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International Journal of Current Research
Vol. 7, Issue, 04, pp.14530-14534, April, 2015

INTERNATIONAL JOURNAL OF CURRENT RESEARCH

ISSN: 0975-833X

RESEARCH ARTICLE

PREVENTION OF CHRONIC KIDNEY DISEASE THROUGH EARLY DETECTION

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ARTICLE INFO

Article History:
Received 10th January, 2015
Received in revised form
14th February, 2015
Accepted 22nd March, 2015
Published online 28th April, 2015

Key words:
Chronic kidney disease,
Proteinuria,
Screening,
Serum creatinine.

ABSTRACT

The current scenario of global burden of diseases comprise of a triple burden of diseases of which non communicable diseases form a huge proportion. Among the non communicable diseases, chronic kidney disease has emerged a major threat in terms of complications, accessibility and availability of treatment, especially in developing countries like India. There are a few studies done on prevalence of kidney disease and our programme targets early detection of kidney disease in the form of screening programmes directed at different segments of the society. The screening programme consists of brief history of medical illness, followed by measurement of body mass index and blood pressure and urine examination to look for proteinuria. Our programme identified prehypertension in 38.7% of the population screened and 24.% were identified with proteinuria. Individuals who were above 45 years of age, and those with proteinuria were found to be significantly associated with abnormal serum creatinine and eGFR. Our screening programme has proven to be efficient in early detection of kidney diseases in the population and has also proven to be cost effective in a country like India where diverse economic conditions exist in the society.

INTRODUCTION

In the modern era of civilization, developing countries face the 'triple burden' of diseases namely communicable diseases, non communicable diseases and socio-behavioral diseases. Among the chronic and non communicable diseases, chronic kidney disease (CKD) is one of the deadly and irreversible diseases. According to World Health Organization, lifestyle and behavior contribute to 46% of the global burden of diseases (http://www.who.int/nutrition/topics/2_background/en/, 2013). Among this, chronic kidney disease has begun to rise rapidly in the recent past. The risk factors for CKD are multitude, including diabetes mellitus, hypertension, persistent proteinuria, recurrent urinary tract infections, etc. According to the first report of the CKD registry that was published in India in 2012, diabetic nephropathy has been established to be the single most common cause of CKD (31%), followed by CKD of undetermined etiology (16%), chronic glomerulonephritis (14%) and hypertensive nephrosclerosis (13%) (Madhusudhan Vijayan *et al.,* 2013). It has been evidenced that there is a steady rise in the incidence of chronic kidney disease and is further bound to increase, owing to the adverse lifestyle factors. Overall, the prevalence of kidney disease is higher in urban areas. In the Screening and Early Evaluation of Kidney disease (SEEK) study done all over India, the prevalence of CKD in 12 cities was found to be 17.2% (Ajay *et al.,* 2013).

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Whereas, the prevalence of CKD in other developing countries like Thailand was 17.5%, Nepal was 10.6%, Taiwan was 11.9% for CKD stage 1-5 and 5.7% in Saudi Arabia. In the developed countries like United States of America and Japan, the prevalence of CKD was 14% and 13% respectively (Madhusudhan Vijayan *et al.,* 2013). Therefore, it is evident from the above facts that extensive research is required with regards to developing countries like India. Chronic Kidney Disease is a disease which causes physical, mental and socioeconomic burden to the individual and his family. This is more so in a country like India. India being a developing country, spends a bare minimum of 3.9% of its GDP on health (Madhusudhan Vijayan *et al.,* 2013). Moreover, according to a survey done by the Government of India, 29.8% of the nation's population lies below poverty line, of which 17.1% are in Tamil Nadu (www.indexmundi.com/india/population_below_poverty_line.html). Also the average per capita income for 2013 being USD1499 in India (www.data.worldbank.org/indicator/NY.GDP.PCAP.CD), the money spent on health is USD 61 per capita per year in 2013 (http://data.worldbank.org/indicator/SH.XPD.PCAP).

