

# Effect of Calcium Channel Blockers on Quality of Life: An Observational Study Among Newly Diagnosed Hypertensive Patients

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**Abstract—Background:** The treatment of essential hypertension with Calcium channel blockers as first line therapy for newly diagnosed patients is the rise. The effect of CCB based therapies on quality of life among patients has produced conflicting results. It's known that this class of drugs have some distressing side effects which can negatively on quality of life, which has implication for adherence. The aim of this study therefore, is to evaluate their effect on health related quality of life (HRQoL) among newly diagnosed hypertensive patients. **Methods:** This was an eight week prospective observational study among newly diagnosed patients placed on six CCB based therapies. A total of 193 patients complete the eight domain SF-36 quality of life survey which was carried out at the point of diagnosis, fourth week and at the end of the study. The score for each domain was calculated according to standard procedure. The influence of reported side effects and demographic variables on HRQoL was assessed using either Students t test or Chi square as appropriate. P values  $\leq 0.05$  was considered statistically significant. **Result:** The effect of antihypertensive regimen(s) on HRQoL was mixed across the eight domains of the instrument. While there was insignificant effect on perception of "general health", the number of side effects and some demographic variables were associated with reduction to HRQoL scores. **Conclusion:** The effect of CCB based therapies on HRQoL was mixed, though there was no significant change in the overall patient's perception of their health status.

**Keywords—** Hypertension, Health related quality of life, Calcium channel blockers, side effects, SF-36, demographic variables, Amlodipine, Nifedipine.

## I. INTRODUCTION

Hypertension is an ever growing chronic disease of public health importance, reported to affect more than a third of all adult population globally [1]. The burden is believed to be rising more rapidly in low and middle income countries where access to effective treatment is limited [2]. The prevalence of hypertension in Nigeria has witnessed an upward trend over the last few decades [3, 4]. It is also estimated that undiagnosed hypertension remain endemic in 13-64% of adult population in the country [5, 6]. Evidence from randomized controlled clinical trials showed that effective treatment significantly reduce incidence of cardiovascular related morbidity and mortality, stroke and other heart related diseases [7, 8, 9].

Hypertension is generally asymptomatic which makes its early detection rather difficult until secondary complications have occurred. While most patients with undiagnosed hypertension usually feel well, however some studies suggest that it negatively affect health related quality of life (HRQoL) [10, 11], however this conclusion was not replicated in other studies [12]. One study suggested that the quality of life of hypertensive patients may even improve over time [13].

The relationship between psychosocial factors, hypertension and HRQoL remain unclear and literature evidence is often contradictory [14, 15, 16]. While some studies reported that at least 10% of hypertensive patients have underlying depressive symptoms [17], there is still controversy as to which one precede the other. Several studies have noted the

relationship between diagnosis of hypertension and stress [18, 19], which is believed to arise from increased need to use healthcare services [20]. Some epidemiological studies have reported that individuals with anxiety disorders have a higher risk of hypertension [21, 22, 23], other studies however reported the opposite effect [20]. There are also disputes to claims of influence of anxiety on hypertension or vice versa [24, 25], with one study which reported that anxiety decrease blood pressure among patients with essential hypertension [26].

The wide variability in HRQoL outcomes may be traceable to multiple factors including drugs used for treatment [27], study design, assessment tools and outcome measures [28]. Other influencing factors include obesity, target organ damage, side effects of medicines [29, 30, 31, 32, 33]. The definition of "HRQoL" used in various studies has also contributed to the often contrasting outcomes of studies [34, 35, 36]. Pharmacotherapy have demonstrated effectiveness in blood pressure control and prevent development of complications, however their side effect of drug(s) have been known to affect HRQoL [36].

