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Impact of Pharmacist Clinical Interventions on Treatment Outcomes in Hypertensive Patients: An Outcomes Study

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Abstract:- Pharmacists' clinical interventions are an important aspect of pharmacy practice that improve blood pressure reduction and medication adherence. These unique clinical interventions address many barriers to hypertension treatment outcomes, such as blood pressure, and medication adherence. Pharmacists' clinical interventions also directly improve patient's and caregiver's knowledge and understanding about the patient's current medication therapy. The general aim of the study was to assess the impact of pharmacists' clinical intervention on treatment outcomes among hypertensive patients. A multi-cluster, prospective, randomized intervention of 473 Nigerian hypertensive patients in which the impact of pharmacist's clinical interventions was assessed and compared to the routine Standard Medication Dispensing (SMD) practices among adult hypertensive patients. Patients' baseline and end of study blood pressure measurements and medication adherence scores were recorded from baseline to a three months' follow-up visit. The data were collected by using a four-part questionnaire. The data collated were analyzed by descriptive statistics, and Independent t-test. Four hundred fourteen patients completed the study. The results showed that mean blood pressure reductions from baseline and endpoint was statistically significant in the Intervention group. Pharmacists' clinical interventions when implemented have immense benefits of improving treatment outcomes among patients with hypertension. For any health care system to thrive in its management of hypertension, the involvement of pharmacists' clinical interventions is strongly recommended.

Keywords:- *Blood Pressure; Pharmacist; Hypertension; Clinical Pharmacy; Medication Adherence; Clinical Interventions.*

I. INTRODUCTION

Medication adherence (henceforth referred to "adherence") is defined as the level to which a patient's medication taking behavior and/or implementation of lifestyle changes tallies with agreed recommendations from a health care provider.[1] Patients' adherence to medications and lifestyle changes improve treatment outcomes and reduces the risks of premature mortality. However, more than half of the patients diagnosed with hypertension often failed to attain adequate blood pressure [BP] reduction due to poor adherence.[2,3] Poor medication adherence often results in adverse treatment outcomes and hospital readmissions and an increased cost of healthcare.[4]

Achieving adequate BP treatment outcomes is challenging due to multiple reasons, such as, long duration of therapy, unpleasant medication side-effects, forgetfulness, poor treatment related knowledge, often lack of finances/resources to purchase medications and/or patients' dissatisfaction with their health status.[5,6] Hypertension refers to systolic blood pressure (SBP) ≥ 140 mmHg and diastolic blood pressure (DBP) ≥ 90 mmHg.[7]

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The increased prevalence of hypertension demanded the development of many different forms of interventions to reduce BP to an acceptable level. One of the easiest and most commonly recommended interventions for achieving favorable outcomes is the home BP monitoring (HBPM). HBPM is "easy to perform, reliable, reproducible", cost-effective and reduces physician's office visits and the number of hypertension medications intake.[8,1,9] In addition to the HBPM, pharmacists' clinical interventions are increasingly employed by healthcare systems to improve treatment outcomes among patients with chronic medical conditions.

A pharmacist's clinical intervention (PCI) is defined as a structured, critical examination of a patient's medications with the objectives of reaching an agreement with the patient about treatment, optimizing the effects of medications, minimizing the number of medication-related problems and reducing wastes.[10] These clinical interventions focus on improving patients' knowledge about their current medications and also target high risks patients who are on multiple medications and involve a review of all the patient's current medications, including over-the-counter, complementary and prescription-only-medications.[11] These interventions are a care-model built on team-based care principles that are effective in influencing and optimizing treatment outcomes.[12,13] Pharmacists' clinical interventions are distinct from the routine or Standard Medication Dispensing (SMD) practices in that these clinical interventions are more concentrated on improving patients' knowledge of their current medications and detecting, resolving or preventing medication-related problems.[11]

Pharmacists' clinical interventions (PCIs) have shown immense benefits of improving treatment outcomes among patients with hypertension.[11] In a prospective randomized controlled trial of 197 Portuguese hypertensive patients, systolic blood pressure (SBP) was significantly ($p = 0.002$) reduced by 10.7 ± 11.6 mm Hg in those who received the pharmacist's clinical interventions. In contrast, treatment outcomes were unchanged in the control group (3.2 ± 12.1 mmHg, P=0.361). When the pharmacist's clinical interventions were further applied to the control group, there was a reduction in SBP of 6.9 ± 12.1 mmHg ($P = 0.047$).[14] Therefore, pharmacist's clinical interventions have showed huge paybacks in terms of patients clinical, economic, humanistic outcomes among hypertensive patients.

