

EVALUATION OF NONADHERENCE AND ITS DETERMINANTS AMONG PATIENTS ON LONG-TERM ANTIHYPERTENSIVE THERAPY AT A TERTIARY HEALTHCARE FACILITY IN MAKURDI, NORTH CENTRAL NIGERIA.

*Chiomma Catherine Idoko and Paul Otor Onah

Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmacy, University of Benin, Benin City, Edo State, Nigeria.

*Corresponding Author's E-mail: pinkjewelone@yahoo.co.uk

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Abstract

Background: Adherence to long-term antihypertensive therapy is a basic requirement for blood pressure control and prevention of secondary complications. Several studies have reported highly variable levels of non-adherence among patients on long-term medication therapy. Therefore, the major aim of this study is to assess adherence and its determinants among patients on long-term antihypertensive therapy.

Methods: This was a six-month prospective study among a cohort of 125 eligible patients on therapy for at least four months. The enrollees included males (65.6%) and females (34.4%) with a mean age of 59.1 ± 11.8 years. Data on medications, comorbidities, duration of therapy and complications was obtained from medical records. Adherence was measured using the Morisky medication adherence scale questionnaire (MMAS-8) and scores were calculated accordingly. The association between sociodemographic variables and adherence was carried out using the Chi-square test and Fisher's exact test as appropriate and P values ≤ 0.05 were considered statistically significant.

Results: The results showed that the percentage of patients with adequate adherence was 47.3% [MMAS score ≥ 6] compared to those with low adherence [52.7%]. Demographic variables like age [$p = 0.011$], educational level [$p = 0.038$], marital status [$p \leq 0.001$], comorbidity [$p \leq 0.001$], place of residence [$p = 0.008$] and frequency of physician consultations [$p \leq 0.001$] were associated with non-adherence. There is a need for pharmacists to provide solicited and unsolicited adherence support as part of their regular pharmaceutical care services to patients on long-term antihypertensive therapy.

Conclusion: The level of satisfactory adherence to antihypertensive medications was less than half of the subjects enrolled in the study. Adherence was found to be associated with the presence of comorbidity, marital status, age, educational status, rural/urban residence, and frequency of physician consultations. Poor adherence poses a significant increase in the risk of stroke and other complications.

Keywords: Adherence, antihypertensives, demographic variables, association, determinants

Introduction

Hypertension is a major public health challenge globally and it is directly responsible for cardiovascular and renal diseases as well as stroke, all of which significantly increase the risk of premature mortality [1,2]. The global prevalence of hypertension was estimated to be 22% of the adult population, although recent projections are much higher in developing countries. The global prevalence of hypertension is estimated to be about 1.13 billion people of which two-thirds live in low- and middle-income countries [2]. Hypertension is increasingly becoming a contributory factor to premature mortality; a recent estimate indicates that up to 9 million deaths were directly attributable to hypertension and its complications [2]. In Sub-Saharan Africa (SSA), the prevalence of hypertension among the adult population vary between 6 and 48% and recent projections indicate that cases will rise to about 68% by 2025 [3,5]. A systematic review and meta-analysis of recent literature however revealed a higher prevalence of between 14.7 – 69% in SSA [6]. In Nigeria, cases of hypertension have been steadily rising over the last few decades [7,8], and recent projections showed that it is found in 13 – 64% of the adult population [9,10]. Hypertension as a chronic disease that require sustained blood pressure control if the reduction of secondary complications is to be achieved on the long term [11,12]. It is therefore important that patients adhere to treatment over the course of lifetime therapy.

Adherence which is defined as the extent to which patients take their medications as prescribed by their healthcare providers [12] is critical to effective management of hypertension like in all chronic diseases [13-15]. Medication non-adherence is a major public health challenge to effectiveness of pharmacotherapy of chronic diseases including hypertension [16,17]. There is a direct relationship between medication non-adherence and uncontrolled hypertension [18,19]. Literature and clinical evidence have shown that even a 10mm/Hg reduction in systolic blood pressure (SBP) significantly reduce the risk of major cardiovascular events by 20%, coronary heart diseases by 17%, strokes by 27%, heart failure by 28% and overall mortality rate by 13% [20]. Non-adherence is reported to be responsible for 33 – 69% of avoidable hospitalizations in the United States [21], longer hospitalizations [22] and increased mortality among patients with chronic diseases [23].

