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Original Research Article

FACTORS IMPACTING THE REFERRAL TIME TO NEPHROLOGISTS IN CHRONIC KIDNEY DISEASE PATIENTS IN SOUTH PUNJAB, PAKISTAN

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Abstract: *To assess the social, demographic, clinical and health factors impacting the referral time to a nephrologist in chronic kidney disease patients. A prospective study was carried out at Nephrology Department of Nishtar Medical Hospital, Multan from October 2021-October 2022. A total of 150 chronic kidney disease patients who were undergoing dialysis were selected for the study. Early and late referral time was evaluated by the time period between referral and dialysis initiation. All the patients were interviewed for evaluation of factors affecting the referral time. The analysis showed that 92 patients (61.3%) were in early referral and 58 patients (38.6%) were in late referral among which 21 patients were referred to a nephrologist almost 90 days prior to the dialysis initiation. Patients in the late referral mostly had diabetes, congestive heart failure or hypertension, whereas patients in early referral were non-smokers, women and patients with glomerulonephritis. The multivariate analysis revealed the following independent risk factors for late referral: kidney disease (diabetes mellitus, hypertension, male sex, congestive heart failure, profession (labourer, mechanic, farmer) and assisted walks. Diabetes and hypertension patients have a later referral time than patients with glomerulonephritis. In addition, men with congestive heart failure practicing physically active professions and assisted ambulation were referred late.*

Keywords: Dialysis, chronic kidney disease, nephrology

Introduction

The two factors that play an important role in the improvement of chronic kidney disease patients are appropriate care and timely consultation with the nephrologist. According to research, the patients who were referred to the nephrologist at an initial stage mostly did not require immediate dialysis or catheters and urgent renal replacement therapy and were recommended peritoneal dialysis or kidney transplant as initial treatment (Shlipak et al., 2021). The management of the disease is also better in early referral patients in spite of comorbidities like cardiovascular disorders (de Boer et al., 2020). In addition, timely referral results in an increased chance of survival, better lifestyle and nutritional status (Marie Patrice et al., 2019; Shah et al., 2018). The treatment costs and hospital stays are also reduced in such patients. Studies have reported that dialysis patients who were referred at an early stage had a low risk of cardiovascular mortality, lower medical costs and better lifestyle (Clyne, 2021; Pyart et al., 2020).

Although the importance of early referral has been highlighted repeatedly, the majority of chronic kidney disease patients are referred to nephrologists late before the initiation of dialysis. The recurrence of late referrals varies significantly across the globe. On average, 20-35% of CKD patients are referred late to the nephrologist (Ghimire et al., 2022). In Pakistan, the ratio of late referrals is comparatively low than developing countries such as the UK (30%), Denmark (38%), Mexico (50%) and the USA (34.7%) (Anees et al., 2018). To analyze the causes of late referral, the clinical and socio-economic factors influencing it must be evaluated. Very limited data regarding this subject is available in Pakistan. We conducted this study to assess the social, demographic, clinical and health factors impacting the referral time to a nephrologist in chronic kidney disease patients.

Methodology

A prospective study was conducted in the Nephrology Department of Nishtar Medical Hospital, Multan from October 2021-October 2022. A total of 150 chronic kidney disease patients older than 18 years undergoing dialysis were selected for the study. The patients with incomplete data on

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nephrologists' visits and start dates of dialysis were excluded. All the patients signed informed consent to become a part of the study. The Ethical board of the hospital approved the study design of the study.

Early and late referral time was evaluated by the time period between referral and dialysis initiation. An early referral was defined as a referral to the nephrologist more than 1 year before the start of dialysis and a late referral was defined as a referral within less than 1 year before the start of dialysis. The patients in the ultra-late referral group were referred to the nephrologist 3 months before the start of dialysis. All the patients were interviewed about their demographics, marital status, employment status, education, history of smoking, medical history, laboratory tests, dialysis modality, medications and comorbidities. The e-GFR was calculated for each patient and the Charlson comorbidity index was used at the time of dialysis.

All the data were analyzed by SPSS version 21. Mean and standard deviation and the percentage were used to express continuous and categorical variables respectively. T-tests were performed for the comparison of data between groups. The logistic regression method was used to evaluate factors affecting late and ultra-late referrals. A p-value less than 0.05 was regarded as statistically significant.

Results

A total of 150 patients were included in the study among which 93 patients were referred early, 22 patients were referred late and 35 patients were referred ultra-late. In the early referral group, age, blood pressure, BUN, serum creatinine, and phosphorus levels were less at the time of referral than in late referral patients. Early referral patients mostly had glomerulonephritis and late referral patients had diabetes or hypertension. At the start of dialysis, age, haemoglobin and calcium levels in the early referral group were higher. The late referral patients mostly had congestive heart failure and the ultra late referral had hypertension. The patients' characteristics are shown in Tables I and II.