The impact of antihypertensive regimen(s) on HRQoL have been reported in literature often with contrasting outcomes [37, 38, 39, 40]. The diversity of study designs and outcome measures has made it rather difficult to make valid inter-study comparisons and to draw general inferences [37]. In recent years, the use of Calcium channel blockers [CCB] as first line antihypertensive therapies has risen dramatically among newly diagnosed treatment naïve patients in developing countries [41, 42, 43]. This is largely because of their good safety profile,

single daily dosage, low cost and near absence of expensive long term routine monitoring of organs involved with their metabolism [44]. There is however limited literature on the impact of commonly prescribed CCBs on HRQoL in developing countries, where their prescription appear to be on the rise [42, 43]. The major objective of this study is to evaluate the effect of two commonly prescribed CCBs on HRQoL among newly diagnosed hypertensive patients.

## II. METHODS

**Settings:** The study was carried out in General Hospital north Bank Makurdi and Bethesda hospital Oju in Benue State Nigeria, Nigeria

**Study design:** This was a prospective observational study involving newly diagnosed hypertensive patients treated with Amlodipine, Nifedipine and their combinations with diuretic [Bendrofluthiazide] or an ACEI [Lisinopril].

### Eligibility criteria

- Newly diagnosed patients with hypertension  $\geq 140/90$  mm/Hg]
- Patients with no pre-existing chronic diseases
- Age  $\geq 30$  years
- Female must not be pregnant
- Patients who achieved 90% of adherence

**Sample size:** A total of 250 newly diagnosed hypertensive patients enrolled and 193 successfully completed the eight week study.

**Subject enrolment:** Patients were recruited from outpatient departments following diagnosis of essential hypertension and upon obtaining informed consent. Patients who were prescribed Amlodipine 10mg [AML], Nifedipine 20mg [NIF], Amlodipine 10mg + Bendrofluthiazide 5mg [AML+BDF], Nifedipine 20mg + Bendrofluthiazide 5mg [NIF+BDF], Amlodipine 10mg + Lisinopril 5mg [AML+LIS], and Nifedipine 20mg + Lisinopril 5mg [NIF+LIS]

**Quality of life assessment:** Health related quality of life was measured using SF-36 generic instrument for health outcomes. It consist of 36 items subdivided into eight domains and scored on a scale of 0 – 100, the higher the score the higher the quality of life [domain 1- physical functioning, domain 2 – physical health limitations, domain 3 – emotional health limitations, domain 4 – energy/fatigue, domain 5 – emotional wellbeing, domain 6 – social functioning, domain 7 – pain and domain 8 – general health]. Patients were surveyed upon enrolment and at the fourth and eight week of therapy and HRQoL scored according to standard procedure.

**Analysis:** The data was analyzed using SPSS 21 for descriptive and inferential statistics. The HRQoL scores were compared using student t test and P values  $\leq 0.05$  was considered statistically significant.

**ETHICAL APPROVAL:** The health research ethics committee of Benue State Ministry of Health gave approval for the study [MOH/STA/204/vol.1/118].

## III. RESULTS

The demographic data showed that more than half of all study participants were males [54.4%] and most were married

[64.7%] and reside in rural areas [62.2%]. Majority of them had no formal education [38.7%] and were mostly farmers [29.2%]. More than half of patients earn less than \$100 per month and about quarter of them earn less than the country’s minimum wage [24.4%] [Table 1].

The percentage of patients on antihypertensive regimens showed that monotherapies accounted for 26.9%, while combinations with BDF [43.6%] and Lisinopril [29.5%] accounted for remaining prescriptions [Figure 1]

The side effects commonly reported by patients included ankle edema (29%), Headaches (24.9%), GIT upset (11.9%), reduced libido (9.8%), dizziness (8.8%) and muscle cramps (7.8%). Patients on monotherapies and BDF appeared to experience more edema and headaches compared to Lisinopril treated groups (Figure 2).

