

Epidemiology and Demography of Chronic Kidney Disease in Pakistan- A Review of Pakistani Literature

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Abstract

Background:

CKD is spreading like an epidemic. There is a dire need to understand the true prevalence as well as the causes of CKD in both urban and rural areas of Pakistan in relevance to age and gender. In this background, there is a need to know what has been done so far to understand the status of CKD in Pakistan.

Materials and Methods:

We selected the articles published through PubMed and Google scholar and the following keyword were used, epidemiology, demography, prevalence, chronic kidney disease, chronic renal insufficiency, etiology, and causes of CKD, Pakistan. We found four articles that evaluated the prevalence and five articles that dealt with the causes of CKD. We included all articles in our analysis.

Results:

The overall prevalence among all age groups was found to be 21.2%. The highest CKD prevalence was reported as 29.9% and the lowest at 12.5%. The highest prevalence was found in patients more than 50 years of age (43.6%). Two studies showed male predominance (62% and 54.4%), while two showed a female majority (64%,52%). The most common cause of CKD was found to be Diabetic nephropathy (27.1%), followed by CKD of unknown etiology (16.6%) and renal stone disease (12.4%)

Conclusion:

The prevalence of CKD is high, especially in the older population. Similarly, the leading causes of CKD are also different in all studies due to center dependence, hospital-specific and urban locations.

Keywords: Pakistan, chronic kidney disease, prevalence, epidemiology.

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DOI: 10.53778/pjkd71209

Received: Sep 20,2022. Accepted March 23, 2023.

PJKD 2023;7(1):2-7

Introduction:

Pakistan is among the most growing nation with a population of 207 million with an annual growth rate of 2.7. It is extrapolated that if the growth rate goes at the same pace, it will be 330 million in 2030.¹ Besides this growing population, the infrastructure of the health sector is badly neglected. This was the reason despite six decades of journey the planning and policy formation in this domain is capable of merely at the preparation level but not at the execution level.² It seems there are unresolved inherent problems in the health care system of the country which are refraining from developing strategies to combat the deteriorating health structure. For example, there is no thought to address the changing pattern of the diseases due to the deteriorating global environment, growing inequalities and disparities between provinces, challenges due to the availability of expert human resources, and questionable quality of care in both private and public hospitals.

Kidney diseases are now recognized as one of the leading causes of death and disability along with the epidemic of Diabetes mellitus which is driving CKD at very high momentum.³ For example, in South Asia alone DM prevalence is estimated to increase by over 150 % between 2000 to 2030.⁴ In addition, specific to this region increasing population is recognized to suffer CKD of unknown etiology (CKDu) in agricultural communities in Sri Lanka and India.^{5,6} CKD leads to a wide range of fatal diseases. CKD is considered one of the major risk factors for developing cardiovascular disease.⁷ Besides the deteriorating effect on individual life, CKD also affects

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the social spectrum of a person and is responsible for the loss of productivity. The most common form of social impact due to CKD is a financial burden.⁸ CKD is a progressive disease and ultimately succumb to end-stage renal disease (ESRD) which requires costly management like hemodialysis, peritoneal dialysis, and renal transplantation.

The exact burden of CKD in Pakistan is not known, but in a review of available data on CKD in Pakistan, the estimated prevalence in the neighboring countries was 17%.⁹ If we extrapolate this number on the existing population of 207 million, there will be 35,326, 000 (3.5 crores) persons with impaired kidney functions residing in Pakistan. The data on contemporary CKD prevalence to better inform future projections is somewhat sparse, similarly, the renal registry as in the other part of Asia is mostly restricted to systematic data collection of hemodialysis patients.¹⁰ There are very few individual reports that suggest wide variation in CKD prevalence.

This situation forced us to feel a dire need to review the existing data on Pakistan delineating the prevalence as well as etiology of CKD. This will pave the way to design a community-based (both in urban and rural areas) evaluation of CKD prevalence and etiologies.

Methods:

The articles were selected through PubMed and Google scholar and the following keyword were used, epidemiology, demography, prevalence, chronic kidney disease, chronic renal insufficiency, etiology, and causes of CKD, Pakistan. Very few articles published on CKD epidemiology and causes of CKD. We included all original articles which discussed the population data on the etiology and prevalence of CKD, although we excluded review articles, editorials, and book chapters. Since very few studies were available in the context of the Pakistani population in a span of 25 years the quality appraisal of the studies was not done, but all studies were published in PubMed and renowned national and international journals. All studies used although different but creatinine-based equations to measure GFR.

