Pharmacists-led diabetes care in Nigeria (2000-2022): A systematic review

Emmanuel A. David[1,2] , Rebecca O. Soremekun[2], Isaac O. Abah[3], Muhammed Y. Katagum[4], Adefolarin A. Amu[5], Roseline I. Aderemi-Williams[2]

[1] Department of Clinical Pharmacy and Pharmacy Practice, Faculty of Pharmaceutical Sciences, Gombe State University, Gombe State Nigeria

[2] Department of Clinical Pharmacy and Biopharmacy, Faculty of Pharmacy, University of Lagos, Idi-Araba, Surulere, Lagos State Nigeria

[3] Department of Pharmaceutical Services, Jos University Teaching Hospital, Plateau State Nigeria

[4] Department of Clinical Pharmacy and Pharmacy Administration, Bauchi State University, Gadau Bauchi State Nigeria

[5] Department of Pharmacy, Faculty of Health Sciences, Eswatini Medical Christian University, Mbabane, Eswatini

ARTICLE INFO

ABSTRACT

Background: Diabetes mellitus (DM) is a noncommunicable disease of global health concern, which is targeted for reduction according to the Sustainable Development Goals 3.4. The burden in Nigeria rose from 2.2% in 1997 to 5.77% in 2018. It is associated with high morbidity and mortality, thus requiring a collaborative care approach involving the patients and all healthcare providers to ensure optimal care. Pharmacists worldwide are involved in diabetes care, with evidence of positive outcomes, but the contributions of pharmacists in diabetes care have not been extensively reviewed in Nigeria. This review was aimed at describing the trends, geographical spread and quality of pharmacist-led diabetes care/research in Nigeria

Methods: To identify diabetes-care research conducted by pharmacists in Nigeria, literature search for articles published between January 1, 2000 and June 5, 2022 was conducted, using databases such as PubMed/Medline, African Journal Online, Clinical Trials Registries, and Google Scholar. Medical subject headings (MeSH) and search terms combined with Boolean operators were among the keywords and search terms used for article identification. Only studies published in English language were considered.

Results: Of the 62 studies retained for review, 51 were conducted in the southern zone of Nigeria (South-West 25, South-East 15 and South-South 11) and 11 in the north (North-East 6, North-Central 4 and North-West 1). Most of the studies (92%) were published between 2010 and 2022, with 83.9% conducted using cross-sectional design, 4.8% were Quasi-Randomized Studies and 11.3% were Randomized Controlled Trials. This review revealed that compared to usual care, patients who received pharmacist-delivered care had significantly improved medication adherence, quality of life and other clinical variables, with more cost-effective management outcomes.

Conclusion: The contributions of pharmacists to diabetes care in Nigeria have significantly improved over the last decade. Majority of studies (82.3%) were conducted in the country's southern zone and only 11.3% were Randomized Controlled Trials with significant improvement in patients' treatment outcomes. More pharmacist-led high quality patient care research are recommended at the state (especially northern states) and national levels to improve on the current evidence of pharmacists' contribution to diabetes management in the Nigeria

1. Introduction

Diabetes Mellitus is a chronic degenerative disease that results from the body's inability to produce or respond to insulin or both[1,2]. It affects protein, carbohydrate and fat metabolisms[1] and is often associated with comorbid conditions including hypertension, dyslipidemia, obesity and atherosclerosis[2]. Micro- and macrovascular complications such as retinopathy, nephropathy, neuropathy, coronary artery disease, peripheral arterial disease and stroke are also commonly found among diabetic populations[1,2], warranting treatment with variety of medications, in addition to non-pharmacological strategies. The non-drug measures are medical nutrition therapy

