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Causes of End Stage Renal Disease in patients undergoing regular hemodialysis in Assiut University Hospital

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Abstract— ESRD is a global public health issue, with rising incidence and prevalence, high costs, and poor outcomes. Diabetic nephropathy, hypertension, glomerulonephritis, interstitial nephritis, pyelonephritis, polycystic kidney disease, and obstructive nephropathy are the most common causes of CKD. Aim of the work: (1)To find out the possible etiologies of ESRD in patients undergoing regular hemodialysis in Assiut university hospital. (2)Registry of ESRD patients undergoing regular hemodialysis in our dialysis unit of Assiut university hospital. **Patients and Methods**: Descriptive cross-sectional study was conducted in dialysis unit of Assiut University Hospitals from August 2018 to August 2019.The study enrolled 150 ESRD patients on regular haemodialysis for more than six months and aged more than 18 years old. All patients included in the study are subjected to detailed history, complete physical examination, laboratory investigations. **Results:** The study showed that Diabetes mellitus was the most disease contributed to ESRD (31.1%) followed by stones-pyelonephritis (14.7%), then hypertension and CKD-U (12.7%). **Conclusion**: Our study revealed that DM, stones- pyelonephritis and hypertension serve as major risk factors to ESRD among patients undergoing regular hemodialysis in Assiut university hospital.

Keywords: End Stage Renal Disease (ESRD),DM, HTN

Introduction

End-stage renal disease (ESRD) is increasing worldwide. Renal replacement therapy (RRT) and kidney transplantation are increasing the burden on health care systems. This condition is espicially serious in developing countries due to limited resources (1).

Chronic kidney disease (CKD) was ranked as the 18th most prevalent cause of death in the 2010 Global Burden of Disease Study (annual death rate 16.3/100 000), up from 27th in 1990 (age-standardized annual death rate 15.7/100 000)(2).

Diabetic nephropathy, hypertension, glomerulonephritis, interstitial nephritis, pyelonephritis, polycystic kidney disease, and obstructive nephropathy are the most common causes of CKD. untreated acute kidney injury (AKI) caused by infections, drugs, toxic chemicals, and heavy metals such as lead, cadmium, mercury, and chromium can also contribute to CKD(3).

The number of people receiving renal replacement therapy (RRT) was more than 2.5 million in 2010 and was expected to reach 5.439 million (3.899–7.640) in 2030 . In 2014, there were 3.37 million ESRD patients worldwide, up from 2.3 million in 2008, while the number of patients

undergoing RRT increased only from 1.77 million to 2.67 million from 2008 to 2014. Among reasons of such an increase in patients receiving RRT are widening acceptance criteria for RRT, an improved survival of the general population, reduction in the mortality of dialysis patients, larger access to dialysis therapy in low- and middle-income countries, an increase in the incidence of CKD(4).

In Europe, the frequency increased from 760 patients per million (pmp) in 2004 to 899 pmp in 2008 (5).In Egypt, according to the Egyptian Society of Nephrology and Transplantation's (9th Annual Report of The Egyptian Renal Registry), the prevalence of ESRD has increased to 483 people per million(1) . Hypertension is the leading cause of ESRD in Egypt, followed by diabetes, with unknown reasons accounting for about 15% of cases(6).

PATIENTS AND METHODS:

Study Design and place:

A descriptive cross-sectional study was conducted in dialysis unit of Assuit University Hospitals in the period from August 2018 to August 2019 . by using questionnaire and direct interviewing technique with ESRD patients, in addition to using medical records for our data collections

Design:

The study enrolled 150 ESRD patients on regular haemodialysis for more than six months and aged more than 18 years old. We exclude ESRD patients less than 18 years old, patients on dialysis for less than 6 months and patients with AKI.

All patients who included in the study were subjected to:

1-full medical history: through questionnaire developed in native language of respondents (Arabic) and organized into four parts

- **The first part** of the questionnaire included the objectives and the importance of the study.
- **The second part** included background information (Gender, Age, place of living, Smoking, Weight and Height at the start of dialysis).
- **The third part** was devised to collect information about the patient's family history, (diabetes mellitus, hypertension, cardiovascular diseases, kidney diseases and ESRD).
- **The fourth part** collected information about patient's medical history to determine the possible etiology of ESRD (diabetes mellitus, Hypertension, Congenital abnormality, Kidney stone, Urinary tract infection, and Analgesic drug abuse, nephritic or nephrotic syndrome). Renal biopsy was reviewed if available to know the possible etiology.