With respect to factors affecting late referral time, the following were the independent risk factors: kidney disease (diabetes mellitus, hypertension, male sex, congestive heart failure, profession (labourer, mechanic, farmer) and assisted walks. These factors are shown in Table III.

Table I: Patients' Characteristics According to Referral Time

	Total (n=150)	Early referral (n=93)	Late referral (including ultra late referrals) (n= 57)	P-value
Findings at the time of referral				
Age, years	51.2 ± 13.4	50.5 ± 13.2	53.2 ± 13.0	0.001
Gender, male	90 (60%)	55 (59.1%)	36 (63.1%)	0.040
Underlying kidney disease				
Diabetes mellitus	86 (57.3%)	51 (54.8%)	34 (59.6%)	<0.001
Hypertension	23 (15.3%)	12 (13%)	10 (17.5%)	
Glomerulonephritis	24 (16%)	16 (17.2%)	8 (14.0%)	
Others	17 (11.3%)	14 (15%)	5 (8.7%)	
Systolic BP, mm Hg	143.8 ± 24.3	140.2 ± 23.5	147.5 ± 26.8	<0.001
Diastolic BP, mm Hg	82.3 ± 15.3	81.3 ± 14.9	83.5 ± 15.5	0.001
Haemoglobin, g/dL	9.9 ± 1.8	10 ± 1.9	7.8 ± 1.2	<0.001
Albumin, mg/dL	2.7 ± 0.5	2.8 ± 0.5	2.4 ± 0.5	<0.001
Serum creatinine, mg/dL	3.55 ± 3.21	1.99 ± 1.55	6.08 ± 3.66	<0.001
eGFR, mL/min/1.73m2	23.1 ± 21.3	32.4 ± 22.5	10.6 ± 10.1	<0.001
Time from referral to dialysis, month	40.4 ± 53.6	63.8 ± 57.1	2.0 ± 2.4	<0.001
At the time of dialysis				
Age, years	54.3 ± 12.6	55.2 ± 12.1	53.3 ± 13.1	0.001
Modified Charlson comorbidity index	4.6 ± 1.7	4.7 ± 1.7	4.0 ± 1.8	0.010
Systolic BP, mm Hg	140.3 ± 21.4	139.6 ± 21.3	141.8 ± 22.0	0.169
Diastolic BP, mm Hg	77.0 ± 13.1	76.4 ± 12.7	78.4 ± 13.2	0.004
BMI, kg/m2	22 ± 2.6	22 ± 2.6	22 ± 2.4	0.900
Haemoglobin, g/dL	8 ± 1.2	8 ± 1.2	7.9 ± 1.2	0.012
Calcium, mg/dL	7.1 ± 1.0	7.2 ± 1.0	7.2 ± 1.0	0.010

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Phosphate, mg/dL	4.9 ± 1.5	4.8 ± 1.4	4.5 ± 1.8	0.035
LDL cholesterol, mg/dL	88.3 ± 37.0	86.3 ± 37.2	92.0 ± 36.5	0.001
Profession				
Professional specialist	10 (6.6%)	7 (7.5%)	2 (3.5%)	0.028
Office worker	8 (5.3%)	5 (5.3%)	2 (3.5%)	
Housewife and student	35 (23.3%)	22 (23.6%)	12 (21.0%)	
Mechanic	5 (3.3%)	4 (4.3%)	3 (5.2%)	
Labourer	10 (6.6%)	6 (6.4%)	3 (5.2%)	
Farmer	7 (4.6%)	2 (2.1%)	3 (5.2%)	
Unemployed	75 (50%)	47 (50.5%)	32 (56.1%)	
Education				
Uneducated	8 (5.3%)	6 (6.4%)	3 (5.2%)	0.048
Educated	142 (94.6%)	87 (93.5%)	54 (94.7%)	
Smoking history				
Smokers	16 (10.7%)	8 (8.6%)	7 (12.2%)	0.001
Non-smokers	90 (60%)	56 (60.2%)	29 (50.8%)	
Former smokers	44 (29.3%)	29 (31.1)	21 (36.8%)	
Comorbidities				
Coronary heart disease	20 (13.3%)	13 (13.9%)	7 (12.2%)	0.055
Peripheral vascular disease	11 (7.3%)	8 (8.6%)	3 (5.2%)	0.570
Congestive heart failure	17 (11.3%)	8 (8.6%)	8 (14.0%)	<0.001
Connective tissue disease	14 (9.3%)	10 (10.7%)	4 (7.0%)	0.001
Mild liver disease	8 (5.3%)	6 (6.4%)	2 (3.5%)	0.001
Cerebrovascular accident	4 (2.7%)	3 (3.2%)	1 (1.7%)	0.128
Tumours	10 (6.6%)	7 (7.5%)	2 (3.5%)	0.010
Ambulation status				
Normal	130 (86.6%)	82 (88.1%)	47 (82.4%)	0.040
Walks with assistance	11 (7.3%)	6 (6.4%)	6 (10.5%)	
Wheelchair	5 (3.3%)	2 (2.1%)	3 (5.2%)	
Bedridden	4 (2.7%)	2 (2.1%)	1 (1.7%)	
Medications				
ACE inhibitor	14 (9.3%)	8 (8.6%)	5 (8.7%)	0.075
Angiotensin receptor blocker	77 (51.3%)	47 (50.5%)	31 (54.3%)	0.492
Diuretics	81 (54%)	51 (54.8%)	29 (50.8%)	0.847
Beta-blocker	78 (52%)	49 (52.6%)	31 (54.3%)	0.971
Calcium channel blocker	90 (60%)	58 (62.3%)	34 (59.6%)	0.119
Vitamin D	26 (17.3%)	17 (18.2%)	7 (12.2%)	0.028
Phosphate binder, calcium	89 (59.3%)	57 (61.2%)	31 (54.3%)	0.034