Many adherence studies have reported contrasting results partly because of differences in study setting, population group, disease condition, outcome measure used and assessment methods employed in the study [24-29]. Several studies in sub-Saharan Africa (SSA) have reported non-adherence rates of between 30 – 49%, although comparatively lower and higher rates have also been reported. For instance, a recent review of non-adherence studies has shown varying rates of non-adherence in countries such as Ethiopia 35.4% [30,31], Tanzania 44% [32] and Nigeria 47.9-49% [33,34], however, higher rates have been reported in some other SSA countries [18,35,36]. In high-income countries, non-adherence is reported to be generally lower compared to low- and middle-income countries [37,38]. Many studies that used questionnaire-based methods, reported higher adherence rates compared to those that employed biochemical methods, which frequently reported lower rates [29,39,40].

Several factors have been frequently reported to promote non-adherence among patients on long-term medication therapy, some of which include polypharmacy [29,41,43], advanced age [44,45], educational attainment [46], presence of comorbidities [45], socioeconomic factors [47,48], rural residence [49], duration of therapy [50,51] and provider relationship with patients, [11] to mention but a few. The major aim of this study is therefore to assess adherence among patients and its determinants among patients on long-term antihypertensive therapy.

Methods

Setting

The study setting, Federal Medical Centre Makurdi, Benue State, is a 400-bed federal government-owned tertiary healthcare facility. The facility offer a range of healthcare services in medical specialties including general medicine, radiology, cardiology, ophthalmology, Obstetrics/gynaecology, orthopaedics, dental and psychiatry.

Study design

This was a prospective observational cohort study carried out among patients who have been on antihypertensive therapy for at least four months. The recruited patients were followed up for a duration of six months and their medication adherence evaluation carried out upon enrolment and at every eight weeks.

Sample size

The sample size was calculated using an Open EPI calculator at 95% confidence interval, power 80% which gave a sample size of 98, although 125 subjects completed the study and data used for analysis.

Sampling technique

A convenience sampling technique was used for the study. Patients who provided consent for participation were enrolled on the study during regular physician consultations.

Eligibility criteria

- Patients must be 30 years and above.
- They must be on antihypertensive therapy for at least four months before enrolment.
- Women participants must not be pregnant.
- The patient must have attended at least three clinic visits within the study period.

Outcome variables

Patients at the point of enrolment into the study should have blood pressure above the target of 140/90 mm/Hg on the day of enrolment. The major outcome variables include the achievement of a target blood pressure of $\leq 140/90$ mm/Hg and an adequate adherence level set at MMAS-8 score of ≥ 6 at the end of the study period.

Enrolment

Eligible patients were enrolled during regular physician consultations upon filling out a consent form. A total of 125 patients completed the study after removing those who were lost to follow-up or failed to make up to three consultations within the study period.

MMAS-8 questionnaire

This instrument consists of eight items covering reason(s) for missing medication (items 1- 7) and frequency of missing medications (item 8). It has been used with high reliability in several studies in Nigeria^(52 - 54) to measure adherence. It is used to measure adherence based on factors such as carelessness, forgetfulness, and stoppage of medication [items 1 – 7] with a yes or no answer, while the eighth item is on a five-point Likert scale. The responses of items 1 – 7 were scored as 0 or 1 for yes or no except for item 5 which was reversed before scoring. The first question on item 8 was scored as 1 while the other questions were scored zero. The scores were totalled, and the results ranged between 0 and 8, where the total score of 8, $6 < 8$ and ≤ 5 were considered high, medium, and low respectively.

Data collection

Demographic data, blood pressure, medication(s), duration of therapy, place of residence and comorbidity were obtained upon enrolment, while blood pressure measurement was done during each physician consultation. The MMAS-8 questionnaire was also self-administered on the day of enrolment, eight weeks and at the end of the study period.

