RESEARCH ARTICLE

The prevalence and risk factors of kidney disease in first degree relatives of patients with ESRD treatment – single center study

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Abstract

Objective: To determine the prevalence and risk factors of kidney disease in first degree relatives of patients undergoing treatment for end-stage renal disease.

Method: The prospective, cross-sectional study was conducted at the Sindh Institute of Urology and Transplantation, Karachi, from May 1 to July 31, 2021, and comprised patients undergoing treatment for end-stage renal disease at the pre-transplant out-patients clinic, and their first degree relatives. Risk factors of chronic kidney disease, including age, gender, body mass index, hypertension, diabetes mellitus, and the causes of index cases were investigated alongside proteinuria, haematuria and estimated glomerular filtration rate. Diagnosis was made according to the criteria of the National Kidney Foundation-Kidney Disease Outcomes Quality Initiative. The participants were divided chronic kidney disease group 1, and healthy group 2. The risk factors were compared between the groups. Data was analysed using SPSS 22.

Results: Of the 1,406 subjects assessed, 266(19%) were ESRD patients; 175(65.8%) males and 91(34.2%) females with mean age 34.04±11.19 years. 1,140(81%) first degree relatives of these 266 ESRD patient were assessed; 595(52.2%) males and 545(47.8%) females with mean age 36.78±13.76 years. Among the relatives, 146(12.8%) had chronic kidney disease out of which 54 (4.7%) were already aware of their underlying disease. Older age, hypertension and diabetes mellitus were among the risk factors for chronic kidney disease ($p<0.05$), while gender was not significantly different between groups 1 and 2 ($p>0.05$). The relatives of index cases with underlying stone disease were at higher risk of haematuria 39(22.4%), whereas the relatives of index cases with chronic glomerulonephritis were at higher risk of proteinuria 67(28.03%) compared to index cases of other kinds ($p<0.05$).

Conclusion: Screening in the high-risk population might help to identify early chronic kidney disease patients for making suitable interventions to prevent disease progression.

Key Words: ESRD, First degree relatives, CKD. (JPMA 73: 2397; 2023) **DOI: 10.47391/JPMA.10927**

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Introduction

Chronic kidney disease (CKD) is an important non-communicable disease responsible for contributing significantly to morbidity and mortality[1] With results obtained after searching for observational studies and renal registries, the total population of people in 2010 having end-stage renal disease (ESRD) and on renal replacement therapy (RRT) exceeded 2.5 million worldwide, and is predicted to more than double to 5.439 million by 2030, with most growth in Asia, from 0.968 million to a projected 2.162 million.[2]

A number of risk factors contribute to the development of CKD, including advancing age, hypertension (HTN), obesity, diabetes mellitus (DM) and family history of CKD. Early detection and treatment of these factors are necessary in order to prevent and delay progression and to achieve improved outcomes[3].

The familial risk of relatives of ESRD is higher for CKD.[4] A study published in southern China estimated a prevalence of 29.7% in relatives of CKD patients in China[5] A more recent study showed a prevalence of 15.8% in relatives of patients dependent on haemodialysis (HD). However, variability exists because of ethnic differences and screening methods.[6] In Pakistan, the exact prevalence of CKD is not clear. Screening of family members of dialysis patients done at Rawalpindi in 2017 showed raised creatinine in 8% patients.[7]

The current study was planned to identify the prevalence and risk factors of kidney disease in first degree relatives of patients undergoing ESRD treatment.

Subjects and Methods

The prospective, cross-sectional, experimental study was conducted at the Sindh Institute of Urology and Transplantation (SIUT), Karachi, from May 1 to July 31,

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2021. After approval from the institutional ethics review committee, the sample size was calculated using EpiInfo calculator(8) based on the 8% prevalence,[7] margin of error 1% and confidence interval (CI) 95%.

The sample was raised using simple random sampling technique.

Those included were individuals aged >18 years irrespective of genderThose excluded were were individuals having hereditary disorders, like adult polycystic kidney disease (APCKD) and Alport syndrome, women who were pregnant or menstruating, and people with acute kidney injury (AKI). First degree relatives already diagnosed with CKD at SIUT or outside facility were also included.

