Salman et al., J Nephrol Ren Dis 2017, 1:1
DOI: 10.4172/2576-3962.1000105

Journal of Nephrology & Renal Diseases

Research Article A SCITECHNOL JOURNAL

# The Causes of Chronic Kidney Disease in Adults in a Developing Country

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## Abstract

**Introduction:** Diabetes mellitus (DM) and hypertension (HTN) are considered as the leading causes of CKD all around the world. But the causes of CKD differ from region to region. In developing countries the population is heterogeneous therefore regional causes of CKD need to be evaluated.

**Material and method:** This cross sectional study included all adult CKD patients, who visited to nephrology service in two tertiary care hospitals in metropolitan city Karachi in Pakistan. The sociodemographic data was collected by interview through a structured questionnaire while laboratory data was collected from patients records.

**Results:** Diabetic nephropathy (DNP) was the main cause of CKD (37.5%) followed by hypertensive nephropathy (17.1%) and obstructive nephropathy (ONP) (12.7%). ONP and hereditary disorders (HD) were more prevalent in males than females (70. 1% vs. 29.9%) and (75% vs. 25%) respectively, while urinary tract infection (UTI), drug induced kidney disease and tubulointerstitial nephritis (TIN) were more common in females than in males (87.5% vs. 12.5%), (75.8% vs.24.2%) and (64.7% vs. 35.3%) respectively. Gender, area of residence and socioeconomic status were the factors which affect the cause of CKD ($p \leq 0.05$).

**Conclusion:** DNP and hypertensive nephropathy were more prevalent in urban, educated males with high socioeconomic background. On the other hand CKD of unknown etiology and stone diseases were more common in rural, uneducated, males with low socioeconomic background.



### Keywords

Diabetes Mellitus; Hypertension; Kidney disease; Nephritis


## Introduction

The decrease in the clearance capacity of the kidney is associated with devastating effect on almost every organ of the body. The detrimental outcome caused by chronic kidney disease (CKD), include End Stage Renal Disease (ESRD), progressive cardiovascular disease (CVD), early mortality and profound morbidity that has considerable economical impact, especially in developing countries [1,2].

Globally, diabetes mellitus (DM) and hypertension (HTN) are recognized as the principal causes of CKD, while infectious diseases, indigenous medicines, environmental and industrial pollution are also important in low income countries [3]. Due to the diversity of population in low income countries, it is a distinct challenge to determine the cause of CKD in this region. The population in this area is heterogeneous in terms of socioeconomic growth, ethnic configuration, rural urban division, disparity and access to health facilities as compared with the developed countries. This is the reason it is hard to identify the population at particular risk and therefore, it becomes a burden to extrapolate any preventative measures on this population. Hence, there is a large group of CKD patients in which cause of CKD remains "unknown". Similarly, preventable causes of end stage renal disease (ESRD) like renal stones still prevail in the etiology of ESRD in these parts of the world [4-6].

The incidence of kidney stones disease is rising all over the world possibly due to global warming as well as change in dietary habits [7]. Recurrent stone formation puts the patients at risk of developing CKD. An early screening of the population at risk, along with aggressive medical treatment to prevent recurrent kidney stones may decrease the risk for CKD [8]. In our country, data regarding incidence and prevalence of stone disease and its effect on kidney function is sparse [9], but its profound morbidity due to acute and chronic kidney disease has been observed in pediatric population [10].

The CKD of unknown-etiology (CKDu) has recently been recognized as major threat of CKD especially in developing countries, which could not be explained by the traditional risk factors. Different risk factors have been highlighted, like drinking water contaminated with heavy metals [4], regional nephropathies like Mesoamerican nephropathy [11], Sri Lankan agricultural nephropathy [12] Udhanam endemic nephropathy in India [13], low birth weight [14]. Growing number of patients come from different parts of the country and are admitted in our emergency departments with advanced uremia and bilateral small kidneys, the etiology of which is difficult to ascertain. There might be environmental, ethnic and regional factors which are the culprits which unfortunately increases its incidence.

