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Prevalence and Pattern of Resistant Hypertension among Dialysis Naïve Chronic Kidney Disease Patients in Ilorin

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ABSTRACT

Hypertension (HTN) is common in CKD and represents a major target for intervention to prevent progression of renal disease. Prevalence of resistant HTN is high in nephrology clinics and adequate control of blood pressure in CKD patients is crucial as they are more likely to die from CVD before reaching ESRD and lack of BP control hastens progression of CKD to ESRD. There is thus concern about the low rate of BP control in CKD, but whether it has improved in recent times is not known in our environment. We sought to determine prevalence and pattern of resistant HTN in dialysis naïve CKD patients in Ilorin, using the newer treatment guidelines.

The case files of renal patients seen in University of Ilorin Teaching Hospital (Jan. 2001 to Dec. 2010) were retrieved from the records department. Patients that met criteria for CKD, but are yet to commence renal replacement therapy were retrospectively studied. Resistant hypertension was taken as persistence of blood pressure above 130/80mmHg despite regular use of maximal tolerated doses of three anti-hypertensive drugs including a diuretic for at least one month.

Total of 180 patients (121 males, 59 females) was studied. Mean age was 49.05±15.48 years, mean systolic and diastolic BP were 146.01±24.57mmHg and 88.44±14.62mmHg respectively. Prevalence of resistant HTN was 69% while isolated diastolic and systolic HTN accounted for 9% and 4% respectively. Overall, 82% had at least one form of resistant HTN with only 18% achieving target treatment goals. Most common combination of drug classes was angiotensin receptor blockers, angiotensin converting enzyme inhibitors, calcium channel blockers and diuretics accounting for 35%.

Resistant HTN was very high among our CKD patients using the newer guidelines on Bp control. Ignorance, poverty and poor compliance to treatment were associated with resistant HTN. We advocate aggressive management including use of more than three drugs at increasing doses especially in those having diagnosis of PKD and CGN. Health education with emphasis on regular clinic attendance and compliance with medication in a bid to forestall ESRD epidemic should be vigorously pursued.

Keywords: *Chronic Kidney Disease, Resistant Hypertension, Prevalence, Ilorin, Nigeria*

INTRODUCTION

The incidence and prevalence of chronic kidney disease (CKD), is increasing globally with majority of the patients dying prematurely from cardiovascular disease [1, 2]. People from developing nations including Nigeria are worst hit by the menace of CKD, because they can hardly afford the cost of treatment. Hypertension (HTN) is very common in CKD and represents a major target for intervention to prevent progression of the disease [3]. Approximately 70-80% of patients with CKD develop HTN at some point in

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the course of the disease and its prevalence increases as glomerular filtration rate declines [3]. Hypertensive renal damage is the main cause of end stage renal disease (ESRD) and development of cardiovascular events in black populations of United Kingdom and Africa [4-7].

Resistant hypertension is defined as failure to achieve goal blood pressure with utilization of maximum tolerated doses of three anti-hypertensive drugs including a diuretic for at least one month [8]. Prevalence of resistant HTN ranges from 5% in general medical practice to more than 50% in nephrology clinics [9]. The guideline identifying CKD as a high risk group recommends treatment goal of less than 130/80mmHg for these category of patients [10]. The objective of HTN therapy in CKD is not only lowering of systemic blood pressure but more importantly, reduction in cardiovascular mortality risk and slowing of progression of CKD [10]. Adequate control of blood pressure in CKD patients is crucial as they are more likely to die from CVD before reaching ESRD and lack of BP control hastens progression of CKD to ESRD [11]. Patients with CKD have been shown to have low rate of BP control [12-14], but whether it has improved in recent times is not known in our environment. This study determines the prevalence and pattern of resistant hypertension in dialysis naïve CKD patients in Ilorin, using the newer treatment guidelines.

MATERIALS AND METHODS

The case files of renal patients seen in nephrology clinic or discharged from the renal wards of University of Ilorin Teaching Hospital from January 2001 to December 2010 were retrieved from the records. Patients that met criteria for CKD [15] but are yet to commence renal replacement therapy were studied. Information obtained from the notes included; bio-data, blood pressure at first presentation, blood pressure during subsequent follow-up, anti-hypertensive drugs, occupation and social habits. CKD was defined by an estimated glomerular filtration rate less than 60mls/min/1.73m^2, using MDRD study equation and/or presence of dipstick protenuria for more than three months [3]. The etiological diagnosis of CKD followed the pattern of a previous study in our environment [26].

