Adherence to statin therapy among patients with hypercholesterolemia in a tertiary health facility in south-south Nigeria

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ABSTRACT

Background: Hypercholesterolemia may be a predictor of cardiovascular diseases and global prevalence of hypercholesterolemia is about 38%. Statins do not increase or decrease the risk of subsequent intracerebral hemorrhages, but do reduce the risk of ischemic stroke. Patients on statins for prevention of cardiovascular disease have an increased risk of cardiovascular events and mortality if they do not adhere to treatment.

Objective: The aim of this study was to assess the level of statin adherence among hypercholesterolemic patients in a tertiary health facility.

Methods: Three hundred and fifty-three hypercholesterolemic out-patients were recruited from a tertiary hospital through systematic random sampling. A validated self-reported questionnaire was used to obtain demographics characteristics, hypercholesterolemia profile and adherence to statin therapy. Data collected were organized and analysed using descriptive statistics and Chi square. Ethical considerations were observed.

Results: Response rate was 99.7%. Majority of the respondents were females (63.1%). Most of the patients had tertiary level of education (67.9%). A total of 168(47.7%) of the participants were private workers. Majority of the participants were urban dwellers (89.5%), 55.1% of the participants has cholesterol level greater than 200mg/dl. About 34.7% had an onset of the disease at age <40 and 68.2% of the participants had a family history of the disease. Atorvastatin was the most used statin drug (54.0%) followed by Rosuvastatin (34.1%) and lastly Simvastatin (11.9%). Hypertension is the most common comorbidity (89.5%) followed by diabetes (59.4%) and lastly myocardial infarction (6.0%). According to rate of adherence among participants, 57.1% showed moderate adherence while 42.9% showed non adherence.

Conclusion: This study has reported moderate adherence to statin, especially among patients with high educational status. Patients on rovastatin were more likely to take their medicine as prescribed than those on the other statins. Adherence apps on android devices are recommended.

Keywords: Statins, adherence, hypercholesterolemia, cardio vascular disease

Adhésion au traitement par statines chez les patients souffrant d'hypercholestérolémie dans un établissement de santé tertiaire du sud-sud du Nigeria

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RÉSUMÉ

Contexte: L'hypercholestérolémie peut être un facteur prédictif des maladies cardiovasculaires et la prévalence mondiale de l'hypercholestérolémie est d'environ 38%. Les statines n'augmentent ni ne diminuent le risque d'hémorragies intracérébrales ultérieures, mais réduisent le risque d'accident vasculaire cérébral ischémique. Les patients sous statines pour la prévention des maladies cardiovasculaires présentent un risque accru d'événements cardiovasculaires et de mortalité s'ils n'observent pas le traitement. L'objectif de cette étude est d'évaluer le niveau d'observance des statines chez les patients de l'hypercholestérolémie dans un établissement de santé tertiaire.

Méthodes: Trois cent cinquante-trois patients ambulatoires d'hypercholestérolémie ont été recrutés dans un hôpital tertiaire par échantillonnage aléatoire systématique. Un questionnaire auto-administré validé a été utilisé pour obtenir les caractéristiques démographiques, le profil de l'hypercholestérolémie et l'observance du traitement par statine. Les données recueillies ont été organisées et analysées à l'aide de statistiques descriptives et du chi carré. Les considérations éthiques ont été respectées.

Résultats: Le taux de réponse était de 99,7%. La majorité des répondants étaient des femmes (63,1%). La plupart des patients avaient un niveau d'éducation supérieur (67,9%). Au total, 168 (47,7%) des participants étaient des travailleurs du secteur privé. La majorité des participants étaient des citadins (89,5%), 55,1% des participants avaient un taux de cholestérol supérieur à 200 mg/dl. Environ 34,7% des participants ont contracté la maladie à un âge < 40 ans et 68,2% des participants avaient des antécédents familiaux de la maladie. L'atorvastatine était la statine la plus utilisée (54,0%), suivie de la rosuvastatine (34,1%) et enfin de la simvastatine (11,9%). L'hypertension est la comorbidité la plus courante (89,5%), suivie du diabète (59,4%) et enfin de l'infarctus du myocarde (6,0%). Selon le taux d'observance parmi les participants, 57,1% ont montré une observance modérée tandis que 42,9% ont montré une non-observance.

