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Comparing different estimated glomerular filtration rate equations in assessing glomerular function in full age spectrum based on serum creatinine

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Abstract
Background: Glomerular Filtration Rate (GFR) will measure the filtration capacity of kidney. The estimated GFR play important role in clinical management of various diseases and altered renal function influence the use of the therapeutic agents. Serum creatinine estimation is simple and commonly used for estimation of GFR. These methods are simple, cost effective and required less time.
Methods: The study comprised of 175 subjects, of these Children group comprised of 75 healthy childrens The adult and old age people comprised of 100 healthy individuals. In all the participants Serum creatinine are blood urea are estimated. In childrens eGFR was estimated by using Schwartz equations and Counahan-Barrad formula. In adult and old age people the eGFR was estimated by Cockcroft-Gault formula (CG) and Modification of Diet in Renal Disease (MDRD) and Mayo Clinic Quadratic Equation (MCQE).
Results: Schwartz equation given a significantly (p< 0.001) higher GFR values in childrens when compared with Counahan-Barrad. Counahan-Barrad formulae included normal healthy childrens in to GFR $\leq$ 90 mL/min/1.73 m^2. MCQE given a significantly (p< 0.001) higher GFR values in all age groups when compared with CG and MDRD. Both the CG and MDRD formulae included around 50% of population under category with a GFR less than <90 ml/min/1.73m^2.
Conclusion: It was concluded that the present study infers with some degree of reservation that Schwartz is a good formula to provide ease of use in the daily practice in childrens and MCQE formula is acceptable for normal adult and old age group people.

Keywords: glomerular filtration rate, Schwartz equation, mayo clinic quadratic equation

Introduction

Glomerular Filtration Rate (GFR) will measure the filtration capacity of kidney. It is an marker for renal function and without knowledge of GFR, the clinical feature of kidney dysfunction may remain silent and deceptive [1]. Glomerular filtration rate is helpful for early detection of renal impairment. The estimated GFR play important role in clinical management of various diseases and altered renal function influence the use of the therapeutic agents [2].

GFR estimation using inulin and radiolabeled substances are gold standards for GFR estimation but these are can cause adverse effects and not used for routine investigation. Serum creatinine estimation is simple and commonly used for estimation of GFR [3]. Serum creatinine based GFR has its own disadvantages like tubular secretion, Serum creatinine also varies from individual to individual based on muscle mass and significant rise of serum creatinine reflects a fall about 50% of GFR. But still serum creatinine is a acceptable parameter for diagnosis of kidney dysfunction in clinical practice. Measured creatinine clearance for 24 hours urine has its own drawbacks due to inaccurate 24 hour urine collection in childrens and older people [4].

Age is advances GFR will decreases, after thirty years, GFR still decline around 0.75 ml/min/year in normal people. [5] It decreased still further in older age. It is due to either physiological or pathological process such as decreased vascular elasticity of kidney with ageing [6, 7]. GFR estimation will be helpful for identification kidney dysfunction in normal healthy individuals and it is also helpful in staging of chronic kidney disease (CKD) Based on GFR CKD patients classified into five stages. They are stage 1 (GFR $\geq$ 90 ml/min/1.73 m^2), stage 2 (GFR 60 to 89 ml/min/1.73 m^2), stage 3(GFR 30 to 59 ml/min/1.73 m^2), stage 4 (GFR 15 to 29 ml/min/1.73 m^2) and stage 5 (GFR less than 15 ml/min/1.73 m^2) [8].

Estimation GFR can be done by different equations using serum creatinine.

These methods are simple, cost effective and required less time. The most common formula in childrens are Schwartz equations [9] and Counahan-Barrad formula [10]. The most common formulae in adult and old age are Cockcroft-Gault formula (CG) [11] and Modification of Diet in Renal Disease (MDRD) [12] and Mayo Clinic Quadratic Equation (MCQE) [13]. These formulae have their own limitation. The present study was undertaken to estimate and compare the different equations in assessing the GFR from children to old age

Materials and Methods

The study comprised of 175 subjects, of these Children group comprised of 75 healthy childrens who were free of features of kidney disease and were having a normal blood urea and serum creatinine level. Children with less than 2 years and any chronic illness are excluded from study. The adult and old age people comprised of 100 healthy individuals who were free of features of kidney disease and were having a normal blood urea and serum creatinine level. The upper limit for serum creatinine levels was 1.2 mg/dl and the corresponding value for blood urea was 45 mg/dl. Individuals suffering from diseases that are likely to alter these parameters were excluded from the study. Likewise, persons with history of drug intake which cause changes in these parameters were also excluded.

In all the subjects, Height was estimated in centimeters and Weight was measured in kilogram on standard clinical weighing machine. BMI was calculated as Weight in kilogram divided by Height in meters squared. In all these groups blood urea and serum creatinine were measured. The blood urea was estimated by GLDH – Urease method [14]. Serum creatinine was estimated by Jaffes method [15].

