Observational Study

Prevalence and staging of chronic kidney disease among adults in Chennai metropolitan area

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Chronic kidney disease (CKD) has been an emerging threat to the health care, due to the increasing burden of type 2 diabetes mellitus and hypertension. There are few studies in India done to assess the prevalence of CKD. This study was carried out to estimate the prevalence of CKD among adults in Chennai metropolitan area. This study was carried out as a cross sectional study in Chennai among 2796 adults. The sample was distributed among 15 administrative zones of Chennai Corporation and 2 administrative zones of Kanchipuram. We measured serum creatinine levels using isotope mass dilution spectroscopy (IDMS) calibration method, and estimated Glomerular Filtration Rate was calculated using the CKD-EPI equation, based on which CKD was classified into stages. The mean age of study participants was 46.16±13.22 years. About 3.9% had a serum creatinine >1.2 mg/dl, impaired GFR was significantly associated with age above 45 years (p=0.001), female sex (p=0.001), hypertension (p=0.001), and history of diabetes mellitus (p<0.001). The overall prevalence of CKD stage 3-5 by the CKD-EPI formula (<60 mL/mm/1.73m) was 4.24%. A comprehensive prevention programme to combat the risk factors should be in place as a part of public health infrastructure, in order to minimize morbidity, mortality and socioeconomic burden of chronic kidney disease.

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Chronic kidney disease (CKD) has become one of the leading causes of morbidity and mortality in India and other low and middle-income countries[1]. In India, diabetes and hypertension account for 40-60 % of cases of CKD[2]. The age-adjusted incidence rate of ESRD in India is 229 per million population, with more than 100,000 new patients entering renal replacement programs annually[3]. CKD poses an enormous burden on healthcare providers in India.Few studies have been done to estimate the prevalence of CKD in India. In the Screening and Early Evaluation of Kidney disease (SEEK) study done in 2007, the prevalence of CKD was found to be 17.2%[3]. Mani in 2005 estimated the prevalence of CKD in a Tamil Nadu village as 0.86%, with GFR <80 mL/mm/1.73m^2[4,5].

There is a growing awareness about diabetes and hypertension in India, but awareness and detection of early CKD remains low. Screening programmes for early detection of kidney disease in the general population are scarcely carried out. Though there is a CKD registry by the Indian Society of Nephrology which provides data on patients seen by a subset of nephrologists, it represents only the tip of the iceberg, and the disease burden is believed to be enormous[6]. As India is the second mostpopulous and vastly diverse country in terms of cultural practices, socio-economic status, dietary patterns and availability of healthcare resources, the burden of CKD in each region needs to be determined, in order to plan andimplement early detection and prevention strategies.Therefore, this study was done to evaluate the magnitude and burden of CKD in Chennai metropolitan area, which is a major industrial hub with a mix of population from across India.

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Methodology :

This cross-sectional study was done in Chennai metropolitan area and included adults greater than 18 years of age.The sample size was calculated at 95% confidence level, 8.75% limit of accuracy and 10% for predicted non-response, with a literature-based CKD prevalence of 17.2%[3]. The required sample size was calculated as 2,662.Approval from the Institutional Review Board was obtained prior to the data collection. The Corporation of Chennai is divided into 15 administrative zones. We conducted a screening study in 37 sites, spread across all 15 administrative zones of Chennai and 2 suburbs of Kanchipuram from April 2015 to December 2016. Menstruating, pregnant and lactating mothers were excluded. Thestudy was conducted in community-based settings, as

a part of TANKER Awareness and Prevention (TAPP) Programme for early detection of kidney disease. Each participant was explained about the study and informed consent was obtained with an information letter in English and Tamil and for people speaking other languages, the purpose of the study was explained in their local vernacular, prior to data collection. A structured interview schedule by a trained doctor and a community health nurse,was developed to collect information regarding demographic characteristics, personal history, medical history and treatment history. Blood pressure, height, and weight were measured. Urine analysis was carried out using urine dipstick to measure protein and glucose. Proteinuria was defined as 1+ or more on dipstick. Blood pressure was measured in right arm in sitting position using appropriate cuff. Hypertension was defined as systolic blood pressure = 140 mm Hg and/or diastolic blood pressure = 90 mm Hg and/or self-reported history of hypertension on antihypertensive medication. Abnormal blood pressure readings for the first time were repeated after one hour, and the mean of 2 readings were taken. Diabetes was defined as self-reported history of diabetes on antidiabetic medication. Serum creatinine (Scr) was estimated using an auto analyzer, and is traceable to IDMS calibration method.

The data was entered and analyzed using SPSS version 20 software (IBM Corporation, Armonk, USA). The estimated glomerular filtration rate was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula.

CKD –EPI Formula

$GFR = 141 \times \min(S_{cr}/\kappa, 1)^{\alpha} \times \max(S_{cr}/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018$ (if female) × 1.159 (if black)

The prevalence of CKD was described in percentages. Chi square test and logistic regression were used to compare the risk factors with CKD.