The diagnosis of hypertension as a cause of ESRD was made whenThere was long-standing hypertension before the development of ESRD with no evidence suggestive of other diagnoses. The diagnosis of diabetic nephropathy (DN) was made when there was longstanding diabetes with proteinuria and associated diabetic retinopathy. Primary glomerulonephritis (GN) was a biopsy-proven diagnosis. Immune/ collagen secondary GN was diagnosed when there was a history or laboratory data suggestive of immune/ collagen disease with kidney affection or biopsy proven kidney involvement of immune/collagen disease. Hepatitis C virus positivity was defined by a history or laboratory data suggestive of hepatitis C virus infection or as tested by a third-generation enzyme immunoassay.

2-clinical examination

3-Laboratory Investigations which include :

a- Complete blood picture with reticulocytic count using the ADVIA 2120i Hematology System (Siemens Healthcare Diagnostics Inc. Tarrytown, NY 10591, USA) Coagulation profile (PT-PC-INR-APTT) on Sysmex Siemens

b- Serum Urea, serum Creatinine, serum albumin, serum calcium and phosphorus and serum parathyroid hormone (PTH) were done on the automated chemistry analyzer Dimension RxL Max.

c- Viral serology (HBS- Ag, HCV -Ab, HIV-Ab) on ARCHITECT i1000sr immunology analyzer (Abbott, Germany).

Statistical Methods

Analysis of data was performed using software MedCalc v. 19. Description of variables was presented as follows:

- Description of quantitative variables was in the form of mean, standard deviation (SD), minimum and maximum.
- Description of qualitative variables was in the form of numbers (No.) and percent (%).
- Comparison between qualitative variables was carried out by Chi-square test.
- The significance of the results was assessed in the form of P-value which is significant when P-value ≤ 0.05.

Results: this study was enrolled on 150 patients with ESRD on regular hemodialysis in Assiut University Hospital.

Table1: shows baseline data of the studied patients: Mean age of patients enrolled in the study was 49.73 ± 4.26 years with range between 20-78 years and majority of them (55.3%) were males. Mean dry weight of them was 70.82 ± 14.46 with range between 40-115 kg. And mean duration of dialysis was 3.80 ± 2.94 with range between 0.08-12 years.

Demographic data		**ESRD group (n=150)**
Age (years)	Mean ± SD	49.73 ± 4.26
	Range	20-78
Males	N (%)	83 (55.3%)
Females	N (%)	67 (44.7%)
Dry weight (kg)	Mean ± SD	70.82 ± 14.46
	Range	40-115

Duration of hemodialysis (years)	Mean ± SD Range	3.80 ± 2.94 0.08-12

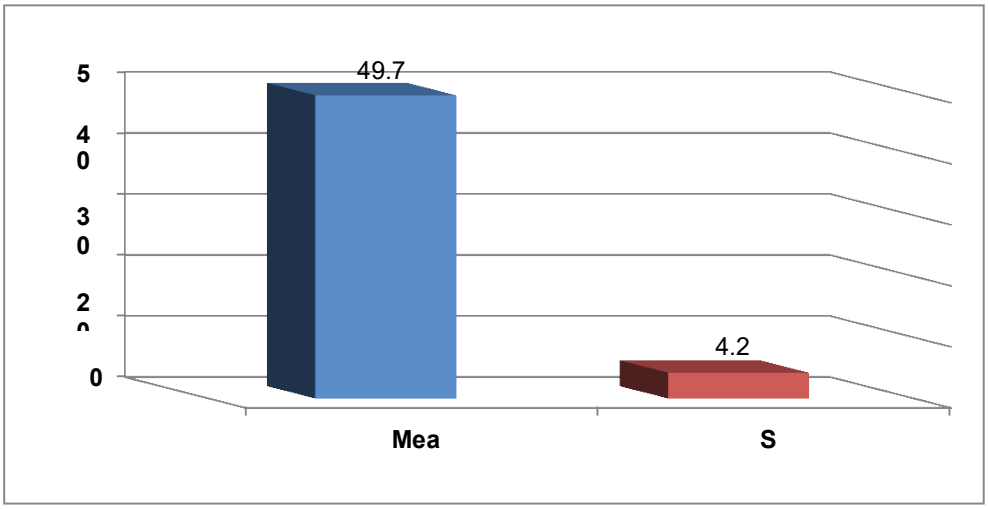

Figure (1): Mean age of the studied group is 49.73 ±4.26 (SD)

