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Antihypertensive Medication Prescribing Patterns and Predictors of Uncontrolled Blood Pressure among Patients with Chronic Kidney Disease and Co-morbid Hypertension in a Nigerian Tertiary Hospital

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Abstract

It is obvious in the literature that the majority of patients with chronic kidney disease (CKD) are concurrently inflicted with hypertension. Hypertension and CKD are both independent risk factors for cardiovascular disease and significantly contribute to disease progression. The study aimed to evaluate the antihypertensive medication prescribing patterns, and assess blood pressure (BP) control and the potential predictors of uncontrolled BP in the study population. This one-year retrospective cross-sectional study was conducted in the Nephrology unit of a tertiary teaching hospital in Maiduguri, Nigeria. This study enrolled adult patients with confirmed diagnoses of any CKD stage and co-morbid hypertension, who received care at the facility between August 2022 and July 2023. Relevant data were collected from 16 January to 15 February 2024 using a predesigned proforma. Study results were presented using descriptive statistics, while binary logistic regression analysis was used to explore the predictors of uncontrolled BP at $p < 0.05$ level of statistical significance. Among 300 patients with CKD and hypertension, 292 (97.5%) patients were prescribed multiple antihypertensive medications. Of 851 antihypertensive medications prescribed for the study population, diuretics (29.5%) mainly furosemide (23.0%) followed by calcium channel blockers [CCBs] (28.7%) were the most frequently prescribed. Furthermore, 213 (71.0%) patients had uncontrolled BP. Age 45 - 54 years (AOR = 4.01, 95 % CI 1.03 to 15.60, P = 0.045), and use of three antihypertensive medications (AOR = 7.08, 95% CI 1.33 to 37.55, P = 0.022), and four antihypertensive medications (AOR = 15.30, 95% CI 1.57 to 149.24, P = 0.019), respectively were significantly independently associated with uncontrolled BP. The study established that an overwhelming number of patients were prescribed multiple antihypertensive medications with diuretics and CCBs being the most common. Uncontrolled BP was highly prevalent in the study population and was significantly associated with middle age, and use of more than two antihypertensive medications. Therefore, interventions targeted at these factors are recommended to improve BP control in this high-risk group.

Key Words: *Chronic Kidney Disease, Hypertension, Antihypertensive Medications, Blood Pressure, Maiduguri*

Introduction

Chronic kidney disease (CKD) is a public health problem that affects 10–15% of the global population with increasing prevalence Coresh *et al*., 2007; Mills *et al*., 2015), due to rise in the most common risk factors, diabetes mellitus, and hypertension (The National Institute of Diabetes and Digestive and Kidney Disease, 2016). Chronic kidney disease is defined as the presence of decreased renal function (an estimated glomerular filtration rate [GFR] < 60 mL/min/1.73 m^2 (Baekken *et al*., 2008) or kidney damage (often indicated by the presence of proteinuria) for three months or more (Stevens and Levin, 2013). Hypertension is a common comorbidity in patients with CKD with a high prevalence of 60-90% (Muntner *et al*., 2010; Taler *et al*., 2013; Stevens and Levin, 2013). Hypertension can cause CKD as well result from it and enhances the progression of the disease (Bidani *et al*., 2004; Brantsma *et al*., 2006; Kestenbaum *et al*., 2008). Pathophysiology of hypertension in CKD is due to many factors involving the renin–angiotensin–aldosterone system, alterations in salt and water balance, and the sympathetic nervous system (Rahman 2020). As renal function declines, the incidence and severity of hypertension inversely increase (Muntner *et al*., 2010).

Hypertension and CKD are both independent risk factors for cardiovascular disease (CVD). The risks of CVD morbidity and mortality are substantially increased when both exist together (Gansevoort *et al.*, 2013). Therefore, blood pressure (BP) control in CKD is essential in preserving renal function, which may delay progression to end-stage renal disease (ESRD), and reduce the incidence of CVD in this patient population (Cheung *et al*., 2017). Hence, the use of antihypertensive agents as well as non-pharmacological measures to control hypertension in CKD is crucial (Peralta *et al*., 2005). Furthermore, antihypertensive medication combinations are often needed to optimize BP control in such patients (Sarafidis *et al*., 2007), however, the increased likelihood of polypharmacy with attendant adherence consequences should be taken into consideration.

