Is There a Chronic Kidney Disease Epidemic? Profile of Chronic Kidney Disease in an Urban Renal Camp in Southern India

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Background: The incidence of chronic kidney disease (CKD) and end-stage renal disease (ESRD) is growing at an alarming rate. It is widely believed that the rising ESRD population is just the tip of the CKD iceberg. Data on early-stage CKD and the prevalence of CKD in India are very limited. Therefore, data from a renal camp organized in connection with World Kidney Day were looked at for renal function.

Methods: This was a cross-sectional study. A renal camp was advertised using a set of eight questions; any person who answered yes to one or more questions were advised to attend the camp. Body weight, height, blood pressure, blood sugar and serum creatinine were measured. Urine examination for sugar, albumin and blood was carried out. Renal function was assessed by calculating the glomerular filtration rate (GFR) using the Cockcroft-Gault (C-G) and Modified Diet in Renal Disease (MDRD) formulas. Kidney function was classified according to estimated GFR (eGFR) and Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines.

Results: A total of 123 people (82.1% male) were studied; 9% were less than 20 years old and 26% were aged 60 years or older. The distribution of eGFR was symmetrical, with the majority of people in the 70–79 mL/min category; 69.9% of the study population had eGFR < 100 mL/min. There was a gradual increase in eGFR from the < 20-year-old group to the 30–39-year-old group (which had the highest eGFR of about 110 mL/min), and then a gradual decline with increasing age. An inverse relation between eGFR and age was observed: eGFR declined by 1 mL/min/year (95% confidence interval, 0.7–1.3). C-G eGFR indicated that about 69% of the study population was normal and 31% had CKD stage I to V. MDRD eGFR indicated that 7.3% had CKD stage III to V. Only in CKD stages IV and V could elevated levels of serum creatinine be seen.

Conclusion: The results indicate low GFR levels and, consequently, a high burden of CKD in the Indian population. It is not clear whether such observations are the result of the transportability problems associated with the GFR prediction equations or with the suitability of K/DOQI guidelines for the classification of CKD in the Indian population or both. Well-planned, larger, community- and hospital-based studies are warranted to clarify these issues. [Hong Kong J Nephrol 2008;10(1):27–33]

Key words: chronic kidney disease, Cockcroft-Gault formula, estimated GFR, K/DOQI guidelines, simplified Modified Diet in Renal Disease formula

背景：慢性腎病 (CKD) 及末期腎病 (ESRD) 的發生率正在與日俱增，其中 ESRD 患者的增加，相信僅能反映 CKD 整體患病人口的冰山一角。在印度，至今關於早期 CKD 及 CKD 盛行率的數據仍相當有限。因此，研究人員在世界腎臟日的一次活動中，對參加者進行了腎功能及相關的檢查。

方法：這屬於一項橫斷面的的研究。在相關活動的宣傳中，列出了幾系列（共 8 題）問題，並建議對其中任何一題回答「是」的人士參與本活動。活動期間，參加者接受了身高、體重、血壓、血糖，及血清肌酐濃度的測量，以及尿液檢查 (糖分、白蛋白、及血球)。腎功能的評估乃採用 Cockcroft-Gault (C-G) 及 Modified Diet in Renal Disease (MDRD) 公式，以計算出腎絲球過濾率 (GFR) 數值。腎功能分級則是基於 GFR 估算值 (eGFR) 及 Kidney Disease Outcomes Quality Initiative (K/DOQI) 的指引進行。
INTRODUCTION

The incidence of chronic kidney disease (CKD) and end-stage renal disease (ESRD) is growing at an alarming rate. It is widely believed that the rising ESRD population is just the tip of the CKD iceberg. For each patient with ESRD, there are over 100 patients with various stages of CKD in the US [1, 2]. It is estimated that about 100,000 people develop ESRD in India each year [3]. However, this figure may be an underestimate as it is projected from only a few tertiary care centers in urban areas. Generally, most CKD patients who report to these tertiary care centers are already in the end stages. Data on early-stage CKD and the prevalence of CKD are very limited [4–7]. In view of this, information on the various aspects of CKD from different geographic regions of a vast country like India will aid in better understanding of the issues related to CKD. A renal camp was organized to coincide with World Kidney Day in the city of Hyderabad; the renal function and CKD of subjects who attended the renal camp were analyzed.

