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The quality of life of chronic kidney disease patients with hypertension treated with angiotensin system-related agents

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ABSTRACT

The chronic kidney disease (CKD) co-exist with hypertension in approximately 80 to 85 per cent of patients. The CKD stages can be defined by glomerular filtration rate (GFR), and the deterioration of kidney function or reduction in GFR has observed in those with uncontrolled blood pressure (BP). We had conducted a prospective study to analyse the impact of the angiotensin system-related agents on the quality of life of CKD patients with hypertension. The SF-36 questionnaire, direct patients interview and medical records were the sources for retrieval of information. We observed that male patients were more prone to CKD than female. Hypertension was the primary (77.8%) aetiology behind the incidence of CKD. The angiotensin-converting enzyme inhibitors (ACEI) was responsible for very low (58%) and low (44%) health disabilities to the patients. In contrast, the angiotensin receptor blockers (ARB) even though it has a limited adverse effect, the patients complained of medium (9%) and high disabilities than the ACEIs. The discontinuation of the antihypertensive drugs by the CKD patients was almost negligible (3.4%). The study concludes that a balanced diet and reasonable blood pressure control is essential to prevent the progression of CKD and to improve the quality of life.

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INTRODUCTION

The Kidney Disease Improving Global Outcomes (KDIGO) has defined chronic kidney disease (CKD) as abnormalities of kidney structure or function presented for greater than three months with implications for health (Kidney International Supplements, 2013). Hypertension and CKD are interrelated and represent global public health challenges. The progression of kidney impairment may be due to changes in the demographics of the population, differences in disease burden among age groups and under-recognition of earlier stages of CKD and risk factors for CKD may partially explain this growth (National Kidney Foundation, 2002). We had conducted an epidemiological study on hypertension with CKD in our locality.

Methodology

The prospective observational study was conducted at the nephrology department of KIMS Al Shifa hospital, tertiary care referral hospital from October 2018 to August 2019. The ethical committee approval and informed consent were obtained.

The chronic kidney disease outpatients with hyper-

tension were enrolled, and they were followed up for three consecutive consultations. The study focused on angiotensin system-related agents; those are the angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB). Patients with acute kidney injury, unconscious or those with serum creatinine greater than 3.5mg/dl are excluded from the study. The SF — 36 questionnaire assessed the patients' quality of life. Direct patient interview, discussion with a physician, medical record database and prescription were the source for retrieval of patient demographics details, aetiology, stage and duration of CKD as well as blood pressure, glomerular filtration rate.

The data collected was spread into an excel sheet which was then imported into Statistical Package Of Social Science (SPSS) software version 23. The Chi-square was applied to relationships among the different variables and the repeatability among clinical parameters, respectively.

RESULTS AND DISCUSSION

Total of 495 patients was enrolled in the study as per the study specification. CKD was prominent among the age group above 60 years (Park *et al.*, 2011). In our study, we observed a similar observation and the least below to the age of 50 years, as per Table 1. However, the pattern had extended down to adults, and this could be due to several factors such as over usage of medicines especially NSAIDs (Baker and Perazella, 2020), inherited disease (Hildebrandt, 2010) and lifestyle changes (Shankar *et al.*, 2006).

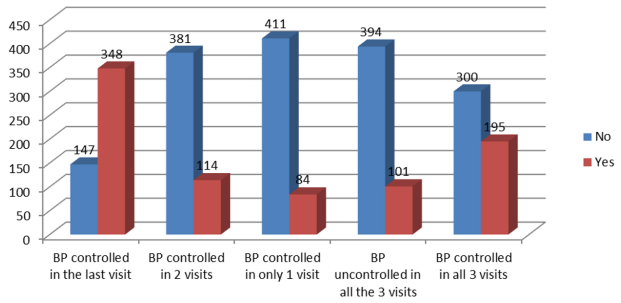

Figure 1: The graph showing the blood pressure of the patients at three consecutive consultations

The people in the United States and Norway had a large density of CKD patients below the age of 65 years (Hallan *et al.*, 2006). The early detection of kidney deterioration may be due to fetal nephrotoxicity of drugs administered by pregnant ladies. The practice of polypharmacy might be a reason for the early age diagnosis of CKD among their offspring (Bernstein *et al.*, 1998).

