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Research Article

Risk factors of progression of chronic kidney disease patients under conservative treatment

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ABSTRACT

Background: Chronic kidney disease (CKD) is recognized as a major health problem affecting approximately 13% of the US population. Early identification and treatment of risk factors of progression of chronic kidney disease can provide marked benefits later in the term of delaying progression to renal replacement therapy.
Methods: The medical chart for 92 CKD patients on regular follow up in low clearance clinic with GFR below 20 ml/min were retrospectively reviewed annually for 4 years regular follow up period. The following variables were recorded for each patient: non-modifiable variables (Age, sex, nationality, BMI, systolic and diastolic blood pressure, smoking status, causes of kidney disease, diabetes status, hepatitis status, medication used (like ACEi/ARBs and Sodium bicarbonate) and modifiable variables which includes: Serum albumin, potassium level, serum bicarbonate level, level of proteinuria, rate of GFR decline (Delta GFR) /year, total cholesterol level and hemoglobin level. Then they were divided into 2 groups according to the endpoint during the follow up period. Group 1 include patients did not start dialysis yet and group 2 which include patients who started dialysis during their regular follow up period.
Results: There is no statistically significant differences between the two groups regarding Age , sex, systolic and diastolic blood pressure and Body Mass Index(BMI), serum albumin and haemoglobin levels (p 0.295, 0.317, 0.220, 0.181,0.805, 0.884 and 0.451 respectively). There is no statistically a difference between the two groups regarding serum potassium level and serum total cholesterol level (p 0.515 and 0.517 respectively). Diabetic patients started dialysis earlier than non-diabetics with statistically significant difference between the two groups (p 0.029). The patients who weren't taking ACEi or ARBs started dialysis earlier than those who were taking (p 0.005), while there was no significant differences between the two groups regarding sodium bicarbonate intake (p 0.256). Low sodium bicarbonate level and severity of proteinuria are of significantly important risk factors for progression of CKD disease (p 0.006 and 0.029 respectively).
Conclusions: The most important risk factors for rapid progression are presence of diabetes, severity of proteinuria and low serum bicarbonate level in advanced stages of chronic kidney disease. Early recognition of these risk factors and their correction may retard the progression of CKD, which will delay the need for renal replacement therapy. In addition, ACEI or ARBs intake are almost renoprotective and may delay the rapid progression of chronic kidney disease especially in proteinuric patients.

Keywords: Chronic kidney disease, Risk factors, Progression

INTRODUCTION

Chronic kidney disease (CKD) is recognized as a major health problem affecting approximately 13% of the US population.[1] The number of patients enrolled in the End-Stage Renal Disease (ESRD) Medicare-funded program has increased from approximately 10,000 beneficiaries in 1973, to 86,354 in 1983, and to 615,899 as of December 31, 2011 The principal outcomes of CKD include progressive loss of kidney function leading to ESRD and the development and progression of cardiovascular disease (CVD).[2-4] Early identification and treatment of risk factors of progression of chronic kidney disease can provide marked benefits later in the term of delaying progression to renal replacement therapy.[5] These risk factors can be divided into 2 categories, the first one is the modifiable risk factors which include systemic infection, diabetes, hypertension, smoking, systemic inflammation, obesity, proteinuria, dyslipidaemia and anaemia. While the second one is non-modifiable risk factors which include gender, age, ethnic minority status and positive family history.[6] Screening and adequate treatment of modifiable risk factors we are able to prevent or delay the progression of the disease. The aim of this study is to provide an overview of the identified risk factors for chronic kidney disease (CKD) progression in our patients under conservative treatment in low clearance clinic.

METHODS

This retrospective study done in low clearance clinic at Hamad medical corporation Qatar. The medical chart for 92 patients with GFR below 20 ml/min were retrospectively reviewed with 4 years regular follow up period in nephrology clinic. The end point of the study is initiation of dialysis. They were divided to 2 groups: group I is CKD patients who did not start renal replacement therapy yet, and group II is CKD patients who ended their follow up by starting haemodialysis. The following variables were recorded for each patient: non-modifiable variables (Age, sex, nationality, Body Mass Index(BMI),systolic and diastolic blood pressure, smoking status, causes of kidney disease, diabetes status, hepatitis status, medication used (ACEi/ARBs and Sodium bicarbonate). The other variables are the modifiable one which includes: Serum albumin, potassium level, serum bicarbonate level, level of proteinuria, rate of GFR decline (Delta GFR) /year, total cholesterol level and haemoglobin level. Table 1 shows the characteristics of all studied patients.

Statistical analysis

Statistical analyses were performed with Statistical Package for Social Sciences version 17.0 for Windows (SPSS Inc., Chicago, IL). Continuous variables are presented as mean ± SD or median and range, and categorical variables are presented as absolute and relevant frequencies. For comparison between Groups, for parametric variable, paired T test was used for the comparison and for non-parametric variable, Chi square test was used for the comparison. Probability values of P 0.05 (two-tailed) were considered statistically significant.

RESULTS

Table 1: Clinical and demographic data for all patients.