METHODS

On March 9, 2006, we organized a free renal camp in Hyderabad, the capital city of the state of Andhra Pradesh in India. The camp was advertised in a few local vernacular dailies 2 weeks before the scheduled date of commencement; the advertisement advised people to attend the camp if they answered yes to one or more of the following questions:

1. Do you have diabetes?
2. Do you have hypertension?
3. Do you have burning micturition?
4. Do you have red colored urine?
5. Do you have difficulty in passing urine?
6. Have you ever passed stones in your urine?
7. Have you ever been told about kidney problems?
8. Is there a history of diabetes/hypertension/kidney disease in your family?

The same advertisement was also broadcast on two local television channels in Hyderabad 2 days before the camp.

However, everyone who turned up for the camp was included in the study, regardless of whether or not they had answered the eight questions. This was because the camp was organized as a free service to the public, with the idea that it might serve to raise awareness and to educate the public in general.

Body weight, height and blood pressure were measured for all subjects attending the camp. Blood was collected for sugar and serum creatinine estimation. Urine was examined for sugar, albumin and blood. Blood sugar was measured using a glucometer; serum creatinine measurement was done by a Hitachi automatic analyzer. The dipstick method was used for urine examination.

Renal function was assessed by calculating the glomerular filtration rate (GFR) with the Cockcroft-Gault (C-G) formula [8] and the simplified Modified Diet in Renal Disease (MDRD) formula [9]. Using these estimated GFRs (eGFRs) and the Kidney Disease Outcomes Quality Initiative (K/DOQI) guidelines, kidney functioning was classified for each subject.

Persons with a low eGFR or who were suspected to have CKD were advised to undergo detailed investigations in the nephrology clinic at Nizam’s Institute.

The distribution of the C-G formula-based GFR was assessed using the coefficient of skewness and kurtosis. Mean, standard deviation (SD), median, range, 5th and 95th percentiles were calculated. The 95% confidence intervals (CI) were calculated. The relation between age and eGFR was assessed using simple linear regression. All analyses were performed using Stata version 9.1 (Stata Corp., College Park, Texas, USA).

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K.V. Dakshinamurty, et al
RESULTS

Description of the study population
A total of 131 people attended the camp. Blood and/or urine sample results were not available for eight subjects so they were excluded from analysis. Data from the remaining 123 subjects were analysed. The majority of subjects (82.1%) were men. The mean age (± SD) of the population was 50.4 (± 15.1) years; 9% were younger than 20 years and 26% were ≥ 60 years old. Mean systolic and diastolic blood pressures were 128.9 ± 17.8 mmHg and 83.6 ± 11.4 mmHg, respectively. About one third of people who attended the camp had diabetes (35%) or hypertension (34%). Both conditions were present in 23 (23/123 = 18.7%). One third of the subjects (33.33%, 41/123) did not report a history of any of the eight problems listed in the advertisement. One of the eight problems was present in 35.77% (44/123) of the subjects, two problems were present in 27.64%, and three were present in 3.25%.

Distribution of eGFR
The distribution of eGFR is shown in Figure 1. It was symmetrical, with the majority of people in the 70–79 mL/min category. The mean and median GFR were close to each other (85.0 and 82.0 mL/min, respectively). More than two thirds (69.9%) of the study population had eGFR < 100 mL/min. Less than 10% had eGFR > 120 mL/min.

The distribution of eGFR was slightly positively skewed (coefficient of skewness, 0.18) and the distribution curve was slightly leptokurtic (coefficient, 3.4). Thus, the distribution of eGFR was close to that of a normal distribution, which has a skewness of zero and kurtosis of 3.0.