Index cases and their first degree relatives were broadly grouped according to the cause of renal failure into 5 categories; relatives of patients with DM, HTN, chronic glomerulonephritis (GN), stone disease, and unknown causes. A family was defined as a group of individuals related to each other by blood or by at least one common blood relative, including first degree relatives (parents and offspring), full siblings, and spouses.

Data was collected from the pre-transplant outpatient department (OPD) from patients coming for their transplant workup. Risk of inheritance of kidney disease was discussed with the index cases, and those families were selected whose patients were willing to call their first degree relatives for screening whether willing or unwilling to donate. The records of index cases were reviewed to obtain age, primary cause of renal failure and mode of dialysis.

Two questionnaires were devised; one the index cases, and the other for the relatives. The questionnaires documented demographic and clinical data, including age, gender and comorbidities, such as HTN, DM, ischaemic heart disease (IHD), kidney disease, cerebrovascular disease, and dyslipidaemia, which were potential confounders, or could potentially affect familial associations. Nephrotoxic drugs were also recorded. Anthropometric measurements were obtained using standard protocols. Venous blood was collected to check for serum creatinine. A midstream morning sample of urine was taken for dipstick analysis (Roche Diagnostics, Mannheim, Germany) and microscopic analysis.

All the relatives also underwent ultrasound of kidney-ureter-bladder (KUB) to explore radiological changes, variation in kidney size or any local pathology. To determine the original cause of renal disease in the index cases, medical records were reviewed.

The exposure of interest was a familial aggregation of CKD. The outcomes of interest were incident CKD and CKD progression, with CKD progression being defined as an incident ESRD.

Proteinuria was assessed by performing dipstick in the first void early morning samples, with negative = none, trace = 15-30mg/dl, +1 = 30-100mg/dl, +2 = 100-300mg/dl, +3 = 300-1000mg/dl, and +4 = >1000mg/dl.

CKD was defined as the presence of kidney damage (proteinuria) with Estimated glomerular filtration rate (eGFR) was categorised as 60-90ml/min/1.73m^2) normal, <60ml/min/1.73m2 low eGFR for 3 months irrespective of the cause proposed by the National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDOQI).[8] The eGFR was calculated using the equation: eGFR = 141 x min(SCr /κ, 1)α x max(SCr /κ, 1)-1.209 x 0.993 Age x 1.018 [if female] x 1.159 [if Black].[9]

ESRD was defined as RRT with eGFR<15ml/min/1.73m2[9]

CKD awareness was defined as participants' self-report that they had been told by a physician that they had kidney disease or impaired renal function.

DM was defined as fasting blood glucose (FBG) >126mg/dl, pre-existing DM and those on hypoglycaemic agents.[10] Blood pressure (BP) was measured using a mercury sphygmomanometer in a seated position at rest for at least 5 minutes. HTN was defined as systolic BP >140mm Hg or diastolic BP >90mmHg, pre-existing HTN and those on anti- hypertensive medications.[11]

The body mass index (BMI) was calculated as weight in kg / height in m^2, and the criteria for Asians was used; normal weight = BMI <23kg/m^2, overweight = BMI ≥23 and up to 25kg/m^2, and obese = ≥25kg/m^2.[12]

Dipstick testing of morning spot urine samples showing haematuria of 1+ or greater were confirmed by microscopic analysis within 2h of the time when the urine samples were collected. Three or more red blood cells (RBCs) per high power field (HPF) were considered abnormal.

Data was analysed using SPSS 22. Continuous variables were expressed as mean ± standard deviation, and were compared using analysis of variance (ANOVA), Categorical variables were expressed as frequencies and percentage, and their proportion differences were evaluated using chi-square test. P<0.05 was considered significant.

Results

Of the 1,406 subjects assessed, 266(19%) were ESRD patients; 175(65.8%) males and 91(34.2%) females with

Table-1: Demographic and clinical characteristics of first degree relatives with respect to their primary diagnosis for chronic kidney disease (CKD).