Resistant hypertension was taken as persistence of blood pressure above 130/80mmHg despite regular use of maximal tolerated doses of three anti-hypertensive drugs including a diuretic for at least one month [8,9]. Systolic HTN and diastolic HTN were taken as >130/<80mmHg and <130/ >80mmHg respectively [8]. An average of two readings of BP measured in the subjects was taken for the purpose of this study. It is the practice in our center to measure Bp after at least 5min of rest, using standard mercury sphygmomanometer and appropriate cuff size. This is applied to exposed right upper arm and rapidly inflated to 30mmHg above level at which the pulse disappeared and then deflated gradually. Phases 1 and 5 of Korotkoff sounds were taken as systolic and diastolic blood pressure respectively. We also obtained information on social class, level of education, occupation, clinic attendance, ability to purchase prescribed drugs and compliance on medication.

Patients was said to be compliant if regular on medication and clinic attendance in the preceding four scheduled clinic visits and those with 75% attendance were regarded to be adherent to treatment. Data analysis was done using SPSS v16. Mean ± Standard Deviation was used for continuous data, student T-test for comparison of means while comparison of proportion was by chi-square test. The level of statistical significance was taken as $P<0.05$.

RESULTS

A total of 180 patients (121 males, 59 females) were studied. The overall mean age was 49.05±15.48 years while mean systolic and diastolic BP were 146.01±24.57mmHg and 88.44±14.62mmHg respectively. Prevalence of resistant HTN was 69% while isolated diastolic and systolic HTN accounted for 9% and 4% respectively (Figure 1).Overall, 82% had resistant HTN with only 18% achieving target treatment goal. Table 1 depicts gender distribution of BP categories. Resistant HTN was commoner in males (73%) than females (61%), but it was not statistically significant (chi-square=2.86, p=0.09). Isolated diastolic HTN was more prevalent in females (12%) than males (7%) which was also not statistically significant (chi-square=1.41, p=0.23). The BP category and aetiology of CKD (Figure 2) showed that resistant HTN was present in more than 80% of patients with essential HTN and CGN while all patients with PKD had resistant HTN. Most common combination of drug classes (Figure 3) was angiotensinII receptor blockers (ARB), angiotensin

Table 1: Gender distribution and BP categories

BP Category	Males (%)	Females (%)
Resistant HTN	88 (72.72)	36 (61.01)
Diastolic HTN	8 (6.61)	7 (11.86)
Systolic HTN	4 (3.31)	3 (5.08)
Target Control	21 (17.35)	13 (22.03)
Total	121 (100)	59 (100)

Resistant HTN = BP >130/>80mmHg
Diastolic HTN = BP <130/>80mmHg
Systolic HTN = BP >130/<80mmHg
Target Control = BP d"130/d"80mmHg

converting enzyme inhibitors (ACEI), calcium channel blockers (CCB) and diuretics (frusemide or bendrofluazide) followed by ARB, ACEI anddiuretics accounting for 35% and 17% respectively.

Table 2: Occupation and BP Category

Occupation	Resistant HT (%)	Diastolic HT (%)	Systolic HT (%)	Good Control (%)	Total
Others	40(71.42)	5(8.93)	-	11(19.64)	6
Students	13(68.42)	2(10.53)	-	4(21.05)	19
Traders	44(66.67)	8(12.12)	4(6.06)	10(15.15)	66
Civil Servants	25(64.10)	2(5.13)	4(10.26)	8(20.51)	39
Total	122	17	8	33	180