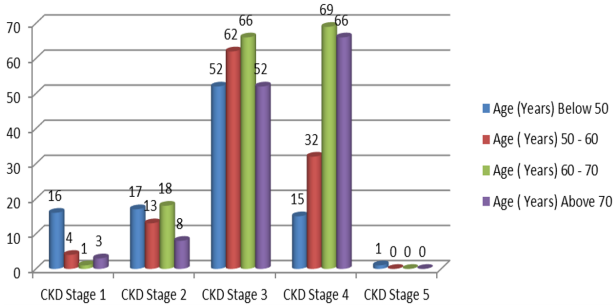

Figure 2: The association between stages of CKD concerning the age of the patient

Man (60.4%) had more prevalence of CKD with hypertension than female (Ojji *et al.*, 2009). When we analysed the chronic kidney disease patient's stage, 46.9% had stage 3 CKD followed by stage 4 (36.8%) and only one person in stage 5 (End-Stage Renal Disease). The study conducted in Karnataka also had a high prevalence of CKD stage 3 patients, then followed by stage 4 (Duan *et al.*, 2019). Only a few patients (16.1%) were identified to be in stage 1(4.8%) and stage 2 (11.3%), as shown in Table 2. From our study, 66 and 69 patients belong to the age group between 60 to 70 had stage 3 and stage 4 CKD, respectively.

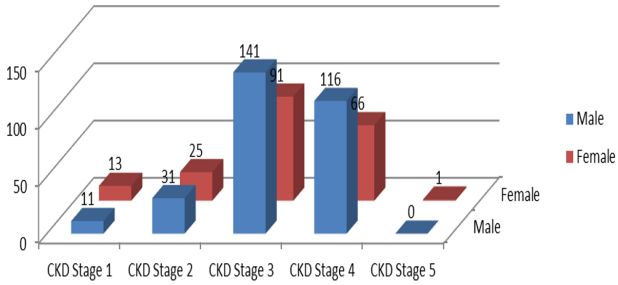

Figure 3: The association between the CKD stage with the gender of the patient

Even though the total patients in stage 2 were small, most patients belonged to 60 to 70 years age group, which was followed by those with age between 50–60 years. Only in stage 1 and stage 5, we observed the patients with age less than 50 years. From Figure 2, the relationship between age and stages of chronic kidney disease was analysed with the chi-square test. There was a statistical difference in the occurrence of various stages of the disease according to age ($P<0.05$). Hence, we reject the null hypothesis; there is significance between the age and the stages of chronic kidney disease.

Only 13 female CKD patients were observed to be more in stage 1 than the male. However, while the stage progressed, the contribution of the male was superior. This association was evaluated with the chi-square test, and the inference showed to have no

Table 1: Demographic details distributed per age, gender, a lean Body weight of the CKD Patients

Particular	Obtained Number	Percentage
Age		
Below 50 Years of Age	101	20.4%
50 to 60 Years of Age	111	22.4%
60 to 70 Years of Age	154	31.1%
Above 70 Years of Age	129	26.1%
Gender		
Particular	Obtained Number	Percentage
Female	196	39.6%
Male	299	60.40%
Lean Body Weight		
Particular	Obtained Number	Percentage
Below 55 Kg	80	16.16%
Between 55 to 65 Kg	179	36.16%
Between 65 to 75 Kg	136	27.47%
Above 75 Kg	100	20.20%

Table 2: Number and percentage of patients based on cause, CKD stages and duration of disease

Particulars	Obtained Number	Percentage
Chronic Kidney Disease Stage		
CKD Stage 1	24	4.8%
CKD Stage 2	56	11.3%
CKD Stage 3	232	46.9%
CKD Stage 4	182	36.8%
CKD Stage 5	1	0.2%
Chronic Kidney Disease Duration		
Particulars	Obtained Number	Percentage
1 to 6 months	29	5.9%
6 to 12 months	74	14.9%
1 to 2 years	90	18.2%
2 to 3 years	76	15.4%
3 to 4 years	53	10.7%
4-5 years	58	11.7%
Above 5 years	115	23.2%
Cause of Chronic Kidney Disease		
Particulars	Obtained Number	Percentage
Hypertension	385	77.8%
Other	110	22.2%

significant difference among male and female for different stages of chronic kidney disease (P>0.05), as observed from Figure 3.