Results:

CKD Prevalence

After completing the search, we found four studies on the prevalence of CKD (11-14) Table 1. Randomization was done in three studies, the study was conducted by Imran et al in a health camp in a busy shopping area, therefore only those who participated were included. Similarly, all three were community-based except the study done by Imran et al. Sample size was adequate the lowest was 300 while the largest was 3034. The minimum age of the population included was 15 years to 40 years. The Glomerular filtration rate (GFR) was estimated by Serum creatinine-based equation. Jafar et al and Alam et al used the MDRD equation, while Imran et al and Jessani et al calculated GFR through the CKD-EPI and the CKD-EPI^{PAK} (Pakistan) equation, respectively. (Table1). The reported prevalence was found to be different in all four studies. The highest CKD prevalence was reported as 29.9% by Jafar et al and the lowest at 12.5% was reported from the same institute and in the same age group by Jessani et al. The overall prevalence among all age groups was found to be 21.2%.

Table: 1 The studies, which were done to evaluate the epidemiology of CKD in Pakistan

Study Name & Author	Jafar et al. 2005 ¹¹	Alam et al. 2014 ¹²	Jessani et al. 2014 ¹³	Imran et al. 2015 ¹⁴
Number of participants	332	461	3143	301
Site of study	Aga Khan University Urban Karachi	The Indus Hospital Urban Karachi	Aga Khan University Urban Karachi	Aga Khan University Urban Karachi
Design of study & sampling technique	Cross-sectional study, random	Cross-sectional study random	Cross-sectional study, random	Cross-sectional study non-random
Assessment of GFR	Creatinine clearance and eGFR (MDRD)	Spot quantitative urine protein and eGFR (MDRD)	Spot quantitative urine protein and eGFR (CKD-EPI Pakistan equation)	eGFR (CKD-EPI)
Age (years)	> 40	≥15	≥ 40	30–80
Gender ratio	54.2% male	36% male	47.8% male	62% male
Prevalence of CKD (overall)	29.90%	16.60%	12.50%	25.60%
Prevalence: age(years) / gender specific	Age-specific: not mentioned/ Male:26.7% Female: 32.5%	Age < 30:10.5% , 30–50:12.7% , > 50; 43.6% / Male:20.6% Female: 14.2%	Age-specific: not mentioned/	Age-specific not mentioned/ Male:26.3% Female: 22.4%

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Age-specific prevalence was only measured by Alam et al and their study showed the highest prevalence among elderly patients more than 50 years of age (43.6%) on the other hand the lowest prevalence among comparatively younger participants aged less than 30 years (10.5%). Table 1.

Gender-specific prevalence was reported by all four studies. Jessani et al and Jafar et al reported a higher prevalence in females, contrary to it Alam et al and Imran et al found men suffered more from CKD.

CKD causes

After completing the search, we found five studies on the causes of CKD in Pakistan (15-19), we added one study under peer review done at District Badin an area of rural Sind (Table 1). All the studies were done in urban Sind except the study done by Shahnawaz et al which was done at District Badin (rural Sind) adjacent to the Thar Desert area. This study was done at District Hospital Badin The Indus Hospital Network and the only data so far presented from this area (under peer review). The sample size of Haren et al was low but it was the first study in this domain done at a large tertiary renal facility. The design of all studies was cross-section and was with non-randomized data collection except for the study done by Salman B et al. the minimum age of the participant in all studies was 15 to 20 years with a mean age of 40-55 years. All have male predominance except the study by KifayatUlah et al who reported an equal number of males and females, Table 2.

Table 2: Studies from Pakistan evaluating the causes of hronic kidney disease in Pakistan.

S. No	Study name and author	Number of participants	Site of study	Design of study & sampling technique	Age(yrs.) mean(n)	Gender ratio
1	Haren K et al 1992 ¹⁵	79	TKC Karachi Urban Sind	Cross section, non-random	15-78 (43)	60.7% males
2	Rizvi et al 2002 ¹⁶	874	SIUT Karachi Urban Sind	Cross section, non-random	17-85 (47.4 ± 14.9)	57.8% males
3	KifayatUlah et al 2015 ¹⁷	500	PIMS Islamabad	Cross section non-Random	20-83 (46.3)	50% males
4	Salman B et al 2017 ¹⁸	1052	TKC Karachi Urban Sind	Cross section. Random	53±15 median (55)	51.4% males
5	Shahnawaz ¹⁸ et al (under publication JPMA-2022-6764) ¹⁹	348	The Indus hospital Badin (rural Sind)	Cross section. Non-random	15-100 40.4±19	52.9% males