The general aim of the study was to assess the impact of pharmacist's clinical intervention on treatment outcomes in hypertensive patients in an out-patient setting.

The specific objectives were:

1. To compare mean blood pressure reductions between patients that received the pharmacists' clinical intervention to those that received routine Standard medication dispensing (SMD) practices.
2. To compare the level of medication adherence between patients that received pharmacists' clinical intervention to those that received routine Standard medication dispensing (SMD) practices.

II. METHODS

The study was a multi-cluster, prospective, randomized intervention of Nigerian hypertensive patients in which the impact of pharmacist's clinical interventions was evaluated and compared to those of the SMD practices. The study was conducted from September to December 2019, in out-patient clinics of the Dadin Kowa Comprehensive Health Center, Jos, Plateau State and the General Hospital Toro, Toro Local Government Area, Bauchi State, Nigeria.

Medication adherence was measured by Morisky Medication Adherence Scale-4 (MMAS-4)[15]. The MMAS-4 is a 4-item questionnaire with 4 yes/no questions, with a scoring scheme of "Yes" = 0 and "No" = 1. The MMAS-4 is quicker to administer and score and can be used to identify barriers to adherence. For the purpose of the current study, higher adherence score indicated better adherence.[11] Adherence score was rated as high adherence (4), medium adherence (3), low adherence (< 2). All patients with adherence score ≤ 3 were considered less-adherent.

Blood pressure was measured in a sitting position with patient's feet flat on the floor after at least ≥ 3 minutes of rest[7] using an OMRON® HEM – 720 – E electronic BP device, manufactured by OMRON Corporation in Kyoto, Japan. Mean blood pressure reduction was achieved by comparing the mean blood pressure reduction between the intervention group and SMD group. Body weight was measured in kilogram (Kg) to the nearest 0.1 kg using an electronic PH – 2015A brand electronic weight scale.

At enrollment, patients' baseline characteristics such as sex, age, weight, risk factors for cardiovascular disease (family history of hypertension) and clinical characteristics (adherence level, BP measurements and antihypertensive medications) were recorded. After the collection of baseline data, patients were follow-up monthly for 3 months. At every follow-up visit, the researchers took standard BP measurements and assessed patient's adherence level. The timing of BP measurements was free in relation to the intake of medication. Medication adherence was assessed by patient's self-reported questionnaire, i.e., the MMAS-4.

Sample size was calculated based on comparison of two independent means formula with an effect size 0.30 and a standard deviation of 10 mmHg. The level of significance was set at $p < 0.05$ and the power was assumed at 80%.[16] These figures were inserted in an online sample size calculator (G* Power 3.1.9.2).[17] The result of the estimated sample size was 322 participants (i.e., $n_1 = 161$, $n_2 = 161$). Considering the possibility of patient's dropout, the number of study participants was increased by 40% more than the estimated sample size.[16] The calculated sample size with was 473.

The routine SMD group was located at General Hospital Toro, Bauchi State while the pharmacist's clinical intervention (PCI) was located at the Dadin Kowa Comprehensive Health Center, Jos, Plateau State. The routine SMD and intervention sites were determined by simple randomization, i.e., by flipping of a coin (heads-SMD and tails-intervention). Participants were randomly assigned to the PCI Group and SMD Group.

All adult hypertensive patients aged ≥ 18 years or must have been taking at least one antihypertensive medication for a period of ≥ 1 month were included. Patients who were not willing to participate, breastfeeding, pregnant, mentally unstable, dementia or cognitively impaired were excluded.

List of Interventions:

- Monthly tailored and targeted written and verbal educational directed to patients in order to improve patients' knowledge about hypertension, their current medications, adherence, and lifestyle changes in order to achieve target blood pressure.
- Monthly blood pressure monitoring.
- Telephone calls and SMS reminders.
- Monthly follow-up assessments.

Standard Medication Dispensing Group:

- The interventions were withheld but they however received monthly blood pressure measurements, telephone call reminders, and monthly follow-up but not for therapeutic purposes.
- Routine care or SMD group receives normal procedures used to treat patients, i.e., normal medication dispensing practices.

Educational intervention:

The education intervention designed for the study was based on the framework of the Joint National Commission for the Detection, Evaluation, and Treatment of Hypertension VIII.[7] This educational intervention encourages the more daily consumption of vegetables and fruits by hypertensive patients. Patient education leads to a change in behavior, such as improvement in medication and lifestyle adherence and reduction in blood pressure.[18] The education comprised of the importance of medication adherence, diet and exercise.

