Influence of Anthropometric Measurements on Serum Creatinine, Urea and eGFR in Healthy Adolescent Subjects

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ABSTRACT

BACKGROUND

Body mass consists of fat and lean body mass. Lean body mass comprises of body cell mass, bone mass and extracellular water. Body cell mass consist of muscle mass. Muscle mass is affected by age and gender and with extremities of age the variation is also found to be higher. Body mass has major influence on serum creatinine. Creatinine is derived from muscle protein, the creatine. Glomerular filtration rate (GFR) is used to estimate the renal glomerular function which is an early indicator of impending renal failure. Estimated GFR (eGFR) is commonly used as a practical alternative for measured GFR. However, most of the formulas used for estimation of eGFR rate takes into consideration age, gender, weight or height but not both. Muscle mass is also not considered into the formula. Hence, we have taken up this study to assess the influence of anthropometric measurements on serum creatinine, urea levels and eGFR in healthy adolescent subjects.

METHODS

It is a cross-sectional, retrospective study; data was collected as a part of larger study. A total of 261 students was included in the study which consisted of 137 female subjects and 124 male subjects. Demographic data, anthropometric measurements like height, weight, Body Mass Index (BMI), estimated lean body mass (eLBM) and fat mass was taken, blood collected was used for estimation of urea and creatinine. Data was analysed by SPSS software by student's t test, Pearson's correlation and ANOVA.

RESULTS

Creatinine values positively correlated significantly with age, height, weight, estimated lean body mass, and blood urea in male subjects; weight, estimated lean body mass, and blood urea levels were recorded in female subjects. Estimated GFR showed statistically significant correlation with anthropometric measurements like Body Mass Index, estimated lean body mass, its percentage and body fat percentage. Age, height and estimated lean body mass percentage showed negative correlation in male subjects whereas in female subjects only age and estimated lean body mass showed negative correlation. Male subjects did not show any statistically significant correlation with height but eGFR of female subjects showed statistically significant correlation with height. Urea did not show any correlation with anthropometric measurements.

CONCLUSIONS

Anthropometric measurements especially the lean body mass influence the serum creatinine and hence the estimated glomerular filtration rate. BMI influences the eGFR, but direct correlation could not be established with creatinine levels.

KEYWORDS

Renal Function Test, eGFR, Lean Body Mass, BMI

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BACKGROUND

Body mass consists of fat and lean body mass. Lean body mass comprises of body cell mass, bone mass and extracellular water. Body cell mass consist of muscle mass. Muscle mass is affected by age and gender and with extremities of age the variation is also found to be higher.[1]

Body mass has major influence on serum creatinine. Creatinine is derived from muscle protein, the creatine. It is synthesized by spontaneous non - enzymatic anhydrous reaction of creatine phosphate in skeletal muscle. Under steady state it is synthesized at a relatively constant rate from body's total skeletal muscle mass.[2,3] In persons with stable renal condition and due to its high correlation coefficient, serum creatinine is sometimes used as an inexpensive and easily available surrogate for muscle mass.[4]

Other factor influenced by muscle mass needing consideration is insulin. Primary target of insulin action is over skeletal muscle. Changes in skeletal muscle mass can trigger insulin resistance further leading to diabetes mellitus which is an important risk factor for chronic kidney disease (CKD). CKD is a risk factor and has been well associated with increased all-cause mortality. Previous studies show obesity and overweight as a major risk factor for renal dysfunction probability due to lipid abnormalities. It has also been indicated that obesity is a risk factor for renal dysfunction.[5]

Importance of early detection of kidney damage is indisputable, as in later stages, the disease is irreversible. Glomerular filtration rate (GFR) is used to estimate the renal glomerular function which is an early indicator of impending renal failure. Measurement of glomerular filtration rate is difficult, time consuming and sometime inaccurate due to improper collection. Estimated GFR (eGFR) is commonly used as a practical alternative for measured GFR.

As the muscle mass can influence the serum creatinine level, it also influences estimated glomerular filtration rate. However, most of the formulas used for estimation of eGFR rate take into consideration age, gender, weight or height but not both. Muscle mass is also not considered into the formula. Lim et al,[6] has suggested the lean body mass in the correction but these formulas are not commonly used. Hence, we have taken up this study to assess the influence of anthropometric measurements on serum creatinine and urea levels and eGFR in healthy adolescent subjects.

