

Original Research Article

Cutaneous adverse effects of antihypertensive medications among hypertensive patients in Enugu state, Nigeria

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ABSTRACT

Background: Antihypertensive drugs are widely used for managing hypertension, especially during this period of increasing prevalence in Nigeria, Africa, and around the world. This study aimed to determine the prevalence of adverse cutaneous drug reactions (ACDRs) to antihypertensives among patients with systemic hypertension. Like other medication classes, side effects can occur and may affect different body systems. The scarcity of data on the profile of ACDRs to antihypertensive medications in Nigeria, despite their growing use, necessitated this study. Cutaneous side effects, being easily visible, could serve as early warning signs to prevent life-threatening complications; therefore, it is important to study them and use the findings to enhance prescriber awareness.

Methods: This cross-sectional descriptive study was conducted at the cardiology clinic of the University of Nigeria Teaching Hospital (UNTH) in Enugu from January to December 2024, among consenting, eligible hypertensive patients. Adverse cutaneous reactions were identified using a medicine-induced symptom checklist and self-report, based on the modified findings of Ranugha and Betkemr.

Results: A total of 70 patients (37 females), aged 26 to 80 years, were studied. The prevalence of ACDRs to antihypertensive medications was 17%. The most common ACDRs to antihypertensive medications among these patients were pruritus (7%), photosensitivity (7%), eczema (5.6%), flushing (4.2%), and vasculitis (4.2%).

Conclusions: There are ACDRs to antihypertensive medications among Nigerians. Increasing awareness of these and potential drug alternatives among prescribers and patients will reduce drug-induced morbidity, leading to better compliance and health outcomes.

Keywords: Antihypertensive drugs, Adverse cutaneous reactions, Awareness creation

INTRODUCTION

Over time, various antihypertensive treatments have been used, but they were often ineffective or poorly tolerated. These included blood-sucking leeches, strict sodium restriction, sympathectomy, and pyrogen therapy.¹⁻⁵ Later, sodium thiocyanate was introduced as the first chemical agent for treating hypertension, but it caused many side effects and was unpopular.^{1,4} Since then, numerous other chemical agents have been tried with mixed results. Odili

et al reported an overall age-standardized hypertension prevalence of 38.1% in Nigeria, with the Southeast region accounting for 52.8%, when broken down by region.⁶ Another study in Enugu, Nigeria, by Ezeala-Adikaibe et al found a prevalence of 27.6%.⁷ A study in Ibadan showed a prevalence of 33.1%, with only 5.1% of those affected actively using antihypertensive medication.⁸ In this study, we examined the common antihypertensive drug groups prescribed at the University of Nigeria Teaching Hospital (UNTH) cardiology clinic and the prevalence of skin-

related side effects due to their use. Our aim was to raise prescribers' awareness of these side effects to enable earlier detection and prevention, thereby reducing patient morbidity and mortality.

An adverse cutaneous drug reaction (ACDR) refers to unwanted effects on the skin, its appendages, or mucous membranes caused by medications currently being used or recently discontinued.^{3,4}

Antihypertensive drugs are widely used, either alone or in combination, to manage hypertension, especially in this era of increasing prevalence in Nigeria, Africa, and globally.⁵

Studies suggest that only around 2-3% of all adverse drug reactions are cutaneous.^{3,9} The Danish National Board of Health reports that ACDR related to antihypertensive medications varies between roughly 10-60%.¹⁰ The occurrence of ACDR is higher in females, immunosuppressed individuals, and the elderly.^{3,11}

Studies in India and Nigeria reported ACDR rates associated with antihypertensives as 2.04% and 2%, respectively.^{4,12} No significant differences were found based on sex or age, but ACDR risk increased with the number of antihypertensive medications used simultaneously. Additionally, combining specific antihypertensives, such as amiloride and hydrochlorothiazide, markedly raises the risk of ACDRs.^{3,4,12,13}

The manifestations of ACDR are generally categorized into exanthematous/eczematous, urticarial, vasculitic, fixed drug eruptions, pustular, blistering, lichenoid, and hypersensitivity syndrome types.^{10,11,14-16}

After the diagnosis is made, the offending antihypertensive is identified; the ultimate goal is to discontinue the offending medication.^{3,10} Risk-benefit ratio analysis is also crucial before discontinuation.³

Treatment for most adverse cutaneous drug eruptions is mainly supportive and depends on the specific type of reaction. Mild eruptions are typically managed with antihistamines, gentle topical steroids, and emollients. In contrast, severe reactions such as Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) might necessitate hospitalization and multidisciplinary care in intensive care units.¹⁰ The insights from this work will improve existing knowledge and aid in lowering the morbidity and mortality associated with ACDRs by increasing awareness among prescribers.

