AGE RELATED CHANGES OF GFR IN A POPULATION OF KERALA
Chitra Kuriakose1, Sebastain Abraham2, Manjula V. D3, V. S. Sumadevi4, Annamma Kurien5

HOW TO CITE THIS ARTICLE:
Chitra Kuriakose, Sebastain Abraham, Manjula V. D, V. S. Sumadevi, Annamma Kurien. "Age Related Changes of GFR in a Population of Kerala”. Journal of Evidence based Medicine and Healthcare; Volume 2, Issue 34, August 24, 2015; Page: 5226-5231, DOI: 10.18410/jebmh/2015/727

ABSTRACT: BACKGROUND: Glomerular Filtration Rate (GFR) is the best index for assessing kidney function. Ethnicity has a potential influence on GFR. Anatomic and physiological changes of ageing kidney influences GFR. AIMS AND OBJECTIVES: To find age related variations of GFR in a population of Kerala. SUBJECTS AND METHODS: A total of 519 subjects of all ages from the community were screened. Blood pressure, diabetes, mellitus, proteinuria, serum creatinine being checked. Estimated GFR (eGFR) assessed using modification of diet in renal disease [MDRD formula]. RESULTS: The mean eGFR of the population was found to be 61.2±18.2ml/min. and the eGFR of normal subjects excluding diabetes, mellitus, blood pressure and proteinuria was found to be 64.49±20.5ml/min. e-GFR was more for males compared to females, 67.5±20ml/min and 55.4±14ml/min respectively. e GFR showed a steady decline as the age advanced and it was statistically significant(p < 0.05). CONCLUSION: The age adjusted eGFR of keralite population is much less compared to western standards. A more detailed study in general population is needed.
KEYWORDS: E GFR, MDRD formula, Ageing.

INTRODUCTION: Glomerular filtration rate gives a rough estimate of the proper functioning of kidney. Mean glomerural filtration rate decreases with age in many cross sectional studies.[1,2,3] This decrease may be regarded as a part of ageing. There can be a potential influence of ethnicity on GFR.[4] Culture and dietary factor may affect it. Different populations are found to have difference in the eGFR. The skeletal muscle mass, height and weight our population is different from that of western population. So the normal values of GFR may also differ in our population. Such a relevant study relating the GFR and age has not been conducted in our population. It has an important clinical implication, in adjusting drug dosage, especially those which is eliminated through kidney, evaluating donors, assessing the potential predisposal ischaemic or toxic renal injury etc. In this context an attempt was made to get an idea of changes of GFR with age and the range of e-GFR values in a Keralite population.

SUBJECTS AND METHODS: After getting the clearance from institutional ethical committee community awareness and detection medical camp program was organized in Kottayam District at two different panchayats in 2008 with the help of nephrology department. Total number of people screened in the camp was 519. People of all age groups attended the camp. Using proforma details of demographic variables like age, sex, history of kidney disease, diabetes mellitus and high blood pressure were collected. Height was measured using measuring tape with a sensitivity of 0.5cm, with patient standing straight with occiput, buttocks and heel touching the wall. Weight was measured using portable weighing machine by instructing subjects to stand
erect without footwear. Blood pressures of all subjects were measured in sitting position in right arm using sphygmomanometer. Informed consent was taken. 5 ml of blood was drawn under aseptic precaution and sent to biochemical laboratory. Serum creatinine, blood glucose and urine protein analysis was done. Those having blood pressure greater than 120/80 mm Hg was considered as hypertensives. Those having RBS greater than 110mg/dl with glucometer was re-evaluated. FBS done and those having FBS>110mg/dl were diagnosed as having diabetes mellitus. Dipstick test is done for detection of proteinuria. Serum creatinine was assessed using Jaffe's method. GFR was assessed using MDRD formula.

\[ GFR = 186 \times (\text{Se.Creat})^{-1.154} \times (\text{Age})^{0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black}) \]

National kidney foundation recommends estimating GFR by MDRD formula.\[5,6,7,8\]

ANALYSIS: Collected data entered in Microsoft excel and was analysed using statistical software SPSS version 11.0. Continuous variables were expressed as mean and standard deviation while categorical variables as percentage. Significant difference in mean values of eGFR between males and females were tested by independent sample t test. Difference in mean e GFR in various age groups was tested by Analysis of variance. Association between age and e GFR was tested by Pearson Correlation. P value of 0.05 is taken as significant.