52.32% of patients had lean body weight between 55 to 65kg, and those below 55 kg were the least. The Cockcroft-Gault equation, the tool widely used to calculate the creatinine clearance (one of a parameter to analyze the kidney function). Accordingly states that, an increase in lean body weight without a proportional increase in serum creatinine will tend to have a favourable impact on the patient (Walker and Whittlesea, 2015). Hence, a healthy diet would improve the patients well being as well as prevent the progress of CKD (Rysz *et al.*, 2017).

The quality of life (QOL) of 93.9% patient under treatment had low or very low disabilities, as shown

in Table 3. The age, gender, stage of CKD and presence of other co-morbidities can affect the quality of life of patients. Anaemia and low-income status were significantly associated with poor QOL (Tannor *et al.*, 2019). A reduction in physical functioning, physical role functioning and in the physical component summary was observed progressively in the different stages of kidney disease. Individuals with higher educational level who were professionally active displayed higher physical component summary values, whereas men and those with a higher income presented better mental component summary values. Older patients performed worse on the physical component summary and better on the mental component summary (Lekpa *et al.*, 2017).

Majority of CKD patients of stage 1,2,3,5 had very low disabilities as observed from Figure 4. However, stage 4 had less health satisfaction compared to other stages. Chi-square test analysis rejected the null hypothesis, and it was found that there was a significant difference in Quality of Life (QOL) among various stages of CKD (P>0.05).

Hypertension is a risk factor for the onset and progression of CKD, a reduction in the glomerular filtration rate (GFR), occurs at a variable rate, ranging from less than 1 to more than 12 mL/min per 1.73 m^2 per year (Levey *et al.*, 2011). The primary cause of progressive kidney damage is found to be due to hypertension which accounts to have a 77.8% distribution among the total chronic kidney disease patient on angiotensin related drugs, as shown in Table 2. This put light that elevated BP is one among the predominant cause of kidney damage than diabetes mellitus (Walker and Whittlesea, 2015).

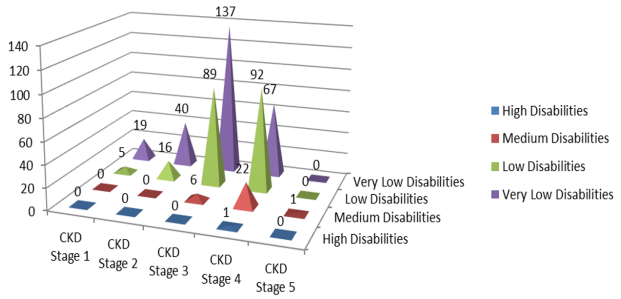

Figure 4: The association between the CKD stage with the patient's Quality of Life

Increased awareness and treatment of hypertension among CKD patients had improved blood pressure control. Each of the antihypertensive agents is roughly equally effective in lowering the blood pressure, producing an excellent antihypertensive response in 30 to 50 per cent of patients. Joint National Committee (JNC) 8 recommends initiating a renin-angiotensin-aldosterone system (RAAS) inhibitor, thiazide diuretic or a calcium channel blocker for normalising the blood pressure in CKD patients. Among them, ACE inhibitors or ARBs was most frequently administered drug (39%) as monotherapy followed by calcium channel blockers, diuretics and beta-blocker (Ridao *et al.*, 2001).

The angiotensin receptor blockers opted by the nephrologist in our study was losartan (37.6%), telmisartan (18.2%) and olmesartan (0.4%). The prescription pattern of the physician also had more ramipril (39.2%) than enalapril (0.4%), as observed in Table 3. In a meta-analysis on 22 studies, Wang et al. indicated that olmesartan provided greater reduction in both diastolic and systolic blood pressure than losartan and systolic blood pressure compared to valsartan (Wang *et al.*, 2012). In the HOPE and EUROPA trails, ramipril had a better outcome than placebo.

