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# Estimate the prevalence of CKD and its risk factors in spouses and first degree relatives (FDR) of ESRD patients

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**ABSTRACT**

***BACKGROUND:*** *Chronic kidney disease (CKD) is now recognized as a global public health challenge[1]. CKD is defined as kidney damage or glomerular filtration rate (GFR) less than 60 ml/min per 1.73 /m$^2$ for 3 months or more, irrespective of cause CKD is classified into stages according to the level of GFR, and stage-specific action plans facilitate its evaluation and management[5,6,7]*

***AIM:*** *Estimate the prevalence of CKD in spouses and first degree relatives (FDR) of ESRD patients.*

***OBJECTIVE OF STUDY:*** *To estimate glomerular filtration rate in the first degree relatives (FDRs) and spouses of patients with End stage renal disease (E.S.R.D) by various formulae.*

***STUDY DESIGN:*** *Cross sectional observational study.*

***MATERIALS AND METHODS:*** *This observation study was carried out in the Department of Nephrology at Gandhi medical college and CAIMS from January, 2014 to December, 2015.Firstdegree relatives and spouses of patients of ESRD disease were counseled about the risk of CKD and asked to volunteer for screening. We calculated eGFR using the equations:*

***STATISTICAL ANALYSIS:*** *Statistical analysis was done using the SPSS package, version 20.0. Descriptive analysis was used to characterize the study population by its demographic (age, gender) medical history and investigations (history of hypertension, diabetes, serum creatinine, and e GFR). Results were expressed as mean ± 1 SD done by ANOVA. Significance was considered for P < 0.05. Reliability test was performed and represented as Cronbach's alpha. Cronbach's* ***α*** *of more than 0.7 says that there is agreement and correlation between two measurements. The more the value the higher is the correlation.*

***RESULTS:*** *Total number of males and females found to be in stage 3 were higher based on CGF equation (10.1%) when compared to M.D.R.D (1.7%) and CKD-EPI (1.3%) Significant numbers of subjects with hypertension are classified to stages 2 and 3 by C.G.F (62.73%), M.D.R.D (54.9%) and CKD-EPI (52.9%). Significant numbers of subjects with diabetes are classified to stages 2 and 3 by C.G.F (89.6 %), M.D.R.D (68.4%) and CKD-EPI (68.4%). Cronbach's a is 0.711 indicating that both C.G.F and M.D.R.D correlated well. Cronbach's a is 0.729 indicating that both C.G.F and M.D.R.D correlated well.*

***CONCLUSIONS:*** *High prevalence of stage 2 and 3 CKD found in both FDRs and spouses by all three equations where as stage 3 CKD is highly prevalent in spouses than in FDRs.*

**KEYWORDS** : CKD-chronic kidney disease, FDR-first degree relatives, GFR-glomerular filtration rate, ESRD-end stage renal disease.

**INTRODUCTION:**

Chronic kidney disease (CKD) is now recognized as a global public health challenge[1]. The adverse outcomes of CKD, including kidney failure, accelerated cardiovascular disease, and premature mortality, have a profound impact on the national economies of low and middle-income countries.[2]The problem is magnified further in India where risk factors for CKD, including hypertension and diabetes, are widely prevalent and increasing.[3,4]

Risk factors for chronic kidney disease include an age of more than 60 years, hypertension, diabetes, cardiovascular disease, and a family history of the disease.[5,6,7] Clinical assessment of kidney function is a routine part of medical practice for overall health evaluation, drug dosing, and administration of intravenous contrast for diagnostic testing and therapeutic procedures.

Screening programs for the early detection of CKD have been suggested across the world[8,9,10]. Some have focused on the entire population, while others have targeted specific groups known to be at high risk for CKD. Large number of patients who have chronic kidney disease, together with the number of people at increased risk for it, requires primary care providers, as well as specialists in areas other than nephrology, to increase their familiarity with the use of GFR estimates. Recommendations for evaluating people at increased risk are to measure urine albumin to assess kidney damage and to estimate the GFR with an equation based on the level of serum creatinine.

Glomerular filtration rate (GFR) is widely regarded as the best indicator of kidney function in both health and disease. GFR can be assessed best by measuring urinary clearance of an ideal exogenous marker like inulin.

Although GFR can be measured directly by using parenteral administration of inulin, iohexol, or iothalamate, direct measurements commonly are not made because of cost, inconvenience, and nonavailability of these tests to the vast majority of patients with chronic kidney disease (CKD). However, GFR often is estimated from serum creatinine level and anthropometric and clinical characteristics of patients.

Thus, GFR estimating equations based on serum creatinine level, age, sex, and body size have been developed and are recommended for routine use in clinical practice.GFR estimating equations provide a more accurate assessment of the level of kidney function than serum creatinine alone.