The most common cause of CKD in this review turned out to be Diabetic nephropathy (27.1%), followed by CKD of unknown etiology (CKDu) (16.6%), which is now recognized as one of the important preventable causes of CKD in agricultural countries like Pakistan. Chronic Glomerulonephritis (14.4%) and hypertensive nephropathy (15.2%) also turn out to be important causes of CKD, although both hypertensive nephropathy and chronic glomerulonephritis were clinical diagnoses in all of the studies and biopsy was done only in 35(4%) of the patients in the study done by Rizvi et al. The definition of both diseases was also not standardized nor defined in all studies, however, there is a gross variation in understanding of these two diseases from one center to another. Kidney stones are prevalent in this region, and it is known as the “stone belt” due to the high incidence of kidney stones and their complications. Shahnawaz et al reported the highest number of cases of CKD due to stone disease (31.1%) which is understandable as Badin is one of the cities which comes under the area of the stone belt. Infections are also an important cause of CKD in two of the studies reported Urinary tract infection as a cause of CKD in their analysis. There is one more reason for CKD in urban areas patients who developed acute kidney injury due to malaria, snake bite, dengue fever, and diarrhea. 21(6.1%). The other enlisted etiologies are not very common, Table 3.

Discussion:

CKD prevalence

This is the first report on the review of literature on the prevalence and epidemiology of CKD in Pakistan. this study revealed that the overall prevalence of CKD in Pakistan is high (21.2%). Jafar et al reported a prevalence of 29.9% which is the highest among the neighboring countries. If we look at the country-specific prevalence in Nepal, Bangladesh, and India the global prevalence of CKD (13.4%) appears high (20). This unprecedentedly high prevalence reported by Jafar et al and somehow Imran et al might be due to the high minimum age in both studies.

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Table 3: Causes of CKD reported in studies from Pakistan.

S. No	Causes of CKD	Haren K et al 1992. Total (79)	Rizvi et al 2002. Total (839)	KifayatUlah et al 2015 Total (500)	Salman B et al 2017 Total (1052)	Shahnawaz et al (under publication) Total (348)	Total 2818
1	Diabetes mellitus n (%)	11(13.9)	172 (19.67)	140 (28)	395 (37.5)	47 (13.7)	765(27.1)
2	CKD of Unknown etiology n (%)	11(13.9)	230(26.3)	53 (10.6)	97 (9.2)	79 (22.7)	470(16.6)
3	Hypertensive nephropathy	7(8.8)	170 (19.45)	73 (14.6)	180 (17.1)	NA	430(15.2)
4	Chronic glomerulonephritis n (%)	35(44.3)	78(9.9)	110 (22)	117 (11.2)	68 (19.4)	408(14.4)
5	Renal stone n (%)	8(10.1)	63 (7.20)	40 (8.0)	134 (12.7)	108 (31.3)	353(12.5)
6	Tubulointerstitial nephritis n (%)	NA	26 (2.97)	67 (13.4)	17 (1.6)	NA	110(3.9)
7	Polycystic kidney disease	5(6.3)	32 (3.66)	7 (1.4)	28 (2.6)	9 (2.6)	81(2.8)
8	Obstructive nephropathy n(%)	1(1.2)	39 (4.46)	NA	NA	NA	40(1.4)
9	Urinary tract infections n (%)	NA	NA	NA	24 (2.3)	16 (4.6)	40(1.4)
10	Drug-induced n (%)	NA	NA	NA	33 (3.1)	NA	33(1.1)
11	Reflux nephropathy n (%)	NA	29 (3.31)	NA	NA	NA	29(1.02)
12	Chronic allograft nephropathy n (%)	NA	NA	NA	27 (2.5)	NA	27(0.96)
13	Unrecovered Acute Kidney Injury n (%)	NA	NA	NA	NA	21 (6.0)	21(.74)
14	Polyarteritis nodosa n (%)	1(1.2)	NA	NA	NA	NA	1(0.03)
15	others	NA	NA	10 (2.0)	NA	NA	10(0.35)
	Total	79	839	500	1052	348	2818

The mean age of the population in the Jafar et al study was 51.4±9.9 (unfortunately the mean age of the population is not reported by others). We know that age itself is a well-known risk factor for CKD, and after the age of 30 to 40 years, there is a decline in GFR and deteriorated further due to the loss of residual renal function after the age of 50-60 years (21). Alam et al mentioned the age-specific prevalence and it is clear from their data that the younger group has less prevalence as compared with the older age group. **Table 1.**