RESULTS:

| Number | Percentage | e GFR [ml/min] | Mean SD |
|--------|------------|----------------|---------|
| Males  | 256        | 49.3           | 67.5    | 20.5    |
| Females| 263        | 50.7           | 55.4    | 14.5    |
| Total  | 519        | 100            | 61.2    | 18.2    |

Table 1: Distribution of e-GFR in the study population

P value<0.01.

Table 1 shows the gender wise distribution of GFR of the whole population with mean and standard deviation. The average effective GFR of males was higher than that of females. The mean e-GFR of males was 67.5±20.5ml/min and females were 55.4±14.5 ml/min. The mean e-GFR of the whole population is 61.2±18.2 ml/min.

| Age group | Number | Percentage | Mean Egfr [ml/min] | Standard Deviation |
|-----------|--------|------------|-------------------|--------------------|
| <30       | 21     | 4.7        | 84.05             | 15                 |
| 31-40     | 80     | 15.41      | 67.17             | 10                 |
| 41-50     | 127    | 24.47      | 61.1              | 12                 |
| 51-60     | 123    | 23.69      | 58.95             | 17                 |
| 61-70     | 103    | 19.65      | 57.87             | 14                 |
| >70       | 65     | 12.52      | 56.15             | 10                 |

Table 2: Distribution of e – GFR in different age groups
Table-2 shows that there was a wide variation in the distribution of study subjects. The mean age was found to be 53.72±19 years. The bulk of the subjects were between 41-70 years. The number of subjects attended the camp below 30 years and above 70 years was 4.7% and 12.5% respectively. The e-GFR showed a negative correlation with age (correlation coefficient -0.134, p value <0.05).

| Effective eGFR | Total number of subjects | Percentage | Total number of normal subjects | Percentage |
|----------------|--------------------------|------------|---------------------------------|------------|
| <60ml/min      | 266                      | 51.2       | 84                              | 43         |
| ≥60ml/min      | 253                      | 48.8       | 110                             | 57         |
| Total          | 519                      | 100        | 194                             | 100        |

Table 3: Percentage distribution of subjects having eGFR < 60ml/min & ≥60ml/min

Table 3 shows comparative distribution of whole population and normal population (Excluding diabetic, hypertensive and proteinuric subjects) having e-GFR greater than and equal to 60 ml/min and e-GFR less than 60 ml/min. Even 43 % of normal population was having e-GFR less than 60ml/min. e-GFR of normal subjects was 64.49±20.5ml/min.

**DISCUSSION:** GFR is a test used to check how well the kidneys are working. They are filters that filter waste from blood. It is the amount of plasma ultra-filtrate formed in bowmans capsule/min. the GFR in a healthy adult is 125 ml/min. In our study e-GFR was assessed by MDRD formula.

Our study showed a progressive decrease in GFR as the age increases. Many studies showed similar decrease.[9,10] The decrease maybe due to normal physiological ageing with structural changes.[11] The mean number of nephrons in adults is around 900,000 ranging from 200,000 to 2,000,000[12] The number of functioning nephrons shows 30 to 45% reduction in older kidney donors compared to younger.[13]

In our study the males are having greater GFR than females. According to Poggio et al women showed greater GFR than males[14] but Gross JL et al showed lower GFR for females[9] while Granerus G et al[15] showed similar GFR in males and females.

