ORIGINAL ARTICLE

Frequency, Factors and Pattern of Delayed Presentation for Dialysis in Advanced Kidney Disease Patients Visiting Tertiary Care Hospital

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ABSTRACT

Background: Globally the burden of chronic kidney diseases is increasing. It is often a silent disease until the most advanced stages when symptoms develop. Late referral and presentation to a nephrologist for CKD management is the major issue.

Objective: To determine the frequency, factors and pattern of delayed presentation for dialysis in advanced kidney disease patients visiting tertiary care hospitals.

Methods: The current cross-sectional study was conducted in Memon Medical Institute Hospital and Dow University of Health Sciences Ojha Campus Karachi Pakistan from December 2019 to March 2020. Patients who presented in the hospital for first-time dialysis with advanced kidney diseases were included in the study. The threshold of patient presentation after a month of advice for dialysis is used to categorize the patient presentation as delayed or non-delayed. Proforma was designed to collect data and SPSS version 21 was used for analyzing the collected data.

Results: A total of 214 participants were recruited into the study. The median age of the participants was 40 (29.75 - 53) years. The majority were male (71%) and belonged to rural areas (63.1%). 50.9% of the patients presented with a delay of more than a month. The delayed presentation was significant among those belonging to rural areas (p=0.009) with higher median creatinine (p=0.002) and lower levels of education (p=0.001). The most frequent presentation was high blood pressure (89.3%), followed by oliguria (66.8%). Oliguria was significant among patients with delayed presentation (p=0.003). Patient perception for the delayed presentation was looking for transplant (69.2%) and fear of needle prick (52.3%).

Conclusion: Delayed presentation for dialysis at tertiary care centers is a frequently seen issue particularly in patients belonging to rural areas presenting with a symptom of oliguria and fluid overload. Seeking alternative options such as renal transplants and fear of needles are the major reasons for delayed presentations in our study.

Keywords: Hemodialysis, delayed presentation for dialysis, oliguria, hypertension, chronic kidney disease.

INTRODUCTION

Global burden of disease study 2015 reported that there is an enormous increase in global life expectancy [1]. However, with this good news, the aging population is increasing and so the chronic kidney diseases. Half of the people in the western world are going to develop chronic kidney disease (CKD) during their lifetime [2]. It is often a silent disease until the most advanced stages when symptoms develop. The Kidney Disease: Improving Global Outcomes (KDIGO) recommended that patients with CKD should be referred to a nephrologist when the glomerular filtration rate (GFR) declines to less than 30 ml/min [3]. The decision to start hemodialysis in CKD stage 5 depends on the presence of serositis, acid-base or electrolyte abnormalities, pruritus, inability to control volume status or blood pressure, progressive deterioration in nutritional status refractory to dietary intervention, or cognitive impairment [3].

Late referral to a nephrologist for CKD management is the major issue that has been studied internationally [4], regionally in India and Pakistan [5, 6]. When such patients are referred to a nephrologist for dialysis it is too late in the term of timely management, dealing with complications and formation of vascular access for dialysis.

There is limited literature as the data is sparse/scanty and few studies were conducted in developing countries to assess or determine the frequency, factors and patterns leading to delay in seeking dialysis and these factors vary in different areas due to socioeconomic status, education level and infrastructure or availability of dialysis facility. One reality for a late referral or delayed presentation is the lack of specialized nephrology services in large parts of Pakistan that forces patients to travel to hospitals located far from their homes [7].

Therefore, the current study aimed to determine these factors in our part of the world and determination of these factors may help out in providing better care and improving the outcomes of end-stage renal disease

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patients that include a timely arrangement of dialysis plan, counseling regarding vascular access issues and management of socioeconomic burden for the patients.

METHODOLOGY

This is a cross-sectional study that was conducted at Memon Medical Institute Hospital and Dow University of Health Sciences Ojha Campus Karachi Pakistan from December 2019 to March 2020 after the approval of the institutional review board/ethical committee. A previously conducted study in Pakistan showed that 51.4% of patients with stage IV or V presented in hospital for the first time [6]. Online available sample size calculator Open-Epi was used for sample size calculation. The calculated sample size was 196 patients at a 95% confidence interval and precision of 7%. The calculated sample size was increased to 214 to account for a non-response rate of 9%. Patients who presented in the outpatient department or were admitted to the hospital for first time dialysis with a confirmed diagnosis of advanced kidney diseases or end-stage kidney disease (ESRD) were included in the study. All patients with acute kidney injury due to any reason requiring dialysis were excluded.