METHODS

Ethical committee clearance was obtained for the cross-sectional, retrospective study with certificate number PESIMSR / IHEC / 205. Data was collected as a part of larger study done for knowing reference range of urea and creatinine in adolescents. Government and private high schools around our medical college were approached; appropriate permissions were taken from school authorities. Multiphasing cluster random sampling was done, after taking consent from parents and accent from children to collect the blood, subject's demographic data and blood sample was collected. Questionnaire for lifestyle factors, history of illness or medication and demographic data were filled. All healthy, well built, students willing to take part in the study with their parents' consent were included in the study. All children with any acute or chronic illness or on any medication were excluded from the study. A total of 261 students were included in the study which consisted of 137 female subjects and 124 male subjects. Demographic data also included anthropometric measurements; height (ht.) in meters (mts.) weight (wt.) in kilograms (Kg). BMI was calculated using formula wt. in Kg / ht. in meters.[2] estimated lean body mass (eLBM) was calculated using Boer's formula,[7] for males: eLBM (Kg) = 0.407 W (Kg) + 0.267 H (cms) - 19.2 and for females: eLBM (Kg) = 0.252 W (Kg) + 0.473 H (cms) - 48.3. Percentage lean body mass was calculated using formula (eLBM / Wt. in Kg) X 100 and percentage fat mass was calculated using the formula (100 - eLBM %).[7] 3 mL of venous sample was taken in serum separator tubes from Becton, Dickinson and company (BD) vacutainer.[8] Samples were transported to laboratory in cold storage box. After centrifugation at 3000 RPM for 10 minutes as per our standard protocol, all samples were analysed for urea and creatinine in Vitros 5.1 FS autoanalyzer from orthoclinical diagnostics.[9] The methodology followed for urea estimation was urease method and for creatinine it was sarcosine method.[9] Estimated glomerular filtration rate (eGFR) was calculated as per Cockcroft-Gault [10,11,12] formula which is eGFR (mL / min) = [140 X age (yrs.)] X [weight (Kg) / 72 X serum creatinine (mg / dL)] multiply by 0.85 if female.

Statistical Analysis

Sample size was calculated using the formula by Daniel.[13] With 90% confidence interval (CI) and 5 % error margin the sample size was calculated to be 270.[13] Data were updated in Microsoft excel. The anthropometric parameters were expressed in mean + standard deviation (SD). Urea and creatinine were expressed as mean + SD mg / dl. eGFR was expressed as mL/min/1.73 mts.[2] SPSS software version 16 was used for statistical analysis. Pearson's correlation was done for all the anthropometric parameters with blood urea, creatinine values and with eGFR calculated using Cockcroft Gault.[10,11,12] The subjects were adolescent children, hence the subjects were categorized as low normal BMI (< 18.49), normal BMI (18.5 - 22.9) and high normal BMI (> 22.9) and groups were compared using ANOVA for renal function tests serum creatinine, urea and estimated GFR.

RESULTS

When male subjects were compared with female subjects using student's t test, height and blood urea levels showed statistically significant differences. Creatinine values positively correlated significantly with age, height, weight, estimated lean body mass and blood urea in male subjects, and weight, estimated lean body mass and blood urea levels in female subjects. Urea values positively correlated significantly with age, height and serum creatinine values in male subjects and only with creatinine in female subjects, other anthropometric measurements did not show any significant correlation with urea values.

N=261	Male Subjects (Mean + SD)	Female Subjects (Mean + SD)	Students t Test P Value
Age (Years)	15.3 + 1.24	15.42 + 1.13	0.206
Weight (Kg)	49.76 + 7.02	47.3 + 6.28	0.149
Height (mts)	1.60 + 0.09	1.56 + 0.06	0.00**
BMI (Kg / mt^2)	19.5 + 1.86	19.48 + 1.86	0.630
eLBM (Kg)	43.67 + 4.99	37.22 + 4.12	0.055
eLBM %	88.12 + 4.2	79.01 + 4.83	0.237
Body fat %	11.88 + 4.2	20.99 + 4.83	0.237
Urea (mg / dl)	19.37 + 5.64	18.84 + 5.23	0.001**
Creatinine (mg / dl)	0.62 + 0.14	0.53 + 0.09	0.850
eGFR by Cockroft Gault (Pierrat) (mL / min / 1.73 m^2)	143.08 + 29.72	135.45 + 26.51	0.178