On comparing the GFR values with the western population e-GFR in our studies is very much less.[16] Barai et al[16] investigated potential kidney donors in India and found the GFR is much less. The mean GFR value of young healthy Indian adult is 81.4±19.4ml/min which is significantly less. Another study in healthy Indian population showed an average GFR value of 87.39±10ml/min and the range of normal creatinine between0.97-0.99.[17] The mean estimated GFR in our study conducted in Kerala was found to be 61.2±18.2ml/min. Similar studies in Denmark showed a variation of GFR from 110-72ml/min. and France between107-86ml/min. Another study in Sweden showed a normal GFR of 105±13ml/min.[18] A Chinese study showed GFR values higher than that of Indian adults but less than that of western population.[19,20] The differences may be due to peculiarities of dietary intake in different population, differences in GFR measurement methods or ethnicity itself.[4] Or might be due to anatomical/ functional change, size/ number or function of nephrons may differ in different population.
In our study 51% of the total population is having GFR <60ml/min. Out of this 31.5% have no associated illness. Associated kidney disease is seen more in persons with low GFR. The normal GFR of healthy Indian adults coincides with the GFR in CKD stage 2 which is between 60 to 89 ml/min. So further studies have to be undertaken in this respect. If necessary CKD classification for Indians has to be changed. It is important for the characterization of various renal diseases, evaluating the effect of different therapies, adjusting the doses of various drugs and ensuring the potential kidney donors having normal renal function.

Limitation of the study was a small study group and the data was obtained from a camp organized for awareness and detection program. It was not a door to door survey. A more detailed study to assess GFR in general population of Kerala is needed to formulate reference value. But this is an eye opener.

CONCLUSION: Data from the study indicates that the estimated GFR decreases as the age advances. Mean e-GFR by MDRD formula of the study population from Kerala is 61.2±8.2ml/mt. The mean eGFR in normal subjects excluding diabetics, hypertensives and proteinuric population is 64.49+/−20.5ml/mt. e GFR of keralite population is much lower when compared to western standards. A more organized study has to be conducted to establish a reference range value of GFR among keralite population.

ACKNOWLEDGMENTS: I am immensely grateful to Dr. Vimala A, retired professor of nephrology and Binu Areekal for their valuable directions in carrying out the study.