End-stage renal disease (ESRD) or advanced kidney disease is defined as an irreversible decline in a person's kidney function, which is severe enough to be fatal in the absence of dialysis or transplantation. ESRD is included under stage 5 of the National Kidney Foundation Kidney Disease Outcomes Quality Initiative classification of chronic kidney disease (CKD), where it refers to individuals with an estimated glomerular filtration rate less than 15 mL per minute per 1.73 m2 body surface area, or those requiring dialysis irrespective of glomerular filtration rate [8]. Hypertension was defined as systolic blood pressure (SBP) of 140 mm Hg or more, or diastolic blood pressure (DBP) of 90 mm Hg or more, or taking antihypertensive medication. Hyperkalemia was defined as a serum potassium concentration greater than approximately -5.5 mEq/L in adults and limits such as >5.5,>6.0, or >7.0 mEq/L are used to indicate severity. Oliguria was considered when urine output was less than 400ml/ 24 hours. Hypervolemia was measured with certain signs like crepitation in the chest, raised jugular venous pressure above 4cm, and leg pitting edema up to 2mm or more. Reduced appetite was labelled if the patient missed one or two meals in a day or reduced the meal intake by about 50% as compared to a regular meal which persisted for more than a week.

There is no conclusive definition of delayed presentation for dialysis, however, it is the time from one month to six months before the first session of hemodialysis after a visit to the nephrologist who advises to start hemodialysis [5]. The threshold of patient presentation after a month of advice for dialysis is used to categorize the patient presentation as delayed or non-delayed. Performa was designed to record the factors leading to delay. Patient demographics like age, gender, marital status,

residence, educational status, mode of referral, patient's presenting complaints, patients' perception regarding delay and etiology of CKD, were documented at the time of presentation (**Table 1**). Creatinine clearance (Cr. Cl) or estimated glomerular filtration rate (eGFR) at the time of the first presentation at the hospital were recorded. Creatinine clearance (Cr. Cl) was evaluated by the Cockcroft-Gault equation.

Data were entered into SPSS version 20 for analysis. Frequencies and percentages were computed for categorical variables. Median and inter-quartile ranges were presented for numerical values after assessing the assumption of normality with the Shapiro-Wilk test. Chi-square or Fisher-Exact test was applied to compare categorical variables among patients who presented within a month and after a month while Mann-Whitney U test was applied to compare numerical variables. A two-tailed p-value <0.05 was taken as statistically significant.

RESULTS

A total of 214 participants was recruited into the study. Participants' socio-demographic characteristics are depicted in Table **1**. The overall median age of the participants was 40 (29.75 - 53) years. The majority of the study participants were male (71%), married (80.4%), unemployed (55.6%), intermediate as per education level (41.1%) and belonging to rural areas (63.1%). About half of the participants presented with a delay of more than a month (50.9%) whereas the remaining presented within a month of symptoms onset. Clinical characteristics are presented in (**Table 2**).

Table **3** depicts the association of participants' characteristics with their status of presentation. Patients' educational status (p=0.001) and area of residence (p=0.009) was significantly different among patients

Table 1: Socio-demographic characteristics of study participants.

Patients' Characteristics	Frequency (%)
Age (in years)#	40 (29.75 - 53)
Gender	
Male	152 (71)
Female	62 (29)
Marital status	
Married	172 (80.4)
Unmarried	42 (19.6)
Education	
Illiterate	30 (14)
Primary	50 (23.4)
Middle	25 (11.7)
Intermediate	88 (41.1)
Graduate or above	21 (9.8)
Employment status	
Employed	95 (44.4)
Unemployed	119 (55.6)
Residence	
Urban	79 (36.9)
Rural	135 (63.1)

Table 2: Clinical characteristics of study subjects.

Variables	Frequency (%)
Hemoglobin# (gm/dl)	8 (7.26 – 8.73)
Creatinine# (mg/dl)	9 (7.78 – 10.62)
eGFR# (ml/min)	9.01 (6.84 – 10.68)
Presentation status	
Presented within a month	105 (49.1)
Presented after a month	109 (50.9)
Referral pattern	
Self	176 (82.2)
Clinic	38 (17.8)
Presenting complaints	
Poor appetite	142 (66.4)
Shortness of breath	61 (28.5)
Nausea	131 (61.2)
Body swelling	132 (61.7)
Oliguria	143 (66.8)
Hicupps	60 (28)
Fluid overload	135 (63.1)
Hyperkalemia	69 (32.2)
High blood pressure	191 (89.3)
Patients' perception regarding delay	
Cost of dialysis	27 (12.6)
Fear of dialysis/needle prick	112 (52.3)
Life time dependency	61 (28.5)
Looking for transplant	148 (69.2)
Etiologies of CKD	
Chronic glomerulopathy	13 (6.7)
Diabetic nephropathy	65 (30.4)
Hypertensive	154 (72.0)
Renal stone	22 (10.3)
Obstetric complications	3 (1.4)
Unknown	2 (0.9)