Variables	All Patients
Age (Y)	55.7±14.3
Sex: Male/Female	51/41
Diabetics	57/35
Smokers	2/90
Systolic BL p mmHg	143.05±21.7
Diastolic BL p mmHg	74.0±9.8
BMI	29.5±5.2
Hepatitis C Yes/No	5/87
ACEi/ARBS intake Yes/NO	18/74
Nahco3 Intake Yes/No	52/40
Albumin g/l	38.6±5.2
Potassium mmol/l	4.8±0.7
Haemoglobin g/dl	11.02±1.52
Cholesterol mmol/l	4.0±1.09
Urine Protein mg/mmol	337.6±327.6
Hco3 level mmol/l	22.1±4.5

Ninety two Patients were selected for this study, their mean age was 55.7±14.3 years, 51 patients were male and 41 patients were females. 57 of them were diabetics, 2 patients were smokers and 5 patients having hepatitis-C positivity. The mean systolic blood pressure was 143.05±21.7 mmHg and the mean diastolic blood pressure was 74.0±9.8 mmhg. The mean of BMI was 29.5±5.2. The number of patients who were on sodium bicarbonate was 52 patients while the number of patients who were on ACEI or ARBs was 18 patients. The mean albumin level was 38.6±5.2 g/l, the mean potassium level was 4.8±0.7 mmol/l, the mean haemoglobin level was 11.02±1.52 g/ dl, the mean cholesterol level was 4.0±1.09 mmol/l, the mean serum bicarbonate level was 22.1±4.5 mmol/l, while the mean protein/creatinine ratio was 337.6±327.2 mg/mmol (Table 1).

All Patients were divided into 2 groups according to their endpoint after 4 years follow up, Group I (53 patients) is the group of patients on regular follow up and not started haemodialysis yet and Group II (39 patients) who are the other patients who started haemodialysis during their regular follow up in our clinic. There is no statistically significant differences between the two groups regarding Age, sex, systolic blood pressure, diastolic blood pressure and BMI, (p is 0.295, 0.317, 0.220, 0.181 and 0.805 respectively (Table 2).

Although the albumin level was lower in dialysis group, there is no statistically a difference between the two

groups p 0.884. Also, haemoglobin level was lower in haemodialysis group but there are no statistically differences between the two groups p 0.451. There are no statistically differences between the two groups regarding serum potassium level and serum total cholesterol level p 0.515 and 0.517 respectively (Table 2).

Table 2: Comparison between the 2 groups regarding modifiable risk factors.

Variables	CKD Not started Dialysis. N:53	CKD Started Dialysis. N39	T	P
Age (Y)	56.7±15	54.3±13.4	1.109	0.295
Systolic BL p mmHg	138.7±18.4	148.9±24.5	1.526	0.220
Diastolic BL p mmHg	72.9±8.1	75.4±11.7	1.815	0.181
BMI	29.3±5.4	29.8±5.09	0.061	0.805
Delta eGFR	-7.9±4.7	-2.0±3.0	3.435	0.067
Albumin g/l	39.3±4.9	37.7±5.5	0.021	0.884
Potassium mmol/l	4.8±0.70	4.9±0.74	0.426	0.515
HB g/dl	11.38±1.59	10.5±1.29	0.572	0.451
Cholesterol	4.01±1.17	3.9±0.99	0.423	0.517
Urine Protein (PCR) mg/mmol	231.7±234.3	481.5±380.8	5.268	0.024
Hco3 mmol/l	22.9±3.3	20.9±5.7	8.041	0.006

Table 3: Comparison between the 2 groups regarding non-modifiable risk factors.

	CKD Not started Dialysis. N:53	CKD Started Dialysis. N39	P
Sex			0.317
Male	31	20	
Female	22	19	
Diabetes			0.029
Non-Diabetics	25	10	
Diabetics	28	29	
Causes of CKD			0.179
Diabetes	18	19	
Hypertension	12	5	
Reflux	1	0	
Unknown	18	7	
Interstitial Nephritis	2	3	
FSGS	2	1	
APKD	0	2	
Others	0	1	
Obstruction	0	1	
Hepatitis			0.291
Y/N	4/49	1/38	
	5		
Smoking Y/N	1/52	1/38	0.671
ACE/ARBs			0.005
NO	52	38	
Yes	1	1	
Nahco3			0.256
No	21	19	

Diabetic patients started haemodialysis earlier than non-diabetics with statistically significant difference between the two groups p 0.029.The patients who weren't taking ACEi or ARBs started dialysis earlier than those who were taking p 0.005, while no significant differences between the two groups regarding sodium bicarbonate intake p 0.256. The causes of CKD and hepatitis status did not affect the outcome of the study with no statistical difference between the two groups' p 0.179 and 0.291 respectively (Table 3).

The most important risk factors that can lead to rapid declining of the kidney function and so earlier starting of dialysis are low bicarbonate level and the severity of proteinuria as in group I the bicarbonate level was 22.9±3.3mmol / l while in group II; it was 20.9±5.7 with p value 0.006. While the level of proteinuria (reflecting as protein / creatinine ratio) was 231.7±234.3 in group I and 481.5±380.8 in group II with p value 0.024 (Table 2).