Table II: Patients' characteristics of Late and Ultra-late referral

	Late referral (including ultra-late referrals) (n= 57)	**Ultra-late referral (n=35)**	**P-value**
Findings at the time of referral			
Age, years	53.2 ± 13.0	54.2 ± 13.4	0.480
Gender, male	36 (63.1%)	23 (65.7%)	0.419
Underlying kidney disease			
Diabetes mellitus	34 (59.6%)	19 (54.3%)	0.004
Hypertension	10 (17.5%)	8 (22.8%)	
Glomerulonephritis	8 (14.0%)	4 (11.4%)	
Others	5 (8.7%)	4 (11.4%)	

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At the time of dialysis			
Age, years	53.3 ± 13.1	53.1 ±13.5	0.479
Modified Charlson comorbidity index	4.0 ± 1.8	3.7 ±1.9	0.002
Diastolic BP, mm Hg	78.4 ± 13.2	79.5 ± 14.2	0.045
Haemoglobin, g/dL	7.9 ± 1.2	7.7 ± 1.2	0.118
Calcium, mg/dL	7.2 ± 1.0	7.2 ±1.0	0.482
Phosphate, mg/dL	4.5 ± 1.8	4.7 ± 2.0	0.092
PTH, Intact	255.1 ± 215.4	286.0 ± 241.2	0.018
b2-Microglobulin	20.0 ±8.3	21.4 ± 9.7	0.031
HbA1c, %	5.9 ± 1.1	5.8 ± 1.0	0.009
LDL cholesterol, mg/dL	92.0 ± 36.5	95.0 ± 37.3	0.049
Profession			
Professional specialist	2 (3.5%)	1 (2.8%)	0.372
Office worker	2 (3.5%)	1 (2.8%)	
Housewife and student	12 (21.0%)	6 (17.1%)	
Mechanic	3 (5.2%)	2 (5.7%)	
Labourer	3 (5.2%)	1 (2.8%)	
Farmer	3 (5.2%)	2 (5.7%)	
Unemployed	32 (56.1%)	22 (62.8%)	
Comorbidities			
Peripheral vascular disease	3 (5.2%)	2 (5.7%)	0.023
Congestive heart failure	8 (14.0%)	5 (14.3%)	0.763
Connective tissue disease	4 (7.0%)	2 (5.7%)	0.639
Mild liver disease	2 (3.5%)	1 (2.8%)	0.548
Ambulation status			
Normal	47 (82.4%)	29 (82.9%)	0.771
Walks with assistance	6 (10.5%)	4 (11.4%)	
Wheelchair	3 (5.2%)	2 (5.7%)	
Bedridden	1 (1.7%)	1 (2.8%)	
Medications			
ACE inhibitor	5 (8.7%)	3 (8.5%)	0.321
Diuretics	20 (50.8%)	18 (51.4%)	0.001
Calcium channel blocker	34 (59.6%)	20 (57.1%)	0.045