Age-wise distribution of eGFR
Table 1 depicts the age-wise distribution (frequency, mean, 95% CI of mean, median, range, 5th and 95th percentiles) of eGFR. On average, the highest values of eGFR were observed in the age group of 30–39 years, where it was about 110 mL/min. The 5th and 95th percentiles in this age group were 71 and 157 mL/min, respectively. There was a gradual increase in eGFR from the < 20-year-old group to the 30–39-year-old group, and then a gradual decline with increasing age.

Association of eGFR with age
Figure 2 shows the relation between age and eGFR; there was an inverse relation between the two. Simple linear regression analysis indicated that eGFR declined by 1 mL/min (95% CI, 0.7–1.3) with each 1 year increase in age.

CKD stages in the study population
Assuming that traces of albumin in the urine is transient albuminuria and 1+ to 4+ is persistent albuminuria, the various stages of CKD, as per the K/DOQI guidelines, in the study population is shown in Table 2. C-G formula-based eGFR indicated that about 69% of the study population was normal (GFR > 60 mL/min and no signs of renal damage as evidenced by albuminuria). About 31% had CKD stage I to V. Even after considering albuminuria of 1+ as transient, this proportion remained high (23.6%). Using MDRD-based eGFR, only 7.3% had CKD stage III to V. The corresponding frequency for C-G formula-based eGFR was 16.2%, indicating a significant disparity between the two formulas.

GFR and creatinine in various stages of CKD
The correspondence between eGFR and serum

Figure 1. Distribution of estimated glomerular filtration rate (GFR) calculated by the Cockcroft-Gault equation.
creatinine values among the various stages of CKD (as per K/DOQI definition) is presented in Table 3. It is interesting to note that the creatinine levels were not elevated even in stage III CKD, although GFR indicated the presence of the disease. Only in CKD stages IV and V could elevated levels of serum creatinine be seen. This indicates that if we depend on serum creatinine alone, there is a high probability of missing the diagnosis of CKD when it is in the early stages.

Table 1. Age-wise distribution of estimated glomerular filtration rate (GFR) calculated by the Cockcroft-Gault equation

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Freq</th>
<th>Mean (95% CI)</th>
<th>Median</th>
<th>Range</th>
<th>5th percentile</th>
<th>95th percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 20</td>
<td>3</td>
<td>102.7 (72.81–132.53)</td>
<td>90</td>
<td>85–133</td>
<td>85</td>
<td>133</td>
</tr>
<tr>
<td>20–29</td>
<td>8</td>
<td>101.2 (88.47–114.03)</td>
<td>96.5</td>
<td>77–126</td>
<td>77</td>
<td>126</td>
</tr>
<tr>
<td>30–39</td>
<td>22</td>
<td>107.3 (94.49–120.06)</td>
<td>110</td>
<td>13–164</td>
<td>71</td>
<td>157</td>
</tr>
<tr>
<td>40–49</td>
<td>24</td>
<td>93.4 (83.34–103.41)</td>
<td>95</td>
<td>15–154</td>
<td>70</td>
<td>115</td>
</tr>
<tr>
<td>50–59</td>
<td>30</td>
<td>79.6 (71.85–87.35)</td>
<td>79.5</td>
<td>21–149</td>
<td>55</td>
<td>125</td>
</tr>
<tr>
<td>≥ 60</td>
<td>32</td>
<td>62.2 (56.19–68.25)</td>
<td>60.5</td>
<td>30–114</td>
<td>38</td>
<td>101</td>
</tr>
<tr>
<td>Unknown</td>
<td>4</td>
<td>88.5 (77.00–100.00)</td>
<td>86</td>
<td>78–104</td>
<td>78</td>
<td>104</td>
</tr>
<tr>
<td>All ages</td>
<td>123</td>
<td>85.0 (80.06–89.89)</td>
<td>82</td>
<td>13–164</td>
<td>44</td>
<td>127</td>
</tr>
</tbody>
</table>

Table 2. Distribution of chronic kidney disease (CKD) according to Kidney Disease Outcomes Quality Initiative definitions