Table 1. Anthropometric Measurements and Renal Function Tests of Study Subjects

**p value <0.001 is statistically significant

N=261	Male Subjects (N = 124)		Female Subjects (N = 137)	
	Pearson's Correlation	P Value	Pearson's Correlation	P Value
Age (Age)	0.276	0.002**	0.118	0.170
Height (mts.)	0.449	0.00**	0.157	0.067
Weight (Kg)	0.296	0.001**	0.231	0.007**
BMI (Kg / m^2)	- 0.110	0.225	0.026	0.760
eLBM (Kg)	0.394	0.00**	0.221	0.01*
eLBM %	0.068	0.455	-0.049	0.569
Body fat %	- 0.068	0.455	- 0.049	0.569
Urea (mg / dl)	0.356	0.00**	0.387	0.00**

Table 2. Pearson Correlation of Creatinine with Anthropometric Measurements in Male and Female Subjects

*P Value <0.01 is Statistically Significant, **P Value <0.001 is Statistically Significant

	Male subjects (N = 124)		Female Subjects (N = 137)	
	Pearson's Correlation	P Value	Pearson's Correlation	P Value
Age (Years)	0.282	0.001**	0.070	0.415
Height (mts)	0.058	0.052*	- 0.091	0.292
Weight (Kg)	- 0.043	0.634	- 0.011	0.894
BMI (Kg / mts^2)	- 0.126	0.162	0.127	0.132
eLBM	0.05	0.959	0.27	0.75
eLBM %	0.116	0.20	0.141	0.1
Body fat %	- 0.116	0.20	0.141	0.1
Creatinine (mg / dl)	0.356	0.00**	0.387	0.00**

Table 3. Pearson Correlation of Urea with Anthropometric Measurements in Male and Female Subjects

**P Value < 0.001 is Statistically Significant, *P Value < 0.05 is Statistically Significant

	Male subjects (N = 124)		Female subjects (N = 137)	
	Pearson's Correlation	P Value	Pearson's Correlation	P Value
Age (years)	- 0.195	0.031*	-0.18	0.035*
Height (mts)	- 0.008	0.926	0.523	0.00**
Weight (Kg)	0.037	0.00**	0.254	0.03**
BMI (Kg / mts^2)	0.489	0.00**	0.518	0.00**
eLBM (Kg)	0.182	0.043*	0.378	0.00**
eLBM %	- 0.488	0.00**	- 0.380	0.00**
Body fat %	0.488	0.00**	0.380	0.00**

Table 4. Pearson's Correlation of eGFR by Cockcroft-Gault (Pierrat) with Anthropometric Measurements

**P Value <0.001 is Statistically Significant, *P Value <0.05 is Statistically Significant

As estimated GFR is calculated using weight, hence weight and all weight derived parameters of anthropometric measurements like Body mass index, estimated lean body mass, its percentage and body fat percentage showed statistically significant correlation. Age, height and estimated lean body mass percentage showed negative correlation in male subjects whereas in female subjects only age and estimated lean body mass showed negative correlation. Male subject did not show any statistically significant correlation with height but eGFR of female subjects showed statistically significant correlation with height.

RFT parameters	BMI <18.5 Mean + SD	BMI 18.5 - 22.9 Mean + SD	BMI > 22.9 Mean + SD	P Value
Male subjects (124)				
	N=51	N=65	N=8	
Creatinine	0.64 + 0.16	0.61 + 0.12	0.6 + 0.10	0.46
Urea	20.06 + 6.5	19.11 + 5.0	16.9 + 2.2	0.31
eGFR	131 + 26.9	148 + 27.43	169 + 36.37	0.00**
Female subjects (137)				
	N=55	N=71	N=11	
Creatinine	0.516 + 0.089	0.53 + 0.089	0.518 + 0.075	0.474
Urea	17.6 + 4.8	19.5 + 5.39	20.1 + 5.36	0.101
eGFR	126 + 22.06	136 + 23.8	176 + 22.06	0.00**

Table 5. Comparison of Renal Function Tests With Body Mass Index

**P Value <0.001 is Statistically Significant

On comparison of renal function test with low normal, normal and high normal body mass index groups, urea and creatinine did not show any statistically significant differences but eGFR showed high statistically significant difference among these group with p value of 0.00 for both male and female subjects.

DISCUSSION

Urea is an end product of aminoacid metabolism. It is synthesized in liver. Amino acids give ammonia, biotransformation of ammonia to convert it into more water-soluble urea happens in the liver. Water soluble waste substance urea is released into the blood and finally excreted through kidneys. Creatinine is non-enzymatically produced from creatine phosphate in the muscle. Creatinine phosphate acts as an energy reserve in the muscle, however finally creatinine is synthesized, and it is also excreted through kidneys.