Table III: Factors Affecting Referral Time

	Time From Referral to Dialysis, Month	**P-value**
Gender		
Male	45.0 ± 58.3	0.009
Female	37.7 ± 50.5	
Underlying kidney disease		
Diabetes mellitus	30.2 ± 39.2	<0.001
Hypertension	40.2 ± 54.0	
Glomerulonephritis	62.1 ± 70.9	
Others	63.4 ± 73.6	
Profession		
Professional specialist	47.1 ± 53.9	0.025
Office worker	51.8 ± 66.4	
Housewife and student	44.5 ± 58.0	
Mechanic	32.1 ± 51.1	
Laborer	37.3 ± 46.5	
Farmer	34.9 ± 60.3	
Unemployed	40.0 ± 52.4	

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Marital status		
Married	41.4 ± 56.0	0.255
Unmarried	42.2 ± 54.4	
Education		
Uneducated	43.5 ± 48.6	0.010
Educated	45.2 ± 59.2	
Smoking history		
Smokers	27.4 ± 46.3	<0.001
Non-smokers	44.3 ± 57.0	
Former smokers	37.6 ± 50.3	
Comorbidities		
Coronary heart disease	34.8 ± 42.2	0.869
Peripheral vascular disease	37.1 ± 41.6	0.440
Congestive heart failure	26.4 ± 39.3	<0.001
Connective tissue disease	61.1 ± 72.3	<0.001
Mild liver disease	46.3 ± 45.1	0.458
Cerebrovascular accident	45.1 ± 55.0	0.842
Tumors	53.3 ± 67.1	0.149
Ambulation status		
Normal	41.5 ± 54.7	0.060
Walks with assistance	37.1 ± 56.0	
Wheelchair	25.5 ± 28.4	
Bedridden	30.0 ± 32.9	
Medications		
ACE inhibitor	32.2 ± 40.2	0.059
Angiotensin receptor blocker	40.0 ± 52.5	0.309
Diuretics	37.4 ± 51.6	0.138
Beta-blocker	38.0 ± 51.4	0.125
Calcium channel blocker	41.7 ± 54.0	0.089
Vitamin D	52.8 ± 63.2	<0.001
Phosphate binder, calcium	41.6 ± 55.0	0.095
Iron		
Oral	40.1 ± 52.2	0.472
IV	37.4 ± 53.8	
Oral+IV	56.2 ± 71.9	
ESA		
Epoetin alpha	42.1 ± 55.0	0.184
Epoetin beta	34.6 ± 45.6	
Darbepoetin alpha	36.8 ± 49.1	
CERA	50.3 ± 64.3	

Discussion

This study was conducted to assess the social, demographic, clinical and health factors impacting the referral time to a nephrologist in chronic kidney disease patients. It was found that diabetes, profession, assisted ambulation and congestive heart failure were independent risk factors of late referral. On the other hand, patients who were smokers and had congestive heart failure were associated with early referral.

The cause of kidney disease also determines the referral time as glomerulonephritis is always referred to early worldwide as this disease is associated with the nephrology department (Caro Martínez et al., 2019; Dhanorkar et al., 2022; Greer et al., 2019). Similarly, CKD patients with diabetes mellitus are also referred early to increase the chances of survival and disease treatment (Smart et al., 2014; Wu et al., 2020). Other studies have also reported the early referral of diabetes mellitus patients before the start of dialysis (Chen et al., 2019; Mutatiri et al., 2022). Kessler et al (Kessler et al., 2003) and Kinchen et al (Kinchen et al., 2002) noted an average time of 4 to 12 months for referral of diabetes mellitus patients. However, our study showed contrary results as diabetes patients were referred to later than glomerulonephritis patients. This discrepancy may be due to differences in definitions of referral time.

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With regards to comorbidities, the late referral group mostly had congestive heart failure as advanced kidney failure is a risk factor for heart failure (Kottgen et al., 2007). Heart failure in CKD patients may increase the mortality risk by accelerating the disease progression (McClellan et al., 2004; Xiong et al., 2019). Congestive heart failure was less common in early referral patients due to proper medication, diet and awareness which resulted in low diastolic blood pressure.

Early referral results in the delayed need for renal transplant, better lifestyle, less hospital stay and costs and increased survival (Chou et al., 2022). Jones et al (Jones et al., 2006) reported that nephrologist referral had a positive impact on the glomerular filtration rate due to appropriate care. Early referral patients had a high haemoglobin level, low phosphorus levels, and low LDL cholesterol levels.

Our study had some limitations including a small sample size and a short study period.

Conclusion

Diabetes and hypertension patients have a later referral time than patients with glomerulonephritis. In addition, men with congestive heart failure practicing physically active professions and assisted ambulation were referred late.

Conflict of interest

The authors declared absence of conflict of interest.

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