Data analysis

The data was recorded in Microsoft Excel, cleaned, and loaded into SPSS version 21 (IBM Corp, Armonk, NY, USA). Data analysis was carried out using descriptive (percentage) and inferential statistics (Chi-square or Fisher's exact test) for association between adherence and demographic variables. P values ≤ 0.05 were considered statistically significant. Adherence was computed from the sum of scores according to standard procedures⁽⁵⁵⁾. Adherence scores from the three surveys were averaged and expressed as a percentage of patients who were adherent or non-adherent. Patients who scored 6 and above were considered adherent and those below were non-adherent.

Ethical approval

Ethical approval was obtained from the human research ethics committee of the Federal Medical Centre, Makurdi (*Ref No: FMH/FMC/MED.108/Vol. I*).

Results

Demographic data showed that males constituted about two-thirds of patients [65.6%] and most were illiterate [46.4%]. The major occupations were farming (25.6%), and civil service (20.8%), while others were either self-employed (16.8%) or unemployed (19.2%). The majority of patients were married (68.8%) and reside in urban areas (64.8%). The mean age of patients was 59.1 ± 11.8 years [Table 1].

Table 1: Demographic data

Variable	Number [%]
Gender	
Male	82 [65.6]
Female	43 [34.4]
Education	

Illiterate	58 [46.4]
Primary	21 [16.8]
Secondary	9 [7.2]
Tertiary	37 [29.6]
Occupation	
Farming	32 [25.6]
Civil service	26 [20.8]
Self-employed	21 [16.8]
Unemployed	24 [19.2]
Housewife	5 [4]
Retired	17 [13.6]
Marital status	
Married	86 [68.8]
Divorced	2 [1.6]
Widowed	35 [28]
Separated	2 [1.6]
Residence	
Urban	81 [64.8]
Rural	44 [35.2]
Age [yrs.]	
≤ 30 – 40	9 [7.2]
41 – 50	20 [16]
51 – 60	33 [26.4]
61 – 70	43 [34.4]
≥ 71	20 [16]
Mean age	59.1 ± 11.8

There was an association between age [P=0.011], marital status [P=<0.001], education [P=0.038], place of residence [P=0.008], comorbidity [P=<0.001], number of drugs [P=0.025] and frequency of hospital visits [P=<0.001] and nonadherence to antihypertensive therapy. Other sociodemographic variables like gender, occupation, length of therapy, drug formulation, and distance to hospital have an insignificant association with adherence [Table 2]

Table 2: Adherence and association with demographic factors

Variable	Non-adherent [%]	Adherent [%]	X ² value	P value
Gender				
Male	27 [21.6]	55 [44]		
Female	9 [7.2]	34 [27.2]		0.213*
Age [yrs.]				
≤ 40	2 [1.6]	2 [1.6]		
41 – 50	9 [7.2]	3 [2.4]		
51 – 60	10 [8]	26 [20.8]		
61 – 70	8 [6.4]	29 [23.2]		
≥ 71	11 [8.8]	25 [20]	12.953 ^a	0.011**
Occupation				
Farming	12 [9.6]	22 [17.6]		
Civil service	16 [12.8]	10 [8]		
Self-employed	7 [5.6]	14 [11.2]		
Unemployed	10 [8]	6 [4.8]		
Housewife	6 [4.8]	12 [9.6]		
Retired	4 [3.2]	6 [4.8]	8.380 ^a	0.136**
Marital status				
Married	9 [7.2]	72 [57.6]		
Divorced	5 [4]	2 [1.6]		
Widowed	18 [14.4]	11 [8.8]		

Separated	3 [2.4]	5 [4]	35.064 ^a	<0.001**
Education				
Illiterate	44 [35.2]	14 [11.2]		
Primary	17 [13.6]	4 [3.2]		
Secondary	3 [2.4]	6 [4.8]		
Tertiary	24 [19.2]	13 [10.4]	8.431 ^a	0.038**
Residence				
Urban	7 [5.6]	74 [59.2]		
Rural	12 [9.5]	32 [25.6]		0.008*
Comorbidity				
Yes	22[17.6]	33[26.4]		
No	6 [4.8]	64 [51.2]		<0.001*
Duration of therapy [yrs.]				
≤ 5	8 [6.4]	42 [33.6]		
6 – 10	10 [8]	25 [20]		
11 – 15	5 [4]	16 [12.8]		
16 – 20	6 [4.8]	13 [10.4]	2.775 ^a	0.428**
Distance to facility [km]				
≤ 20	4 [3.2]	38 [30.4]		
20 – 40	12 [9.6]	21 [16.8]		
41 – 60	8 [6.4]	13 [10.4]		
61 – 80	5 [4]	12 [9.6]		
81 – 100	2 [1.6]	6 [4.8]		
>100	2 [1.6]	2 [1.6]	10.555 ^a	0.061**
Frequency of consultations				
Regular	18 [14.4]	82 [65.6]		
Occasional	7 [5.6]	3 [2.4]		
Seldom	10 [8]	5 [4]	24.835 ^a	<0.001**