	First Degree Relatives n=1140	Relatives of DM n=168 (14.7%)	Relatives of HTN Minimum n=442 (38.8%)	Relatives of Chronic GN n=239 (21%)	Relatives of Stone dx N=174 (15.3%)	Relatives of Unknown n=117 (10.3%)	*P*- value
Mean Age (yrs)	36.78 ± 13.76	35.57 ± 13.25	38.51 ± 14.06	34.89 ± 13.65	35.91 ± 12.68	37.16 ± 14.51	0.00
Gender (%)							
Male	595 (52.19%)	82 (48.8%)	237 (53.6%)	122 (51%)	81 (46.6%)	73 (62.4%)	0.07
Female	545 (47.81%)	86 (51.2%)	205 (46.4%)	117 (49%)	93 (53.4%)	44 (37.6%)	
Relationship to index patient (%)							
Parents	241 (21.1)	12(7.1)	90(20.36)	63(26.35)	36(20.68)	40(34.18)	<0.05
Siblings	766 (67.2)	74(44.04)	315(71.2)	175(73.2)	127(72.9)	75(64.10)	
Off springs	133 (11.7)	82(48.80)	37(8.37)	1(0.41)	11(6.32)	3(2.56)	
BMI (%)							
<23	986 (86.5%)	140 (83.3%)	380 (86%)	212 (88.7%)	159 (91.4%)	95 (81.2%)	0.07
≥23	154 (13.5%)	28 (16.67%)	62 (14%)	27 (11.3%)	15 (8.6%)	22 (18.8%)	
DM (%)	114 (10%)	33 (19.6%)	46 (10.4%)	14 (5.9%)	10 (5.7%)	11 (9.4%)	0.00
HTN (%)	189 (16.6%)	22 (13.1%)	99 (22.4%)	40 (16.7%)	14 (8%)	14 (12%)	0.00
CKD (%)	54(4.7%)	1(0.6%)	16((3.6%)	27(11.3%)	3(1.7%)	7(6%)	<0.05
IHD (%)	27 (2.4%)	4 (2.4%)	10 (2.3%)	4 (1.7%)	4 (2.3%)	5 (4.3%)	0.67

DM: Diabetes mellitus, BMI: Body mass index, HTN: Hypertension, CKD: Chronic kidney disease, IHD: Ischaemic heart disease.

Table-2: Markers of chronic kidney disease (CKD) in first-degree relatives of haemodialysis patients.

	First Degree Relatives n=1140	Relatives of DM n=168 (14.7%)	Relatives of HTN Minimum n=442 (38.8%)	Relatives of Chronic GN n=239 (21%)	Relatives of Stone dx N=174 (15.3%)	Relatives of Unknown n=117 (10.3%)	*P*- value
CKD (%)	146 (12.8%)	20 (0.6%)	52 (3.6%)	39 (11.3%)	20 (1.7%)	15 6%)	0.48
Haematuria (%)	95 (8.3%)	3 (1.8%)	32 (7.2%)	11 (4.6%)	39 (22.4%)	10 (8.5%)	0.00
Proteinuria (%)	229 (20.1%)	27 (16.07%)	72 (16.29%)	67 (28.03%)	44 (25.29%)	19 (16.24%)	0.003
eGFR (%)							
>90	923 (81%)	142 (84.52)	350 (79.18%)	194 (81.17%)	147 (84.48)	90 (76.07%)	
<90	161 (14.1%)	26(15.47%)	66(14.9)	23(9.6)	25 (14.36)	21 (17.9%)	0.00
<60	56 (4.91%)	0	26(5.88)	22(9.20)	1(0.57)	7(5.98)	
ESRD	19(1.7%)	0	3(0.67)	13(5.43)	1(0.57)	2(1.70)	<0.05
Ultrasound (%) Normal	1004 (88.07%)	167 (99.4%)	412 (92.6%)	207 (86.61%)	111 (63.8%)	107 (91.45%)	
Echogenic	48 (4.2%)	0 (0%)	12 (2.69%)	26 (10.88%)	2 (1.15%)	8 (6.84%)	
Stone ± Obstruction	79 (6.92%)	0 (0%)	15 (3.37%)	5 (2.09%)	59 (33.91%)	0 (0%)	0.00
Simple cyst	5 (0.44%)	0 (0%)	0 (0%)	1 (0.42%)	2 (1.15%)	2 (1.71%)	
Asymmetrical	3 (0.26%)	1 (0.6%)	2 (0.45%)	0 (0%)	0 (0%)	0 (0%)	
Solitary	1 (0.08%)	0 (0%)	1 (0.22%)	0 (0%)	0 (0%)	0 (0%)	