REFERENCES:
1. Hoang K, Tan JC, Derby G, et al. Determinants of glomerular hypofiltration in aging humans. Kidney Int. 2003; 64(4): 1417-1424.
2. Rowe JW, Shock NW, De Fronzo RA. The influence of age on the renal response to water deprivation in man. Nephron. 1976; 17(4): 270-278.
3. Edwards MS, Wilson DB, Craven TE, et al. Associations between retinal microvascular abnormalities and declining renal function in the elderly population: the Cardiovascular Health Study. Am J Kidney Dis. 2005; 46(2): 214-224.
4. Ariana Aguiar Soares1, Aline Bodanese Prates1, Letícia Schwerz Weinert1, Francisco Veríssimo Veronese2, Mirela Jobim de Azevedo1,3 and Sandra Pinho Silveiro1,3 Reference values for glomerular filtration rate in healthy Brazilian adults Soares et al. BMC Nephrology 2013, 14:54 http://www.biomedcentral.com/1471-2369/14/54.
5. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF III, Feldman HI, et al: A new equation to estimate glomerular filtration rate. Ann Intern Med 2009, 150: 604–612.
6. Nyman U, Grubb A, Sterner G, Björk J: The CKD-EPI and MDRD equations to estimate GFR. Validation in the Swedish Lund-Malmö study cohort. Scand J Clin Lab Invest 2001, 71: 129–138.
7. Miller WG: Estimating glomerular filtration rate. Clin Chem Lab Med 2009, 47: 1017–1019.
8. Soares AA, Eyff TF, Campani RB, Ritter L, Weinert LS, Camargo JL, et al: Performance of the CKD Epidemiology Collaboration (CKD-EPI) and the Modification of Diet in Renal Disease (MDRD) study equations in healthy South Brazilians. Am J Kidney Dis 2010, 55: 1162–11635.
9. Gross JL, Friedman R, de Azevedo MJ, Silveiro SP, Pecis M: Effect of age and sex on glomerular filtration rate measured by 51Cr-EDTA. Brazilian J Med Biol Res 1992, 25: 129–134.
10. Rule AD, Amer H, Cornell LD, Taler SJ, Cosio FG, Kremers WK, et al: The association between age and nephrosclerosis on renal biopsy among healthy adults. Ann Intern Med 2010, 152: 561–567.
11. McLachlan MSF: The aging kidney. Lancet 1978, 2: 143–145.
12. Walker AK, Bertram JF: Kidney development: core curriculum 2011. Am J Kidney Dis 2011, 57: 948–958.
13. Tan JC, Busque S, Workeneh B, Ho B, Derby G, Blouch KL, et al: Effects of aging on glomerular function and number in living kidney donors. Kidney Int 2010, 78: 686–692.
14. Poggio ED, Rule AD, Tanchanco R, Arrigain S, Butler RS, Srinivas T, et al: Demographic and clinical characteristics associated with Glomerular filtration rates in living kidney donors. Kidney Int 2009, 75: 1079–1087.
15. Granerus G, Aurell M: Reference values for 51Cr-EDTA clearance as a measure of glomerular filtration rate. Scand J Clin Lab Invest 1981, 41: 611–616.
16. Barai S, Bandopadhayaya GP, Patel CD, Rathi M, Kumar R, Bhowmik D, et al: Do healthy potential kidney donors in India have an average glomerular filtration rate of 81.4 ml/min? Nephron Physiol 2005, 101: 21–26.
17. Chakravarthi, R.; Hussaini, S.; Prasad, K. Mahesh; Naidu, S.; Harikrishana; Shekhar; Laxmi estimation of GFR in healthy Indian population., Indian Journal of Nephrology; Jul-Sep. 2007, Vol. 17 Issue 3, p105.
18. Ulf Nyman1/ Anders Grubb2/ Anders Larsson3/ Lars-Olof Hansson3/ Mats Flodin3/ Gunnar Nordin4/ Veronica Lindström2/ Jonas Björk5; 6The revised Lund-Malmö GFR estimating equation outperforms MDRD and CKD-EPI across GFR, age and BMI intervals in a large Swedish population, Clinical Chemistry and Laboratory Medicine (CCLM) Volume 52, Issue 6 (Jun 2014).
19. Ma YC, Zuo L, Chen L, Su ZM, Meng S, Li JJ, et al: Distribution of measured GFR in apparently healthy Chinese adults. Am J Kidney Dis 2010, 56: 420–421.
20. Rule AD, Gussak HM, Pond GR, Bergstralh EJ, Stegall MD, Cosio FG, et al: Measured and estimated GFR in healthy potential kidney donors. Am J Kidney Dis 2004, 43: 112–119.
AUTHORS:
1. Chitra Kuriakose
2. Sebastain Abraham
3. Manjula V. D.
4. V. S. Sumadevi
5. Annamma Kurien

PARTICULARS OF CONTRIBUTORS:
1. Assistant Professor, Department of Physiology, Government Medical College.
2. Assistant Professor, Department of Nephrology, Government Medical College.
3. Professor, Department of Community Medicine, Government Medical College.
4. Retired Professor, Department of Physiology, Government Medical College.

NAME ADDRESS EMAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Chitra Kuriakose,
Assistant Professor,
Department of Physiology,
Government Medical College,
Kottayam.
E-mail: chitrasabin@yahoo.in

Date of Submission: 14/08/2015.
Date of Peer Review: 15/08/2015.
Date of Acceptance: 17/08/2015.
Date of Publishing: 21/08/2015.