www.jmscr.igmpublication.org
Impact Factor 5.84
Index Copernicus Value: 83.27
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v5i7.251

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Research Article

Effect of Age on Estimated Glomerular Filtration Rate

Author
Pallavi Mahajan
Demonstrator, Department of Biochemistry, Government Medical College, Jammu, J&K, India
Corresponding Author
Dr Pallavi Mahajan
Demonstrator, Department of Biochemistry, Government Medical College, Jammu, J&K
Phone no. 9419114012, Email: *pallavi31mahajan@gmail.com*

Abstract
Glomerular filtration rate is the best determinant for the evaluation of renal function. It is important for the differentiation of various kidney diseases, for the evaluation of the effect and dose adjustment of various drugs. For the estimation of GFR precise methods and appropriate reference values are to be used and it is often estimated from equations that include variables like age, sex, race, creatinine and cystatin C. In the earlier studies, the variable results of the effects of age and sex on renal function were observed. So, the present study was conducted to estimate and compare the eGFR both creatinine and cystatin C based in apparently healthy subjects of different age groups. It was observed that there was decline in estimated GFR in both creatinine and cystatin based with increase in the age in both the genders. Hence, depending on the equation used for the estimation of GFR, the reference range adjusted for different age groups should be taken into consideration.
Keywords: *Glomerular filtration rate, age, sex, eGFR*

Introduction

Glomerular filtration rate (GFR) is the best measure for the assessment of renal function. GFR is important for the categorization of different renal diseases, for the evaluation of the effect and adjustment of dose of various drugs and to check the renal function in potential kidney donors. For the determination of GFR accurate methods and adequate reference values are to be used. In the previous studies, the effects of age and sex on renal function showed variable results [(1)]. GFR is often estimated from equations that include age, sex, race, creatinine and cystatin C as main variables [(2)]. In a normal adult population, serum creatinine shows modest correlation with age, whereas the creatinine clearance (CCL) decreases appreciably with age [(3)]. The decrease in the GFR with age is the main reason for the predisposition of chronic kidney disease (CKD) in old age [(4)]. The definition of chronic kidney disease by the US National Kidney Foundation recommends, regardless of the age, a single GFR cut-off of 60 ml/min/1.73m^2 [(5)]. The various equations for the calculation of estimated GFR (eGFR) includes the Cockcroft and Gault (CG) formula and the simplified modified diet in renal disease (MDRD) equation, reexpressed MDRD equation, CKD-EPI equations both based on creatinine and cystatin C. The MDRD formula gives a direct estimate of GFR whereas the original CG formula gives an

estimate of CCL [3]. In the past decade, there has been increase in the awareness of CKD. The guideline issued by the Kidney Disease Outcomes Quality Initiative (K/DOQI) from the National Kidney Foundation has increased the interest in CKD worldwide. In the past various studies showed that there is decline in eGFR in older age as compared to younger patients. Though eGFR is an excellent forecaster of progression to end stage kidney disease (ESKD) in patients of all age groups, but there is huge difference in the absolute risk of ESKD in patients of different age having similar levels of eGFR and at any given level of eGFR, the older patients are less likely to develop ESKD [6]. In the general population, male gender, hypertension, diabetes, older age are the well-built risk factors for development of kidney disease but the involvement of hypertension with succession of renal disease may be decreased at older ages [7]. So, the present study was conducted to estimate and compare the eGFR both creatinine and cystatin C based in apparently healthy subjects of different age groups.

Material and Method

The present study was conducted in the department of Biochemistry, Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. 100 apparently healthy subjects in the age range of 17 years and above of either sex were selected. They were further divided into two groups according to their age i.e 17-49 years and 50 years and above. Under all aseptic conditions, 5 ml of venous blood sample was collected from antecubital vein of the subjects after an overnight fasting of 10-12 hours for biochemical analysis. Serum Cystatin C estimation was done by Enzyme Linked Immunosorbent Assay (ELISA) as described by Pergande M[8]. The serum creatinine was estimated by Jaffe's Alkaline Picrate method [9]. The estimated GFR was calculated using creatinine-based (eGFR-creatinine) and cystatin C-based (eGFR-cys) equations.

The "reexpressed" Modification of diet in renal disease (MDRD) study equation for standardized serum creatinine: [10]

eGFR (mL/min/1.73 m^2) = 175 x serum creatinine (mg/dL)$^{-1.154}$ x age(years) $^{-0.203}$ x 0.742 (if female) x 1.212 (if black)

CKD-Epidemiology Collaboration (EPI) cystatin C equation adjusted for age, sex, and race: [10]

eGFR = 127.7 x serum cystatin C (mg/L) $^{-1.17}$ x age (years) $^{-0.13}$ x 0.91 (if female) x 1.06 (if black)

Results

In the present study, 100 apparently healthy subjects in the age range of 17 years and above were selected. They were further divided into two groups according to their age i.e. 17-49 years and 50 years and above. The mean eGFR-cys in 17-49 years was 195.96 ml/min/1.73 m^2 and in the age group 50 years and above, the mean eGFR-cys was 119.76 ml/min/1.73 m^2. When the comparison was done between the mean eGFR-cys in both the age groups, the p-value was 0.001, which is statistically significant. The comparison was also done between the mean eGFR-creatinine in both the age groups. It was observed that the mean eGFR-creatinine in 17-49 years age group was 93.82 ml/min/1.73 m^2 and in the 50 years and above age group, the mean eGFR-creatinine was 74.76ml/min/1.73m^2, on comparison the p-value <0.001(which is statistically significant). When the comparison of eGFR both cystatin C and creatinine based were done in the males and females of both age groups, significant difference was observed. There is decrease in the eGFR both creatinine and cystatin C based with age in both the genders.