Results

This study was carried out among 2,796 adults in Chennai metropolitan area. The mean age of study participants was 46.16 ± 13.22 years. About 60.5% were males, 18.5% were on drugs for diabetes mellitus, and 14.8% of the participants were on drugs for hypertension. In this study, 37.9% were overweight and 12.2% were obese. Prehypertension was present in 12.2 % of the population, who were not previously diagnosed as hypertensives. Urine protein excretion was in traces for 21.4% of the participants. Table 1 shows the prevalence of CKD, after applying the CKD-EPI formula.

The overall prevalence of CKDstage 3-5 by CKD-EPI (<60 mL/mm/1.73m) was 4.24 %. Table 2 depicts the association through chi Square test between certain risk factors and abnormal eGFR (<90 ml/min/1.73 m^2 by CKD-EPI equation). It was observed that impaired kidney function was associated with age above 45 years (p<0.001), female sex (p<0.001), body mass index >25kg/m^2 (p=0.016), hypertension (p<0.001), history of diabetes mellitus (p<0.001), proteinuria (p<0.001), and glucosuria (p<0.001). On using logistic regression as shown in Table 3, impaired GFR was significantly associated with age above 45 years (p=0.001), female sex (p=0.001), hypertension (p=0.001),and history of diabetes mellitus (p<0.001). Those with eGFR< 90 ml/min/1.73 m^2 had an average BMI of 25.3 ± 4.4 kg/m^2, while those with normal eGFR had an average BMI of 24.8 ± 4.3 kg/m^2 (p=0.007). Table 4 shows the prevalence of proteinuria among various stages of CKD in our population. The correlation between eGFR and age of the participant is shown in figure 1. It was observed that age was negatively correlated with eGFR. The observed difference was statistically significant r=-0.602; p<0.001).

Table 1 — *Prevalence and stages of CKD (<90 ml/min/1.73 m^2)*

Stage of CKD	eGFR (ml/min/1.73m^2)	Males (n=2796)	Females	Total	Percentage
Stage 2	60-89	557	424	981	35.1
Stage 3A	45-59	26	36	62	2.2
Stage 3B	30-44	12	22	34	1.2
Stage 4	15-29	10	10	20	0.7
Stage 5	<15	4	0	4	0.14

Table 2 — *Association between risk factors and abnormal eGFR through CKD EPI (<90 ml/min/1.73 m^2) through chi Square test*

Variable	Characteristics	N	Abnormal eGFR (<90 ml/min/1.73 m^2)	Chi sq	p value
Age (years)	> 45	1498	859 (57.3 %)	436.282	<0.001
	≤ 45	1298	510 (39.3 %)		
Sex	Male	1693	609 (36.0 %)	20.856	<0.001
	Female	1103	492 (44.6 %)		
Body mass index (kg/m^2)	≥ 25.0	1399	582 (41.6 %)	5.799	0.016
	<25.0	1397	519 (37.2 %)		
Hypertension	Present	1243	584 (47.0 %)	54.225	<0.001
	Absent	1553	517 (33.3 %)		
History of diabetes mellitus	Present	517	319 (61.7 %)	132.423	<0.001
	Absent	2279	782 (34.3 %)		
Proteinuria	Present	493	234 (47.5 %)	16.397	<0.001
	Absent	2303	867 (37.6 %)		
Glucosuria	Present	612	298 (48.7 %)	28.479	<0.001
	Absent	2184	803 (36.8 %)		

Discussion

In our study, abnormal eGFR by the MDRD formula was associated with age >45 years (p=0.001), female sex (p=0.001), hypertension (p=0.001) and history of diabetes mellitus (p<0.001). There was also an association with body mass index > 25 kg/m^2, proteinuria and glucosuria, however, it did not have statistical significance on using logistic regression. Those with eGFR< 90 ml/min/1.73 m^2 had an average BMI of 25.3 ± 4.4 kg/m^2, while those with normal eGFR had an average BMI of 24.8 ± 4.3 kg/m^2 (p=0.007). The prevalence of CKD in India is roughly pro-

Table 3 — *Association between risk factors and abnormal eGFR through CKD-EPI (<90 ml/min/1.73 m²) through logistic regression*

Variable	B	Exp (B)	Wald	df	P value
Age>45 years	1.607	4.989	305.760	1	0.001*
Female sex	0.298	1.348	11.561	1	0.001*
BMI >25 kg/m²	-0.083	0.921	0.907	1	0.341
Proteinuria	0.174	1.190	2.398	1	0.121
Glucosuria	0.077	1.080	0.533	1	0.465
History of diabetes mellitus	0.554	1.740	23.355	1	<0.001*
Hypertension	0.286	1.331	10.676	1	0.001*
Constant	-1.744	0.175	325.950	1	<0.001*