Therefore, we feel that there is need to determine the causes of kidney failure with reference to ethnicity, socioeconomic status, rural or urban dwelling, gender and age of the population. In this study, we evaluated the causes of CKD in different groups of the population in two referral tertiary care hospitals.

## Materials and Methods

This cross sectional study was the sub analysis of another study conducted in the nephrology unit of Dow University Hospital and The Kidney Centre Post Graduate Training Institute. These two hospitals are located in metropolitan city, Karachi in Pakistan. We included all adult CKD patients, admitted or on visit as inpatient or outpatient respectively during a period of eight months from May 2015 to December 2015. Patients are referred to these hospitals from all over the province and adjacent provinces and the population is heterogeneous in terms of their rural and urban distribution.

It is difficult to define rural and urban areas in this region, since many villages have no health care facilities at all. It gets harder to

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**Received:** February 15, 2017 **Accepted:** February 17, 2017 **Published:** February 24, 2017

classify urban cities due to the fact that some cities are devoid of tertiary care hospitals and availability of hemodialysis and kidney specialists. Therefore, we have labeled these non-equipped cities as rural. We defined uneducated, as those who were not able to read and write their name and even they did not get basic religious education. In the category of primary education we included those patients who could read the Holy Book or they received education in school till class V. All patients who got education up to class X were categorized in secondary education. In graduate and above education category, we included those patients who acquired education of more than and equal to XIV years. For ease in final analysis we merged these categories into two main categories educated and uneducated.

A face-to-face interview was conducted by the principal investigator in the OPD and wards of both institutes. A structured questionnaire was developed, which was used to collect the data on sociodemographic characteristics. A pilot study of 10 patients was done first, to check any inconvenience in collecting the data through questionnaire. Variables included in the study were gender, age, marital status, area of residence, ethnicity, smoking status and level of education. Variables like comorbid conditions and cause of chronic kidney disease were taken from patient's records.

### Statistical analysis

Data analyses were performed by using software IBM SPSS license version 21. Descriptive analysis of variables was presented in form of frequencies and percentages. To measure association of cause of CKD with categorical study variables, chi-square test was executed. Level of significance was considered at 5%.

## Results

The study included 1052 patients; males were slightly more than the females (51.4%) versus (48.5%). The age group from 41-60 years was predominantly high (46.2%). Most of the patients who came to our hospitals were resident of urban areas 86.8%. Among different linguistic groups, Urdu speaking were most prevalent (50.8%) followed by Sindhi speaking patients (16.3%). Majority of the patients were married (79.1%). When sociodemographic status was investigated, it was observed that higher number of patients belonged to middle class (53.8%). The education status of the patients showed that graduate and higher educated patients were more frequent (24.2%), followed by secondary educated patients (22.6%). While evaluating the working status of the patients, we found that most of the females were doing house work (44.6%), while higher numbers of male patients were doing field works (13.5%). The analysis of smoking status showed that patients who never smoked cigarette were (82.6%) (Table 1).

Various comorbid conditions are associated with CKD patients and in our sample population; the most prevalent comorbid was HTN (86.7%) followed by DM (49.9%) and IHD (19.6%) (Table 2).

Among the different causes of CKD, the most frequent cause was DNP (37.5%). Hypertensive nephropathy was (17.1%) followed by ONP (12.7%) (Tables 3-5).

Cross tabulation of gender with causes of CKD showed that gender was highly associated with causes of CKD ($p$<0.001). For instance, ONP and hereditary disorders(HD) were more prevalent in males than females (70.1% vs. 29.9%) and (75% vs. 25%) respectively. On the other hand urinary tract infection, drug induced kidney disease and tubulointerstitial disease as the cause of CKD were more common in females than in males (87.5% vs. 12.5%), (75.8% vs. 24.2%) and (64.7% vs. 35.3%) respectively (Table 3).