Demographic variables had significant association with HRQoL except drug regimen. These associations was independent of specific CCB or add on medication prescribed for patients (Table 2)

TABLE 1: Demographic data

Variable	N (%)
<b>Gender</b>	
Male	105 [54.4]
Female	88 [45.6]
<b>Marital status</b>	
Single	22 [11.4]
Married	125 [64.7]
Divorced	26 [13.5]
Widowed	20 [10.4]
<b>Education</b>	
Illiterate	75 [38.7]
Primary	28 [14.1]
Secondary	49 [25.5]
Tertiary	41 [21.7]
<b>Residence</b>	
Urban	73 [37.8]
Rural	120 [62.2]
<b>Occupation</b>	
Farming	57 [29.5]
Civil service	49 [25.5]
Business	87 [45.1]
<b>Income [\$]</b>	
$\leq 40$	47 [24.4]
41 – 80	62 [32.1]
81- 120	39 [20.2]
121 – 160	23 [11.9]
161 – 200	14 [7.3]
$> 200$	8 [4.1]
<b>Age [yrs.]</b>	
30 – 40	21 [10.9]
41 – 50	47 [24.4]
51 – 60	67 [34.7]
61 – 70	45 [23.3]
$\geq 71$	13 [6.7]
<b>Mean age</b>	54.5 $\pm$ [10.9]

The HRQoL related to monotherapies was generally low to average except for “social functioning and pain” where the score was high. There was significant reduction in scores related to “physical health limitations” and “emotional wellbeing” [P= < 0.001], as well as patients perception of “general health” [P = < 0.001] [Table 3].

TABLE 2: HRQol and demographic variables

Variable	N [%]	X <sup>2</sup>	P value
<b>Gender</b>			
Male	105 [54.4]		
Female	88 [45.6]	26.06 <sup>a</sup>	<b>0.001</b>
<b>Age [yrs.]</b>			
< 50	58 [30.1]		
51 – 69	117 [60.6]		
≥ 70	18 [9.3]	25.78 <sup>a</sup>	<b>0.057</b>
<b>Education</b>			
Illiterate	70 [36.6]		
Primary	55 [28.5]		
Secondary	47 [24.3]		
Tertiary	21 [10.9]	37.34 <sup>a</sup>	<b>0.002</b>
<b>Weight [Kg]</b>			
50 – 60	47 [24.4]		
61 – 70	75 [38.9]		
71 – 80	41 [21.2]		
81 – 90	30 [15.5]	144.00 <sup>a</sup>	<b>0.000</b>
<b>BMI [kg/m<sup>2</sup>]</b>			
Healthy	75 [38.9]		
Overweight	80 [41.4]		
Obese	38 [19.7]	111.62 <sup>2</sup>	<b>0.000</b>
<b>SBP drop</b>			
≤ 10	26 [13.5]		
11 – 20	41 [21.2]		
21 – 30	58 [30.1]		
31 – 40	56 [29]		
41 – 50	12 [6.2]	144.00 <sup>a</sup>	<b>0.000</b>
<b>DBP drop</b>			
≤ 10	26 [13.5]		
11 – 20	129 [68.8]		
21 – 30	38 [19.7]		
<b>Side effects [N]</b>			
None	45 [23.3]		
One	115 [59.6]		
Two	28 [14.5]		
Three	5 [2.6]	32.59 <sup>a</sup>	<b>0.008</b>
<b>Drug regimen</b>			
AML	28 [14.5]		
NIF	24 [12.4]		
AML + BDF	42 [21.8]		
NIF + BDF	42 [21.8]		
AML + LIS	35 [18.1]		
NIF + LIS	22 [11.4]	6.00 <sup>a</sup>	1.000