Conclusion: Cette étude fait état d'une observance modérée à la statine, en particulier chez les patients ayant un niveau d'éducation élevé. Les patients sous rovastatine étaient plus susceptibles de prendre leur médicament comme prescrit que ceux sous autres statines. Les applications d'observance sur les appareils Android sont recommandées.

Mots clés: Statines, observance, hypercholestérolémie, maladie cardio vasculaire

INTRODUCTION

It has been estimated that 38% of the global adult population has hypercholesterolemia with total cholesterol levels over 5.0 mmol/L.[1] A patient has hypercholesterolemia when he or she has three or more of the following: High total cholesterol level (greater than 200 mg/dl), low HDL-C <40 mg/dl in men < 50 mg/dl in women, High LDL-C>100 mg/dl This metabolic disorder hypercholesterolemia has been linked to an increased risk of coronary artery disease[2] but may no longer be associated with myocardial infarction and stroke[3]. Statins are a common name for a class of drugs known as 3-hydroxyl-3-methylglutaryl coenzyme A (HMG - COA) inhibitors that lower blood cholesterol levels thereby preventing heart attacks caused by coronary artery disease. Mutations in genes encoding the low-density lipoprotein receptor, apolipoprotein B, proprotein convertase subtilisin/kexin type 9 and the low-density lipoprotein receptor adapter protein 1 are the most common causes of familial hypercholesterolemia (FH) (LDIRAP). Statins have efficacy for these familial hypercholesteremia but not for Lipoprotein(a), a genetic form of low-density lipoprotein associated with atherosclerotic disease and aortic stenosis. About 20-25% of people globally have a genetic version of cholesterol called lipoprotein(a). There is no known cure for this type of dyslipidemia but a test drug, muvalaplin passed the first stage of clinical trials in healthy participants.[4] Statins do not increase or decrease the risk of subsequent intracerebral hemorrhages, but do reduce the risk of ischemic stroke.[5] Both hereditary and environmental variables have a role in the development of hypercholesterolemia; poor dietary and lifestyle choices in developed nations are major causes. Statins are the first-line medications for the prevention of primary and secondary atherosclerotic cardiovascular disease because they help to reduce low density lipoprotein cholesterol (LDL-C) levels by up to 55%.[6] Statins enhance endothelial function, restrict immune cell proliferation and activation, and decrease inflammation by reducing the expression of numerous proteins involved in the production of arteriosclerotic plaque. Statins are clinical indicated for lowering cholesterol levels, reduction of hyperplasia and restenosis.[7]

Treatment effectiveness is largely dependent on patient's adherence to treatment.[8] The World Health Organization defines medication adherence as "the extent to which a patient's actual behaviour conforms to the agreed upon advice of their healthcare professional".[9]

Several publications have reported that dyslipidaemia is widespread in every region of Nigeria with the highest incidence in South-South Nigeria. The prevalence of hypercholesterolemia among adults aged 20 and above rose from 17% to 26% between 1992 and 2015 in Nigeria. Using UN population predictions for Nigeria and assuming that the extracted information was gathered between 1992 and 2015, we find that the prevalence of hypercholesterolemia increases with age, p = 0.012. A staggering 21.9 million people (26% of the population) now have hypercholesterolemia, a 166% rise since 2000. This trend is suspected to be linked to urbanisation and lifestyle in the Country.

The aim of this study was to assess the level of statin adherence among patients with hypercholesterolemia in a tertiary health facility.

METHODS

Study design

This was a descriptive cross-sectional study of patients diagnosed with hypercholesterolemia and have been on statin therapy for at least 3 months. This study was conducted between March and November 2022.