Some studies have investigated BP control among patients with CKD and hypertension in Nigeria (Rafiu *et al*., 2011; Taslim and Oluwafemi, 2015; Okaka *et al*., 2017; Mamven *et al*., 2023). However, none of these studies attempted to evaluate the antihypertensive medication prescribing patterns in this group of patients. The evaluation of current drug management of hypertension in CKD is crucial for the effective management of the disease. The study's findings provide useful insights into the current management of hypertension and BP control in patients with CKD in the study setting. The study aimed to evaluate the antihypertensive medication prescribing patterns and assess BP control and the potential predictors of uncontrolled BP among patients with CKD in the study setting.

Methods

This one-year retrospective study was conducted in the Nephrology Unit of the University of Maiduguri Teaching Hospital, Maiduguri, Borno State. This hospital is currently about a 500-bed capacity tertiary teaching healthcare facility that serves as a

referral hospital for residents of Borno State and other neighbouring States including the neighbouring countries, such as Chad, Cameroon and Niger Republic.

The study population comprised patients with CKD and co-morbid hypertension who received care at the Nephrology Unit of the study hospital between August 2022 and November 2023. The minimum sample size of 286 required was calculated based on Yamane's (1967) sample size formula with a total population of 1000 CKD patients with hypertension in the facility and a 0.05 margin of error. This was rounded to 300 patients to boost the statistical power of the study.

The eligibility criteria were, being 18 years or above, confirmed diagnosis of all stages of CKD and co-morbid hypertension, having two documented BP values taken three months apart within the audited year, and received care in the Nephrology unit of the study hospital during the period under review.

The study protocol was reviewed and ethical approval was granted by the Research and Ethics Committee of the study hospital. Confidentiality of patients' information and anonymity of data collected were maintained throughout the study period.

The medical case files of study patients were randomly selected using systematic sampling with an interval of five. Data were collected from 16 January to 15 February 2024. The information collected included patients' sociodemographic data, such as age, sex, marital status, religion, educational level, and occupation. Blood pressure, creatinine values, and prescribed antihypertensive medications during the period under review were also collected.

In this study, hypertension was defined as systolic blood pressure (SBP) ≥ 140 mm Hg and/or diastolic blood pressure (DBP) ≥ 90 mm Hg and/or antihypertensive medication prescription. Blood pressure control was defined as SBP < 140 mm Hg and/or DBP < 90 mm Hg and was assessed using two BP values taken three months apart. The GFR was estimated with using CKD-EPI Creatinine 2021 Equation (https://www.kidney.org/professionals/gfr_ calculator). For binary logistics regression analysis, controlled and uncontrolled BP were assigned appropriate weights (controlled BP = 0, uncontrolled BP = 1).

The extracted data were first entered into a Microsoft Excel spreadsheet 2019, cleaned, coded, and transferred to Statistical Products and Services Solution (SPSS) version 25 (IBM Corporation) for Windows software for analyses. Study results were presented using descriptive statistics (means and standard deviations, frequencies, and percentages). Binary logistic regression analysis was used to explore the predictors of uncontrolled BP at the $P < 0.05$ level of statistical significance.

Results

The study enrolled 300 patients with CKD and hypertension as a comorbidity. Most of these patients were females (63.7%). The average age of the participants was 54.5±13.2 years, while those within 45 – 54 years (29.0%) dominated other age groups. A remarkable proportion of the participants was married (82.6%), while CKD stages 4 and 5 were dominant as presented in Table 1.

Overall, a total of 851 antihypertensive medications were encountered in the

prescriptions of participants during the period under review with diuretics (29.5%) as the highest prescribed class followed by calcium channel blockers [CCBs] (28.7%), and angiotensin receptor blockers [ARBs] (20.7%) (Figure 1). Furosemide (23.0%), and losartan (20.8%) were the most prescribed individual antihypertensive medications (Figure 2).

The analysis of single and combined antihypertensive medication prescriptions revealed that most patients received three (75.0%), and two (16.7%) antihypertensive medication combinations per encounter, respectively (Figure 3). Of 225 (75.0%) patients who received three antihypertensive medication prescriptions, most were prescribed ARB+CCB+Diuretic (35.0%) followed by ACEI+CCB+Diuretic (19.7%) (Figure 3). On the other hand, out of 50 (16.7%) patients who were prescribed two antihypertensive medications per prescription, most were prescribed ARB+CCB (9.0%), and ARB+Diuretic (2.3%) (Figure 3).