Therefore, the public health care system is the only long term option towards a better health in India. Unfortunately, the public health care system is emphasized through the three tier system of care of which primary health care caters to the majority of the population while tertiary health care is narrowed to referrals. Therefore, it is a major challenge to address the problem of CKD through the masses. Moreover,

the nephrology force in India is 1 per 1.1 million population of which a majority of them are restricted to urban areas, and more to the private sector (Madhusudhan Vijayan *et al.,* 2013). Also, the quality of care for CKD patients is better in the private sector compared to the public system. Though several health care financing models like health insurance and public private partnerships have recently emerged in India, the cost of treatment continues to be of certain financial burden to an average Indian. These above factors justify the need for prevention and early detection of kidney disease, and its risk factors namely diabetes mellitus and hypertension. Since factors attributed to the kidney disease are preventable, it is essential to detect them at an early stage and address them adequately in order to prevent complications. The prevention programme for kidney diseases is best achieved through primary and secondary prevention by means of creating awareness and early detection through screening respectively. An ideal screening tool has to be cost effective, with high sensitivity and specificity, especially when applied to populations. It has been established that detection of proteinuria at an early stage is an effective method of stalling the progress of CKD. Proteinuria is a sensitive indicator of renal function. Among the several methods available for detection of protein in the urine, studies have shown that estimation of proteinuria by urine dipstick method has a sensitivity of 83% to 98% and a specificity of 59% to 86% (BMJ Best Practice). In comparison with cardiovascular screening which includes ECG and echocardiogram, and gastrointestinal screening which includes endoscopy and other radiological investigations, the screening tests for kidney disease is far more cost effective, incurring between 1.2 USD to 1.6 USD per person per time. Therefore, examination of protein in the urine by dipstick method is an ideal method for early detection of kidney disease in the population.

Objectives

This study was carried out to

1. Assess the effectiveness of proteinuria as a screening tool for early detection of kidney disease.
2. Estimate the prevalence of CKD and abnormal renal function.
3. Estimate the prevalence of risk factors for CKD.

MATERIALS AND METHODS

This study was carried out as a population based cross sectional study in Chennai city among all the adults above 18 years of age. Based on the previous studies done to estimate the prevalence of CKD, the prevalence was found to be 17.2% in India as per SEEK study. Based on this, sample size was calculated to be 1188.8, with a limit of accuracy of 12.5% at 95 % level. Accounting for non response, the final sample size was arrived at 1551. The population of Chennai city as per 2011 census was 46,46,732 (http://www.citypopulation.de/php/india-tamilnadu.php). Chennai city is divided into 15 zones and each zone is further subdivided into wards for administrative purposes. For this study, Zone VIII with a population of 2,04,165 was randomly selected, which is further divided into 14 wards. The ward wise list of population for this zone was obtained and based on this, 1551 individuals were selected by simple random sampling using computer generated random numbers. Ethical committee approval was obtained prior to data collection. The data collection was based on the KEEP guidelines for screening emphasized by the National Kidney Foundation (National Kidney Foundation, 2013). It consisted of a questionnaire containing background information including diet history, family history of chronic diseases, previous health related issues and focused history on diabetes mellitus, hypertension, smoking, alcohol consumption and use of alternate medicines. This is followed by measurement of the blood pressure, calculating the body mass index, urine analysis on the spot and estimation of serum creatinine. Informed consent was obtained prior to the data collection. The nurses and technicians were trained prior to the examination of urine and blood. Individuals with abnormal results of urine analysis, serum creatinine or eGFR were referred to the tertiary centres of both public and private sectors for further evaluation at low cost and were followed up.

Definitions of diagnostic tools

History of diabetes mellitus was elucidated as a self reported history of diabetes mellitus, or receiving medications for diabetes mellitus.

Blood pressure was measured in sitting position in the right arm using the standard cuff. The blood pressure was classified based on the JNC 7 classification as normal (<120/80 mmHg) pre hypertension (systolic 120-139mmHg or diastolic 80-89mmHg) hypertension stage 1(systolic 140-159mmHg or diastolic 90-99mmHg), hypertension stage 2 (systolic >160 mmHg or diastolic >100 mmHg) (http://www.nhlbi.nih.gov/guidelines/hypertension/phycard.pdf. Accessed on August 2013).

Body mass index was calculated by the formula weight (kg)/ height (metre) (http://apps.who.int/bmi/index.jsp?introPage=intro_3.html). The body mass index was classified based on the WHO classification as underweight (<17.5 kg/m^2) normal (17.5-22.99 kg/m^2) overweight (23.00-27.99 kg/m^2) obese (>28 kg/m^2).