Study site

This study was carried out in the Consultant Outpatient Department (COPD) of the University of Benin Teaching Hospital(UBTH) in Benin City. This is the major Federal tertiary health facility in southern Nigeria serving States like Ondo, Delta, and Kogi . UBTH is a leading academic and medical centre in West Africa, providing a wide range of professional services. It was established in Benin City on May 12, 1973 after an edict (number 120 of the Nigeria National Health Act) was passed.

The COPD consists of various specialties in internal medicine including cardiology, oncology, urology, nephrology, gynecology, ophthalmology, mental health e.t.c. There are different pharmacy units in the COPD, including the main or primary pharmacy, National Health Insurance Scheme (NHIS) pharmacy and the antiretroviral pharmacy section etc. The primary pharmacy for COPD was where the respondents were recruited and data collected.

Study population

About 4,306 patients were receiving treatment with statins at the time of the study. This information was collected from the COPD primary pharmacy ledger book.

Sample size determination

Calculation of sample size was done using the Cochran formula[10]:

$SS = Z^2 x\, pq/e^2$

Where

SS = Sample size

Z = Z value (e.g. 1.96 for 95% confidence level)

P = estimated proportion of an attribute that is present in a population (50% approx.0.5)

q = p - 1.

e = margin of error (5% approx.0.05).

The sample size derived from the calculation above is used to calculate the sample size for a finite population (where the population is less than 50,000).

NEW SS = SS $^{+}$[1 + (ss - 1) /POP

POP = Population

Study Population = 4,306

Using the formula's above

$SS = 1.96^2 x\, 0.5\, x\, (1 - 0.5)/0.05^2$

= 384.16

NEW SS = 384.16 $^{+}$[1 + (384.16 - 1)/4,306]

= 384.16 $^{+}$[1 + (384.16 - 1)/4,306]

= 384.16 $^{+}$[1 + 0.089]

= 384.16 $^{+}$.089

$\simeq$ 353

NEW SS = 353

Calculation for sampling interval:

Sampling Interval, $R = \frac{N}{n}$

Where N = Total Population = 4,306

n = New Population = 353

$R = \frac{N}{353} = 12$

Therefore, the **Sampling Interval = 12**

Instrument for data collection

A validated 28 item self-structured questionnaire was developed. The questionnaire was divided into three sections representing the major study variables of this study; (i) demographic characteristics of participants (ii) Clinical variables (iii) participants' adherence to prescribed statin therapy.

The validity of the questionnaire was checked by doing a pre-test on 20 participants. Modification of the tool was made based on the pre-test result. Cronbach's alpha test was carried out and 0.86 was obtained, indicating excellent internal consistency in their responses.

Inclusion criteria; Adult patients diagnosed with hypercholesterolemia and on statin treatment at the University of Benin Teaching Hospital. Only out-patients who were willing to participate were included.

Exclusion criteria; Patients below the age of 18 years were excluded; patients who didn't give informed consent were excluded.

Data Collection

The Head of Department of Pharmacy in the University of Benin Teaching Hospital consultant outpatient department was informed and the questionnaires were distributed to the patients. In order to ensure a high response rate, a proper presentation was carried out by the Researcher and an intern pharmacist. The questionnaires were only distributed on the clinic days (Tuesday and Thursday) and were collected in person.

Data analysis

The data obtained were sorted, coded and entered into a Microsoft Excel spread sheet. All data were analyzed using the Statistical Package for the Social Science version 24 9IBN: SPSS INC.). Mean of the sample, standard error of mean, Chi square, variance and standard deviation were calculated.

Calculation for adherence

From the 16 items on the adherence, a score of 8 and above indicates adherence while a score below 8 indicates non-adherence.

Percentage of participants that were adherent to Statins

$$= \frac{\text{Total Number Of Adherence}}{\text{Total Sample Size}} \text{ X } 100\%$$

Percentage of participants that was non-adherent to Statins

$$= \frac{\text{Total Number Of Non-adherence}}{\text{Total Sample Size}} \text{ X } 100\%$$

Patients will be considered adherent if they score 80% or more, moderate adherence if they score 50% to 79%, and non-adherence if they score below 50% 11.