(MNT), graduated physical activities or exercises and tobacco cessation program. Pharmacotherapy include the use of oral antihyperglycaemic agents (OAHAs), insulin therapies, blood pressure lowering medications, antilipidaemic agents (ALAs) and glucose-friendly nutraceuticals[3,4]. It is therefore expected that the management of diabetes mellitus (DM) would require a multidisciplinary team approach, involving physicians, pharmacists, nurses, diabetes educators, nutritionists and other healthcare specialists to ensure optimal treatment outcomes including blood glucose control (less than 7% glycated haemoglobin concentration or less than 7mmols/L of fasting blood glucose levels), weight reduction (body mass index: 18.5 kg/m^2 and 24.9kg/m2), blood pressure (average of less than 140/80 mmHg) and controlled lipid concentrations (total cholesterol <5.2mmol/L, low density lipoprotein cholesterol <2.6mmol/L high density lipoprotein cholesterol >1.3mmol/L, triglycerides <1.7mmol/L)[5,6,7]. With the myriad of medications usually prescribed for DM treatment, especially type 2 diabetes mellitus (T2DM), the inclusion of pharmacists in diabetes care team is highly recommended to ensure optimisation of care outcomes[8,9]. The pharmacy-related services (PS) include prescription validation, patient education, medication adherence counselling, medication reconciliation, medication therapy management including identification and resolution of drug therapy problems, provision of drug therapy information to both patients and other healthcare professionals, pharmacovigilance, medication dispensing and referrals[10,11,12]. Previous diabetes-related reviews in Nigeria have focused on the burden of prediabetes, prevalence, hospitalization, mortality and risk factors associated with DM[13,14,15,16], but the scope of pharmacists' involvement in diabetes care in Nigeria has not been extensively reviewed. This review was aimed at describing the geographical spread and quality of pharmacists-led diabetes care research in Nigeria.

2. Methods

2.1 Study location: Nigeria is one out of the seventeen (17) countries in the West African sub-region, often regarded as the most populous black nation in the world, with an estimated population of 216,468,451 as at June 13th, 2020[17,18]. The population is projected to hit 264 million by the year 2030 and cross the 300 million threshold somewhere around 2036[18]. The country has a total land area of 923,769 square kilometers (Km^2) and is divided into six (6) geopolitical zones, with thirty-six (36) states and a federal capital territory.

2.2 Inclusion criteria: Studies were considered eligible for this systematic review if they met the following criteria: 1) conducted by pharmacists in Nigeria. 2) Conducted among people with DM in Nigeria. 3) Conducted between January 2000 and June 2022. 4) Articles are published in English language. 5) Observational or outcomes studies.

2.3 Exclusion criteria: Diabetes care studies published by other healthcare professionals (non-pharmacists), articles of animal- or laboratory-based diabetes studies, publications of studies with no outcome evaluations and pharmacist-led studies which focused on non-diabetes outcomes were excluded.

2.4 Search strategies: An extensive literature search was conducted to extract articles published between January 1, 2000 and June 5, 2022 using databases including PubMed/Medline, African Journal Online (AJOL), Clinical Trials Registries and Google Scholar to identify pharmacist-led diabetes care studies conducted in Nigeria. The keywords and search terms used for article identification included medical subject headings (MeSH) and text terms combined with Boolean operators: The different search terms entered were a combination of "Pharmacists" and "Diabetes care" and "Nigeria", " "Pharmaceutical care" and "Diabetes care in Nigeria", "Pharmaceutical care" and "Glycaemic control." Grey literatures were identified through the web search in additional to some article reference lists and included. No process to obtain or confirm these findings from authors or investigators was initiated as only their publications' contributions from the mentioned search engines were considered for this review.

2.5 Study selection: Titles and abstracts retrieved from the electronic databases were screened by the reviewers in accordance with predefined criteria and the full texts of most (89.7%) of the potentially eligible articles were obtained, where possible. The retained studies were individually assessed for suitability before final inclusion in the review and all areas of disagreements were resolved through consensus.

2.6 Data extraction and synthesis: The reviewers extracted relevant data from the studies retained in the review including geographical zone, authors' surname, year of publication, study setting (hospital or community), study design, study population (type 1 diabetes patients, type 2 diabetes patients, community pharmacists and hospital

pharmacists), sample size and study outcome (s). A summary of the data extracted is given in table 2:

2.7 Grading quality of studies included: The quality of eligible studies retained in the review were assessed using the grading recommendations provided by Petrisor & Bhandari. Randomized controlled trials (RCTs) were scored "high quality" (1), Quasi-randomized studies were scored "moderate quality" (2), Observational/Cross-sectional studies were scored "low quality" (3) and other evidence like case series or expert opinion "very low quality" (4)[19].

2.8 Ethical Considerations: This systematic review consists of published articles of studies conducted by pharmacists in Nigeria (secondary data) and does not require ethical board approval.

