma creatine (Pcr) from mg/dl to mmol/L conversion factor of 88.4 was used. The mathematical derivation for the modified formula is as under Schwartz formula: GFR = 0.45L/Pcr; 0.45 x length (cm) / Pcr (mg/dl); 0.45 x 50 x 88.4/Pcr (mmol/L), where, 50 cm is the rounded off length, and 88.4 is the conversion factor for creatinine from mg/dl to mmol/L. After simplifying, the equation becomes 1989/Pcr (mmol/L). Modified formula (Manzar formula): GFR = 1989/Pcr. To test this formula against the Schwartz formula we conducted this study.

The study was conducted over a 6-month period between January and June 2003 at the Royal Hospital, Muscat, Sultanate of Oman, which is a tertiary referral center for neonates with a birth rate of approximately 5,000 infants annually. Details of all admission and discharge or death are both kept as case files in the Medical Records Department and on the computer database using Visual Dbase Program. Term infants, defined as infants born after 37 completed weeks of gestation, were selected for the study and the data were extracted from the computer database. Each baby's identification number and length in centimeters that was taken by the nurses at the time of admission was retrieved from Visual Basic Database. Each baby's first Pcr value was recovered from the online hospital data storage system (Medicom), which as a protocol, is estimated within 24 hours of admission.

A total of 83 term neonates, out of 311 admission during the specified 6-month period had complete information needed for the study. The Pcr values were reported in SI units as mmol/L by our laboratory using auto-analyser technique (ALEX 20, USA). The GFR was then calculated from the creatinine value using both the methods, the Schwartz formula and modified formula. To convert mmol/L to mg/dl the conversion factor of 88.4 was used, as described. As the nature of the study was retrospective and laboratory based, and no intervention was carried out on the infants, formal approval by the Institution Review Committee and informed parental consent were not considered. This being a pilot study, no sample size calculation was performed. The mean values of GFR were calculated using statistical package for social sciences (SPSS) version 7.5 for windows. Correlation between the variables was performed using Pearson correlation test. A p value of < 0.05 was considered statistically significant. A total of 83 samples from 83 term infants were analyzed. The mean value of GFR was noted to be 32.5 ± 16.9 and 31.8 ± 15.4 ml/min/1.73m^2 by Schwartz and modified method. A statistically significant correlation ($r=0.99$, $p=0.0001$) was obtained between the 2 methods for estimating GFR.

In the present study, we were able to demonstrate that the simplified formula for estimating GFR in term neonates (GFR = 1989/Pcr) is comparable with the Schwartz method (GFR = 0.45L/Pcr). Our finding indicated that rounding off and standardizing length to 50 cm for estimating GFR had no significant effect on GFR calculations. The possible reasons for no significant difference could

be in 2 folds. First, there is usually no wide variation in the length of term babies.[5] Secondly, the muscle mass for term babies does not differ much. It was reported to be 24% of body weight.[1] Thus, including some of the body measurement parameter in the formula for estimating GFR, as carried out for older children, may not be applicable to neonates. The simple reason is that the variation in length and muscle mass in older children is likely to be higher. These facts and that growth, development, size and age profoundly affect GFR estimation is shown recently in a meta-analysis of previous published reports.[6] In our group of term infants the mean value of GFR was noted to be 31.8 ± 15.4 ml/min/1.73m^2 (modified method) which was not different from the normal ranges reported earlier.[3] However, a wide variation was observed ranging from 8.5 to 79 ml/min/1.73m^2. One known reason for the wide variation is the variability of Pcr in the first 72 hours of life.[7] The other reason for the observed variation is in view of the fact that we selected term neonates who were in the intensive care unit with different disease pathology. They were not in a steady state. The ideal study group for that purpose should be the term healthy stable neonates in the postnatal ward. However, to draw extra blood merely for Pcr estimation without indication may not be justified or ethical. Thus, for the study purpose we had to rely on the available creatinine values from the relatively unstable term babies.

It is obvious from the above discussion that GFR is inversely proportional to Pcr. The lower the Pcr the higher will be the GFR or vice versa. Thus, one could argue regarding the fact that instead of GFR one could use Pcr alone for assessing renal function. Schwartz provided the answer to this possible argument in his review on GFR estimation.[3] He suggested that the creatinine value is critically dependent on the percentage of muscle mass, in addition to renal function. In addition, it is easier to grasp a change in GFR as compared to Pcr (for example: a change of 40 ml/min/1.73m^2 in GFR corresponds to 0.2 mg/dl of creatinine). However, with expression of creatinine in SI unit this point loses its strength (0.2 mg/dl means 17.2 mmol/L). However, the advantage of using GFR instead of Pcr in acute renal failure is proven beyond doubt. It has been stated that in cases of acute renal failure when GFR falls abruptly it takes several days for Pcr to reach new constant level and similarly as the failure improves there may be several days before a stable Pcr value is attained. The clinical implication of GFR has been gaining interest. Recently, it has been shown to be an effective prognostic factor in the outcome of infants with posterior urethral valve.[8] Previously, the troublesome and time-consuming methods of GFR estimation could be one of the reasons for under utilization of GFR in clinical settings. Now with the availability of much simpler way of GFR estimation, as described in the study, more could be known regarding the GFR in relation to common neonatal problems. We have already embarked on a prospective study relating GFR to the outcome of asphyxiated neonates with different stages of hypoxic-ischemic-encephalopathy.

In conclusion, the modified formula for GFR estimation, as described in the present study, is a simple, reliable, rapid and a bedside method. To look at the other potential clinical benefits of our modified formula further studies are warranted.

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