Ethical consideration

Ethical approval was obtained from the University of Benin Teaching Hospital Ethical Review Board (Ref. no: ADM/E 22/A/VOL. VII/14831276). Informed consent was obtained from each Participant, identities were kept anonymous and data obtained were used only for academic purpose.

RESULTS

A total of 352 questionnaires were valid for analysis giving a response rate of 99.7%.

Socio demographic Characteristics

About 110(31.3%) of the participants were between the ages of 35-44 years, 90 (25.6%) were above 65 years. Majority of participants; 222 (63.1%) were females. Details of the socio demographic characteristics are illustrated in Table 1. A total of 168 (47.7%) of the participants were private workers and 139 (39.5%) were Civil Servants. Majority of the participants were educated up to the tertiary level while 10(2.8%) were uneducated. Most of the participants, 315(89%) were Urban residents.

Table 1: Socio demographic characteristics of participants

Variables	Frequency (%) *N* (352)
Age group (years)	
35-44	110 (31.3)
45-54	72 (20.5)
55-64	80 (22.7)
>65	90 (25.6)
Gender	
Male	130 (36.9)
Female	222 (63.1)
Occupation	
Unemployed	6 (1.7)
Civil Servant	139 (39.5)
Private worker	168 (47.7)
R etired	39 (11.1)
Educational Level	
Primary	25 (7.1)
Secondary	78 (22.2)
Tertiary	239 (67.9)
Uneducated	10 (2.8)
Marital Status	
Single	23 (6.5)
Married	271 (77.0)
Divorced	23 (6.5)
Widowed	35 (9.9)
Residence	
Rural	37 (10.5)
Urban	315 (89.5)

Clinical variables

The profile of hypercholesteremia (>200mg/dl) is presented in Table 2. A total of 194 (55.1%) participants at the time of filling the questionnaire had a cholesterol level greater than 200mg/dl indicating uncontrolled hypercholesteremia. About 188 (53.4%) patients had age of onset less than 55 years while 122 (34.7%) had an early onset at ages <40 years. From the results, 68.2% reported a family history of hypercholesteremia. Atorvastatin was the most common prescribed hypolipidemic drug with 190 (54.0%) of the participants being on it, followed by Rosuvastatin with 120 (34.1%) and lastly Simvastatin. From the results, 89.5% had hypertension as a comorbidity to hypercholesteremia, 59.4% also had diabetes while 21 (6.0%) reported prior myocardial infarction.

Table 2: Profile on hypercholesteremia (>200mg/dl)

Variable	Frequency, n (Percentage %)
Cholesterol level	
<200mg/dl	158 (44.9)
>200mg/dl	194 (55.1)
Age of onset (years)	
<40	122 (34.7)
<55	188 (53.4)
<70	42 (11.9)
Family history of hypercholesteremia	
Yes	240 (68.2)
No	112 (31.8)
Current hypolipidemic drugs	
Atorvastatin	190 (54.0)
Simvastatin	42 (11.9)
Rosuv astatin	120 (34.1)
Comorbidities	
Diabetes	209 (59.4)
Hypertension	315 (89.5)
Myocardial infarction	21 (6.0)

Adherence status of participants

From the analysis, 57.1% showed moderate adherence while 42.9% showed non adherence.

About 66.7% of the participants on rosuvastatin were adherent compared with 55.3% on atorvastatin. This indicates that rosuvastatin allowed better adherence than the other medications. Details of adherence status of participants are illustrated in Tables 3 and 4.

Adherence was statistically significant with the current hypolipidemic drug with a p value of 0.004. Males had a higher tendency to be non-adherent to their medications with 63.1 percent being non-adherent compared with 46.4% non-adherence among females. This however was not statistically significant (p = 0.83). Among the age groups the highest adherence was in the 35-44 while the lowest adherence was seen in the 45-54 age group. Participants with tertiary education were the most adherent to their medications; likewise, urban residents were more adherent than rural residents.