The interventions were conducted Tuesdays and Thursday while sessions for the SMD practices were Mondays, Wednesdays and Fridays. The intervention lasted for 12 weeks (October to December, 2019), and each session lasted for about 15 minutes per patient during a follow-up visit. The contents and educational materials used for the intervention were guided by previous study.[19] The intervention commenced immediately after baseline data were collected. intervention data were also collected through monthly follow-ups of patients during their clinic visits, through short-message-service (SMS) and phone calls.[13]

Outcome Measures

Primary outcome was any change in medications adherence level. Reductions in mean systolic blood pressure (SBP) and mean diastolic blood pressure (DBP) were the final outcomes.

Data Analysis

Categorical variables such as gender, marital status and family history of hypertension, were analyzed by descriptive frequencies while the change in blood pressure was analyzed using sample paired t-test. Missing values as a result of a participant's not responding to certain items or withdrawal from the study were analyzed by performing missing value analysis (chi square = 8.649, df = 22, p = 0.995). All missing values were purely by chance and excluded from the data analyses. Statistical significance was set at $p < 0.05$. The analyses were performed using the IBM SPSS 25.0 (IBM Corp., Armonk, NY, USA).

Ethics Approval and Consent to participate

The study was approved by the Health Research Ethics Committee of the Plateau State Hospital Management Board (**Ref: HMN/ADM/423/II/682)** and Ethical Committee on Research Projects, Bauchi State Ministry of Health (**Ref: MOH/GEN/S/1409/I**). Participants were fully informed about the study objectives, their role, the risks involved in the study, voluntary nature of their participation and that they could decline or pull out of the study any time they wished. Copies of the questionnaires and intervention were administered only after receiving written informed consent from all participants.

III. RESULTS

At baseline, 473 participants were recruited[20] with the PCI group composing of 62.8% females with a mean (SD) age of 55.3 ± 12.46 years, while the SMD group comprised 75.5% females with a mean age of 54.2 ± 12.44 years. The mean (SD) weight of the PCI group was 77.7 ± 16.66 kg while the mean (SD) weight of the SMD group was 69.74 ± 16.57 kg (Table 1). At the endpoint of the study, the attrition rate was 12.5%.

The medication adherence levels of the PCI group at baseline and endpoint were 2.96 ± 1.25 and 3.66 ± 0.52 respectively (Table 2). The SBP and DBP reductions of the PCI group at the endpoint were 128.80 ± 10.63 mmHg and 82.78 ± 6.88 mmHg respectively. The mean SBP and DBP reductions were -15.70 mmHg [95% CI: -11.53 to -19.90; p = 0.001] and -5.40 mmHg [95% CI: -4.33 to -9.28; p = 0.001] respectively.

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Table 1: Sociodemographic characteristics of study participants

Characteristics	Total		Intervention Group		SMD Group	
	N	%	N	%	N	%
Sex of Participants						
Males	140	29.6	71	37.2	69	24.5
Females	333	70.4	120	62.8	213	75.5
Marital status						
Married	406	85.8	141	34.7	265	65.3
Widowed	53	11.2	40	75.5	13	24.5
Educational status						
Informal	262	55.4	24	9.2	238	90.8
Primary	63	13.3	36	57.1	27	42.9
Tertiary	91	19.2	86	94.5	5	5.5
Occupational status						
Farmers	39	8.3	7	18.0	32	82.0
Traders	82	17.3	24	29.3	58	70.7
Civil servants	58	12.3	55	94.8	3	5.2
Public servants	59	12.5	53	89.8	4	10.2
Family history of hypertension						
Present	225	47.6	119	52.9	106	47.1
Purposeful exercise						
Never	125	26.9	52	41.6	73	58.4
At least once a week	340	73.1	134	39.4	206	60.6
Caffeine intake						
Never	299	63.6	73	24.4	226	75.6
At least once a week	171	36.4	118	69.0	53	31.0
Home Blood Pressure Measurements						
Never	339	72.0	95	28.0	244	72.0
At least once a week	132	28.0	96	72.7	36	27.3
Medications regimen						
Taking a single	127	27.1	67	52.8	60	47.2
Taking multiple pills	344	72.9	125	36.3	219	63.7

Table 2: Clinical Characteristics of the Participants at Dadin Kowa Comprehensive and Toro General Hospital