#: variables are summarized as median (inter-quartile range)

who presented within a month and after a month on symptom onset. Median creatinine was significantly higher in patients presented after a month of symptoms onset [delayed] (p=0.002). Oliguria was significantly more frequent among patients who presented with a delay than those who were on time (p=0.003). None of the patients' perception and etiologies of CKD were significantly different among patients presented within a month or after a month of symptoms onset (delayed).

DISCUSSION

The current study focused to determine the frequency, factors and pattern of delayed presentation for dialysis in advanced kidney disease patients. Previously conducted studies in Pakistan determined the factors of late referral and refusal of hemodialysis among patients with CKD patients [6, 9]. Once a patient reaches stage 4 CKD, he or she should be under a nephrologist's care who will start a multidisciplinary program that includes patient and family education, early choice of appropriate renal replacement therapy and elective creation of dialysis access. Late referral or presentation leads to psychological and physiological stress [5] with

Table 3: Association of patients' characteristics with their presentation status.

Study Variables	Status of Patients' Presentation		p-value
	Presented within a month [Non delayed] n(%)	Presented after a month [Delayed] n(%)	
Socio-demographic			
Age (in years)#	40(28.5 - 53)	42(30.5 - 53)	0.690
Gender			
Male	74(70.5)	78(71.6)	0.861
Female	31(29.5)	31(28.4)	
Marital status			
Married	81(77.1)	91(83.5)	0.243
Unmarried	24(22.9)	18(16.5)	
Residence			
Urban	48(45.7)	31(28.4)	**0.009
Rural	57(54.3)	78(71.6)	
Employment status			
Employed	49(46.7)	46(42.2)	0.511
Unemployed	56(53.3)	63(57.8)	
Education			
Illiterate	3(2.9)	27(24.8)	**<0.001
Primary	20(19)	30(27.5)	
Middle	5(4.8)	20(18.3)	
Intermediate	61(58.1)	27(24.8)	
Graduate or above	16(15.2)	5(4.6)	
Referral			
Self	83(79)	93(85.3)	0.230
Clinic	22(21)	16(14.7)	
Clinical Presentations			
Poor appetite	66(62.9)	76(69.7)	0.288
Shortness of breath	32(30.5)	29(26.6)	0.531
Nausea	63(60)	68(62.4)	0.720
Body swelling	63(60)	69(63.3)	0.619
Oliguria	60(57.1)	83(76.1)	**0.003
Hicupps	31(29.5)	29(26.6)	0.635
Fluid overload	66(62.9)	69(63.3)	0.946
Hyperkalemia	35(33.3)	34(31.2)	0.738
High blood pressure	95(90.5)	96(88.1)	0.570
Hemoglobin#	8(7.5 - 9)	8(7.05 - 8.6)	0.984
Creatinine#	8.4(7.44-9.90)	9.50(8.30-11.12)	**0.002
eFGR#	9.47(7.19-11.09)	8.73(6.52-10.34)	0.274
Patients' perception regarding delay			
Cost of dialysis	11(10.5)	16(14.7)	0.355
Fear of dialysis/ needle prick	49(46.7)	63(57.8)	0.103
Life time dependency	26(24.8)	35(32.1)	0.234
Looking for transplant	68(64.8)	80(73.4)	0.172
Etiologies of Chronic kidney diseases			
Chronic glomerloupathy	4(3.8)	9(8.3)	0.173
Obstetric complications	3(2.9)	0(0)	†0.116
Diabetic nephropathy	31(29.5)	34(31.2)	0.791
Renal stone	11(10.5)	11(10.1)	0.926
Hypertensive	74(70.5)	80(73.4)	0.635