CKD: Chronic kidney disease, eGFR: Estimated glomerular filtration rate, ESRD: End-stage renal disease.

mean age 34.04±11.19 years. There were 1,140(81%) first degree relatives; 595(52.2%) males and 545(47.8%) females with mean age 36.78±13.76 years. Among the relatives, 146 (12.8%) had CKD out of which 54 (4.7%) already had awareness of underlying diagnosed chronic kidney disease where as the rest were diagnosed upon sampling. For the sampled first degree relatives, the most common primary diagnosis of ESRD patients was HTN 442(37.59%), followed by chronic GN 239(21.05%), DM 168 and stone disease 174 (approx. 15% each), while the remaining 117(10.9%) were those who presented with small-sized kidneys and were categorised as cases of unknown aetiology (Table 1).

Among the relatives screened, siblings were 766 (67.2%), BMI <23kg/m2 was noted in 986(86.5%), pre-existing HTN, DM, IHD and CKD were found in 189(16.6%), 114(10%), 27(2.4%) and 54(4.7%), respectively. CKD awareness was found more in relatives of chronic GN 27(11.3%) (p<0.05)

The overall prevalence of CKD in the first degree relatives of haemodialysis patients was 146(12.8%) compared to 54(4.7%) among those who were aware of CKD status at the time of screening (Table 2).

Table-3: Correlation between chronic kidney disease (CKD) markers and demographic variables in relatives of haemodialysis (HD) patients.

	Proteinuria (%)	P value	Haematuria (%)	P value	eGFR<90(%)	P value
Age (yrs)						
18-39	13.20%	<0.001	7.9%.	0.8	5.28%	<0.001
40-62	26.30%		8.67%		33.33%	
≥63	55.71%		10%		81.43%	
Gender						
Male	19.49%	0.67	8.23%	0.9	19.83%	0.158
Female	20.74%		8.40%		20%	
Relatives						
Parents	33.19%	<0.001	7.80%	0.046	49.37%	<0.001
Siblings	19.06%		9.40%		12.60%	
Offsprings	2.25%		3%		0.75%	

eGFR: Estimated glomerular filtration rate.

Table-4: Comparison of associated risk factors between relatives of haemodialysis (HD) patients with and without chronic kidney disease(CKD).

Variables	Group 1 (CKD) n= 146	Group 2(Non-CKD) n=994	P value
Gender (%)			
Male	70(47.94)	525(52.81)	0.156
Female	76(52.05)	469 (47.18)	
BMI (%)			
<23	117 (80.13)	869 (87.42)	<0.014
>23	29 (19.86)	125(12.57)	
DM (%)	71(48.63)	43 (4.32)	<0.05
HTN (%)	89 (60.95)	100 10.06)	<0.05
IHD (%)	18 (12.3)	09 (0.9)	<0.05
Haematuria (%)	27 (18.49)	68 (6.84)	<0.05
Proteinuria (%)	136 (93.15)	93 (9.35)	<0.05

DM: Diabetes mellitus, BMI: Body mass index, HTN: Hypertension, IHD: Ischaemic heart disease.

Haematuria, proteinuria and eGFR <90ml/min were noted in 95(8.3%), 229(20.1%) and 217(19%) first degree relatives, respectively (Table 3) Moreover, 136(12%) of the relatives had positive sonographic evidence in terms of echogenicity, stones and cyst, while 19 (1.7%) were also dialysis-dependent.

Among the relatives, with CKD, age, BMI, HTN, DM, IHD, haematuria and proteinuria were significantly different between the relatives having CKD than those in the non-CKD group ($p<0.05$). Gender was not significantly different between the groups (Table 4).

Discussion

CKD is a serious health issue, and health system planning requires careful assessment regarding its epidemiology, but data for morbidity and mortality of this disease is scarce or non-existent in many countries[1]. In developing countries, like Pakistan, especially, patients present or are referred to a nephrologist usually after renal dysfunction or CKD has set in. This happens because of lack of proper screening, which leads to delayed diagnosis and referral to a nephrologist. Even families with strong family history of kidney disease are unaware of the need and sometime reluctant for screening of the rest of the family members for timely diagnosis of kidney disease.