The GFR was estimated by using following formula in childrens Schwartz equations K* X Ht/SCr [9] and Counahan-Barrad 0.43X Ht/SCr [10]

The GFR was estimated by using following formula in adult and old age Cockcroft-Gault Creatinine Clearance (ml/min) [11]= (140 - age) x (weight in kg) / Serum Creatinine (mg/dl) x 72 (Multiply with 0.85 if female)CG formula is adjusted to body surface area (BSA) by using DuBois, DuBois method, BSA = (W $^{0.425}$ x H $^{0.725}$) x 0.007184

MDRD Creatinine Clearance (ml/min/1.73m2) [12] = 186 x (Serum Creatinine (mg/dl))$^{-1.154}$ x (age in years)$^{-0.203}$ x 0.742 (Multiply with 0.742 if female) The MCQE estimated GFR (ml/min /1.73 m2) [13] = exp [1.911 + 5.249 / SCr – 2.114 / SCr2 – (0.00686 x age (years)] (– 0.205 if female).

All the Data was expressed in Mean and Standard deviation (mean ±SD). Statistical significance between control and cases groups Z test was performed using Microsoft Excel and SPSS software 16.0. The statistical significance was determined at 5% ($p < 0.05$) level.

Results

In the present study was a total of 75 Childrens subjects were included.

Table 1: Demographic Profile of Childrens

	Childrens
Number	75
Age (mean±SD) years	9.27±3.09
Sex (males %)	63
(females %)	37
Body Mass Index	18.22±8.90
Blood urea (mg/dl)	8.22±4.90
Serum Creatinine (mg/dl)	0.55±0.09

Table1 shows the mean age of the Children was 9.27years±3.09. The blood urea and serum creatinine within the normal range.

Table 2: Shows eGFR by Schwartz and Counahan-Barrad equations in childrens p<0.001

	Children (n=75) Mean±SD
Schwartz (ml/min/1.73m2)	168.09 ± 67.18**
Counahan-Barrad (ml/min/1.73m2)	121.44 ± 59.22

Table 2 shows the mean eGFR of in Children by Schwartz formula it is 168.09 ± 67.18 and by Counahan-Barrad equations it is 121.44 ± 59.22.

Table 3: Shows Distribution of childrens in different stages on the basis of eGFR equation

	Schwartz (ml/min/1.73m^2)	Counahan-Barrad (ml/min/1.73m^2)
≥ 90 ml/min/1.73m^2	72 (96 %)	57 (76 %)
≤ 90 ml/min/1.73m^2	3 (4 %)	18 (24 %)

Table 3 shows the distribution of childrens based on Schwartz and Counahan-Barrad equation. Counahan-Barrad included a much higher number of normal individuals are having eGFR value below <90 mL/min/1.73m^2.

Table 4: Demographic features in adult and old age group

	Control (n=100)
Age (mean±SD) years	45.02±14.67
Sex (males %)	69 %
(females %)	31 %
Body Mass Index	20.67±5.17
Blood urea (mg/dl)	28.55±8.16
Serum Creatinine (mg/dl)	0.90±0.13

Table 4 shows the mean age of the Children was 45.02 years±14.67. The blood urea and serum creatinine within the normal range.

Table 5: Age wise eGFR in adult and old age group by using CG, MDRD and MCQE

Age	CG (ml/min/1.73m^2)	MDRD (ml/min/1.73m^2)	MCQE (ml/min/1.73m^2)
20-29 (n=19)	112.89±18.65	107.36±21.84	132.56±13.84**
30-39 (n=21)	102.92±15.92	98.50±19.89	123.27±16.77**
40-49 (n=23)	88.36±12.97	88.02±17.97	110.13±16.04**
50-59 (n=20)	78.88±11.04	85.02±15.98	104.98±14.30**
60-70(n=17)	73.03±9.74	82.38±14.04*	99.77±12.79**

*p<0.05; **p<0.001

Table 5 shows eGFR comparison age wise in adult and old age group, it was noticed that there was no significant difference in the 20-29, 30-39, 40-49 and 50-59 years range with respect to CG and MDRD equation (p=not significant). But in the age range of 60-70 years, the eGFR is significantly higher (p< 0.05) as per the MDRD equation. In all the age groups in controls the GFR as per MCQE method was significantly higher when compared with CG and MDRD (p<0.001).

Table 6: Distribution of adult and old age group in to different stages on the basis of eGFR

Stages	CG (ml/min/1.73m^2)	MDRD (ml/min/1.73m^2)	MCQE (ml/min/1.73m^2)
50-59 ml/min/1.73m^2	02 (2 %)	02 (2 %)	0 (0 %)
60-89 ml/min/1.73m^2	46 (46 %)	48 (48 %)	10 (10 %)
>90-120 ml/min/1.73m^2	52 (52 %)	50 (50 %)	90 (90 %)

Table 6 shows adult and old age group both CG and MDRD equation included a much higher number of normal individuals are having eGFR value below <90 mL/min/1.73m^2 this constitute 46% 48% with respect to CG and MDRD thus many control cases which apparently normal are included as CKD patients with stage 2 and stage 3. As per MCQE method only 10% of control cases belong to stage 2 of CKD. Therefore MCQE is a comparatively better method for assessing GFR in healthy control individual.