<table>
<thead>
<tr>
<th>CKD status</th>
<th>C-G formula* n (%)</th>
<th>C-G formula† n (%)</th>
<th>MDRD formula n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>85 (69.11)</td>
<td>94 (76.42)</td>
<td>114 (92.68)</td>
</tr>
<tr>
<td>Stage I</td>
<td>8 (6.50)</td>
<td>3 (2.43)</td>
<td>–</td>
</tr>
<tr>
<td>Stage II</td>
<td>10 (8.13)</td>
<td>6 (4.88)</td>
<td>–</td>
</tr>
<tr>
<td>Stage III</td>
<td>17 (13.82)</td>
<td>17 (13.82)</td>
<td>5 (4.07)</td>
</tr>
<tr>
<td>Stage IV</td>
<td>2 (1.63)</td>
<td>2 (1.63)</td>
<td>2 (1.63)</td>
</tr>
<tr>
<td>Stage V</td>
<td>1 (0.81)</td>
<td>1 (0.81)</td>
<td>2 (1.63)</td>
</tr>
<tr>
<td>Total</td>
<td>123 (100)</td>
<td>123 (100)</td>
<td>123 (100)</td>
</tr>
</tbody>
</table>

*Assuming traces of albuminuria as transient; †assuming traces and 1+ of albuminuria as transient. C-G = Cockcroft-Gault; MDRD = Modified Diet in Renal Disease.

Figure 2. Association of estimated glomerular filtration rate (GFR) with age. Regression equation: \( GFR = 136.62 - (\text{age} \times 1.03) \).
**DISCUSSION**

We examined the renal function of a sample of an urban population who attended a renal camp. The distribution of GFR in the study population was estimated by the C-G formula as a quick and feasible method suitable for the study setting.

We observed an average GFR level of 85 mL/min in this population, which is on the lower side of the generally accepted values for normal GFR estimates. About 40% of our study population had GFR > 90 mL/min, which might be due to the camp approach as more people with renal problems would attend the camp, leading to the observation of poor or low GFR profiles. We do not know the average GFR level in the Indian community and hence it is difficult to make any conclusions. On the other hand, there could be reasons for overestimation of GFR in our study population. First, the samples were obtained during the day, when GFR is expected to be at its highest [10]. Second, it has been reported that the C-G formula overestimates true GFR [11]. Despite these, an observation of a low profile of eGFR indicates that the general level of GFR in the Indian community and hence it is difficult to make any conclusions. On the other hand, there could be reasons for overestimation of GFR in our study population. First, the samples were obtained during the day, when GFR is expected to be at its highest [10]. Second, it has been reported that the C-G formula overestimates true GFR [11].

The age-wise distribution of GFR indicated that the peak was in the age group of 30–39 years. Gender-specific analysis confirmed similar observations in both males and females. Though not significant, GFR was, on average, 4 mL/min lower in females than in males.

As per the K/DOQI definition of CKD, we observed a very high proportion (30.9%) of CKD in the study population. Even if albuminuria of 1+ grade was taken as transient, 23.6% of the study population would be categorized as having CKD stage I to V. The same arguments for the observation of low GFR profiles hold for this observation too. In addition, it also raises the question of whether or not the cut-offs recommended by the K/DOQI guidelines for the various stages of CKD are applicable for all populations worldwide. Ideally, any international recommendations should be based on international data. However, a number of investigators believe that the use of prediction equations in population-based studies suggest a surprisingly high prevalence of CKD [12–14]. This leads to doubt in the utility of these equations in epidemiologic research. The transportability problem [15], i.e. validity of these formulas to other populations with different characteristics, needs to be addressed before commenting on this. Another contributing factor may be related to the issue of measurement methodology and calibration of serum creatinine [16].

The apparently lower level of eGFR results in problems of staging due to fixed cut-offs in the K/DOQI classification of CKD stages. Actually, it is not known if the classification can be applied to the Indian population. Whether the lower level of GFR in the population indicates a greater susceptibility to developing ESRD or proportionately lower cut-off values at each stage are required is not known.