#: variables are summarized as median (inter-quartile range),

†: denotes Fisher-exact test is reported, **Significant at p<0.01

the placement of a temporary catheter which might be associated with catheter-related blood infections if permanent access is delayed [10, 11]. In our study, 50.9% of patients presented late which is comparable to other studies conducted in past as in developing country Nigeria that showed the prevalence of 50% and 44.8% [12, 13]. The study conducted in Pakistan also reported that 51.4% presented in the hospital first time either with stage IV or V [6]. In our study median age of the patient is 40 years with advanced kidney disease whereas another study conducted in Sindh Institute of Urology and Transplantation which is the largest tertiary care center for Kidney diseases in Karachi reported an average age of 46 years [14]. Early age at initiation of dialysis reflects the early onset of diabetes, hypertension, kidney stone disease and glomerulopathy in the general population with poor compliance and control of the disease. Due to the prevalence of risk factors of CKD including hypertension and diabetes, eGFR is reduced in adult men and women in Pakistan [15]. The majority of our patients were male (71%) which may reflect the presence of more co-morbid, early development of advanced kidney disease and behavior of our society to seek medical care in the male population as compared to the female gender. Women are also said to have a low risk of CKD due to blood pressure stability, hormonal status and lifestyle modification that is less consumption of smoking, alcohol, salt and protein intake [16].

Delay in dialysis was significant in patients with low education level which reflects the fact that understanding of wellbeing status, seeking medical attention and response to the advice of nephrologist were lacking. Education affects physical and mental health as it generates more social and economic resources which help to cope with stressors in life and development of a better strategy for a healthy lifestyle. Another demographic parameter which is highlighted in this study is that majority are from rural areas (63.1%) which is explained by the fact that Memon Medical Institute Hospital and Dow University of Health Sciences Ojha Campus both are located near to rural areas of the city that is why these two institutes are easily accessible to rural residents due to shorter distance from their residence. Delay was statistically significant among patients belonging to rural areas that might explain the fact that travelling and seeking dialysis facilities with background questionable knowledge about disease and dialysis might have an impact on the delay. Moreover, our study population presented with markedly reduced hemoglobin raised creatinine and reduced eGFR, typical of neglected, poorly managed CKD patients [17] as lack of awareness among general physicians to deal with such situations at early stages [18] and lack of compliance issues on the part of patients.

Major presenting symptoms were poor appetite, nausea, body swelling and reduced urine output (oliguria) which are typical of advanced kidney disease with [19] clinical signs of fluid overload (63.1%) in the majority of patients and frequency of fluid overloaded was not significantly different among patients presenting with and without delay. Generally, patients come to a dialysis facility or nephrologist when they have difficulty in breathing likely due to fluid overload. Reduced urine output (oliguria) was significant in late referrals which reflects that this symptom when appeared, patients then realized to seek medical attention as literature shows it is commonly the late symptom of advanced kidney disease [20]. The majority of the patients were hypertensive and diabetic that turn into the main etiology of CKD that is 72% and 30.4% respectively. These two co-morbid are also the main reason for advanced renal disease globally [21]. Diabetes and hypertension are considered as major attributable causes of CKD and ESRD in the developed world and recent data suggest that the developing world has increasing trends for both these diseases [8, 21]. Renal stone disease, chronic glomerulopathy and obstetric complications remain relatively fewer reasons for kidney failure as in previous international literature [22] as well as in locally available literature [23].

Surprisingly looking for transplant and fear of dialysis are the possible reasons for delay followed by lifetime dependency as compared to cost. Awareness of looking for the transplant is increasing due to successful transplants in Pakistan [24] so most of our group population sought information for renal transplantation with background fear of dialysis as needle fear is common among the general population usually and specifically in ESRD patients [25]. Interestingly, in this study perception of cost burden was not significantly different among two groups of patients as the cost has been documented as one of the factors causing delayed healthcare seeking [26]. However, regarding the cost issue in Pakistan with a total GDP of USD 314.6 billion (2018) [27] with health expenditure per capita of 45 US dollars in 2017 [28], an increased burden due to CKD can be very hard on families.

We did not measure the disease-related knowledge of the patients which could be the predictor of the delay. We could enroll a larger sample size but due to the COVID-19 pandemic, we did not achieve more sample size as there was a restriction on attending patients in out-patient departments like a usual routine. Moreover, the duration of symptoms is just based on self-reporting of the patients which might not be accurate. With the estimated population of 207.8 million, referral of chronic kidney disease patients generally and end-stage kidney disease patients specifically is a difficult task and can overburden the nephrology services in Pakistan. However, with the involvement of internists and general practitioners, timely management and appropriate referral is possible.

CONCLUSION

Delayed presentation for dialysis at tertiary care centers is a frequently seen issue particularly in patients belonging to rural areas presenting with a symptom of oliguria and fluid overload. Seeking alternative options such as renal transplants and fear of needles are the major reasons for delayed presentations in our study.

ETHICS APPROVAL

The ethical approval was taken from Memon Medical Institute Hospital before conducting the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the Helsinki declaration.

CONSENT FOR PUBLICATION

Not applicable.

FUNDING

None.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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