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suggested across the world. Some have focused on the entire population, while others have targeted specific groups known to be at high risk for CKD.

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Estimatation of GFR used for Detection of Chronic kidney Disease, Monitoring the progression of Chronic Kidney Disease, Evaluation and Management of Complications, also when to refer the patient to Nephrologist and administration of medication doses depend upon the filtration rate and lastly to assess the complication particularly Cardiovascular Disease risk as CKD are more prone to premature mortality

The present study is intended to evaluate the GFR levels in FDRs and spouses of our patient population by C.G.F, M.D.R.D and CKD-EPI equations.

**METHODS AND MATERIAS:**

This observation study was carried out in the Department of Nephrology at Gandhi medical college and CAIMS from January, 2014 to December, 2015.Firstdegree relatives and spouses of patients of ESRD disease were counseled about the risk of CKD and asked to volunteer for screening.

**Inclusion criteria :** A total of 294 First degree relatives and Spouses of ESRD patients who are ≥18 years, out of these 184 FDR and 110 spouses found eligible were enrolled into the study after obtaining the informed consent. We calculated e-GFR using the various equations:

During the study period a detailed history including age, relation with the patient, and history of hypertension, diabetes mellitus, and physical examinations including height and weight and blood pressure (BP) were documented. Body mass index (BMI) was calculated as weight (kg) divided by height squared ($m^2$).

The subjects were considered to be hypertensive if they used medications for hypertension and those with a systolic blood pressure (SBP) of 140 mm Hg or greater and or diastolic blood pressure (DBP) of 90 mm Hg or greater at screening. A participant was considered to have diabetes if a history of diabetes or usage of antidiabetic medications was given. Serum creatinine was measured by the kinetic Jaffe method in a central laboratory accredited by the N.A.B.L

**GFR Estimation:**

We calculated e-GFR using the following equations:

**1) 4-variable MDRD** Study equation : $186 \times SCr^{-1.154} \times Age^{-0.203} \times 0.742$ [if female]

**2) CKD-EPI** creatinine equation: $141 \times \min(Scr/k, 1)^{\alpha} \max(Scr/k, 1)^{1.209} \times 0.993^{Age}$ [×1.018 if female] [×1.159 if black], where Scr is serum creatinine (in mg/dl), k is 0.7 for females and 0.9 for males, α is -0.329 for females and -0.411 for males, min is the minimum of Scr/k or 1, and max is the maximum of Scr/k or 1

**3) C.G.F equation** (140-Age×body weight) /Scr× 72 (0.85 if females).

**RESULTS & DISCUSSION:**

In this study we evaluated GFR in FDRs and spouses of ESRD patients by three equations. A total of 298 subjects were evaluated of which 184 were FDRs and 110 were spouses. In this study the number of spouses with hypertension and diabetes were found to be more compared to the FDRs.

Mean serum creatinine value in spouses (0.89± 0.15) is higher than in first degree relatives (0.87± 0.14) and Mean glomerular filtration rate by various equations is lower in spouses than in first degree relatives [Table-1]

In this study we found that [Table-2] CGF and MDRD equations underestimated GFR. CGF equation underestimated GFR in 51 subjects thus classifying them to stages 2, 3 and where as M.D.R.D classified 20 subjects to stages 2, 3 who are classified to stage 1 by CKD-EPI. This finding by CKD-EPI and M.D.R.D correlated well in all stages and in all age subgroups.

This study showed a higher prevalence of e-GFR of <60ml/min (stage 3) in both FDRs and spouses. In this study,[Table-3] amongst FDRs, 74 (39.35%) by C.G.F, 47 (24.9%) by M.D.R.D and 39(20.75%) subjects by CKD-EPI have e-GFR <90ml/min.Amongst spouses, by C.G.F 63 subjects (57.26%), by M.D.R.D 59 subjects (53.6%) and By CKD-EPI 49 subjects (44.53%) have an eGFR<90ml/min. More number of female subjects have eGFR<60 ml/min (stage3) as compared to males by all three equations. In this study old age, hypertension, and diabetes mellitus have shown statistically significant association with eGFR <90 ml/min.