Of 300 patients included in the study, only 87 (29.0%) had controlled BP in the last three months as shown in Figure 4. The analysis for the predictors of uncontrolled BP showed that patients within the age group of 45-54 years had significantly highest odds of having uncontrolled BP (Adjusted odds ratio [AOR] 4.01, 95% CI 1.03-15.60, P = 0.045) compared to other age groups. Also, those who received three and four antihypertensive medications had significantly higher odds of having uncontrolled BP (AOR 7.08, 95% CI 1.33-37.55, P = 0.022, and AOR 15.30 95% CI 1.57-149.24, respectively) than those that received only one antihypertensive medication (Table 2).

Discussion

The use of multiple antihypertensive medications in this study is not surprising as the majority of the patients with CKD often have co-morbid hypertension, involving multiple pathways such as volume overload, vasoconstriction, and activation of the renin-angiotensin-aldosterone system. The same pattern has been reported in some previous studies (Muntner *et al*., 2010; Yan *et al*., 2018; Magvanjav *et al*., 2018). Overall, diuretics followed by CCBs were the most commonly prescribed antihypertensive medication classes in the present study. The high use of diuretics may be linked to a higher proportion of participants with ESRD which often is accompanied by fluid overload. Also, diuretics are an integral component of the management of hypertension in CKD because patients with CKD are particularly sensitive to sodium and water retention. In contrast, a previous study reported that only a few of the included patients were prescribed diuretics (Yan *et al*., 2018). While this previous study enrolled patients with predialysis CKD only, the present study enrolled those with both predialysis and dialysis CKD with a very high proportion of participants with ESRD. Hence, the very high prescriptions of diuretics in this study. In addition, CCBs are commonly used to manage hypertension in CKD due to their low risk of hyperkaleamia (Weinberg *et al*., 2009).

Furosemide, losartan, nifedipine, and lisinopril were the dominant prescribed individual antihypertensive medications

among the study participants. These are individual medications of typical primary antihypertensive classes (diuretics, ARBs, CCBs, and angiotensin-converting enzyme inhibitors [ACEIs]) commonly used in the management of hypertension in CKD. Apart from BP control in CKD, furosemide, a loop diuretic helps to reduce oedema and relieve pulmonary congestion (Arumugham *et al*., 2024). However, furosemide use in CKD requires careful monitoring due to potential side effects, such as volume depletion, electrolyte imbalances, worsening renal function, and ototoxicity (Khan *et al*., 2024). In addition, why losartan, an ARB is commonly used to control BP in CKD, it possesses renoprotective effect (Kobori *et al*., 2013), anti-fibrotic and anti-inflammatory effects (Kaschina *et al*., 2024), and lower risk of cough than ACEIs (Goyal *et al*., 2024). Nonetheless, regular monitoring of renal function and electrolytes is crucial during losartan therapy (Comparison chart, 2021). Similarly, nifedipine, a CCB, is frequently used in CKD for effective BP control because of its synergistic effects with other antihypertensive medications and cost-effectiveness (Saito *et al*., 2008). Lisinopril, an ACEI, is also commonly used to control BP in CKD. Its high use could also be due to other effects seen with losartan though it has a lower risk of hyperkaleamia than ARBs (Sadjadi *et al*., 2009). Nevertheless, it is also essential to monitor patients with CKD on lisinopril for potential side effects, such as hyperkalaemia, cough, angioedema, and worsening renal function (Comparison chart, 2021).

The high proportion of patients with uncontrolled BP may indicate suboptimal management of hypertension in these patients which might necessitate the use of multiple antihypertensive medications to achieve adequate BP control. This is in agreement with a previous Nigerian study (Mamven *et al*., 2023) and comparable with other studies conducted in Germany and Tanzania, respectively (Schneider *et al*., 2018; Katatwire and Meremo, 2023). On the contrary, a study conducted in the US reported a lower proportion of participants with uncontrolled BP (Muntner *et al*., 2010). These disparities could be due to differences in patients' specific factors, stages of CKD, geographic locations, healthcare systems of various countries, and care received by the patients.