The residence of the CKD patients has an impact on etiology of CKD ($p$=0.006). Among different causes of CKD, the ONP and CKD of unknown etiology were more prevalent in residents of rural areas (22.3% vs. 11.5%), and (11.5% vs. 8.9%) respectively, while the DN is more common in urban patients than rural patients (39.2% vs. 26.6%) (Table 4).

While comparing the socioeconomic status with causes of CKD in our patient's population, it was observed that both were highly associated ($p$<0.001). The patients who belonged to higher socioeconomic class had more DN than middle and low socioeconomic classes (49.5%), (36.7%) and (31.5%) respectively, while ONP was more frequent in lower class rather than middle and higher classes (18.8%), (11.7%) and (6.7%) respectively. In the same manner unknown cause of CKD was also more common in low socioeconomic class than other classes (13.4%) (Table 5).

## Discussion

In this analysis DM and hypertension emerged out as the main causes of chronic kidney disease, followed by ONP and glomerular disease. The fifth largest group which causes CKD was of unknown etiology. As we discussed, the developing countries' population is complex in structure, in terms of socio-economic differences and ethnic variety, which have an impact on ESRD incidence and prevalence. Therefore, we considered these factors as well in

**Table 1:** Socio Demographical variables of the CKD patients.

| | | N (%) |
|---|---|---|
| **Gender** | Female | 511 (48.6) |
| | Male | 541 (51.4) |
| **Age Category** | 18-40 years | 217 (20.6) |
| | 41-60 years | 486 (46.2) |
| | >60 years | 349 (33.2) |
| **Area of Residence** | Urban | 913 (86.8) |
| | Rural | 139 (13.2) |
| **Ethnicity** | Urdu Speaking | 534 (50.8) |
| | Sindhi | 171 (16.3) |
| | Punjabi | 126 (12.0) |
| | Balochi | 51 (4.8) |
| | Pakhtoon | 72 (6.8) |
| | Any other | 98 (9.3) |
| **Marital Status** | Married | 832 (79.1) |
| | Single | 220 (20.9) |
| **Socioeconomic Status** | Low | 298 (28.3) |
| | Medium | 566 (53.8) |
| | High | 188 (17.9) |
| **Education** | Un-educated | 205 (19.5) |
| | Primary | 217 (20.6) |
| | Secondary | 237 (22.5) |
| | Intermediate | 138 (13.1) |
| | Graduate and above | 255 (24.2) |
| **Job** | None | 116 (11.0) |
| | House wok | 469 (44.6) |
| | Field job | 142 (13.5) |
| | Office job | 101 (9.6) |
| | Business | 107 (10.2) |
| | Retired | 117 (11.1) |
| **Smoking Status** | Never | 869 (82.6) |
| | Ever Smoker | 183 (17.4) |

**Table 2:** Comorbid conditions of the CKD patients.

| | N (%) |
|---|---|
| Hypertension (HTN) | 912 (86.7) |
| Diabetes Mellitus (DM) | 525 (49.9) |
| Ischemic Heart Disease (IHD) | 206 (19.6) |
| Renal Stone | 129 (12.3) |
| Hepatitis C | 83 (7.9) |
| Tuberculosis | 40 (3.8) |
| Hepatitis B | 29 (2.8) |
| Thyroid Disease | 29 (2.8) |
| Cerebrovascular Accident (CVA) | 25 (2.4) |
| Osteoarthritis | 25 (2.4) |
| Asthma | 24 (2.3) |
| Partial Villous Atrophy (PVA) | 14 (1.3) |
| Prostate Disease | 13 (1.2) |
| Systemic Lupus Erythematosus (SLE) | 8 (0.8) |
| Blood Disorders | 8 (0.8) |
| Rheumatoid Arthritis (RA) | 6 (0.6) |
| Chronic Obstructive Pulmonary Disease (COPD) | 6 (0.6) |
| Dyslipidemia | 3 (0.3) |