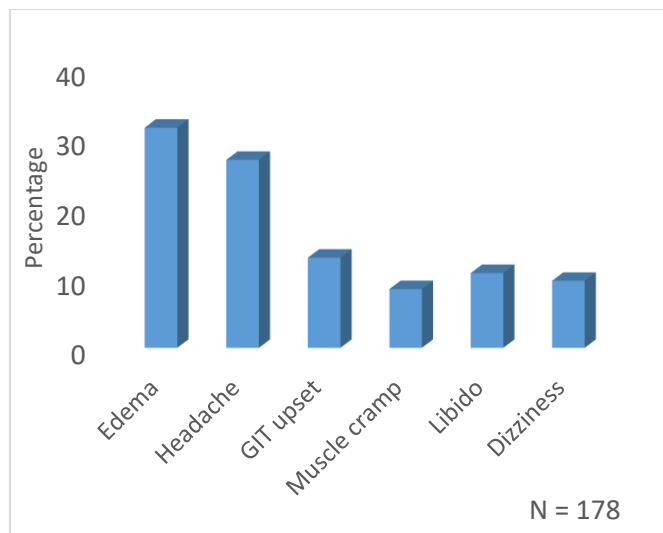


Figure 2

TABLE 3: HRQol associated with monotherapies

	Pretest	Posttest	TS	P value
<b>Domain 1</b>				
Amlodipine	38.6	34.7	1.226	0.206
Nifedipine	34.1	32.1	1.606	0.109
<b>P value</b>	0.104	0.118		
<b>Domain 2</b>				
Amlodipine	33.8	23.5	5.760	<b>0.001</b> ↓
Nifedipine	46.8	16.4	17.000	<b>0.001</b> ↓
<b>P value</b>	<b>0.001</b>	<b>0.001</b>		
<b>Domain 3</b>				
Amlodipine	31.4	33.3	1.195	0.233
Nifedipine	31.2	34.4	2.013	<b>0.045</b> ↑
<b>P value</b>	0.899	0.489		
<b>Domain 4</b>				
Amlodipine	59.3	58.1	1.382	0.168
Nifedipine	59.8	58.5	1.497	0.135
<b>P value</b>	0.565	0.565		
<b>Domain 5</b>				
Amlodipine	56.7	74.9	17.408	<b>0.001</b> ↑
Nifedipine	74.2	75.2	0.956	0.339
<b>P value</b>	<b>0.001</b>	0.774		
<b>Domain 6</b>				
Amlodipine	71.7	69.5	1.524	0.128
Nifedipine	71.5	67.6	2.701	<b>0.007</b> ↓
<b>P value</b>	0.889	0.189		
<b>Domain 7</b>				
Amlodipine	79.1	78.3	0.747	0.455
Nifedipine	78.5	77.3	1.121	0.263
<b>P value</b>	0.567	0.351		
<b>Domain 8</b>				
Amlodipine	59.9	64.4	3.574	<b>0.001</b> ↑
Nifedipine	59.2	64.1	3.892	<b>0.001</b> ↑
<b>P value</b>	0.578	0.812		

Key: ↑ - increase, ↓ - decrease

The same pattern of HRQol was observed with the addition of BDF except for “emotional wellbeing, social functioning and pain”. While Nifedipine group reported significant decline in quality of life [emotional wellbeing and energy/fatigue (P = <0.001)], Amlodipine group had decline with “physical health limitations” [P = 0.005]. Overall, there was no significant change in perception of “general health” among patients on BDF containing combination therapies [Table 4].