As expected, middle age is a common time for uncontrolled BP. This could be due to a combination of factors, such as increased stress, weight gain, decreased physical activity, hormonal changes, and underlying medical conditions among others. The finding of the present study is in agreement with that of some previous Nigerian studies (Okaka *et al*., 2017; Mamven *et al*., 2023). Therefore, targeted interventions among this group of patients can help them achieve improved BP control. In contrast, 50 years of age or more was reported in Tanzania as a significant predictor of uncontrolled BP (Katatwire and Meremo, 2023). The disparities in results could be due to differences in the geographic locations, cultural and religious practices, quality of care, and genetic makeup of patients included in these studies.

Furthermore, antihypertensive pill burden can impact negatively on medication

adherence of patients with CKD. Therefore, prescribers need to simplify antihypertensive regimens wherever possible, with consideration given to the quantity. Again, patient disease education, and medication counselling from a clinical pharmacist to ensure active patient participation in care and regular drug therapy monitoring are recommended to promote antihypertensive medication adherence which could translate to improved BP control in this high-risk patient group.

The study had some limitations, which included a cross-sectional study design, the inability to assess antihypertensive medication adherence to establish its influence on BP control, and the collection of data from one hospital which may affect generalisation of the findings. Therefore, multi-centered longitudinal studies that include an additional objective such as, an assessment of antihypertensive medication adherence are recommended.

Conclusion

The study established that the majority of study patients were prescribed multiple antihypertensive medications with diuretics, mainly furosemide followed by CCBs ranking highest. Uncontrolled hypertension was highly prevalent and was associated with middle age, and using more than two antihypertensive medications. Therefore, interventions targeted at middle-aged patients and those using three or more antihypertensive medications are needed to improve the quality of care and optimize BP control among patients with CKD and co-morbid hypertension.

Declaration of interest:

The authors declared no conflict of interest.

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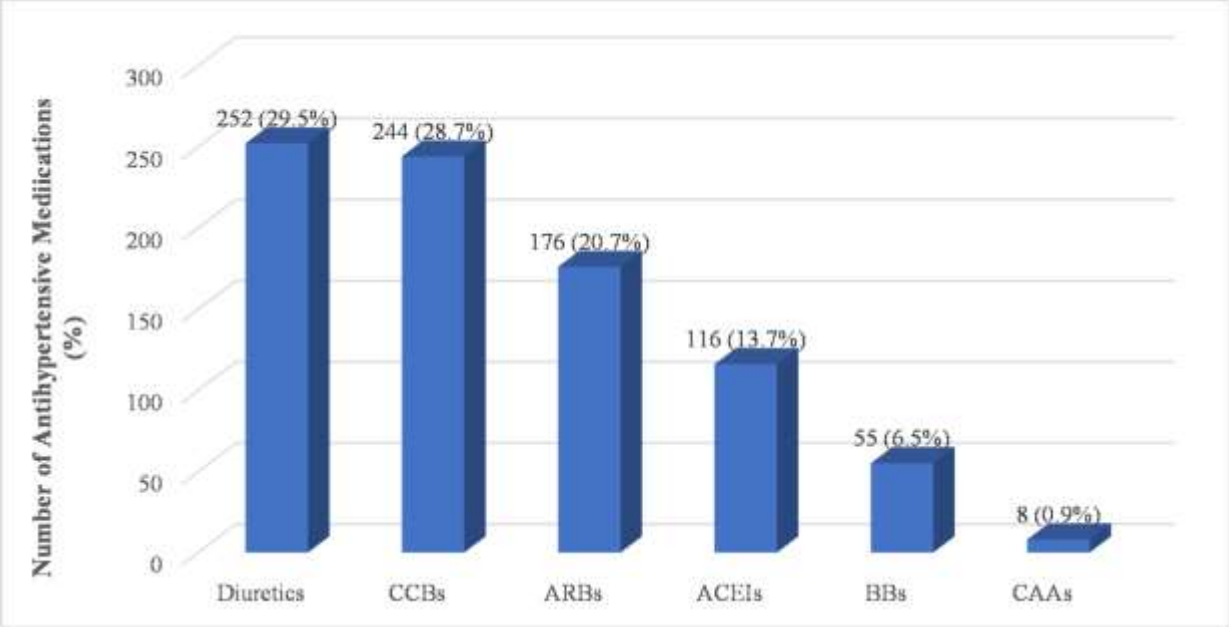
Table 1: Baseline Characteristics of the Study Population according to CKD Stage (N=300)