A total of 16 was scored for the participants according to their response. A score greater than 8 was considered

adherent, while a score less than 8 was considered non-adherent.

Calculation for adherence:
Percentage of participants that were adherent to Statins

$$= \frac{\text{Total Number Of Adherence}}{\text{Total Sample Size}} \text{ X } 100\%$$

$$= \frac{201}{352} \text{ X } 100\% = 57.1\%$$

Percentage of participants that was non-adherent to Statins

$$= \frac{\text{Total Number Of Non-adherence}}{\text{Total Sample Size}} \text{ X } 100\%$$

$$= \frac{151}{352} \text{ X } 100\% = 49.9\%$$

Table 4: Patterns of adherence among participants

Variables	Adherent	Non -Adherent	p-value
Age group (years)			
35-44	69 (62.7)	41 (37.3)	0.900
45-54	33 (45.8)	39 (54.2)	
55-64	43 (53.8)	37 (46.3)	
>65	56 (62.2)	34 (37.8)	
Gender			
Male	48 (36.9)	82 (63.1)	0.830
Female	119 (53.6)	103 (46.4)	
Occupation			
Unemployed	4 (66.7)	2 (33.3)	0.369
Civil Serva nt	75 (54.0)	64 (46.0)	
Private worker	95 (56.5)	73 (43.5)	
Retired	27 (69.2)	12 (30.8)	
Educational Level			
Primary	14 (56.0)	11 (44.0)	
Secondary	42 (53.8)	36 (46.2)	0.857
Tertiary	140 (58.6)	99 (41.4)	
Uneducated	5 (50.0)	5 (50.0)	
Marital Status			
Single	19 (82.6)	4 (17.4)	0.083
Married	150 (55.4)	121 (44.6)	
Divorced	12 (52.2)	11 (47.8)	
Widowed	20 (57.1)	15 (42.9)	
Residence			
Rural	18 (51.4)	19 (48.6)	0.272
Urban	183 (58.1)	132 (41.9)	
Cholesterol level			
<200mg/dl	97 (61.4)	61 (38.6)	0.142
>200mg/dl	104 (53.6)	90 (46.4)	
Family history of Hypercholesteremia			
Yes	138 (57.5)	102 (42.5)	0.825
No	63 (56.3)	49 (43.8)	
Current hypolipidemic drugs			
Atorvastatin	105 (55.3)	85 (44.7)	
Simvastatin	16 (38.1)	26 (61.9)	**0.004**
Rosuvastatin	80 (66.7)	40 (33.3)	
Age of Onset (years)			
<40	72 (59.0)	50 (41.0)	0.074
<55	99 (52.7)	89 (47.3)	
<70	30 (71.4)	12 (28.6)	

DISCUSSION

Adherence to statins reduces the devastating consequences of hypercholesterolemia.[12] In this study, patients' adherence to statin for hypercholesterolemia was generally moderate. This is comparable to a study which revealed that about 60% of the Kuwaiti participants reported medium adherence.[13] In a study conducted over a three-year period, Aubert *et al* (2010) observed the effects of statin adherence on subsequent hospitalizations.[14] Patients with higher adherence (PDC>80%) had fewer hospitalizations (16% vs 19%, P<0.01) and reduced medical expenses. Patients with >80% adherence had considerably decreased hospitalization rates. Adherence to drug therapy has been improved with mobile health which involves the use of smartphone applications on mobile devices such as medPlan®.[15] Healthcare professionals can recommend the use of smartphone medication reminder applications for patients on statins to improve adherence and therapeutic outcomes.