Table 2: Comparing distribution of underlying kidney disease of ESRD in the study group: Within the study group of ESRD, there is statistically significant difference in distribution of original kidney disease. Diabetes represents the highest distribution (31.3%), followed by stones, pyelonephritis (14.7%), hypertension (12.7%), unknown causes (12.7%), hereditary (8.7%), obstruction reflux (6.7%), pregnancy (4%), systemic lupus (3.3%), glomerulonephritis (2.7%) analgesia (2.7%), neoplasm represents the lowest distribution (0.7%).

Underlying kidney disease	N	%
Diabetes	47	31.3
Stones-pyelonephritis	22	14.7
Hypertension	19	12.7
Unknown	19	12.7
Hereditary	13	8.7
Obstruction-reflux	10	6.7
Pregnancy	6	4

Systemic lupus	5	3.3
Glomerulonephritis	4	2.7
Analgesia	4	2.7
Neoplasm	1	0.7
Total	150	100
Chi-squared	127.053	
P. value	< 0.0001*	

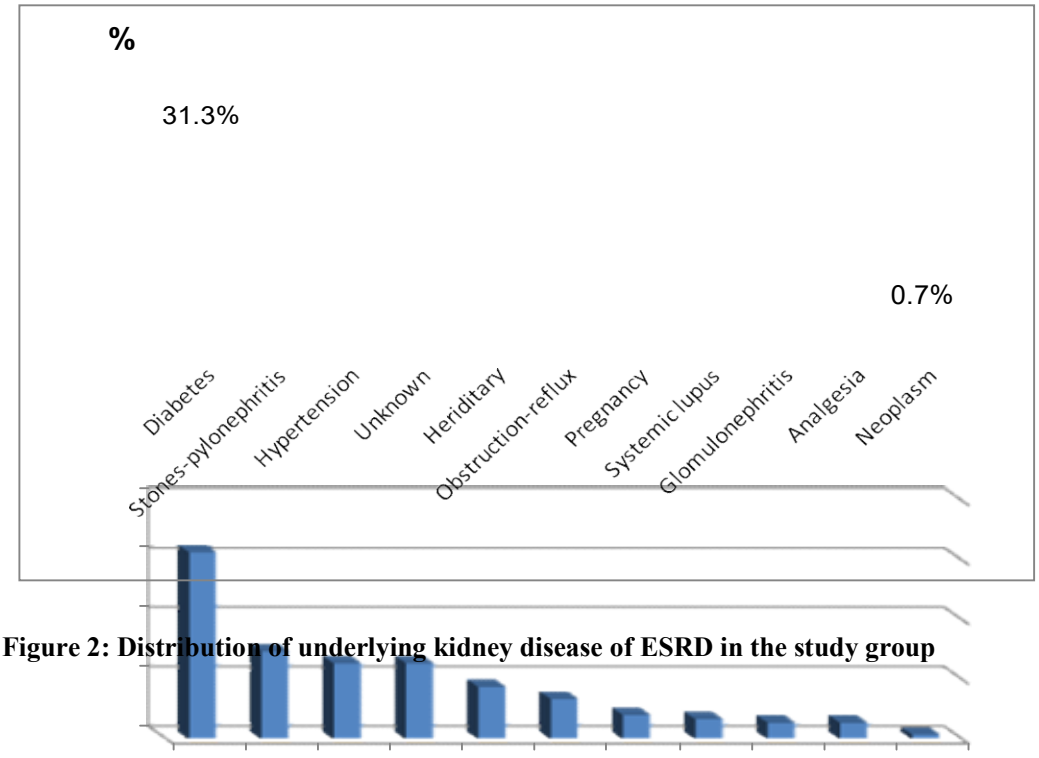

Figure 2: Distribution of underlying kidney disease of ESRD in the study group

Table 3: Comparing distribution of hypertension in the study group

Within the study group of ESRD, There is statistically insignificant difference between distribution of cases with hypertension (58%) and cases without hypertension (42 %).