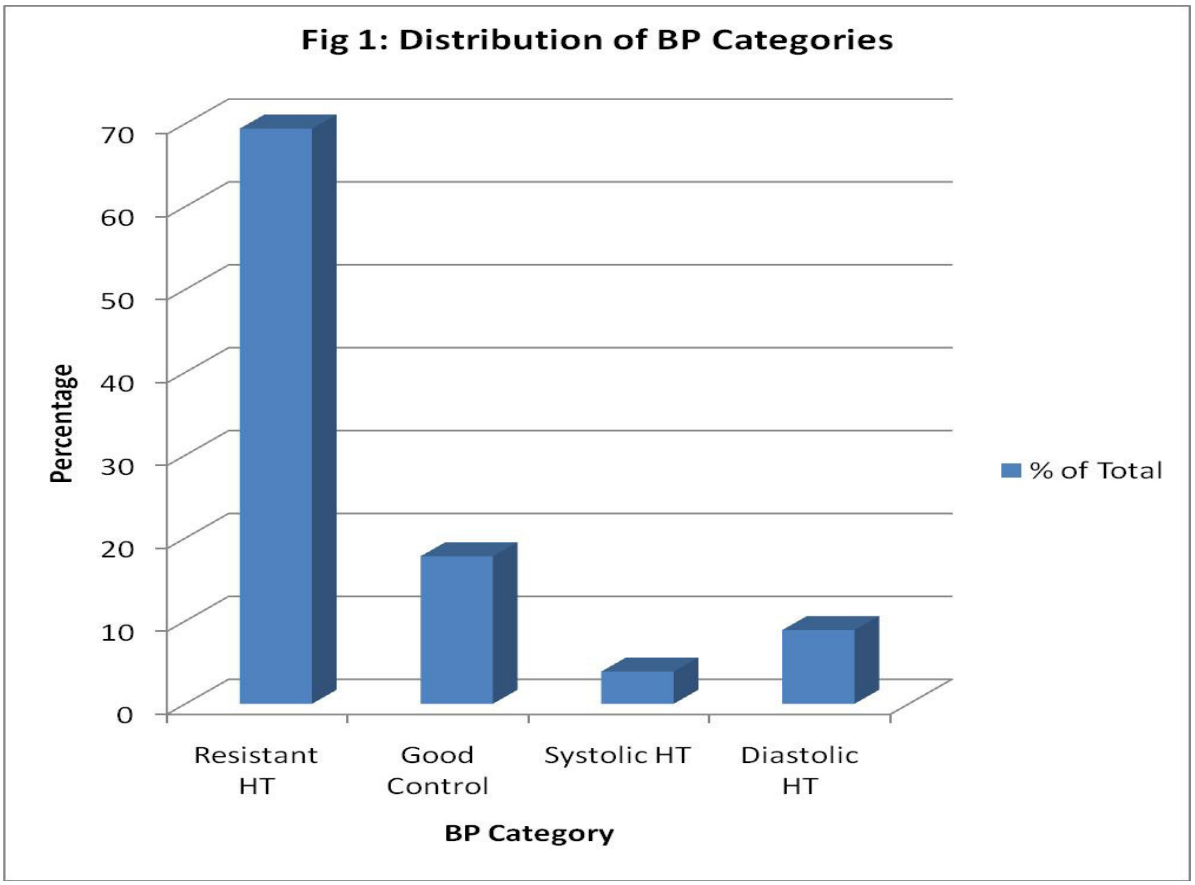
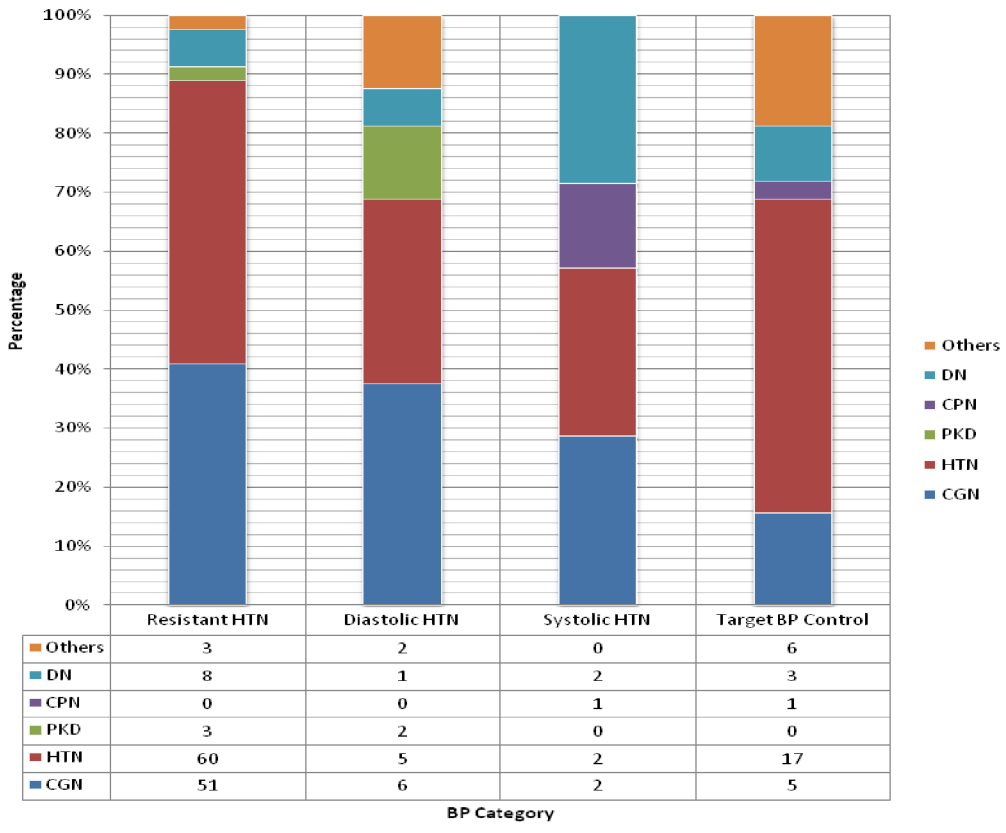