Table 1: Mean eGFR in both the age groups

	Age group	Number	Mean ($ml/min/1.73m^2$)	Standard deviation ($ml/min/1.73m^2$)	p-value
eGFR of cystatin c	17-49 years	50	195.96	126.713	0.001
	50 years & above	50	119.76	82.286	
eGFR of creatinine	17-49 years	50	93.82	16.684	<0.001
	50 years & above	50	74.76	14.211	
p-value<0.05,statistically significant					

Table 2: Mean eGFR in males and females of both the age groups

	Age group	sex	number	Mean ($ml/min/1.73m^2$)	Standard deviation ($ml/min/1.73m^2$)	p-value
eGFR of cystatin c	17-49 years	Female	23	196.04	135.152	0.031
	50 years & above	Female	16	110.94	82.757	
eGFR of creatinine	17-49 years	Female	23	84.52	14.343	<0.001
	50 years & above	Female	16	66.38	11.803	
eGFR of cystatin c	17-49 years	Male	27	195.89	121.671	0.008
	50 years & above	Male	34	123.91	82.978	
eGFR of creatinine	17-49 years	Male	27	101.74	14.453	<0.001
	50 years & above	Male	34	78.71	13.653	
p-value<0.05,statistically significant						

Table 3: Reference value of eGFR by different researchers

Researchers	Sample size	Age range (years)	Population	GFR ($ml/min/1.73m^2$)
Hogeman et al (17)	36 men 20 women	20-30	Healthy	122±13 men 124±13 women
Wesson et al (18)	347 men 141women	1-89	Healthy status not confirmed	130 men 120 women
Back et al (19)	67	21-77	Healthy volunteer, healthy status confirmed	20-50 years, 100±22 51-65 years, 83±25 66-80 years, 72±20
Vervoort et al (20)	23 men 23 women	28±6	Healthy volunteer, healthy status confirmed	107±11
Hoang et al (21)	94 men 65 women	18-88	Healthy volunteer, healthy status confirmed	>40 years,104±15 <55 years,81±17
Fehrman-Ekholm and Skeppholm (22)	32 men 20 women	71-110	Elderly, active subjects	68±11
Grewal and Blake (15)	208 men 216 women	19-72	Living kidney donors, healthy status confirmed	>40 years, 103±16
Barai et al (13)	250 men 360 women	20-45	Indian Living kidney donors, healthy status confirmed	81±19

Discussion

In the present study, it was observed that both eGFR-creatinine and eGFR-cys decreases with age in both the sexes. Similar results were observed by other researchers (Table 3). It was believed that the process of senescence is associated with decline in GFR, and it is a universal phenomenon in individuals after the age of 30 years. Besides aging, the presence of co-morbid disorders in the elderly can also influence the rate of decline of GFR. This phenomenon was also observed in females, but the value of GFR in

advanced age is usually lower in women as compared to men [11]. This decrease in GFR with age is usually accompanied by alterations in renal structure [12]. As the age advances there is steady increase in the percentage of glomeruli affected by glomerulosclerosis. By and large there in decrease in the number of functioning nephrons with aging even in the absence of any disease. However, it was supposed that the decline in GFR was due to progressive alteration in the vascular tree or due to angiotensin II or oxidative stress and telomere shortening. The process of "normal" aging is associated with progressive loss of nephron mass, glomerulosclerosis, nephrosclerosis, and an increase in interstitial volume [11]. In a cohort study conducted by Hare et al, it was observed that, at eGFR ≥ 45 ml/min per 1.73 m^2, there was rapid decline in GFR in older patients as compared to younger patients and when the eGFR≤ 45 ml/min per 1.73m^2, the eGFR declined more slowly in older than in younger patients [6]. Wetzels et al demonstrated that the reference value of MDRD-GFR decreases with age. In their study, for men >60 years and women >50 years, GFR of 60 ml/min/1.73m^2 is within the normal reference range (12). In another study conducted by Barai et al, on potential kidney donors, it was found that no significant difference in the GFR between males and females in 20–30 or 30–40 year age groups, but significantly higher GFR was observed in females than in males in the age group of 41–45 years, suggesting slow or no progression in females with age[13]. Many authors have showed decline in GFR with age but without taking gender into consideration [1]. In a meta-analysis study, a decline of 4 ml/min/1.73m^2 up to 50 years and 10ml/min/1.73m^2 after 50 years using inulin or radioactive EDTA was shown [14]. In a study conducted by Grewal et al also observed that the GFR remained stable till the age of 40 years and thereafter declined at a rate of 9.1ml/min/1.73m^2 per decade [15]. In the MDRD study, patients with normal renal function were not included and thereby lacking precision and the systematic underestimation of GFR around 60 mL/min/1.73m^2. The K-DIGO recommendation defines GFR below 60 mL/min/1.73m^2 as a disease, without considering the age. This recommendation was based on eGFR and the greater risk of mortality with eGFR below 60 mL/min/1.73m^2. Though the bias was less significant with the new CKD-EPI equation, but the meticulousness remains suboptimal [16].