This study aimed to determine how common ACDRs are from antihypertensive medications, identify potential offending drugs, and evaluate the most frequent types of ACDRs among patients with systemic hypertension attending the UNTH cardiology clinic.

METHODS

This cross-sectional descriptive study took place from January to December 2024. The participants were patients with systemic hypertension who were on antihypertensive medications. Inclusion criteria specified patients with hypertension who had been on treatment for over a year, had no severe co-morbidities, and gave informed consent. Patients with poorly controlled co-morbidities, mental impairments, or those who did not consent were excluded. Ultimately, 70 patients meeting the criteria were enrolled in the study.

The researcher and the trained assistants administered the pretested questionnaire, based on the findings of Ranugha and Betkemr, to the participants.⁹ Afterward, their skin was examined thoroughly from head to toe under good lighting, with privacy ensured, to facilitate an accurate diagnosis and exclude other causes. Diagnoses were made clinically.³ Individuals with ACDRs or other skin conditions received free consultations, appropriate treatments, and some were referred for further care.

The collated data were analyzed using statistical package for the social sciences (SPSS) version 23.0. Descriptive statistics, including frequency and percentages, were used to summarize categorical variables, while means and standard deviations were calculated for continuous variables. Associations between categorical variables were made using logistic regression, Chi-square, and Fisher's exact test.

Means of continuous variables were compared using the student t-test. P value <0.05 was considered statistically significant. Results were presented in tables and charts.

RESULTS

Study demographics

About of 74.6% of the patients were 55 years or older, with a mean age of 60.9 years, a standard deviation of 11.24, and minimum and maximum ages of 26 and 80 years, respectively. There were more female patients (52.1%) than male patients (47.9%). The patients were predominantly married (87.3%), and 35.2% had a tertiary education. The patients were mainly civil servants (32.4%), traders (31%), and farmers (18.3%) (Table 1).

Prevalence of adverse cutaneous drug reactions

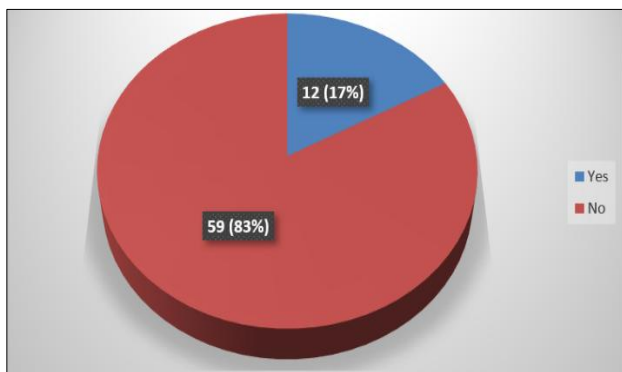
The prevalence of ACDR to antihypertensives in the study population was 17% (Figure 1).

Adverse cutaneous drug reactions to antihypertensives

The most common reactions, listed in order, were pruritus (7%), photosensitivity (7%), eczema (5.6%), flushing (4.2%), and vasculitis (4.2%) (Table 2).

Table 1: Demographic characteristics of the patients.

Variables	Frequency	Percent
Age group (years)		
26-35	2	2.8
36-45	6	8.5
46-55	10	14.1
56-65	27	38.0
66+	26	36.6
Sex		
Female	37	52.1
Male	34	47.9
Marital status		
Single	2	2.8
Married	62	87.3
Separated	1	1.4
Widowed	6	8.5
Level of education		
No formal education	12	16.9
Primary	14	19.7
Secondary	20	28.2
Tertiary	25	35.2
Religion		
Christianity	71	100.0
Occupation		
Farmer	13	18.3
Trader	22	31.0
Civil servant	23	32.4
Retiree	8	11.3
Others	5	7.0

**Figure 1: Prevalence of ACDR to antihypertensives among the patients.**

Types of antihypertensive drug classes commonly prescribed in the clinic

The antihypertensive drug classes, listed from most to least common, were calcium channel blockers (62%), angiotensin receptor blockers (59.2%), diuretics (57.7%), beta-blockers (45.1%), angiotensin-converting enzyme inhibitors (14.1%), and centrally acting agents (5.6%) (Table 3).