**Table 3.** Correspondence between glomerular filtration rate (GFR) and serum creatinine level among various stages of chronic kidney disease (CKD)

<table>
<thead>
<tr>
<th>CKD status</th>
<th>Freq</th>
<th>GFR</th>
<th>Creatinine</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Mean (95% CI)</td>
<td>Median</td>
</tr>
<tr>
<td>Normal</td>
<td>85</td>
<td>92.1 (87.71–96.55)</td>
<td>90</td>
</tr>
<tr>
<td>Stage I</td>
<td>8</td>
<td>121.1 (99.91–142.34)</td>
<td>108</td>
</tr>
<tr>
<td>Stage II</td>
<td>10</td>
<td>74.7 (72.27–77.13)</td>
<td>74.0</td>
</tr>
<tr>
<td>Stage III</td>
<td>17</td>
<td>50.4 (46.48–54.23)</td>
<td>54.0</td>
</tr>
<tr>
<td>Stage IV</td>
<td>2</td>
<td>18.0 (12.12–23.88)</td>
<td>18.0</td>
</tr>
<tr>
<td>Stage V</td>
<td>1</td>
<td>13.0 (--)</td>
<td>13.0</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>85.0 (80.06–89.89)</td>
<td>82.0</td>
</tr>
</tbody>
</table>
The finding that there is a consistently lower prevalence of decreased GFR among African Americans across all age groups and yet a disproportionately higher frequency with ESRD (compared to White Americans) indicates that there is a differential risk [12]. In other words, there exists heterogeneity in the risk of progressive renal disease for the same cross-sectional category of GFR. The crucial question is whether the lower GFR levels in the Indian population indicate a greater risk for developing CKD early or if a different set of guidelines from the existing K/DOQI guidelines are required.

While staging CKD as per the K/DOQI classification, we considered only albuminuria as an evidence of kidney damage; cases of hematuria were ignored. An effect of this might be that the incidence of CKD was underestimated, however minimal the effect might be.

The staging of CKD based on the C-G and MDRD formulas show divergence. The prevalence of stage III CKD was 13.82% according to the C-G formula, but 4.07% according to the MDRD formula. However, stage V prevalence as calculated by the C-G formula was only about half of that calculated by the MDRD formula (0.81% vs. 1.63%). The divergence between the two formulas is well known because the biases of the two formulas may be quite different in selected populations, defined by age, sex, body mass index and also level of GFR [17]. Regarding the MDRD formula, it may be stated at present that in its available form, it only picks up stage III or above.

We observed a linear negative correlation between age and GFR. The proportion of variation in GFR explained by age \( r^2 \) was 32.0% \( p < 0.001 \). GFR declined by 1 mL/min for each 1 year of increase in age. This is in agreement with other reports based on cross-sectional data [12], but slightly more than the decline based on longitudinal data [18,19].

The correspondence between eGFR and serum creatinine values among the various stages of CKD led to the interesting observation that serum creatinine levels were not elevated even in CKD stage III, though the GFR indicated derangement or presence of disease. Only in CKD stages IV and V could elevated levels of serum creatinine be seen. Thus, if we depend on serum creatinine alone, there is a possibility of missing the diagnosis of the disease when it is in its earlier stages. Similar views have also been reported previously [20,21].

Our results are based on only 123 subjects, who were likely to be different from the general population of the community by virtue of them attending the renal camp in response to the advertisement listing the eight problems. The results therefore need to be interpreted with this in mind. Only one-time measurements of urinary albumin and serum creatinine, and a lack of calibration of the measurement of serum creatinine are some of the limitations of the study.

To conclude, the results of this study indicate that GFR levels in the Indian population are on the lower side of the generally accepted normal values. The burden of CKD, even if we consider the high-risk nature of the camp population, was much higher than expected. It is not clear whether this observation was the result of the transportability problems associated with the GFR prediction equations or with the suitability of the K/DOQI guidelines for classifying CKD in an Indian population or with both. Well planned and larger community- and hospital-based studies are warranted to clarify these issues. Pending such studies, revisiting the data from earlier reports that estimated the prevalence of CKD, based on serum creatinine, in India would help to assess the prevalence of various stages of CKD and the GFR profiles in the community. The lack of correspondence between serum creatinine and eGFR should be accepted and eGFR should be adopted for the early diagnosis of CKD.

**References**