Measures	Baseline Mean (±SD)	End of study Mean (± SD)	Mean BP Change [95% CI]	95% CI: P < 0.05
SBP				
PCI/mmHg	141.01 ± 19.97	128.80 ± 10.63	-15.70 [-11.53 -9.90)	0.001
SMD group/mmHg	146.44 ± 24.87	144.70 ± 24.1	-1.47 [-2.04 – 4.98]	0.410
DBP				
PCI/mmHg	86.19 ± 12.44	82.78 ± 6.88	3.70 [1.56 – 5.83]	0.001
SMD group/mmHg	90.55 ± 15.32	89.88 ± 14.68	1.00 [-1.29 - 2.61]	0.500
Medication adherence				
PCI	2.96 ± 1.25	3.66 ± 0.52		0.001
SMD group	3.45 ± 0.71	3.27 ± 0.85		0.009

*SBP – Systolic Blood Pressure, DBP - Diastolic Blood Pressure, SD – Standard Deviation, CI – Confidence Interval, Mm Hg – millimeter mercury, IG – Intervention Group, SMD – Standard Medication Dispensing Group

Table 3: Commonly Prescribed Antihypertensive medications at Dadin Kowa and Toro General

Characteristics	Total		SMR Group		SMD Group	
	N	%	N	%	N	%
Amlodipine	356	36.7	115	26.9	241	43.4
Lisinopril	304	31.4	83	19.4	221	39.8
Vasoprin	43	4.4	2	0.5	41	7.4
Metformin	50	5.2	24	5.6	26	4.7
Glimepiride	23	2.4	22	5.2	1	0.2
Moduretic	193	19.9	183	42,9	10	1.8

IV. DISCUSSION

Findings from the study revealed that many participants had a family history of hypertension, inadequate physical activities and had high intake of caffeine (Table 1**).** Home Blood Pressure Monitoring was a major concern in the current study. Many participants did not monitor their BP at home or in their communities. This could be due to the cost of purchasing a blood pressure monitoring device, which is very expensive. Hence many of the patients were dependent on blood pressure measurements from healthcare providers during their next hospital visit.

Many patients were prescribed multiple medications to reduce their blood pressure. Previous study shows that multiple antihypertensive medications control blood pressure.[21] The current study shows that Amlodipine was the most prescribed antihypertensive followed by Lisinopril and Hydrochlorothiazide, when compared to previous Nigerian studies.[22,23] Multiple medications during treatment is that multiple anti-hypertensive medications have been shown to reduce blood pressure thereby preventing complications and reducing mortality among hypertensive patients.[7]

The mean blood pressure reductions and mean blood pressure change of -10mmHg are consistent with previous studies[13,14] where pharmacist clinical interventions significantly improved treatment outcomes among hypertensive patients.[24,25] Blood pressure was reduced in the PCI following the implementation of the intervention for a 3-months period.

Poor medication adherence is an important problem in the management of hypertension. At baseline, there was medium medication adherence in the PCI and this was significantly improved post-intervention ($p = 0.001$). This result is similar to another study[26] where patients were educated about the importance of medication adherence in order to reduce blood pressure and improve treatment outcomes.

The baseline and endpoint outcomes in the SMD group showed high level of medication adherence. However, findings revealed poor blood pressure reduction despite high level of medication adherence in the SMD group. This could be due to several factors, such as, patient forgetting to take their medications, intentional lack of adherence, duration of treatment or cost of therapy and often unpleasant medications side effects. This then indicated that poor blood pressure reduction was not related to poor medication adherence alone.[20] Several studies found that the most common reason for poor BP reduction was clinical inertia and drug-related causes.[27,28,29] High adherence and poor blood pressure reduction among the SMD group demonstrated that medication adherence is self-reported and may not be reliable as patients may give positive responses in order to satisfy health care workers.[30]

V. CONCLUSION

Medication adherence is a health problem that is difficult to obtain among hypertensive patients. Based on the outcomes of the 3-months pharmacist clinical intervention, blood pressure reduction and medication adherence were significantly improved compared with the routine/SMD practices. The use of this team-based strategy to control blood pressure and improve medication adherence has proven effective in the reduction of high blood pressure. Therefore, for any health care system to thrive in its management of hypertensive patients, the involvement of pharmacist clinical among hypertensive patients is strongly recommended.

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Authors' contributions

GFS, MPD and EIN conceived the study. EFH, KCS, EAD and JTP provided technical inputs. All authors read the document for academic content and approved the final version for publication.

Conflict of Interest

The authors declared no conflict of interest.

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