	CKD stages n (%)			
Variables	**2 N=1**	**3 N=2**	**4 N=22**	**5 N=275**
Sex				
Female	1(100.0)	-	15 (68.2)	175 (63.6)
Male	-	2 (100.0)	7 (31.8)	100 (36.4)
Age group (years)				
20-34	-	1 (50.0)	2 (9.1)	12 (4.4)
35-44	-	-	6 (27.3)	46 (16.7)
45-54	-	-	6 (27.3)	81 (29.5)
55-64	1 (100.0)	1 (50.0)	5 (22.7)	76 (27.6)
≥ 65	-	-	3 (13.6)	60 (21.8)
Marital status				
Divorced	-	-	1 (4.5)	10 (3.6)
Widowed	-	-	1 (4.5)	23 (8.4)
Single	-	-	1 (4.5)	16 (5.8)
Married	1 (100.0)	2 (100.0)	19 (86.4)	226 (82.2)
Religion				
Islam	-	1 (50.0)	20 (90.9)	210 (78.4)
Christianity	1 (100.0)	1 (50.0)	2 (9.1)	58 (21.6)
Educational levels				
None	-	-	8 (36.4)	57 (20.7)
Primary	-	-	1 (4.5)	16 (5.8)
Secondary	1 (100.0)	-	7 (31.8)	63 (22.9)
Tertiary	-	2 (100.0)	6 (27.3)	139 (50.6)
Occupation				
None	1 (100)	-	14 (63.6)	104 (37.8)
Retired	-	-	3 (13.6)	45 (16.4)
Civil servant	-	-	4 (18.2)	59 (21.5)
Business person	-	2 (100.0)	1 (4.5)	67 (24.3)
Number of antihypertensives				
1	-	-	3 (13.6)	5 (1.8)
2	1 (100.0)	-	6 (27.3)	43 (15.6)
3	-	2 (100.0)	10 (45.5)	213 (77.5)
4	-	-	3 (13.6)	14 (5.1)

Table 2: Predictors of Uncontrolled BP among the Study Patients

Variables	AOR (95% CI)	P value
Sex		
Female	1.00	
Male	1.05 (0.51-2.17)	0.902
Age (years)		
20-34	1.00	0.345
35-44	2.78 (0.71-10.87)	0.141
45-54	4.01 (1.03-15.60)	0.045*
55-64	3.58 (0.93-13.86)	0.065
≥ 65	3.31 (0.80-13.61)	0.097
Marital status		
Divorced	1.00 (0.22-4.49)	0.996
Widowed	0.63 (0.21-1.84)	0.394
Single	0.88 (0.23-3.10)	0.836
Married	1.00	
Religion		
Islam	1.00	
Christianity	0.77 (0.39-1.52)	0.450
Educational levels		
None	3.49 (1.38-8.85)	0.080
Primary	0.65 (0.20-2.07)	0.460
Secondary	1.65 (0.78-3.49)	0.188
Tertiary	1.00	
Occupation		
None	1.00	
Retired	2.22 (0.70-7.02)	0.173
Civil Servant	1.64 (0.65-4.14)	0.300
Business	1.14 (0.47-2.73)	0.778
Number of antihypertensive medications per prescription		
1	1.00	
2	3.31 (0.58-18.80)	0.177
3	7.08 (1.33-37.55)	0.022*
4	15.30 (1.57-149.24)	0.019*
End-stage-renal-disease (ESRD)		
No	1.75 (0.60-5.17)	0.309
Yes	1.00	0.213

**Significant at P < 0.05*



ARBs=Angiotensin receptor blockers; ACEIs=Angiotensin converting enzyme inhibitors; BBs=Betablockers; CAA=Centrally acting agents; CCBs=Calcium channel blockers

Figure 1: Overall, Classes of Antihypertensive Medications Prescribed (N=851)