Association between age, gender, duration of treatment, and prevalence of ACDRs

No significant link was found between age, gender, treatment duration, and the occurrence of ACDRs to antihypertensives in patients ($p>0.05$) (Table 4).

Table 2: Adverse cutaneous drug reactions to antihypertensives among patients.

Variables	Frequency	Percent
Angioedema	1	1.4
Pruritus	5	7.0
Photosensitivity	2	2.8
Eczematous eruptions	2	2.8
Gingival hyperplasia	2	2.8
Flushing	3	4.2
New-onset psoriasis	2	2.8
Facial and truncal telangiectasia	1	1.4
Photosensitivity	5	7.0
Purpuric exanthems	1	1.4
Sub-acute cutaneous lupus erythematosus	1	1.4
Oral ulcers	1	1.4
Eczematous eruptions	1	1.4
Psoriasiform eruptions	1	1.4
Vasculitis	3	4.2
Photodermatitis	2	2.8
Erythema multiforme	1	1.4
Eczema	4	5.6

Table 3: Types of antihypertensive drug classes commonly prescribed for patients.

Variables	Frequency	Percent
Angiotensin converting enzyme inhibitors	10	14.1
Angiotensin receptor blockers	42	59.2
Calcium channel blockers	44	62.0
Beta blockers	32	45.1
Diuretics	41	57.7
Centrally acting agents	4	5.6
Alpha-1 blockers	0	0.0
Angiotensin converting enzyme inhibitors	10	14.1
Angiotensin receptor blockers	42	59.2
Calcium channel blockers	44	62.0
Beta blockers	32	45.1
Diuretics	41	57.7
Centrally acting agents	4	5.6
Alpha-1 blockers	0	0.0

Association between the type of antihypertensive class and prevalence of ACDRs

Angiotensin-converting enzyme inhibitors were significantly associated with ACDRs in patients ($p=0.006$, $OR=7.714$, 95% $CI=1.776-33.501$). Patients using these drugs were about 8 times more likely to experience adverse

cutaneous drug reactions than those not on the medication. Similarly, beta-blockers were significantly associated with ACDRs ($p=0.031$, $OR=4.696$, 95% $CI=1.149-19.185$). Patients taking beta-blockers were approximately 5 times more likely to develop adverse cutaneous drug reactions than non-users (Table 5).

Table 4: Association between age, gender, duration of treatment, and prevalence of ACDRs to antihypertensives in the patients.

Variables	ACDR to hypertensives			
	Yes, N (%)	No, N (%)	χ^2	P value
Age group (years)				
26-35	1 (50.0)	1 (50.0)	3.925	0.416
36-45	0 (0.0)	6 (100.0)		
46-55	2 (20.0)	8 (80.0)		
56-65	6 (22.2)	21 (77.8)		
65+	3 (11.5)	23 (88.5)		
Sex				
Female	5 (13.5)	32 (86.5)	0.631	0.427
Male	7 (20.6)	27 (79.4)		
Duration of treatment				
1-5	5 (13.5)	32 (86.5)	5.812	0.121
6-10	2 (15.4)	11 (84.6)		
11-15	4 (44.4)	5 (55.6)		
16+	1 (8.3)	11 (91.7)		

Table 5: Association between type of antihypertensive class and prevalence of ACDRs to antihypertensives in the patients.

Type of antihypertensive class	ACDR to hypertensives				
	Yes, N (%)	No, N (%)	P value	OR	95% C.I for OR
Angiotensin converting enzyme inhibitors					
Yes	5 (50.0)	5 (50.0)	0.006	7.714	1.776-33.501
No	7 (11.5)	54 (88.5)			
Angiotensin receptor blockers					
Yes	5 (11.9)	37 (88.1)	0.184	0.425	0.120-1.502
No	7 (24.1)	22 (75.9)			
Calcium channel blockers					
Yes	9 (20.5)	35 (79.5)	0.315	2.057	0.504-8.393
No	3 (11.1)	24 (88.9)			
Beta blockers					
Yes	9 (28.1)	23 (71.9)	0.031	4.696	1.149-19.185
No	3 (7.7)	36 (92.3)			
Diuretics					
Yes	8 (19.5)	33 (80.5)	0.495	1.576	0.427-5.815
No	4 (13.3)	26 (86.7)			
Centrally acting agents					
Yes	2 (50.0)	2 (50.0)	0.100	5.700	0.718-45.260
No	10 (14.9)	57 (85.1)			