In this study, hypercholesterolemia tends to be more common in women than in men. This was similar to study carried out in Iran that showed hypercholesterolemia was more common among the Iranian women.[16] This was in contrast to a study carried out in Saudi Arabia, the frequency of hypercholesterolemia was found to be greater in males than in females, and a subsequent university study confirmed this trend.[17]

This might be attributable to gender roles and religious demands in developing countries which cause women to spend most of their time at home caring for children and doing housework which increases their risk of obesity[18].

In this study, hypercholesterolemia is common among the elderly (age above 45years). This might be due to less activity by the elderly people compared to the younger ones. This was in line with a study carried out by Odenigbo *et al* (2009) which reported that hypercholesterolemia was common among the elderly in Asaba, Delta state, South-South Nigeria[19].

Most of the participants in this study were urban-resident, diet from artificial sources and sedentary lifestyle are more common among the urban dwellers than the rural dwellers. This is similar to a study carried out by Adeloye *et al* (2019) where urban dwellers had a significantly higher rate[20].

From our study, participants showed better adherence to Rosuvastatin than Atorvastatin, this may be due to a more convenient dose interval than the other statins. Atorvastatin was the most common hypolipidemic drug prescribed, followed by Rosuvastatin and lastly, Simvastatin. This is similar to the findings of Akunne *et al* (2016) and another study carried out in China on adherence to statins and its impact on clinical outcome. Atorvastatin was the most used statin at a rate of 44.2%. [21,22]

.This study reported an association between individuals with low socioeconomic levels and poor adherence.This finding is similar to the study reported by Zhao *et.al*, (2020). This may be due to the inability of the low socioeconomic individuals to easily purchase their statins medication thereby reducing adherence rate.[22] A study carried out by Clark *et al* (2009) reported that individuals with a first acute myocardial infarction are more likely to have poor medication adherence if they are classified as having a lower socioeconomic level.[23] One in eight individuals with cardiovascular disease claim non-adherence due to the expense of their medication.[24] Low socioeconomic status is connected with limited access to doctors, pharmacists and health insurance that covers prescription drugs.[25]

The results of this study reveal that older age and family history of hypercholesterolemia are positively related with elevated cholesterol levels, this is in line with previous studies.[17] In this study, non-adherent participants reported to have stopped taking their medication when they felt their symptoms had subsided, this may be responsible for high cholesterol observed in about half of of the participants. A similar work carried out in China reported that poor medication adherence to drugs like statins was linked to a lack of "health literacy" among Chinese patients, who may not realize that they still need to take their medicine even if their symptoms have subsided.[26]

There was poor adherence among the uneducated and the secondary school level compared to the tertiary level where there was moderate adherence. A similar study was carried out on factors affecting adherence to statins in hypercholesterolemia Kuwaiti patients. Their results revealed that the highly educated participants were more adherent to their statins medication than the less educated participants.[13]

In this study, hypertension had the highest percentage as comorbidity to hypercholesterolemia followed by diabetes and lastly, myocardial infarction. This is in line with a study carried out by Zhao *et al* (2020) on adherence to statins and its positive impact on clinical outcomes. Their results revealed that hypertension has the highest rate as comorbidity to hypercholesterolemia followed by type 2 diabetes.[22]

A patient's failure to adhere to their prescribed statins may lead to several unwanted outcomes therefore clinical pharmacists should provide pharmaceutical care which takes responsibility for these patients' drug therapy. Adherence to treatment is a patient outcome affected by numerous health care interventions. Adequate patient education, counselling, follow-up and monitoring will encourage patient adherence to statins.

CONCLUSION

Adherence to statin medication is moderate among the study population in this study. Adherence to statin medication was higher among individuals with higher levels of education compared to those with lower levels of education. Patients on rovastatin were more likely to take their medicine as prescribed than those on the other statins.

Statin education is important for people with hypercholesterolemia because it increases the likelihood that they will take their medicine as prescribed.

As many patients struggle to afford statins owing to their expensive cost price and ongoing usage, the government should aid to subsidize the cost price of these medicines. Patients on statins should take advantage of mHealth adherence apps on their phones as reminders to take their medications.

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