**Table 3:** Association of causes of CKD with gender.

| | | Gender | | Total | *p* Value |
|---|---|---|---|---|---|
| | | Female | Male | | |
| Cause of CKD | Unknown | 53 (54.6) | 44 (45.4) | 97 | <0.001 |
| | Diabetes Mellitus (DM) | 185 (46.8) | 210 (53.2) | 395 | |
| | Hypertension (HTN) | 98 (54.4) | 82 (45.6) | 180 | |
| | Obstructive Nephropathy | 40 (29.9) | 94 (70.1) | 134 | |
| | Hereditary Disorders | 7 (25.0) | 21 (75.0) | 28 | |
| | Glomerular Disease | 57 (48.7) | 60 (51.3) | 117 | |
| | Urinary Tract Infection (UTI) | 21 (87.5) | 3 (12.5) | 24 | |
| | Tubulointerstitial Disease | 11 (64.7) | 6 (35.3) | 17 | |
| | Drug Induced | 25 (75.8) | 8 (24.2) | 33 | |
| | Chronic Allograph Nephropathy | 14 (51.9) | 13 (48.1) | 27 | |
| **Total** | | **511 (48.6)** | **541 (51.4)** | **1052 (100.0)** | |

our analysis. The demography of our patients is representative of metropolitan nature of Karachi located in Sindh province, which is the largest city of Pakistan with majority of Urdu speaking population, with Sindhi speaking population residing mainly in rural areas. The majority of our patients belonged to age group of 41 to 60 years.

Contrary to the DM and hypertension as main causes of CKD all over the world, we identified two large categories of CKD which are different from other parts of the world; firstly, "CKD of unknown etiology" and obstructive nephropathy. This observation is also evident in a study conducted at a large center of renal disease from the same city [5]. They discerned that the largest group of their CKD cohort belongs to unknown-etiology and comprises (19.67%) of the population while obstructive nephropathy comprises (11.67%).

It is difficult to point out the exact factors which lead to CKD of unknown etiology. In Pakistan, there is evidence of high level of cadmium, lead and arsenic in rural as well as in urban areas of all provinces of the country [15-18]. Similarly, being an agricultural country with hot and humid climate, the possibility of kidney diseases in agricultural worker is high, identical to Sri Lankan and Mesoamerican nephropathy. Analogously, low birth weight is associated with high risk of ESRD in 3rd and 4th decade of life [19]. It is estimated that 72% of LBW infants in developing countries are born in Asia. Although there is no study on the prevalence of low birth weight in Pakistan, UNICEF estimates an incidence of 19% [14]. With this high incidence of low birth weight, it will be pivotal to look for this association in this region also.

The other unfortunate factor which is still a threat of ESRD in our population is kidney stones. Although there is rise in the incidence of kidney stone all over the world [20,21], prevalence of ESRD due to stone disease has reduced [22]. We noticed in our study that a large number of our patients develop ESRD from this preventable cause. The reason of this misfortune is lack of a coordinated health system of the country.

DM has risen all over the world especially in developing countries of Asia [23]. The escalating effect has also been observed among all ethnic groups and in both urban and rural population of the country [24,25]. The impact of this venomous rise of DM reflects to an increase in the prevalence of Diabetic kidney disease (DKD). This phenomenon has been observed in our population as well as in other populations both in developing and developed countries [26-34]. We confirmed the same by contemplating our results. We also observed that in the last decade there is a rising trend of CKD due to DM. Rizvi and Manzoor found (19.7%) of their patients had DM in their ESRD Cohort fifteen years ago, while we found that (37.5%) of our population had DKD in the similar population [5].

ONP is more prevalent in male gender in our population which is consistent with other studies as male patients have more stone formation [7,35]. While females predominantly have urinary tract infections and tubulointerstitial disease [36,37].

The residence of the patients significantly affected the cause of CKD in our population. ONP due to Kidney stones and CKD of unknown etiology are more prevalent in rural dwellers [35]. It is observed that access to the health facilities is challenging for rural dwellers as compared to urban, hence their approach to the health facilities is delayed and they suffer more irreversible damage, even of preventable and treatable diseases like kidney stones and urinary tract infections. On the other hand, diabetic kidney disease was ubiquitous in urban patients. This might be due to expeditious change in life style and dietary pattern.