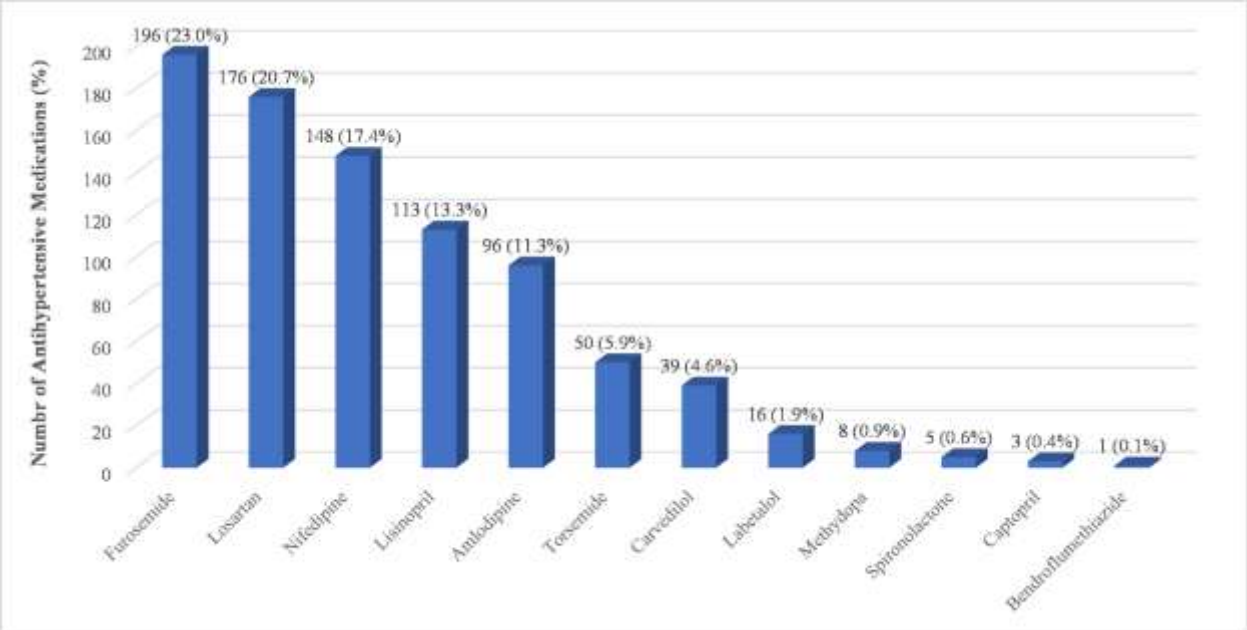
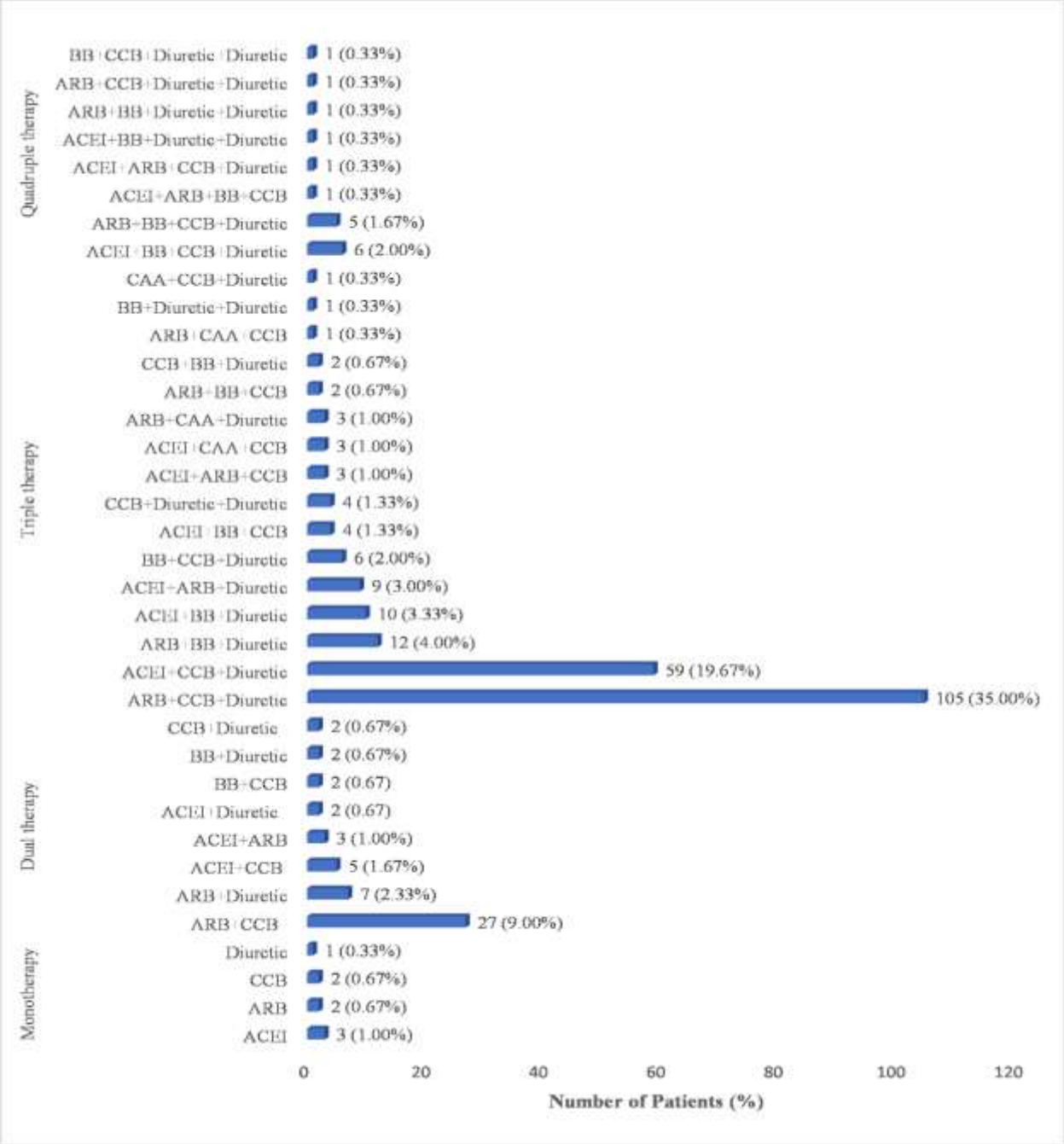