Hypertension	N	%
Yes	87	58
No	63	42
Total	150	100
Chi-squared	3.840	
P. value	0.0500	

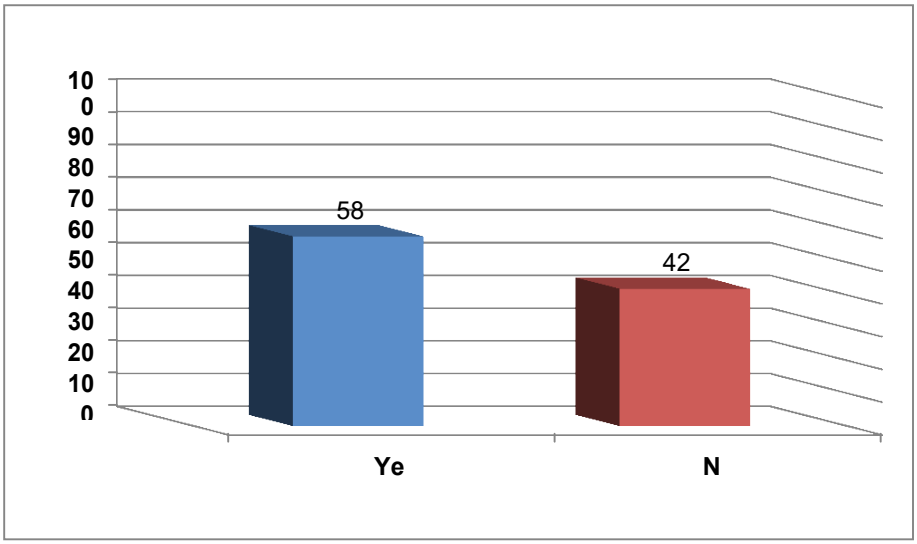

Figure 3: Distribution of hypertension in the study group

Table 4: Comparing distribution of diabetes in the study group

Within the study group of ESRD, most of cases are diabetic (52.7%), with insignificant difference in comparison to non-diabetic cases (47.3%) (P. < 0.05).

Diabetes mellitus	N	%
Yes	79	52.7
No	71	47.3
Total	150	100
Chi-squared		2.025
P. value		0.1547

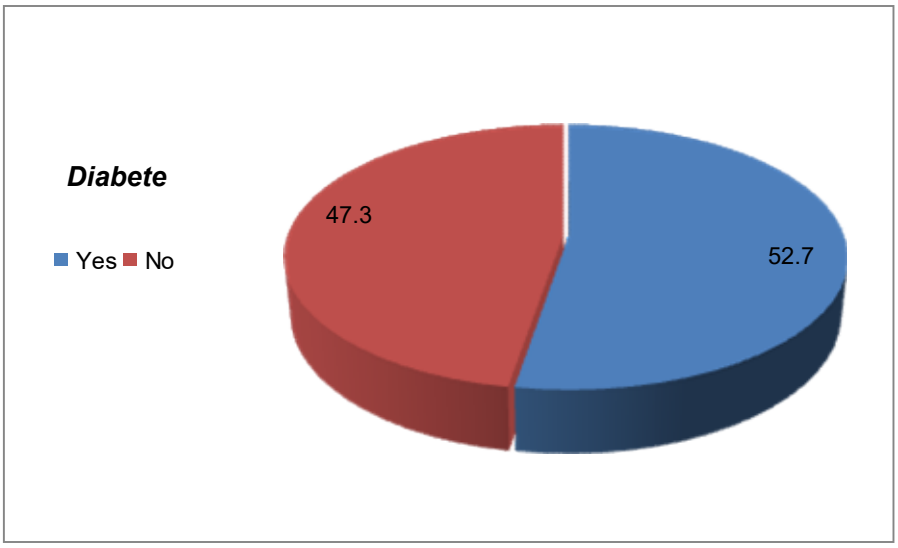

Figure 4: Distribution of diabetes in the study group

Table 5: Comparing distribution of APCKD in the study group

Within the study group of ESRD, most of cases have not APCKD (94.7%), with significant difference in comparison to cases with APCKD (5.3%).