Conclusion

Hence, in the present study, it was observed that there was decline in estimated GFR in both creatinine and cystatin based with increase in the age in both the sexes. So while estimating the GFR the age adjusted reference ranges depending on the equation used should be taken into consideration.

Competing Interests

The data used in the study was a part of the MD (Biochemistry Thesis) of Dr. Pallavi Mahajan at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. The author declares no conflict of interest.

References

1. Berg UB. Differences in decline in GFR with age between males and females. Reference data on clearences of inulin and PAH in potential kidney donors. Nephrol Dial Transplant. 2006; 21: 2577-82.
2. Garasto S, Fusco S, Corica F, Rosignuolo M, Marino A, Montesanto A, et al. Estimating glomerular filtration rate in older people. Hindawi Publishing Corporation. BioMed Res Int. 2014; Article ID: 916542.
3. Douville P, Martel AR, Talbot J, Desmeules S, Langlois S, Agharazii M. Impact of age on glomerular filtration estimates. Nephrol Dial Transplant. 2009; 24: 97-103.
4. Eriksen BO, Stefansson VTN, Jenssen TG, Mathisen UD, Schei J, Solbu MD, et al. Blood pressure and age related GFR

decline in the general population. BMC Nephrol. 2017; 18: 77.
5. National Kidney Foundation. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Initiative. Am J Kidney Dis. 2002; 39: S1-S246.
6. O'Hare AM, Choi AL, Bertenthal D, Bacchetti P, Garg AX, Kaufman JS, et al. Age affects outcome in chronic kidney disease. J Am Soc Nephrol. 2007; 18: 2758-65.
7. Klag MJ, Whelton PK, Randall BL, Neaton JD, Brancati FL, Ford CE, et al. Blood pressure and end stage renal disease attributed to hypertension. Am Engl J Med. 1996; 334:13-18.
8. Pergande M, Jung K. Sandwich enzyme immunoassay of cystatin C in serum with commercially available antibodies. Clin Chem. 1993; 39: 1885-90.
9. Bowers LD. Kinetic serum creatinine assays I. The role of various factors in determining specifity. Clin Chem. 1980; 26(5): 551-54.
10. Stevens LA, Levey AS. How is GFR estimated? Am J Kid Dis. 2009; 53: S17-S26.
11. Glassock RJ, Winearls C. Ageing and the glomerular filtration rate: truths and consequences. Trans Am Clin Climatol Assoc. 2009; 120: 419-27.
12. Wetzels JFM, Kiemeney LALM, Swinkels DW, Willems HL, Heijer MD. Age- and gender-specific reference values of estimated GFR in Caucasians: The Nijmegen biomedical study. Kidney Int. 2007; 72: 632-37.
13. Barai S, Bandopadhayaya GP, Patel CD. Do healthy potential kidney donors in India have an average glomerular filtration rate of 81.4 ml/min? Nephron Physiol. 2005; 101:21-26.
14. Granerus G, Aurell M. Reference values for 51Cr-EDTA clearance as a measure of glomerular filtration rate. Scand J Clin Lab Invest. 1981; 41: 611-16.
15. Grewal GS, Blake GM. Reference data for 51Cr-EDTA measurements of the glomerular filtration rate derived from live kidney donors. Nucl Med Commun. 2005; 26: 61-65.
16. Delanaye P, Schaeffner E, Ebert N, Cavalier E, Mariat C, Krzesinski JM, et al. Normal reference values for glomerular filtration rate: what do we really know? Nephrol Dial Transplant. 2012; 27: 2664-72.
17. Hogeman O. Normal individuals. Acta Med Scand Suppl. 1948; 131: 99-108.
18. Wesson LG. Renal hemodynamics in physiologic states. In: Wesson LG (ed). Physiology of the Human Kidney. New York: Grune & Stratton, 1969, pp. 96-108.
19. Back SE, Ljungberg B, Nilsson-Ehle I et al. Age dependence of renal function: clearance of iohexol and p-aminohippurate in healthy males. Scand J Clin Lab Invest. 1989; 49: 641-46.
20. 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: 1909-13.
21. Hoang K, Tan JC, Derby G et al. Determinants of glomerular hypofiltration in aging humans. Kidney Int. 2003; 64: 1417-24.
22. Fehrman-Ekholm I, Skeppholm L. Renal function in the elderly (>70 years old) measured by means of iohexol clearance, serum creatinine, serum urea and estimated clearance. Scand J Urol Nephrol. 2004; 38: 73-77.