Discussion

A total of 175 subjects were studied including 75 Childrens and 100 subjects including both adult and old age group. In the present study, blood urea and serum creatinine were normal in all age groups with respective ages due to normal kidney function.

Detection of renal impairment can be done by estimating GFR accurate GFR measurement is done by infusion of radio- labelled substances. But these are not cost effective nor free of risk so these are not suitable for routine clinical practice. Serum creatinine based eGFR was simple and cost effective and not required infusion of toxic substances.

The eGFR value is depends upon the performances of the eGFR formulae. The most common serum creatinine based eGFR formulae used in clinical practice depends on anthropometric measurements. In these Schwartz equation is most commonly used eGFR [16]. In clinical practice, it is important to distinguish between children having normal (GFR $\geq$ 90 mL/min/1.73 m2) and abnormal GFR (GFR<90 mL/min/1.73 m2). Serum creatinine based formulas are suitable for use in patients with normal renal function [17].

Schwartz equation given a significantly ($p<0.001$) higher GFR values in childrens when compared with Counahan-Barrad. More or less it is the Schwartz equation which reasonably approximates to normal GFR values in childrens. Counahan-Barrad formulae included normal healthy childrens in to GFR $\leq$ 90 mL/min/1.73 m2 even though there was a normal serum creatinine and no evidence of renal impairment. They comprised 4% GFR less than 90 by Schwartz equation and 24% by Counahan-Barrad formulae. This suggests that Counahan-Barrad formulae underestimate GFR. The Schwartz equation placed 96% of healthy individuals in GFR more than 90 Counahan-Barrad formulae included 76% of population under category with a GFR more than 90 ml/min/1.73m^2. More or less it is the Schwartz equation which reasonably approximates to normal GFR values in childrens groups.

Cockcroft and Gault (CG) formula main purpose is measuring of creatinine clearance but the equation is biased due to body weight parameter in the equation. In obese subjects GFR is overestimated and lean individuals GFR is underestimated by CG equation [18]. It is overcome by adjusting to body surface area. The CG formula inaccurately measures the GFR in older age group individual with normal renal function because the age in the CG formula is inversely proportional to eGFR [19]. MDRD developed in patients with moderate CKD so applicability of MDRD in healthy individuals is not clearly understood. Compare with CG, MDRD not required weight and not need any correction for body surface area. Previous studies reported that it can only measures lower GFR values that is less than 60 ml/min/1.73m^2. [20, 21] Rule (2004) reported that MDRD did not improve performance even after recalibration of serum creatinine and there is still bias in patients with CKD. [13]

CG and MDRD formulae assessing GFR is still debated. Corsonelo (2005) reported that several drugs causes decreased GFR and therefore early stage detection is necessary for therapeutic management where the serum creatinine is near normal value [22]. But both CG and MDRD formulae have maximum disagreement in the low and normal creatinine value and causing inaccuracy. CG and MDRD inaccurately measures GFR in older age group people. Mayo clinic quadratic equation (MCQE) derived by using both normal and CKD patients. Because of both population, the result of creatinine dependent MCQE gave intermediate performance, though it does not underestimate normal GFR. Hence MCQE is found to be a better alternative to CG and MDRD [23].

There is a decline kidney function as age is advances and causes raised serum creatinine with decreased level of eGFR. In the present study, it was observed that there was a progressive decline in GFR as the age advances. When a comparison was made between CG and MDRD methods in respect of older age group, it was reported by both Garg [24] and Wieczorowska [25] that older individuals more than 60 years of age showed a higher value of eGFR by the MDRD method than the CG method. MCQE given a significantly ($p<0.001$) higher GFR values in all age groups when compared with CG and MDRD. More or less it is the MCQE method which reasonably approximates to normal GFR values in all age groups.

CG and MDRD formulae included normal healthy adult and old age group people in to satge 2 and stage 3 of Kidney disease even though there was a normal serum creatinine and no evidence of renal impairment. In case of stage-3 the inclusion of healthy individuals was to the extent of 2% by both the CG and MDRD equations. They comprised 46% in stage 2 by CG and 48% by MDRD. This suggests that CG and MDRD underestimate GFR. Both the MDRD and CG prediction formulae perform poorly in patients with normal or near-normal renal function [26, 27]. The MCQE placed only 10% of healthy individuals in CKD stage 2 and there was not a single case of control in stage 3. Both the CG and MDRD formulae included around 50% of population under category with a GFR less than <90 ml/min/1.73m^2. In Indian study Rajeshwari *et. al.*, (2011) in has reported that CG and MDRD equation classified more than 50% subjects in stage 2 and 0.8 to 1.4% under stage 3 of CKD depending on equation. Therefore the observation in our study in healthy control population is in concurrence with the findings of Rajeshwari (2011) [28].

From the findings of present study, it was concluded that the estimated GFR formulae have its own advantages and disadvantages and there are ambiguous reports in literature regarding estimated GFR. It is very complicated to predict best formulae to estimated GFR. However the present study infers with some degree of reservation that Schwartz is a good formula to provide ease of use in the daily practice in childrens and MCQE formula is acceptable for normal adult and old age group people.

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Declarations
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