Socioeconomic status also influences the cause which leads to CKD. We found Diabetic nephropathy more in higher socioeconomic class which is consistent with many studies around the world [38-40]. This rise in the incidence of DM is expected to increase in adults by 69% in this part of the world as compared with the developed countries due to rapid urbanization [41]. Likewise, infections, kidney stones and CKD of unknown etiology were more common in lower socioeconomic group. The reason of which is hard to describe, but apparently seems to be due to late recognition of disease.

This is the first study in this country which reviewed the CKD population in regional perspective. It will make an impact on further research in this direction to elaborate the underlying causes of CKD. It will furthermore help to design strategies at governmental as well as at private organizations to save our population from preventable causes of this deadly disease.

In conclusion, we found DNP and hypertensive nephropathy were more prevalent in urban, educated males with high socioeconomic background. On the other hand, CKD of unknown etiology and stone diseases were more common in rural, uneducated, males with low socioeconomic background.

**Table 4:** Association of causes of CKD with area of residence.

| | | Area of Residence | | Total | *p* Value |
|---|---|---|---|---|---|
| | | Urban | Rural | | |
| Cause of CKD | Diabetes Mellitus (DM) | 358 (39.2) | 37 (26.6) | 395 (37.5) | 0.006 |
| | Hypertension (HTN) | 157 (17.2) | 23 (16.5) | 180 (17.1) | |
| | Obstructive Nephropathy | 103 (11.3) | 31 (22.3) | 134 (12.7) | |
| | Glomerular Disease | 101 (11.1) | 16 (11.5) | 117 (11.1) | |
| | Unknown | 81 (8.9) | 16 (11.5) | 97 (9.2) | |
| | Drug Induced | 31 (3.4) | 2 (1.4) | 33 (3.1) | |
| | Hereditary Disorders | 22 (2.4) | 6 (4.3) | 28 (2.7) | |
| | Chronic Allograph Nephropathy | 22 (2.4) | 5 (3.6) | 27 (2.6) | |
| | Urinary Tract Infection (UTI) | 23 (2.5) | 1 (0.7) | 24 (2.3) | |
| | Tubulointerstitial Disease | 15 (1.6) | 2 (1.4) | 17 (1.6) | |
| **Total** | | **913 (100.0)** | **139 (100.0)** | **1052 (100.0)** | |

**Table 5:** Association of cause of CKD with socioeconomic status.

| | | Socioeconomic Status | | | Total | *p* Value |
|---|---|---|---|---|---|---|
| | | Low | Medium | High | | |
| Cause of CKD | Diabetes Mellitus (DM) | 94 (31.5) | 208 (36.7) | 93 (49.5) | 395 (37.5) | <0.001 |
| | Hypertension (HTN) | 39 (13.1) | 110 (19.4) | 31 (16.5) | 180 (17.1) | |
| | Obstructive Nephropathy | 56 (18.8) | 66 (11.7) | 12 (6.4) | 134 (12.7) | |
| | Glomerular Disease | 38 (12.8) | 59 (10.4) | 20 (10.6) | 117 (11.1) | |
| | Unknown | 40 (13.4) | 49 (8.7) | 8 (4.3) | 97 (9.2) | |
| | Drug Induced | 9 (3.0) | 19 (3.4) | 5 (2.7) | 33 (3.1) | |
| | Hereditary Disorders | 3 (1.0) | 23 (4.1) | 2 (1.1) | 28 (2.7) | |
| | Chronic Allograph Nephropathy | 7 (2.3) | 12 (2.1) | 8 (4.3) | 27 (2.6) | |
| | Urinary Tract Infection (UTI) | 6 (2.0) | 13 (2.3) | 5 (2.7) | 24 (2.3) | |
| | Tubulointerstitial Disease | 6 (2.0) | 7 (1.2) | 4 (2.1) | 17 (1.6) | |
| **Total** | | **298 (100.0)** | **566 (100.0)** | **188 (100.0)** | **1052 (100.0)** | |

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