The finding of increased prevalence of CKD in FDRs is in concordance with previous studies that family members of patients with ESRD were at high risk of developing CKD and ESRD. This study showed that the prevalence of CKD (low e-GFR) was significantly higher in spouses and FDRs. This result contradicts the previous report by O'Dea et al that spouses of patients with ESRD showed relatively lower prevalences compared with first degree relatives of patients with ESRD. Spousal concordance of health risks and behaviors has been observed in many diseases. They include several major renal risk factors, such as cardiovascular disease, hypertension, metabolic syndrome, and high fasting glucose levels. To elucidate the pathogenic mechanism for spousal concordance of health risk and behaviors, researchers have proposed the hypotheses of assortative mating and shared environmental factors. Previous studies suggested that genetic susceptibility may account for the phenomenon of family clustering of CKD. However, of these renal risk factors, diabetes mellitus, hypertension, and metabolic syndrome are multifactorial diseases under the influence of both genetic traits and non genetic environmental factors. Environmental factors, such as low socioeconomic status and lifestyle of inactivity and smoking, also should be considered as potential contributing factors for CKD.

In this study it was shown that older age, female sex, diabetes mellitus and hypertension act as independent significant risk factors for CKD

**CONCLUSIONS:**

1) High prevalence of stage 2 and 3 CKD found in both FDRs and spouses by all three equations where as stage 3 CKD is highly prevalent in spouses than in FDRs.

2) Although e -GFR estimated by three equations MDRD and CKD EPI equations are correlated well in GFR staging but CGF underestimated GFR when compared to MDRD and CKD-EPI.

**LIMITATIONS**:1) The e-GFR was estimated based on a single laboratory measurement.

2) This screening study was conducted with limited numbers of participants;

3) We did not measure the GFR by a standard method. Lastly we could not assess the native CKD in index patients.

Therefore, a comprehensive and population-based screening program is needed before drawing a definitive conclusion.

| Table-1 | First degree relative | | | Spouse | | |
|---|---|---|---|---|---|---|
| Parameter | Male | Female | Total | Male | Female | Total |
| Creatinine | 0.90± 0.133 | 0.80± 0.123 | 0.87± 0.137 | 0.92± 0.176 | 0.85± 0.107 | 0.89± 0.15 |
| CGF | 100.34± 21.57 | 89.74±2 3.65 | 96.73±2 2.8 | 91.73±2 6.26 | 78.51±1 8.97 | 85.72±2 4.04 |
| MDRD | 108.72± 20.59 | 90.05±1 7.178 | 102.37± 21.4 | 100.26± 23.15 | 78.84±1 2.01 | 90.52±2 1.68 |
| CKD EPI | 109.83± 15.12 | 97.46±1 8.183 | 105.62± 17.21 | 99.12±1 9.63 | 84.82±1 4.37 | 92.62±1 8.77 |

| Table-2 Distribution according to GFR staging | | Total No. | % |
|---|---|---|---|
| GFR stage— CGF | 1 | 161 | 54.0% |
| | 2 | 107 | 35.9% |
| | 3 | 30 | 10.1% |
| GFR stage—MDRD | 1 | 192 | 64.4% |
| | 2 | 101 | 33.9% |
| | 3 | 5 | 1.7% |
| GFR stage– CKD-EPI | 1 | 212 | 71.1% |
| | 2 | 82 | 27.5% |
| | 3 | 4 | 1.3% |

| Table-3: Distribution according to GFR STAGING in subgroups | | | | | |
|---|---|---|---|---|---|
| Parameter | SEX | Stage | CGF (%) | MDRD (%) | CKD-EPI (%) |
| First degree Relatives | Female | 1 | 27(42.2) | 36 (56..3) | 42 (65.6) |
| | | 2 | 31( 48.4) | 27 (42.2) | 21(32.8) |
| | | 3 | 6 ( 9.4) | 1 (1.6) | 1 (1.6) |
| | Male | 1 | 87(70.2) | 105 (84.7) | 109 (87.9) |
| | | 2 | 29( 23.4) | 19( 15.3) | 15( 12.1) |
| | | 3 | 8 (6.5) | | |
| | **Total** | **1** | **114 (60.6)** | **141 (75.0)** | **151(80.3)** |
| | | **2** | **60 (31.9)** | **46( 24.5)** | **36( 19.1)** |
| | | **3** | **14( 7.4)** | **1(0.5)** | **1 (0.5)** |
| Spouse | Female | 1 | 18( 36.0) | 12( 24.0) | 19( 38.0) |
| | | 2 | 21( 42.0) | 36( 72.0) | 30( 60.0) |
| | | 3 | 11( 22.0) | 2 (4.0) | 1 (2.0) |
| | Male | 1 | 29( 48.3) | 39( 65.0) | 42( 70.0) |
| | | 2 | 26( 43.3) | 19( 31.7) | 16( 26.7) |
| | | 3 | 5(8.3) | 2(3.3) | 2 (3.3) |
| | **Total** | **1** | **47(42.7)** | **51(46.4)** | **61(55.5)** |
| | | **2** | **47(42.7)** | **55(50.0)** | **46(41.8)** |
| | | **3** | **16(14.5)** | **4 (3.6)** | **3 (2.7)** |

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