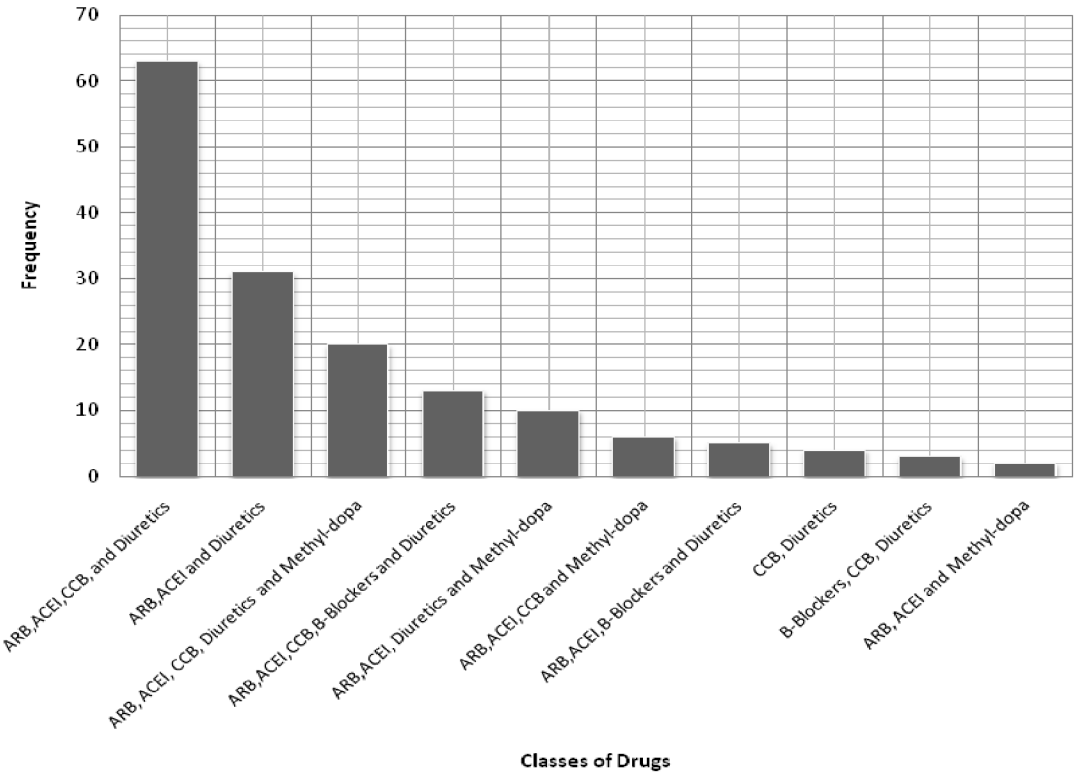
Fig 2: Aetiology of CKD and BP Category



	Resistant HTN	Diastolic HTN	Systolic HTN	Target BP Control
Others	3	2	0	6
DN	8	1	2	3
CPN	0	0	1	1
PKD	3	2	0	0
HTN	60	5	2	17
CGN	51	6	2	5