Key: * - Fishers exact test, ** - Chi-Square test

The use of monotherapies, combination therapies and different drug formulations was not associated with non-adherence [Table 3].

Table 3: Adherence and medication factors

Variable	Non-adherent [%]	Adherent [%]	X ² score	P value
Drug formulation [n=125]				
Single drug	30 [24]	57 [45.6]		
Fixed dose combination	9 [7.2]	29 [23.2]		0.295*
Monotherapies [n=79]				
Lisinopril	8 [10.1]	32 [40.5]		
Losartan	3 [3.8]	6 [7.6]		
Telmisartan	5 [6.3]	3 [3.8]		
Amlodipine	2 [2.5]	3 [3.8]		
Felodipine	2 [2.5]	5 [6.3]		
Nebivolol	3 [3.8]	2 [2.5]		
Methyldopa	2 [2.5]	3 [3.8]	8.257 ^a	0.220**
Combination therapies [n=46]				
Amlodipine + Lisinopril	4 [8.8]	3 [6.5]		
Nifedipine + Lisinopril	6 [3.1]	3 [6.5]		
Amlodipine + Losartan	10 [21.7]	5 [10.9]		
Telmisartan + Hydrochlorothiazide	2 [4.3]	2 [4.3]		
Amiloride + Triamterene	8 [17.4]	3 [6.5]	0.905 ^a	0.924**

Key: * - Fishers exact test, ** - Chi Square test

The patients who were adherent constituted 47.3% [MMAS-8 score ≥ 6] while the non-adherent represented 52.3% of the study population [Figure 1]

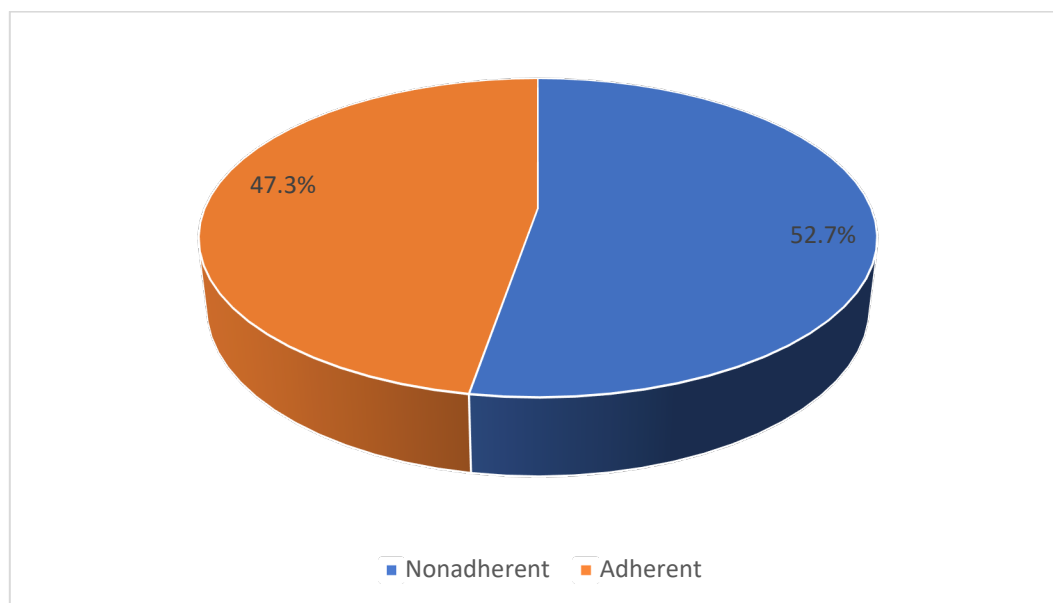


Figure 1: Level of adherence ($n=125$)