Gender-specific prevalence also showed variability and gross differences among all four studies. Two studies (Alam et al and Imran et al) reported male predominance while the other two (Jessani et al and Jafar et al) notified females majority. In both the studies with the female majority the difference in proportion was low in the Jessani et al population (males 11.6%, females 13.3%) as compared with Jafar et study (males 26.7% females 32.5%). This might be due to the use of the Pakistan-specific CKD-EP^{PAK} equation. In a large CKD cohort of nearly 4000 patients, women had a low risk of CKD progression and death as compared with men. It has been hypothesized that gender disparities in the progression of CKD have multiple factors like differences in kidney volume and renal hemodynamics, sex hormones, dietary intake of proteins, and smoking (22). There is a need to investigate the gender-specific prevalence in our CKD population.

CKD causes:

The population of Pakistan is distributed in rural and urban areas and despite the rapid urbanization and migration of the people (a global phenomenon) from rural to urban areas majority (70% -80%) of the population reside in rural areas (23). The large cities are a bit modern, and lifestyle is changing very rapidly, and people are opting for western ways of life. Therefore, the disease pattern is a mix of modern and traditional lifestyles. Along with this Pakistan is an agricultural country and most of the rural population is associated with cultivation, farming,

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etc. This is the reason the diseases of the modern era like DM, Hypertension, and malignancy as well as diseases of developing countries both are prevalent in Pakistan.

All five studies were done in the province of Sind, four published studies were from Karachi which is one of the largest cities in the country with people migrating from all over Pakistan. Unfortunately, not a single study has been published so far to know the demography of CKD in rural populations. The only data is by Shahnawaz et al from Civil Hospital Badin (under publication), which is mostly an agricultural community.

In this review, DM turns out to be the most common cause of CKD which is a well-recognized phenomenon globally (3). The largest population of DM patients is reported by Salman B et al from The Kidney center followed by KifayatUlah et al from the Pakistan Institute of Medical Sciences (PIMS) Islamabad. The Kidney center is a private hospital that caters to a different population mostly affluent as compared to other hospitals funded by philanthropy and government funding.

CKD of unknown etiology is also an important cause of renal failure in our population. It is well recognized in agricultural communities like Pakistan (24,25,26). The disease characteristically involves men who have worked for two or more seasons, are between 20 and 50 years old, are asymptomatic, and have normal or only slightly elevated blood pressure and normal blood glucose levels. The urinalysis shows no or minimal proteinuria (27). Shahnawaz et al reported the highest prevalence in their population and almost all studies showed a high prevalence of CKDu in their data. There is debate about its etiology as it is caused by heat stress and water depletion leads to acute tubular injury or overhydration of contaminated water with heavy metals or pesticides causing tubulointerstitial disease. In a review of water content in different areas of Pakistan Salman et al found a high level of arsenic, ochratoxin, and Zearalenone in areas related to the chicken industry (28). Similarly, in a biopsy series, Ruqaya, and Salman et al found a high prevalence of tubulointerstitial disease in people belonging to these areas (29)

Renal stones are prevalent in this area for this it is recognized as “stone belt” . The exact cause of this high incidence is not known whether it is due to genetic predisposition, dietary habits, water content, or extremely hot climate causing dehydration. Kidney Damage due to stones leading to CKD is rare in other parts of the world although the stone prevalence is high, due to early diagnosis and prompt management and prevention of the recurrence. (30). Unfortunately, nothing has been done so far to understand the cause of renal stone disease in this population. The prevalence of both CKDu and stone disease diseases is high, comprising about 30 to 35% of the CKD population and both are preventable.

Hypertensive nephropathy and Chronic glomerulonephritis also cause significant morbidity. But definitions of both diseases are not equivocal. Most of the time it is a clinical diagnosis for those who have small non-biopsiable kidneys with a history of hypertension of any duration or presence of proteinuria in urinalysis at the time of diagnosis respectively.

Conclusion:

In this review, the overall prevalence of CKD turns out to be 16.7% with a range of 29.9% to 12.5% in all four studies. Diabetic kidney disease and CKDu followed by renal stone diseases is the common cause of CKD in Pakistan. Older age is the risk factor for CKD. There is a need to do a population-based study in both rural and urban areas of Pakistan to evaluate the prevalence and causes of CKD to combat this deadly but preventable disease.

Conflict of Interest: None Declared

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