The current study, to our knowledge, is the first from Pakistan conducted with a large sample size mainly focussing on the prevalence of CKD in first degree relatives of dialysis-dependent patients. A prior study[7] had a very small sample size, and focussed mostly on proteinuria (13%), but did not highlight the exact prevalence of CKD in terms of eGFR among the relatives of dialysis patients.

In the current study, >20% of screened participants had proteinuria, and this percentage increased to >90% in the CKD group. The prevalence of CKD in the study was 12.8%. This was very similar to earlier reports[6,13] of 15.8% in Taiwan and 13.8% in Saudi Arabia. In contrast, a study[3] reported 5.6% prevalence in Egypt. One possible explanation for these discrepancies may be differences in race/ethnicity and comorbid conditions of the studied population. It was noteworthy that DM and HTN were more prevalent diseases among the screened relatives of current patients. The two conditions were found to be the major causes of CKD. This is consistent with earlier data.[14,15] Besides, proteinuria and low eGFR, 8.3% of the study population also had haematuria, and this number double in the CKD group.

There has been evidence that genetic susceptibility may account for the phenomenon of familial predisposition to CKD, and the risk of its development and progression with a substantially higher risk of ESRD.[16,17] The increased risk in the affected family highlighted the fact that CKD is a hereditable condition.[18] However, of these renal risk factors, DM and HTN are multifactorial diseases that share

both genetic traits and non-genetic environmental factors.[19,20] Moreover, prior literature[13,21] also showed high association of risk factors, like older age, female gender and increased BMI, with CKD. The current study also found a strong relation with age, as participants of CKD group were older. But, no association was found in terms of gender distribution and increased BMI as most of the screened population was lean with BMI <23kg/m^2, probably because majority belongs to the low scio-economic class.

The strength of the present study is that it represents one of the largest adult cohort of first degree relatives of ESRD patients from Pakistan, a developing country. Second, it was a prospective study and data was collected in the physical presence of the participants.

However, the current study has several limitations. First, the diagnosis of proteinuria was based on a dipstick. This drawback was minimised as CKD was confirmed only in those who had proteinuria along with low eGFR. Second, given the observational nature of the study, the cross-sectional design has several inherent weaknesses, such as lack of long-term observation for outcome, and difficulty interpreting the association of exposure with outcome. Third, the findings may not be generalisable to the community as the study was conducted at a single centre with limited numbers of participants. Fourth, as data was collected from the pre-transplant OPD where majority of patients were non-diabetic, the most prevalent cause of renal failure in the study was HTN even though worldwide the major is DM[22]. Therefore, a nationwide screening programme is needed before drawing a definitive conclusion.

Conclusion

CKD was found to be present in 12.8% first degree relatives of patients undergoing ESRD treatment. Reduced kidney function was more likely in older relatives and those with HTN, glycosuria, or proteinuria.

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Conflict of Interest: None.