3. Results

A total of 150 diabetes-related studies conducted by pharmacists in Nigeria were identified. The studies were assessed for duplicity and 17 articles were excluded, while 71 other studies were dropped based on the inclusion and exclusion criteria stated above. Thus, a total of 62 studies were finally selected for inclusion in the review (figure 1).

3.1 Study Characteristics: Of the 62 studies retained in the review, 51 were conducted in the southern zone (South-East

15, South-South 11 and South-West 25), while the north accounted for 11 studies (North-East 6, North-Central 4 and North-West 1). Most of the studies (36) were published between 2015 and 2022, followed by 25 articles published through 2008 and 2014, while only one article was found between year 2000 and 2007. In terms of study design and quality, 52 studies were cross-sectional and rated low quality, 3 (quasi-randomized studies) were rated moderate quality and 7 (Randomized Controlled Trials) were rated high quality. Most of the studies (50) were population-based, comprising of patients with T1DM, T2DM and a few non-diabetic individuals in one pre-diabetes study, while 12 articles reported outcomes of researches conducted among community and hospital pharmacists. Fifty three studies (53) were hospital-based, while eight (8) were conducted in community pharmacies and one (1) study involved the hospital and community settings. Outcomes measures for studies retained in the review include assessment of knowledge, attitude and DM self-practice {self-management or monitoring of blood glucose (SMBG)}, pharmaceutical care knowledge, practice and barriers and health related quality of life. Adherence to oral antihyperglycaemic agents and lifestyle changes were also evaluated, as well as factors associated with glycemic control, treatment outcomes in diabetic patients and pharmacoeconomic evaluations.

Table 1: Studies Included in the Review

S/N	Geo-Political Zones	Author	Year of Publication	Study Design	Study Setting	Population	Sample Size	Study Outcome	Quality Grading
1	**South-East**	Adibe et al.[20]	2009	Cross-sectional	Hospital	T1DM & T2DM Patients	426	Diabetes self-care	3
2		Odo et al.[21]	2013	Cross-sectional	Community	Community Pharmacists	60	Practice of Pharmaceutical care Knowledge, & Practice of Pharmaceutical Care	3
3		Ogbonna et al.[22]	2013	Cross-sectional	Hospital	Hospital Pharmacists	130	Diabetes Care Practice of Pharmaceutical Care	3
4		Ogbonna et al.[23]	2015[a]	Cross-sectional	Community	Community Pharmacists	208	Self-care Knowledge	3
5		Adibe et al.[24]	2011	Cross-sectional	Hospital	T2DM Patients	400		3
6		Adibe et al.[25]	2014	Randomized Controlled Trials	Hospital	T2DM Patients	220	Clinical Outcomes	1

S/N	Geo-Political Zones	Author	Year of Publication	Study Design	Study Setting	Population	Sample Size	Study Outcome	Quality Grading
7		Ogbonna et al.[26]	2015[b]	Cross-sectional	Hospital	Hospital Pharmacists	78	Pharmaceutical Care Barriers	3
8		Adibe et al.[27]	2013[a]	Randomized Controlled Trials	Hospital	T2DM Patients	220	Quality of Life	1
9		Adibe et al.[28]	2013[b]	Randomize Controlled Trials	Hospital	T2DM Patients	220	Cost Utility of Pharmaceutical Care	1
10		Ogbonna et al.[29]	2014	Cross-sectional	Hospital	T2DM Patients	399	Practice of pharmaceutical care	3
11		Anene-Okeke et al.[30]	2021	Cross-sectional	Hospital	T2DM Patients	340	Knowledge, Practice & Barriers to Self-care	3
12		Okoro et al.[31]	2018	Cross-sectional	Hospital	T1DM & T2DM Patients	115	Drug Utilization study	3
13		Ogbonna et al.[32]	2015[c]	Cross-sectional	Hospital	T2DM Patients	383	Clinical outcome study	3

Keys: T1DM= Type 1 Diabetes Mellitus; T2DM= Type 2 Diabetes Mellitus; DM= Diabetes Mellitus; HRQoL= Health Related Quality of Life; NHIS= National Health Insurance Scheme; QoL= Quality of Life