Urine for protein was examined by reading the urine dipstick after a minimum period of 30 seconds of collection by uristik method (NKF KDOQI guidelines, 2002). The uristik readings were interpreted as Normal- absence of colour change Abnormal – trace and above.

Serum creatinine (Daniel H Cooper *et al*., 2013) was estimated using auto analyzer. The interpretation of serum creatinine values were Males: 0.7 to 1.5 mg/dl Females: 0.6 to 1.4 mg/dl.

>1.2 mg/dl- abnormal and requires further investigations.

Estimated glomerular filtration rate was calculated from the creatinine values based on the MDRD equation as eGFR= 175 x $sr.creatinine^{-1.154}$ x $age^{-0.203}$ x 1.212 x 0.742(if females)(Estimating GFR, 2013). The interpretation of eGFR values were <60 $mL/min/1.73m^2$ – Abnormal and indicator of renal damage. Requires further investigations >60 $mL/min/1.73m^2$ – does not require further investigations.

RESULTS

A total of 1551 individuals above 18 years of age participated in the study. The mean age of the participants was 46.08 years ± 13.1 years. Table 1 shows the background characteristics of the participants.

Table 1. Background characteristics

S. No	Particulars	Frequency	Percentage
1.	Age of the participant		
	20-40 yrs	596	38.5
	40-60 yrs	732	47.3
	>60 yrs	219	14.2
2.	Sex of the participant		
	Male	841	54.4
	Female	706	45.6
3.	History of type 2 diabetes mellitus		
	Present	331	21.3
	Absent	1220	78.7
3.	Body mass index		
	Underweight	92	5.9
	Normal	439	28.3
	Overweight	693	44.7
	Obese	327	21.1
4.	Blood pressure		
	Normal	752	48.5
	Pre hypertension	600	38.6
	Hypertension stage 1	148	9.5
	Hypertension stage 2	51	3.2
5.	Proteinuria		
	Present	375	24.2
	Absent	1172	75.8
6.	Serum creatinine (mg/dl)		
	<1.2	1457	94.2
	>1.2	90	5.8
7.	Estimated glomerular filtration rate (ml/min/1.73m2)		
	<60	119	7.7
	>60	1428	92.3

Table 2. Association between various factors and abnormal serum creatinine

S. No	Particulars	Abnormal Serum creatinine	percentage	Odds ratio	Chi square	p value	95%CI
1.	Age of the participant						
	>45 yrs	78	9.5	6.1	42.7	0.0001	3.3-11.4
	<45 yrs	12	1.7				
2.	Sex of the participant						
	Male	64	7.6	2.2	10.8	0.001	1.3-3.4
	Female	26	3.7				
3.	Known diabetics						
	Present	30	9.1				
	Absent	60	4.9	1.9	8.2	0.004	1.2-3.04
4.	Body mass index (kg/m^2)						
	>23	45	4.4	0.5	10.5	0.001	0.3-0.8
	<23	45	8.5				
5.	Proteinuria						
	Present	46	12.3	3.6	37.5	0.0001	2.3-5.5
	Absent	44	3.8				
6.	Blood pressure						
	Hypertensive	21	9.5	1.9	6.5	0.010	1.2-3.2
	Normal	69	5.2				

Table 3. Association between various factors and abnormal eGFR

S. No	Particulars	Abnormal eGFR	Percentage	Odds ratio	Chi square	p value	95%C.I
1.	**Age of the participant**						
	>45 yrs	109	13.2	10.8	75.8	0.0001	5.6-20.8
	<45 yrs	10	1.4				
2.	**Sex of the participant**						
	Male	64	7.6	2.2	10.8	0.001	1.3-3.4
	Female	26	3.7				
3.	**Known diabetics**						
	Present	41	12.4				
	Absent	78	6.4	2.1	13.2	0.0001	1.4-3.1
4.	**Body mass index**						
	>23	68	6.7	0.7	4.2	0.039	0.5-0.9
	<23	51	9.6				
5.	**Proteinuria**						
	Present	55	14.7	2.9	33.9	0.0001	2.0-4.3
	Absent	64	5.5				
6.	**Blood pressure**						
	Hypertensive	24	10.9	1.6	3.8	0.052	0.9-2.5
	Normal	95	7.1				