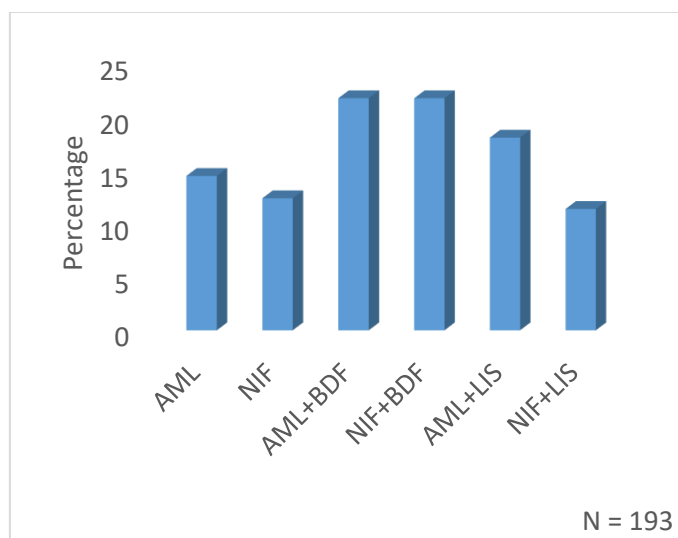


Figure 1: Distribution of treatment groups

TABLE 4: HRQoL with CCB/BDF therapy

	Pretest	Posttest	TS	P value
<b>Domain 1</b>				
AML+BDF	49.4	48.1	0.783	0.434
NIF+BDF	46.1	44.6	0.904	0.367
<b>P value</b>	<b>0.047</b>	0.229		
<b>Domain 2</b>				
AML+BDF	32.7	27.6	2.852	<b>0.005</b> ↓
NIF+BDF	32.1	28.8	1.510	0.132
<b>P value</b>	0.737	0.503		
<b>Domain 3</b>				
AML+BDF	36.4	36.8	0.252	0.802
NIF+BDF	32.6	34.8	1.384	0.167
<b>P value</b>	<b>0.017</b>	0.209		
<b>Domain 4</b>				
AML+BDF	56.9	57.5	0.691	0.491
NIF+BDF	63.7	56.5	8.290	<b>0.001</b> ↓
<b>P value</b>	<b>0.001</b>	0.250		
<b>Domain 5</b>				
AML+BDF	77.5	77.2	0.267	0.774
NIF+BDF	76.7	71.1	5.356	<b>0.001</b> ↓
<b>P value</b>	0.445	<b>0.001</b>		
<b>Domain 6</b>				
AML+BDF	73.7	76.3	1.801	0.073
NIF+BDF	75.1	77.2	1.455	0.147
<b>P value</b>	0.333	0.533		
<b>Domain 7</b>				
AML+BDF	78.8	78.7	0.093	0.926
NIF+BDF	78.8	78.7	0.093	0.926
<b>P value</b>	0.779	0.192		
<b>Domain 8</b>				
AML+BDF	63.3	65.5	1.748	0.081
NIF+BDF	62.9	63.8	0.475	0.475
<b>P value</b>	0.791	0.178		

Key: ↑ - increase, ↓ - decrease, TS - t score

TABLE 5: HRQoL and CCB/Lisinopril therapy

	Pretest	Posttest	TS	P value
<b>Domain 1</b>				
AML+LIS	42.1	46.9	88.210	<b>0.001</b> ↑
NIF+LIS	47.2	55.2	4.821	<b>&lt;0.001</b> ↑
<b>P value</b>	<b>0.002</b>	<b>0.001</b>		
<b>Domain 2</b>				
AML+LIS	39.7	22.1	9.283	<b>&lt;0.001</b> ↓
NIF+LIS	37.2	23.1	7.885	<b>&lt;0.001</b> ↓
<b>P value</b>	0.163	0.576		
<b>Domain 3</b>				
AML+LIS	44.1	33.3	6.794	<b>&lt;0.001</b> ↓
NIF+LIS	46.9	32.1	9.310	<b>&lt;0.001</b> ↓
<b>P value</b>	<b>0.012</b>	0.269		
<b>Domain 4</b>				
AML+LIS	63.7	56.5	8.290	<b>&lt;0.001</b> ↓
NIF+LIS	56.9	55.3	1.842	0.066
<b>P value</b>	<b>0.001</b>	0.168		
<b>Domain 5</b>				
AML+LIS	75.9	77.6	1.626	0.105
NIF+LIS	78.4	79.3	0.861	0.389
<b>P value</b>	<b>0.017</b>	0.105		
<b>Domain 6</b>				
AML+LIS	81.9	84.9	2.078	<b>0.038</b> ↑
NIF+LIS	83.8	86.1	1.593	0.112
<b>P value</b>	0.189	0.406		
<b>Domain 7</b>				
AML+LIS	87.6	88.6	0.934	0.351
NIF+LIS	91.2	90.6	0.560	0.575
<b>P value</b>	<b>0.001</b>	0.033		
<b>Domain 8</b>				
AML+LIS	64.4	65.1	0.556	0.578

NIF+LIS	67.6	67.8	0.159	0.874
<b>P value</b>	<b>0.011</b>	<b>0.033</b>		

Key: ↑ - increase, ↓ - decrease, TS - t score

Among patients on CCB/Lisinopril, there was significant decline in “Physical health, emotional health” domains [P = <0.001]. While HRQoL was similar to other treatment groups, “emotional wellbeing, social functioning, physical functioning and pain” domain scores improved significantly from baseline [P = <0.001]. Overall, there was little change in perception of “general health” among patients [Table 5]