Figure 2: Overall, Individual Antihypertensive Medications Prescribed for the Study Population (N=851)



ARB=Angiotensin receptor blocker; ACEI=Angiotensin converting enzyme inhibitor; BB=Betablocker; CAA=Centrally acting agent; CCB=Calcium channel blocker

Figure 3: Prescribing Patterns based on the Number of Antihypertensive Medication(s) per Prescription (N=300)

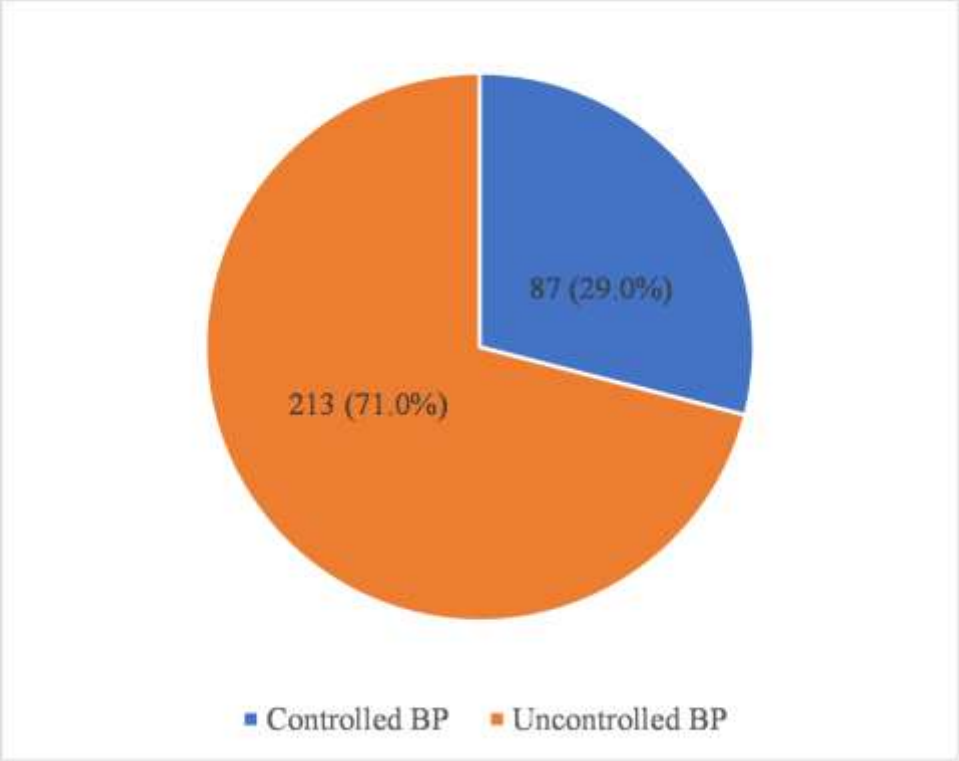


Figure 4: Blood Pressure Control in the Study Population