DISCUSSION

Systemic hypertension is a long-term condition that, if not managed, gradually damages multiple organs and can lead to death or disabilities. This underscores the importance of

lifelong use of antihypertensive medications.¹⁷ Adverse skin reactions are known side effects of antihypertensive drugs.^{3,4,9} This study identified that 17% of patients experienced ACDR to antihypertensives. This rate aligns with the range reported by a Danish study conducted by

the Danish National Board of Health committee (10-60%), but it exceeds the figures from earlier research in Benin City, Nigeria (2%), and India (2.04%).^{4,10,12} The variation is likely due to differences in study design, population characteristics, and the timeframe of each study. Additionally, the other researchers examined all adverse reactions to antihypertensives, without specifically focusing on skin-related side effects, unlike our study. The higher prevalence observed suggests a need for further investigations, as cases of adverse cutaneous drug reactions to antihypertensives appear to be increasing. In this study, the most common adverse skin reactions to antihypertensive drugs included pruritus (7%), photosensitivity (7%), eczema (5.6%), flushing (4.2%), and vasculitis (4.2%). Additional reactions are detailed in Table 2. These findings align with those reported by Talat et al in Pakistan.¹⁸ Olowofela et al in Benin City, Nigeria, identified major symptoms such as swollen ankles/oedema (13.8%), flushing (10.7%), and dry mouth (8.8%), among others.¹² In a review article, Ranugha and Betkerur primarily documented angioedema, pruritus, bullous eruptions, urticaria, photosensitivity, and hair loss, among other symptoms.⁹ Note that ACDRs linked to antihypertensive drugs can appear in various forms, and different medications may lead to multiple clinical presentations.¹⁰ The most commonly prescribed antihypertensive classes were calcium channel blockers (62%), followed by angiotensin receptor blockers (59.2%), diuretics (57.7%), beta-blockers (45.1%), angiotensin-converting enzyme inhibitors (14.1%), and centrally acting agents (5.6%). Olowofela et al, in Benin City, Nigeria, also reported that CCBs were the most frequently prescribed antihypertensives.¹² In another study, calcium channel blockers had the most common ACDRs as gingival hyperplasia (21%) and flushing (10%).⁹ Other observed reactions included facial and truncal telangiectasia, photosensitivity, new-onset psoriasis (including flare-ups), purpura, pemphigoid, and subacute cutaneous lupus erythematosus. Beta-blockers have been linked to pemphigoid drug eruptions, as well as to eczematous and psoriasiform rashes.¹⁹ Beta-blocker-induced skin eruptions can occur many months after starting treatment. In the case of practolol, these reactions were also followed by sclerosis of internal organs. Therefore, when these skin reactions are seen in patients, they should be recognized as potential signs of significant toxicity.¹⁹

There was no significant link between age, gender, or duration of treatment with the occurrence of ACDRs among those using antihypertensives ($p>0.05$), as shown in Table 4. Other research indicates that adverse skin reactions to drugs are more common in women than in men, and older patients tend to experience a higher rate of adverse drug reactions.^{3,20} Furthermore, Olowofela et al found no significant link in their study, despite analyzing all types of adverse reactions to antihypertensive drugs.¹² Our study found that ACEIs were strongly linked to ACDRs, with a p-value of 0.006, an odds ratio of 7.714, and a 95% confidence interval of 1.776 to 33.501. Patients taking ACEIs were eight times more likely to develop

these reactions compared to those not on the medication. Similarly, beta-blocker use showed a significant association ($p=0.031$, $OR=4.696$, 95% $CI=1.149-19.185$), with patients on beta-blockers being five times more prone to adverse skin reactions. In a study from Benin, Nigeria, the most common drugs linked to adverse reactions were diuretics (27.9%), calcium channel blockers (26.8%), and ACEIs (26.8%).¹²

CONCLUSION

This study observed a relatively high prevalence of adverse skin reactions to antihypertensive medications, leading to notable morbidity. Patients frequently experienced pruritus and photosensitivity, with ACEIs and β -blockers showing the strongest link to these adverse reactions. However, there was no significant correlation between age, gender, treatment duration, and the occurrence of ACDRs among patients on antihypertensive drugs.

Recommendations

Targeted prescriber education about adverse cutaneous drug reactions associated with antihypertensive medications to increase the index of suspicion for early detection and intervention. Public enlightenment to improve awareness among users and potential users of antihypertensives and to encourage early feedback to prescribers.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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