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References

1. GBD Chronic Kidney Disease Collaboration. Global, regional, and national burden of chronic kidney disease, 1990-2017: a systematic analysis for the Global Burden of Disease Study 2017. Lancet 2020;395:709-33. doi: 10.1016/S0140-6736(20)30045-3.
2. Liyanage T, Ninomiya T, Jha V, Neal B, Patrice HM, Okpechi I, et al. Worldwide access to treatment for end-stage kidney disease: a systematic review. Lancet 2015;385:1975-82. doi: 10.1016/S0140-6736(14)61601-9.
3. Khamis SSA, El Edel RH, Zahran AM, Ibrahim MA, El Zorkany KMA. Prevalence of Chronic Kidney Disease in Relatives of Chronic Hemodialysis Patients. Open J Nephrol 2020;10:274-81. Doi: 10.4236/ojneph.2020.104027
4. Zhang J, Thio CHL, Gansevoort RT, Snieder H. Familial Aggregation of CKD and Heritability of Kidney Biomarkers in the General Population: The Lifelines Cohort Study. Am J Kidney Dis 2021;77:869-78. doi: 10.1053/j.ajkd.2020.11.012.
5. Wei X, Li Z, Chen W, Mao H, Li Z, Dong X, et al. Prevalence and risk factors of chronic kidney disease in first-degree relatives of chronic kidney disease patients in Southern China. Nephrology (Carlton) 2012;17:123-30. doi: 10.1111/j.1440-1797.2011.01523.x.
6. Tsai JC, Chen SC, Hwang SJ, Chang JM, Lin MY, Chen HC. Prevalence and risk factors for CKD in spouses and relatives of hemodialysis patients. Am J Kidney Dis 2010;55:856-66. doi: 10.1053/j.ajkd.2009.12.021.
7. Kumar J, Butt G, Maqbool F. Screening for Chronic Kidney Disease in Family Members of Dialysis Patients. J Rawalpindi Med Coll 2017;21:262-4.
8. Dean AG, Sullivan KM, Soe MM. OpenEpi: Open Source Epidemiologic Statistics for Public Health, Version: 3.01. [Online] 2013 [Cited 2023 November 22]. Available from URL: https://www.openepi.com/Menu/OE_Menu.htm
9. Florkowski CM, Chew-Harris JS. Methods of Estimating GFR - Different Equations Including CKD-EPI. Clin Biochem Rev 2011;32:75-9.
10. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2018. Diabetes Care 2018;41(Suppl 1):s13-27. doi: 10.2337/dc18-S002.
11. Iqbal AM, Jamal SF. Essential Hypertension. Treasure Island, FL: StatPearls Publishing; 2023.
12. Weir CB, Jan A. BMI Classification Percentile and Cut Off Points. Treasure Island, FL: StatPearls Publishing; 2023.
13. Mousa D, Alharbi A, Helal I, Al-Homrany M, Alhujaili F, Alhweish A, et al. Prevalence and Associated Factors of Chronic Kidney Disease among Relatives of Hemodialysis Patients in Saudi Arabia. Kidney Int Rep 2021;6:817-20. doi: 10.1016/j.ekir.2020.12.029.
14. Kumela Goro K, Desalegn Wolide A, Kerga Dibaba F, Gashe Fufa F, Wakjira Garedow A, Edilu Tufa B, et al. Patient Awareness, Prevalence, and Risk Factors of Chronic Kidney Disease among Diabetes Mellitus and Hypertensive Patients at Jimma University Medical Center, Ethiopia. Biomed Res Int 2019;2019:e2383508. doi: 10.1155/2019/2383508.
15. Wang Y, Zhao L, Zhang J, Wu Y, Zhang R, Li H, et al. Implications of a Family History of Diabetes and Rapid eGFR Decline in Patients With Type 2 Diabetes and Biopsy-Proven Diabetic Kidney Disease. Front Endocrinol (Lausanne) 2019;10:e855. doi: 10.3389/fendo.2019.00855.
16. Raji YR, Mabayoje MO, Bello BT, Amira CO. Albuminuria and Reduced Estimated Glomerular Filtration Rate among First-degree Relatives of Patients with Chronic Kidney Disease in Lagos, Southwest Nigeria. Indian J Nephrol 2018;28:21-7. doi: 10.4103/ijn.IJN_225_16.
17. Galbraith L, Hemmelgarn B, Manns B, Samuel S, Kappel J, Valk N, et al. The association between individual counselling and health behaviour change: the See Kidney Disease (SeeKD) targeted screening programme for chronic kidney disease. Can J Kidney Health Dis 2016;3:e35. doi: 10.1186/s40697-016-0127-4.
18. Drawz PE, Sedor JR, Hostetter TH. Family history and kidney disease. Am J Kidney Dis 2012;59:9-10. doi: 10.1053/j.ajkd.2011.11.012.
19. Lei HH, Perneger TV, Klag MJ, Whelton PK, Coresh J. Familial aggregation of renal disease in a population-based case-control study. J Am Soc Nephrol 1998;9:1270-6. doi: 10.1681/ASN.V971270.

20. Satko SG, Sedor JR, Iyengar SK, Freedman BI. Familial clustering of chronic kidney disease. Semin Dial 2007;20:229-36. doi: 10.1111/j.1525-139X.2007.00282.x.
21. Munshi SK, Vijayakumar N, Taub NA, Bhullar H, Lo TC, Warwick G. Outcome of renal replacement therapy in the very elderly. Nephrol Dial Transplant 2001;16:128-33. doi: 10.1093/ndt/16.1.128.
22. Couser WG, Remuzzi G, Mendis S, Tonelli M. The contribution of chronic kidney disease to the global burden of major noncommunicable diseases. Kidney Int 2011;80:1258-70. doi: 10.1038/ki.2011.368.