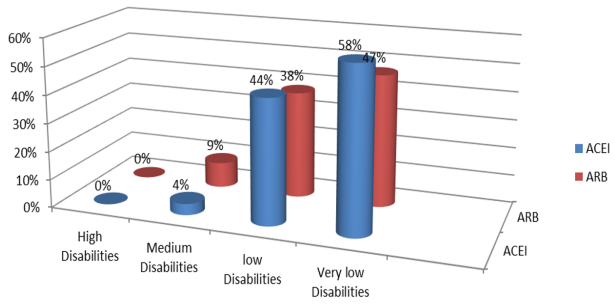

Figure 5: The association between the Quality of Life of the patient with the ACE Inhibitors and Angiotensin Receptor Blockers

We obtained a greater strength (23.2%) among the group who had been diagnosed with the disease more than five years, followed by those with a duration between 1 and 2 years and least was observed in the group with a duration between 1 to 6 months, shown in Table 2. Majority of the CKD population had the long-standing disease (greater than five years), this can be attributed to the suppression of known "causes" of progression by targeting high blood pressure (BP) as well as the impact of renin-angiotensin system (RAS) related drugs (Brenner *et al.*, 2001).

In particular, an elevation of 20 mm Hg accounts for many increased mortality (Forouzanfar *et al.*, 2013). There are two major components to slow the rate of progression of CKD: treatment of the underlying disease, if possible; and treatment of secondary factors that are predictive of progression, such as elevated blood pressure (Coresh *et al.*, 2001).

Among the 495 patients, 348 patients had blood pressure controlled on the last visit. Only 195 patients were stable with the best control on all

Table 3: The number and percentage of patients based on the treatment provided, discontinued and also the quality of life

Particulars	Obtained Number	Percentage
Antihypertensive prescription pattern		
ACE Inhibitors	196	39.6%
Ramipril	194	39.2%
Enalapril;	2	0.4%
Angiotensin Receptor Blockers	299	60.4%
Losartan	186	37.6%
Telmisartan	90	18.2%
Olmesartan	23	4.6%
Incidence of Medicine Discontinuation		
Particulars	Obtained Number	Percentage
Yes	17	3.4%
No	478	96.6%
Distribution of Discontinued Drug		
Particulars	Obtained Number	Percentage
Losartan	4	0.8%
Ramipril	9	1.8%
Telmisartan	4	0.8%
None	478	96.7%
Quality Of Life (score)		
Particulars	Obtained Number	Percentage
High Disability (0-25)	1	0.2%
Medium Disability (25 – 50)	29	5.9%
Low Disability (50 – 75)	202	40.8%
Very Low Disability (75 – 100)	263	53.1%

the three visits. A majority had fluctuated BP during their three consecutive visits, shown in Figure 1. Tozawa et al. also argued that controlling blood pressure within normal levels can prevent the development of ESRD in both male and female patients (Tozawa *et al.*, 2003). We had patients with poor blood pressure control which could be attributed to the advancement of CKD irrespective of gender.

The discontinuation rate was found to low (3.4%), and among them, ramipril (1.8%) was the main culprit, shown in Table 3. ARBs have demonstrated excellent safety profiles alone and in combination with other antihypertensive therapies during the past 20 years. The tolerability profiles of ARBs are similar to placebo and superior to ACE inhibitors.

The risk of discontinuation for an adverse event was reduced by 29% with ARB treatment, by 10% with diuretics, and by 2% with calcium-channel blockers. In contrast, it was increased by 18% with ACE-inhibitors and by 13% with beta-blockers (Barreras and Gurk-Turner, 2003). The health status of patients on ACEIs was better than ARBs, observed in Figure 5. The null hypothesis was accepted using chi-square analysis, and it was observed that there is no significant statistical difference (P>0.05) among the administration of angiotensin related drugs on patients Quality of Life (QOL).

CONCLUSIONS

Proper diet and blood pressure control had more significant impact on the progression of CKD. Hence the administration of a safer drug, ACEI was found to influence the quality of life of the patients. Even though ARBs claim to have a lesser side effect, patients had much better health outcomes with ACEI.

Conflict of Interest

The authors declare that they have no conflict of interest for this study.

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