APCKD	N	%
Yes	8	5.3
No	142	94.7
Total	150	100
Chi-squared	119.707	
P. value	< 0.0001*	

* P < 0.05 is considered significant

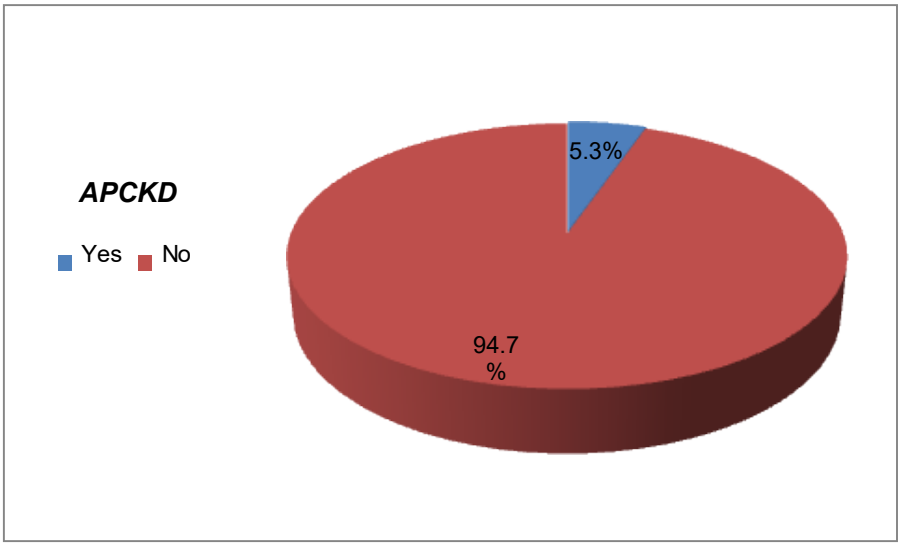

Figure 5: Distribution of APCKD in the study group

Discussion:

Chronic kidney disease is now regarded as a serious threat to global health systems, and a significant percentage of health-care funding is directed to it. The growing trend of non-communicable diseases such as diabetes and hypertension among societies producing end-stage renal disease (ESRD) globally continues to grow higher compared to the annual growth rate of the world population(7).

Our descriptive cross sectional study aimed to find out the possible etiologies of ESRD in patients undergoing regular hemodialysis in Assiut university hospital, this study enrolled 150 patients.

the mean age of patients in our study was (49.73 ± 4.26). In agreement with *El- Minshawy* study, where the mean age was 46 ± 13, and *El-Zorkany* study, where the mean age of was 53.1 years. Reflecting that ESRD increased with age, especially in the age of 50 and higher(8) [11].

In contrast to our study , *Saran et al* demonstrated that the mean age in USA was 59.2 years(10)and in Europe it was 60.3 years(11).

Furthermore, according to the 2015 USRDS annual data report, the prevalence of treated ESKD

per million populations was highest in individuals aged 65–74 years, whereas the prevalence was highest in those aged 75 years and older in Bosnia, Canada, France, Greece, Japan, and Taiwan[14]. *Couchoud et al,* reported that in France, the median age of patients on RRT is 70.4 years[14]. In Japan, the mean age was 66.9 years(12).

Our study found that diabetes mellitus was the leading cause of ESRD (31.1%), followed by Stones-pyelonephritis (14.7%), hypertension, and unknown etiology (12.7 %). This is in concordance with the epidemiology of ESKD in Gulf Cooperation Council nations, which revealed that diabetic nephropathy was the primary cause of ESKD (17%), followed by GN (13%), and hypertensive nephropathy (8%), with a considerable increase in the prevalence of DN.(13).

And also in agree with a USA study as, diabetes (37.47%) was the main cause of ESKD followed by hypertension (25.1%), glomerulonephritis (16.34%), and cystic kidney disease (4.69%)(14). In European countries, European Renal Association − European Dialysis and Transplant Association Registry stated that the most common recognizable cause of ESKD was glomerulonephritis (20.4%), followed by diabetes (15.6%), etiology uncertain (14.6%), and hypertension (10.7%)(15).

Our results were different from those reported in a number of Egyptian governorates. According to the El-Zorkany study, hypertension is the major cause of ESKD (33.4%), followed by diabetic nephropathy (9.2%)(16).