There were 47.3% of individuals between 40-60 years of age and 54.4% were males. In all, proteinuria was present in 24.2% of the individuals and in 5.8% of them, the serum creatinine was greater than 1.2 mg/dl. The blood pressure was normal for 48.5% of the individuals, while 44.7% of them were found to be overweight. In this study, proteinuria had a sensitivity of 51.1% and specificity of 77.5%. Table 2 shows the association between various factors and serum creatinine. It is evident that people of age greater than 45 years are more at risk of developing abnormal serum creatinine (OR- 2.2, $p<0.0001$) . Similarly known diabetics are at increased risk of developing abnormal serum creatinine (OR- 1.9, $p<0.005$). The association between certain risk factors and eGFR is shown in table 3. In our study, non modifiable factors like age and sex were proven to be risk factors for abnormal serum creatinine and therefore at risk of any form of kidney disease. It was observed that individuals more than 45 years of age were 6.1 times at risk of any form of kidney disease (9.5%, $p<0.001$). Moreover, males were found to be more at risk for kidney disease. Among the modifiable risk factors, diabetic status, proteinuria and hypertension were found to be positively associated with the risk of any form of kidney disease. It was observed that known diabetics were 1.9 times more at risk of developing any form of kidney disease (9.1%, $p <0.005$). Similarly, presence of proteinuria was found to be 3.6 times a risk factor for kidney disease (12.3%, $p <0.001$). Moreover, hypertensives were 1.9 times more at risk of having abnormal creatinine (9.5%, $p<0.05$). It was observed that non modifiable risk factors like age and sex of the individuals were risk factors for abnormal eGFR. In this study, individuals more than 45 years of age were 10.8 times at risk of abnormal eGFR (13.2%,$p<0.001$). Among the modifiable risk factors, known diabetics were 2.1 times at risk for abnormal eGFR (12.4%, $p<0.0001$). Similarly, presence of proteinuria was found to be 2.9 times a risk factor for lower eGFR ($p<0.001$).

DISCUSSION

In this study, the mean age of the participants was 46.08 years. In the SEEK study done by AK Singh et al, the mean age of the participants was 45.22 years which is comparable. The prevalence of kidney disease was found to be 5.2% as against 17.2% in a study done by (AK Singh *et al.,* 2013). The mean eGFR was found to be 88.5 ml/min/1.73m^2. According to our study, the prevalence of diabetic nephropathy was 9.1%. In a study done in Chennai, the prevalence of diabetic nephropathy was 2.2% (Ranjit Unnikrishnan *et al.,* 2007). This study has revealed that age and proteinuria are solid risk factors for developing kidney disease. Individuals more than 45 years of age were found to be 10.8 times at risk for an eGFR of <60 ml/min/1.73m^2. This study elucidates the impact of risk factors namely history of diabetes mellitus, age and the presence of proteinuria in the prevalence of chronic kidney disease. It is imperative to follow the KEEP guidelines recommended by the National Kidney Foundation to address all the risk factors of kidney disease further (http://www.kidney.org/news/keep/index.cfm) by assessing body mass index, waist circumference, estimation of plasma glucose, creatinine, hemoglobin, lipids, electrolytes and PTH in the blood, urine examination. In developing countries like India, the cost of screening is an important aspect and screening for kidney disease based on measuring blood pressure, body mass index, proteinuria and estimation of eGFR has been proven to be cost effective as compared to many other screening tools for other chronic diseases and is associated with improvement in the QALYs (Braden Manns *et al.,* 2010).

Conclusion

In India, high prevalence of CKD is due to diabetes mellitus and hypertension followed by other causes. Moreover, only 10% of the population has access to Renal Replacement Therapy in India (World Health Organization, 2013). Therefore, we feel that primary prevention in the form of cost effective awareness programmes coupled with mass screening using simple questionnaire, blood pressure screening, urine analysis, measurement of serum creatinine and estimation of eGFR is the need of the hour and will facilitate early diagnosis and interventions to slow down the progression of CKD. Philanthropic organizations with partnership through government agencies and pharmaceutical industries can take this forward in reducing the morbidity and mortality due to CKD.

Limitations

Apart from estimation of proteinuria, microalbuminuria is a key predictor of early renal damage, especially among people with diabetes mellitus. This study did not look into the prevalence of microalbuminuria due to the logistic difficulties. Though this study has elucidated the importance of diabetic nephropathy, a well worked cohort study is required to assess the causal association between the diabetic status and the onset of nephropathy.

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