Table 4 — *Comparison between proteinuria and stage of CKD (CKD-EPI)*

CKD stages / Proteinuria (mg/dl)	5	4	3B	3A	2	Total
≥ 2000	0	0	0	3	17	20
300	1	1	4	6	26	38
100	0	3	2	5	39	49
30	1	7	11	11	97	127
Trace	0	3	4	11	213	231
Nil	2	6	13	26	589	636
Total	4	20	34	62	981	1101
		Low risk	Moderate risk		High risk	

portional to the prevalence of type 2 diabetes mellitus, obesity, and hypertension[16-18]. Most studies from India have reported a higher prevalence of CKD in men. However, this is the first study from India in which female gender was reported as a potential risk factor for CKD. In our study, women were more likely to have a history of diabetes (p<0.001) and a higher body mass index (p<0.001) compared with men. However, on multivariate analysis, female gender had an independent association with abnormal GFR (p=0.001, Odds ratio=1.348). Higher prevalence of CKD among females has been reported several times in the literature[19-22]. The data from the National Institute of Health and Center for Disease Control and Prevention in the US, report a higher prevalence of CKD stage 1-4 among women[23,24]. A population-based Turkish study reported a higher prevalence of CKD in women compared with men (18.4 % *versus* 12.8 %, p<0.001)[20]. In Iran, a population-based cohort study also showed a higher prevalence of CKD among females[22]. However, the prevalence of stage 5 CKD has been reported to be higher in males. In our study, all 4 patients with CKD-5 were men. This may be due to slower progression of CKD in females, or underestimation of GFR in females by the CKD-EPI equation. A major drawback is that the CKD-EPI formula has never been validated in several countries where the above studies were conducted.

The prevalence of CKD by the SEEK study was reported to be 17.2 %[3]. However, this has been criticized as a significant overestimation. CKD stage 1 is defined as objective kidney damage such as proteinuria for over 3

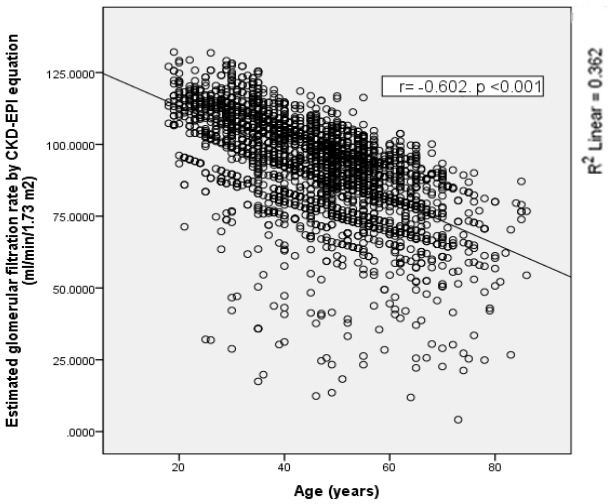

Fig 1 — Scatterplot between age and eGFR by CKD-EPI equation

months, with a GFR of above 90 ml/min/1.73 m². Because we could not rule out false positives in most of our patients, we did not report on the prevalence of stage 1 CKD in our population.

The prevalence of CKD in India is beginning to be determined with a few population-based studies. The prevalence of CKD stage 3 and above is 4.24% of our study population, which is expected to exert a significant burden on the healthcare infrastructure. About 238 per million population are expected to develop ESRD every year, but less than 10% of the population has access to renal replacement therapies[25]. Moreover, the cost of treatment ranges from 300 USD to 3000 USD per month, which is unaffordable for the average Indian. The federal government has recently expanded spending on RRT by setting up dialysis units in every district hospital. The state government pays for haemodialysis costs for underprivileged patients, through the Chief Minister's Comprehensive Health Insurance Scheme (CMCHIS). Haemodialysis reimbursements accounts for a large portion of the CMCHIS spending (personal communication). With increasing incidence of diabetes mellitus and hypertension due to the obesity epidemic in India, the incidence of ESRD is expected to increase and the strain on existing healthcare resources will be enormous. This leaves out prevention as the only effective solution to this burden. A comprehensive screening programme for NCDs that is government-sponsored is essential for the prevention of CKD in India. This screening programme must encompass 3 components which are currently lacking in government programmes, ie,standardized laboratory testing, awareness programmes, and regular follow-up to check for compliance.

Limitations :

We did not collect information about other risk factors

for CKD, such as smoking, history of cardiovascular disease, analgesic abuse and alternative drug use.As with other epidemiological studies, we could not document the chronicity of the abnormal eGFR, which may lead to overestimation of CKD prevalence.

Strengths :

The strengths of the study include representativeness of a metropolitan city with mixed population, due to sampling from all administrative divisions. To our knowledge, this is also the first study which studied risk factors for abnormal eGFR by the CKD-EPI formula.

Conflict of Interest Statement :

The results presented in this paper have not been published previously, in whole or part, except in abstract format.

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