Table 2: Studies Included in the Review Continued

S/N	Geo-Political Zones	Author	Year of Publication	Study Design	Study Setting	Population	Sample Size	Study Outcome	Quality Grading
14		Ogbonna et al.[33]	2015[d]	Cross-sectional	Hospital	T2DM Patients	330	Adherence study	3
15		Adibe et al.[34]	2018	Cross-sectional	Hospital	T2DM Patients	147	Quality of Life study	3
16	South-South	Bello et al.[35]	2012	Quasi-randomized	Hospital	T1DM & T2DM Patients	170	Clinical outcomes study	2
17		Oparah et al.[36]	2009	Randomized Controlled Trials	Hospital	T1DM & T2DM Patients	99	Clinical outcomes study	1
18		Mgbahurike et al.[37]	2018	Cross-sectional	Community	community Pharmacists	190	Practice of Pharmaceutical care	3
19		Odili et al.[38]	2011	Cross-sectional	Hospital	T1DM & T2DM Patients	100	Knowledge of Diabetes	3
20		Odili et al.[39]	2013	Cross-sectional	Community	Community Pharmacists	78	Pharmaceutical Care Barriers	3
21		Eshiet et al.[40]	2021	Prospective Cross-sectional	Hospital	T1DM & T2DM Patients	120	Pattern of Drug Utilization	3
22		Suleiman et al.[41]	2015	Cross-sectional	Hospital	T1DM & T2DM Patients	400	Pharmacoeconomic study	3
23		Ganiyu et al.[42]	2018	Prospective Cross-sectional	Hospital	T1DM & T2DM Patients	430	Health-Related QoL	3
		Suleiman		Cross-		T1DM & T2DM		Clinical outcomes	

S/N	Author	Year	Study Design	Study Setting	Population	Sample Size	Study Outcome	Quality Grading
24	et al.[43]	2014	sectional	Hospital	Patients	263	study	3
25	Ajulo et al.[44]	2018	Observational Cross-sectional	Hospital	T2DM Patients	119	Clinical outcomes study	3
26	Adje et al.[45]	2016	Cross-sectional	Community	Community Pharmacists	107	Practice of Pharmaceutical care	3

Keys: T1DM= Type 1 Diabetes Mellitus; T2DM= Type 2 Diabetes Mellitus; DM= Diabetes Mellitus; HRQoL= Health Related Quality of Life; NHIS= National Health Insurance Scheme; QoL= Quality of Life

Table 3: Studies Included in the Review Continued

S/N	Geo-Political Zones	Author	Year of Publication	Study Design	Study Setting	Population	Sample Size	Study Outcome	Quality Grading
27	**South-West**	Amadi et al.[46]	2018	Cross-sectional	Community	Community Pharmacists	168	Knowledge of DM	3
28		Ekore et al.[47]	2010	Cross-sectional	Hospital	T1DM & T2DM Patients	137	Diabetes self-care	3
29		Amaeze et al.[48]	2018	Cross-sectional	Hospital	T2DM Patients	453	Drug utilization study	3
30		Oyetunde et al.[49]	2014	Cross-sectional	Hospital	T1DM & T2DM Patients	102	Drug utilization study	3
31		Yusuff et al.[50]	2008	Cross-sectional	Hospital	T2DM Patients	200	Adherence study	3
32		Adisa et al.[51]	2009	Cross-sectional	Hospital	T2DM Patients	121	Adherence Study	3
33		Saka et al.[52]	2018	Prospective Cross-sectional	Hospital	T2DM Patients	110	NHIS-related study	3
34		Suleiman et al.[53]	2006	Cross-sectional	Hospital	T1DM & T2DM Patients	277	Pharmacoeco-nomic study	3
35		Adisa et al.[54]	2011	Cross-sectional	Hospital	T2DM Patients	114	Adherence study	3
36		Aje et al.[55]	2017	Cross-sectional	Hospital	Hospital Pharmacists	63	Diabetes care	3
37		Ojieabu et al.[56]	2017	Randomized Controlled Trials	Hospital	T2DM Elderly Patients	150	Clinical Outcomes study	1
38		Ojieabu et al.[57]	2020	Randomized Controlled Trials	Hospital	T2DM Patients	170	Drug utilization study & HRQoL	1
39		Adisa et al.[58]	2013	Prospective Cross-sectional	Hospital	T2DM Patients	176	Drug utilization study	3
40		Adisa et al.[59]	2014	Prospective cross-sectional	Hospital	T2DM Patients	176	Adherence study	3