GFR estimation is very important for a routine evaluation in kidney failure patients. It is also done for early detection of renal failure. However measured GFR, if done by correct procedure is a good measure of glomerular function but it is cumbersome. Estimated glomerular filtration rate (eGFR) hence is used as an alternative to measured GFR. Most of the formulas used to estimate or calculate GFR are creatinine based. As muscle mass remains fairly constant over a period of time, serum creatinine also remains constant over a period of time. 24-hour urinary creatinine excretion also remains constant over a period of time.[14] Due to this relationship serum and urinary creatinine is used to predict muscle mass. Creatinine is synthesized in muscle and hence muscle mass needs consideration in these formulas.

Here in this study we have tried to correlate the renal function tests which included serum creatinine, urea and measured GFR by Cockcroft-Gault,[10,11,12] with the anthropometric measurements including BMI and estimated lean body mass. As urea is derivative of aminoacid the anthropometric measurements did not directly correlate with the urea levels. Creatinine is a derivative of muscle hence most of the anthropometric measurements showed direct

positive or negative statistically significant correlation. Age, weight, height and eLBM showed positive correlation with creatinine for male subjects whereas in female subjects it correlated statistically significantly with weight eLBM.

Estimated lean body mass index calculated using Boer's formula,[7] showed statistically significant correlation with creatinine levels for both male and female subjects. As opposite to the study results of Alessandra et al[15] and Baxmann et al our study showed no correlation of serum creatinine with BMI but estimated GFR by Cockcroft-Gault formula showed significant positive correlation with BMI and lean body mass for both males and females.

In contrast to our study, Swaminathan et al[16] showed that lean body mass has minor contributions to serum creatinine, and they explained their findings by stating that production of creatinine increases with increased lean body mass, however volume of distribution of creatinine also concomitantly increases. This reduces the influence of LBM on serum creatinine. However, their study included only female subjects, as females have lower LBM, females might have lower creatinine thus reducing its contribution. Similar results are seen in our study when female data was analysed. The statistical significance was lower with p value of <0.01 when compared to male subjects with p value of < 0.00, however our study showed statistically significant positive correlation between creatinine and estimated lean body mass even in female subjects.

BMI was categorized as low normal, normal and high normal. Our study did not show any significant differences between groups for urea and creatinine, however statistically significant differences among groups were observed for eGFR. This finding could be due to the fact that both are calculated parameters using anthropometric measurements, however X.-M. Li published in 2014 showed obesity or high BMI clearly as an independent risk factor of kidney damage. Their study showed direct significant correlation between serum creatinine and body mass index (BMI).BMI was found to be an independent predictor of increased creatinine in children of age above 10 years. He also opined that prevention of obesity in childhood was exceptionally important to protect renal function.[18] As evident from above, our study did not show any significant correlation between BMI and creatinine, but showed significant positive correlation with lean body mass. One of the factor contributing to these differences seems to be due to the differences in sample size between both the studies, our study had a sample size of 261 subjects while study by X.-M. Li was a multi-ethnic, community-based, and cross-sectional study which included 5222 study subjects. The study done by X.- M. Li has not correlated lean body mass values with serum creatinine as the hypothesis of the study was to evaluate the correlation between BMI and serum creatinine.[17]

Most of the studies done showed positive correlation with BMI and lean muscle mass. Our study also shows strong positive correlation with lean body mass and serum creatinine. Both urea and creatinine levels are used as the functional markers of kidney; creatinine was influenced by anthropometric measurements especially the lean body mass even in healthy adolescents. Thereby our study humbly reiterates the known relevance of these factors on renal function.

CONCLUSIONS

Anthropometric measurements especially the lean body mass influences serum creatinine, and hence the estimated glomerular filtration rate. BMI influences the eGFR but direct correlation could not be established with creatinine levels. Serum creatinine and hence eGFR is influenced by lean body mass; but these findings have to be confirmed by studies involving actual measurements of GFR, GFR measurements using urinary creatinine levels and lean body mass.

Limitations

We have mainly included well-built study subjects with mean BMI of 19.5 + 1.86 for male subjects and 19.48 + 1.86 for female subjects, as the data was collected for a larger study done to derive biological reference interval of normal adolescents. Further detailed and well-organized study with low BMI, normal BMI and high BMI subjects grouping as malnourished, normal and obese can demonstrate the differences in more detail.

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