DISCUSSION

In this retrospective study, we are trying to study some of risk factors that can be related to rapid deterioration of the kidney function and rapid initiation of renal replacement therapy in CKD patients followed in low clearance clinic. There was no statistical difference between the two groups (group I who did not start renal replacement therapy and group II who started renal replacement therapy) regarding age, blood pressure (systolic and diastolic) in contradiction to other studies which was done before. In one study done by Jungers et al, the proportion of patients who started dialysis was lower in the group aged >75 years than in younger patients (28% vs 48%, p <0.02).[7] In other study done by Harounet al., the higher systolic and higher diastolic BP were associated with a relative hazard for CKD of 1.02 (95% CI 1.01–1.03) and1.04 (95% CI 1.03–1.06), respectively, after adjustment for age, gender, smoking, and diabetes treatment (p < 0.001).[6] This difference in the results between our study and the previous ones can be explained by the well monitored blood pressure in our patient and its strict control in each visit to the clinic. Also in this study, no significant difference was found between the two groups regarding Body mass Index and this can goes with one study done on diabetic patient by David New et al who found that raised BMI did not influence the rate of progression of chronic kidney disease in patients with type 2 diabetes mellitus.[8] In other study done Khedr et al, again no statistical difference in slope of eGFR was found, with a decline of 2.2 mL/min/1.73 m^2per year in the no obese group, and 2.69 mL/min/1.73 m^2 per year in the obese group (p = 0.13).[9]

In this study, no statistically significant differences between the two groups was found regarding haemoglobin level. This is contradictory to some previous studies like The NHANES III study which confirmed a connection between low haemoglobin and renal damage also A Canadian cohort study of patients with CKD showed that at any level of renal impairment, the risk for progression to ESRD is increased by the presence and level of anaemia.[10,11] The explanation for that difference is that all our patients were closely monitored for anaemia and most of them were receiving erythropoietin stimulation agent (ESA) replacement. Also in our study, no statistically significant differences between the two groups was found regarding total cholesterol level and this was contradictory to study results done by Krolewski et al which showed that the prevalence of patients with rapid loss of renal function was racing with increasing level of serum cholesterol.[12] In our study, we found that diabetic patients experienced rapid progression of their CKD with p value 0.029. The importance of diabetic nephropathy as a cause for patient morbidity and mortality is well known. Diabetic nephropathy occurs in ~ 30% of people with type 1 diabetes and 25-40% of people with type 2 diabetes, often irrespective of glycaemic control. Diabetic nephropathy is the single most common cause of end stage renal disease (ESRD) in the United States, accounting for > 50% of new cases of renal failure. Patients who have diabetes and reach ESRD have a poor prognosis because of high cardiovascular events.[13]

In our study, patients who were on ACEi or ARBs have a slow progression of their CKD in comparison to other patients who weren't on this medication p value 0.005. Several trials have demonstrated the renoprotective benefits of controlling proteinuria as well as BP in people with moderate to severe renal disease. Of these studied was the Angiotensin-Converting-Enzyme Inhibitor in Progressive Renal Insufficiency (AIPRI) study, Therapy with benazepril significantly reduced the risk for a composite renal outcome (doubling of baseline serum creatinine or need for dialysis) compared with placebo. This reduction in risk was attenuated but remained significant after adjustment for benazepril's effect on diastolic BP (DBP) and urinary protein excretion.[14] After adjustment for DBP and proteinuria changes, the benefit of benazepril remained significant in the subgroup of patients with mild renal impairment at baseline (risk reduction 65 to 66%) and those with baseline urinary protein excretion ≥3 g/d (risk reduction 52 to 56%). However, the benefit was no longer significant in those with moderate renal impairment or lower levels of urinary protein excretion.[14] In the Ramipril Efficacy in Nephropathy (REIN) study, ramipril therapy prevented the need for dialysis when used for 3 to 4 yrs. in patients with proteinuria and CKD.[15,16] These and other results were consistent with a renoprotective effect exceeding that attributable to BP lowering alone.[17,16] In our study, severity of proteinuria was the most risk factor that can lead to rapid progression of CKD with p value 0.006 and this was consistent with many previous studies. From these studies, there was one done by Jungers et al and concluded that Proteinuria had a strong positive relationship with the decline of GFR in the entire study population.[18] In other study done by de Goeij, they confirmed that proteinuria is a risk marker for progression of CKD in predialysis patients.[19]

In our study, we have found that low bicarbonate level is an important risk factor for CKD progression p value 0.024 and this result goes with cohort study done by Mirela Dobre which concluded that low serum bicarbonate level was an independent risk factor for kidney disease progression, particularly for participants with preserved kidney function.[20]

CONCLUSION

The most important risk factors for rapid progression of advanced stage of chronic kidney disease are the presence of diabetes, severity of proteinuria and low serum bicarbonate level. That is why timely recognition of these risk factors and their correction may retard the progression of CKD, thus delaying the need for renal replacement therapy. Also in those patients, ACEI or ARBs intake are almost renoprotective and may delay the rapid progression of chronic kidney disease especially in proteinuric patients.

Ethical standard

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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