Discussion

Chronic medication therapy generally is challenged by non-adherence which is reported to be partly responsible for poor clinical outcomes. The result of non-adherence in this study was comparable to several previous studies [50,56-58], although higher values have been reported in some developing countries [59]. In sub-Saharan Africa, studies have also consistently reported high levels of non-adherence comparable to the findings of this study [49,60-62]. This contrasts with studies from high-income countries where non-adherence is considerably lower [37,63]. A recent systematic review and meta-analysis of studies in SSA indicated that adherence is generally lower than in Asian, European, and American patients [37]. However, some studies in African countries have however reported high levels of adherence comparable to developed countries [64-67].

This high level of non-adherence among patients on long-term antihypertensive therapy may be reflective of multiple factors; either acting alone or in a complex ways to negatively influence attitudes towards therapy. Some of these factors include socioeconomic, patient, therapy, and health system-related factors. This study showed that age, marital status, education, urban residence, presence of comorbidity, number of drugs and frequency of medical consultations are significantly associated with non-adherence [68,69]. While the relationship between gender and non-adherence has been reported to be significant [70,71], this conclusion is inconsistent with the findings of this study [57,58].

The association between advancing age and non-adherence have been reported [69,72-75], although contrary findings have also been reported [76]. It has been observed that patients with multiple morbidities commonly associated with advancing age would sometimes require complex drug treatments that create confusing dosing schedules which will cause unintentional forgetfulness to take medication. This can be compounded by side effect(s) of drugs and high cost of medications which reduce affordability of drugs. For instance, comorbidity with diabetes mellitus was found to be associated with non-adherence due to high medication costs [68,77], although contrasting results have been reported [49].

The duration of antihypertensive therapy has been previously linked to non-adherence [50,51] which is in contrast to this study finding [11,78]. While long-term medication therapy is believed to have the potential to improve knowledge of disease expected to subsequently improve adherence, the effect of knowledge and adherence has not consistently shown a linear relationship. The place of residence has shown a significant association with non-adherence [79,80], although this has not been demonstrated in studies

carried out in residents of urban and rural areas. It is commonly believed that because urban dwellers typically have better access to health services and medicines, they are likely to be more adherent compared to those in rural areas who have to travel long distances to access medications.

There appear to be a significant relationship between marital status and adherence in this study [57,71], however, there is inconsistency with findings of similar studies [69,78]. This association is reportedly linked to spousal and family influence and authority within the family structure [11]. The level of patient education attainment affect how well patients understand health problems and their involvement in healthcare decision. While this study showed that education has significant association with adherence [72,81], other studies have reported contrasting results [11,70,76]. For instance, some studies reported that illiterate and elementary-grade patients are less likely to achieve adequate adherence [57,69], compared to those with high-level education. This may be due to the fact that not only do they have high health literacy, but are more likely to utilize medical information which is needed for long-term adherence.

The inverse relationship between drug regimens and adherence found in this study have been previously reported [29,43]. It clearly indicate that adherence tends to reduce with increasing burden of medications [75,82], however this is not a consistent finding from other studies [73,74,78]. This can be understood from the fact that the more medications a patient takes, the more the incidence and severity of side effects which are known to negatively affect adherence [69,76]. The distance a patient must travel to receive care has shown no significant association with adherence consistent with previous studies [11,71], although contrasting findings have been reported in literature [30]. One of the possible explanations for this lack of association is that the majority of enrolees reside within the city and nearby communities which may have encouraged attendance to physician appointment and which may have robbed off on adherence.

Conclusion

Non-adherence is a drug therapy problem that requires proactive intervention by clinical pharmacists during regular pharmaceutical care services. It is also important to consider providing unsolicited medication adherence support to all patients on long-term antihypertensive therapy.

Strengths/Limitations of the study

This study highlights the ongoing challenge of adherence to medications among patients on chronic medication therapy. The level of non-adherence to antihypertensive medications can be a pointer to a greater risk of secondary complications. The major limitations were the small sample size and follow-up losses of enrolees which can affect the findings of the study.

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Conflict of interest

The authors declare no conflict of interest.

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