In Cairo, the main cause was hypertension (29.7%), followed by diabetic nephropathy (DN) (12.5). In Canal governorates hypertension was the main cause (27.3%), followed by DN (10.7%)(8) in El-Sharkia governorate, hypertension (31.8%) was first followed by DM (15.5%) (17). The current results differ also with previous one from Menoufia governorate, where hypertension is the main cause followed by DM (18). Also, the causes in recent study in El-Behera were hypertension (31.7%), then diabetes mellitus (18.0%)(19).

Also *Ahmed et al* study in Kafer El-Shakh Governorate, the leading cause was hypertension (34%), followed by diabetes (14%)(20). In *El-Arbagy et al* ESRD was due to hypertension in (21.4%)(21).

Our study result also disagree with results from other African countries as Hypertension is the primary cause in sub-Saharan Africa(22). In another study, in Khartoum State/Sudan, the most common cause was hypertension (34.6%), followed by chronic glomerulonephritis (17.6%) and DM (12.8%)(23).

The high percentage in our study is due to increased incidence and prevalence of DM mainly due to the rise in obesity and other risk factors for type 2 diabetes [T2D]. There has been an associated global increase in the incidence and prevalence of diabetic kidney disease (DKD), a frequent complication of long standing and poorly controlled diabetes (24)

In current study diabetes was considered as a major cause of ESRD. This confirms that there was significant impact of DM on onset of ESRD. These results agree with the findings of other studies conducted in a variety of nations, all of which found a highly significant effect of diabetes mellitus on the beginning of ESRD. The main risk factor for impaired kidney function is DM type II(25).

Stones and pyelonephritis were the second cause of ESRD in current study (14.7%). This finding was reported in other studies as well[28, (27). In *El-Arbagy et al* study but lesser than our results 8.9%(21).

high percentage of stones-pyelonephritis in our study is due to hot climate in upper Egypt causing dehydration, salty food ,obesity ,recurrent urinary tract infections.
CKD of unknown causes represent (12.5%) of current study patient as an etiology of ESRF, we differ with *El-Zorkany* study as unknown etiology accounted for 32.9% of all causes of ESKD(9). The percentage of undetermined etiology was estimated to be 27% in El- Minia governorate and represent the most common cause(8). also in earlier registry by Afifi , the percentage of undetermined etiology was estimated to be 15.2% in Egypt(28)

Etiology of treated ESKD was also unknown or uncertain in 33% of the patients in the area of Tabuk in Saudi Arabia(29). The percentage of uncertain etiology of ESKD was estimated to be 27% in Iran(30) and 14%in Qatar(31). In European countries, 2013 European Renal Association − European Dialysis and Transplant Association Registry found that unknown cause was estimated to be 14.6%(32) and, in Japan, unspecified causes accounted to be 8.5%(33).

This is mirroring the absence of awareness of patients about appropriate time for seeking medical advice and also lack of awareness of primary healthcare and other specialists' physicians about early detection and prevention of CKD especially for those at high risk to develop CKD and early referral to nephrologists. In line with the lack of follow- up and good care of CKD patients.

In our study analgesic nephropathy represents 2,7% differing with(8) where it represent 5%. Reflecting awareness of the people in the US about the hazard of excessive analgesic intake.

In our study, chronic glomerulonephritis represents 2.7% while it was 11% in *El- Minshawy* study. *El-Arbagy et al.* study showed that chronic GN was the cause in 8% of patients in Assiut governorate. glomerulonephritis was (4.5%) in *El-Ballat et al.* study(8) [22, 24].

Our study revealed that Obstructive uropathy was the cause of ESRD in 6.7% differing with *El-Arbagy et al. study* where it accounts for (11%) and (10.8%) in *El-Ballat et al.* study [22,24].

This low incidence may be because of the reduction in the incidences of urinary schistosomiasis and advancements in the treatment of obstructive urinary diseases.

Conclusion

Our study revealed that DM, stones- pyelonephritis and hypertension, serve as major risk factors to ESRD among patients undergoing regular hemodialysis in Assiut university hospital.

Recommendation

As diabetes mellitus, stones-pyelonephritis and hypertension are the most predisposing factors to ESRD, so we recommend

- Proper control of hypertension and diabetes mellitus is an effective method to reduce the number of ESRD patients.
- Proper management of obstructive uropathy and infections e.g. renal stones and pyelonephritis is an effective method to reduce the number of patients with ESRD.

Proper search for the cause of CKD should be applied to every person to reduce the number of patients with idiopathic ESRD (CKD-U).

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