#### IV. DISCUSSION

The influence of antihypertensive therapies on HRQoL among newly diagnosed hypertensive patients has received little investigation among patients in developing countries. While the blood pressure lowering effect of antihypertensives is well documented with either monotherapies and/or combination therapies, there is little information on the impact of drug therapy on the quality of their daily lives. There have been literature evidence of the effect of different antihypertensive regimen(s) on HRQoL often with contrasting outcomes. The result of this study generally showed majority of patients had low to moderate HRQoL across all domains except for “social functioning and pain”. The little improvement in HRQoL among many study participants suggest that their quality of life may be related to other challenges including mental health issues, economic challenges, social and psychological issues.

Some of the outcomes reported ranged from improvement [13, 45, 46], negative effect [38, 47] to insignificant influence on quality of life [48]. The results of this study showed that Amlodipine and Nifedipine monotherapies significantly limit “physical functioning”, while there was mixed results with other domains. The “general health” perception significantly improved during the therapy. While common side effects of CCBS [Headaches, constipation, facial flushing and pedal edema] can negatively affect patient reported HRQoL, it appears that even when/if they occurred, they had little effect patient’s perception of their general health. This may be partly due to emotional relief from knowledge and information obtained from counseling following diagnosis and free treatment. Patients who are well educated about their disease are more likely to have a positive attitude towards treatment and participation in long term management, hence the high score for quality of life.

The combination of the CCBs with diuretic appeared to produce inconsistent but significant reductions in HRQoL in at least three domains [physical health limitations, energy/fatigue and emotional wellbeing], This result contrast with outcomes of a previous study, possibly because of differences in the incidence and severity of common side effects of diuretic therapy, particularly when given in high doses [49]. While side effects were infrequently reported, their severity was not enough to negatively impact on perceived HRQoL. In addition, medication counseling probably helped patients to become aware of these possible side effect, which may help to lower distress if they occur.

The addition of an ACEI [Lisinopril] to CCBs significantly improved the perception of “physical functioning” among patients, though reductions in “physical and emotion health” domains was observed. This was comparable to outcomes from similar studies [38, 45], though a contrasting result was reported in a study [50]. One of the possible reasons for improved physical functioning may be related to the ability of ACEIs to reduce the incidence and severity of ankle edema which is a common side effect of CCB therapy [51].

Drug combination therapies are often associated with increased incidence and severity of side effects which can have negative effect on HRQoL of patients. The often contrasting effect of Amlodipine and Nifedipine based antihypertensive regimen(s) on HRQoL has been previously reported [52] While there is no clinical explanation regarding the wide variations in the effect of drugs from the same class on HRQoL, there have been suggestions that the observation may be related to differences in pharmacokinetic profiles and associated adverse drug reactions. Generally, side effect of antihypertensive medications have been associated with reduced quality of life similar to the results of this study [53, 54]

The HRQoL of hypertensive patients vary widely between studies [30, 55, 56, 57] largely because of differences in settings and assessment tools. In addition, HRQoL is influenced by demographic variables such as gender [58, 59], educational status [60], age [61, 62], body mass index [63, 64, 65], weight [66, 67, 68] and SBP/DBP variability [69, 70] similar to the findings of this study. Furthermore, quality of life is also affected by complex factors acting alone and/in combination with social, economic, psychological and medical factors [32, 71, 72]. In addition to these, non-pharmacological interventions such as increased physical activity [73, 74], education and family support either alone or in conjunction with drug therapy have been shown to have beneficial effect on HRQoL [75, 76, 77]. While these interventions alone may produce some benefits, they also offer opportunities for ongoing pharmaceutical care support [78], promotion of better clinical outcomes, improved adherence as well as achieve and sustain high quality of life even with chronic medication therapy.

#### V. CONCLUSION

The HRQoL is not significantly affected by CCB based antihypertensive therapies. The often mixed results of domains affected presents a point of attention during medication counseling, therapy changes or dose adjustments.

**STUDY LIMITATIONS:** The side effect of drug(s) reported by patients could not be independently verified. Sociocultural factors may influence reporting of effect on libido.

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