BP Category

Fig 3: Common Combination of Drug Classes



The rate of drug compliance was 58% in these patients. Occupation and blood pressure category (Table 2) showed that resistant HTN was commonest among manual workers (71%) followed by students (68%), traders (66%) and civil servants (64%)

DISCUSSION

The published guideline for BP control recommends lower BP targets among patients with CKD [8]. In this study, 69% had resistant HTN using the disease-specific guidelines. This is in accordance with the findings of Plantinga LC, ET al [16] and is similar with 70% reported by Agarwal R, *et al* [17]. The contributory factors to poor BP control in patients with CKD includes lack of understanding of the importance of BP in preventing progression and complication of CKD, cognitive difficulties associated with the disease, intolerance of drug side effects and cost of multiple medications [18]. We found that males with CKD were at greater risk for resistant HTN and it contrasts with previous studies that documented more females [16,19].

The reason for the gender difference is not clear. It may be related to attitude towards drug usage as non-compliance rate was higher in males (56% vs. 44%). Our finding of isolated diastolic hypertension in 9% of the patients is similar to 7% reported in the United States [13]. The prevalence of isolated systolic HTN of 4% in this study contrasts sharply with 59% documented in United States. Young J.H *et al* [20], have alluded to the high prevalence of systolic HTN in CKD and its role in disease progression. The disparity in the prevalence of isolated systolic HTN may be due to differences in lifestyle, choice of anti-hypertensive drugs and predominantly affected age bracket. Majority of our patient were in their third and fourth decade in contrast with fifth and sixth decade in developed countries. Previous studies have documented peak age range in CKD patients to be third to fourth and seventh to eighth decade in Blacks and Whites respectively. This has been linked with differences in the pattern of diseases causing CKD in both populations [22, 24-26].

The relatively young age at which CKD patients present in the tropics has been ascribed to variety of infectious agents implicated in the aetiology of CGN which are present in endemic proportions [22, 27, 28]. The older age of patients with CKD in developed countries may be responsible for high prevalence of systolic hypertension as recent data documented higher prevalence of systolic HTN in elderly CKD patients [19, 29, 30]. Resistant systolic HTN is more prevalent in the elderly because of associated arterial stiffness and natural history of arteriosclerosis [31,14]. Most commonly prescribed combination of drug classes in this study was ACEI, ARB, CCB and diuretics. ACEI and ARB have emerged as first line drugs in treatment of HTN among CKD patients [32]. These drugs inhibit rennin angiotensin system which play crucial role in pathogenesis of hypertension in CKD, slow progression of the disease and reduce risk of death from CVD, independent of their BP lowering effects [33, 34]. The COOPERATE STUDY in which CKD patients were randomly assigned ARB, ACEI or a combination of both drugs showed that the combination treatment safely retards progression of CKD compared to monotherapy [35]. Despite evidence of the benefits of ACEI and ARB in patients with CKD, studies suggest their underutilization [13, 36, 37]. This is in agreement with our findings as multiple drugs including ARB and ACEI was associated with better control of BP. These drugs were underutilized in our patients because of cost as majority could not afford to sustain the therapy

In relation to aetiology, patients with PKD had highest incidence of resistant hypertension followed by CGN and hypertensive nephrosclerosis. This variability in pattern of BP control may be related to differences in pathogenic mechanisms involved in the genesis of HTN in these conditions. Occupation did not appear to influence pattern of BP control in this study. This is in accordance with related study that showed that socio-economic factors including level of education, insurance status and high income were not associated with increased risk of resistant hypertension after adjustment for demographic and clinical characteristics [16]. The foregoing suggests that physiologic factors may dominate socio-economic influence on BP control in CKD patients

In conclusion, resistant HTN was very high among our CKD patients using the recent Bp control guidelines. Ignorance, poverty and poor compliance to treatment among patients with CKD were associated with resistant HTN but occupation and social habits did not appear to have any influence on the pattern of BP control. We strongly advocate aggressive management including use of more than

three drugs at increasing doses especially in those having diagnosis of PKD and CGN. The need for health education with emphasis on regular clinic attendance and compliance with medication in a bid to forestall ESRD epidemic should be vigorously pursued.

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