Keys: T1DM= Type 1 Diabetes Mellitus; T2DM= Type 2 Diabetes Mellitus; DM= Diabetes Mellitus; HRQoL= Health Related Quality of Life; NHIS= National Health Insurance Scheme; QoL= Quality of Life

Table 4: Studies Included in the Review Continued

S/N	Geo-Political Zones	Author	Year of Publication	Study Design	Study Setting	Population	Sample Size	Study Outcome	Quality Grading
41		Onwuchuluba et al.[60]	2019	Cross-sectional	Hospital	T2DM Patients	418	Adherence study	3
42		Ipingbemi et al.[61]	2021	Quasi-randomized controlled study	Hospital	T2DM Patients	201	Adherence & pharmacoeconomic study	2
43		Ajiboye[62]	2013	Cross-sectional	Community	Community Pharmacists	185	Practice of Pharmaceutical care	3
44		Iheanacho et al.[63]	2021	Cross-sectional	Hospital	Non Diabetic Patients	300	Diabetes care	3
45		Ojieabu et al.[64]	2015	Cross-sectional	Hospital	T1DM & T2DM Patients	152	Drug utilization study	3
46		Ipingbemi et al.[65]	2015	Cross-sectional	Hospital	T2DM Patients	52	Pharmacoeconomic study	3
47		Ayeni et al.[66]	2020	Prospective Cross-sectional	Hospital	T2DM Patients	52	Pharmacoenimic study	2
48		Ayeni et al.[67]	2021	Quasi-randomized controlled	Hospital	T2DM Patients	671	Clinical outcomes study	3
49		Segun et al.[68]	2022	Cross-sectional	Community	Community Pharmacists	36	Practice of Pharmaceutical care	3
50		Adisa et al.[69]	2019	Prospective Cross-sectional	Hospital	T2DM Patients	403	Practice of Pharmaceutical care	3
51		Awodele et al.[70]	2015	Prospective Cross-sectional	Hospital	T2DM Patients	152	Adherence study	3

Table 5: Studies Included in the Review Continued

S/N	Geo-Political Zones	Author	Year of Publication	Study Design	Study Setting	Population	Sample Size	Study Outcome	Quality Grading
52	North-Central	Abdullazeez et al.[71]	2014	Cross-sectional	Hospital	T2DM Patients	220	Drug utilization	3
53		Osuafor et al.[72]	2021	Cross-sectional	Community & Hospital	T1DM & T2DM Patients	65	Availability, pharmacoenomics study	3
54		Okunlola et al.[73]	2022	Cross-sectional	Hospital	T2DM Patients	448	Knowledge and practice diabetes self-care	3
55		Bello et al.[74]	2020	Cross-sectional	Hospital	T2DM Patients	262	Diabetes care study	3
56	North-East	Sa'ab et al.[75]	2011	Cross-sectional	Hospital	Hospital Pharmacists	29	Knowledge & Practice of Pharmaceutical Care	3
57		David et al.[76]	2021	Randomize Controlled Trials	Hospital	T2DM Patients	108	Clinical outcomes	1
58		Okoro et al.[77]	2012	Cross-sectional	Hospital	T1DM & T2DM Patients	72	Adherence study	3
59		David et al.[78]	2020	Prospective Cross-sectional	Hospital	T2DM Patients	200	Drug utilization and clinical outcomes study	3

60		David et al.[79]	2019	Cross-sectional	Hospital	T2DM Patients	385	Clinical outcomes	3
61		Sabo et al.[80]	2019	Cross-sectional	Hospital	T1DM & T2DM Patients	77	knowledge of Diabetes	3
62	**North-West**	Adamu et al.[81]	2020	Observational Cross-sectional	Hospital	T1DM & T2DM Patients	216	Clinical outcomes	3

Keys: T1DM= Type 1 Diabetes Mellitus; T2DM= Type 2 Diabetes Mellitus; DM= Diabetes Mellitus; HRQoL= Health Related Quality of Life; NHIS= National Health Insurance Scheme; QoL= Quality of Life
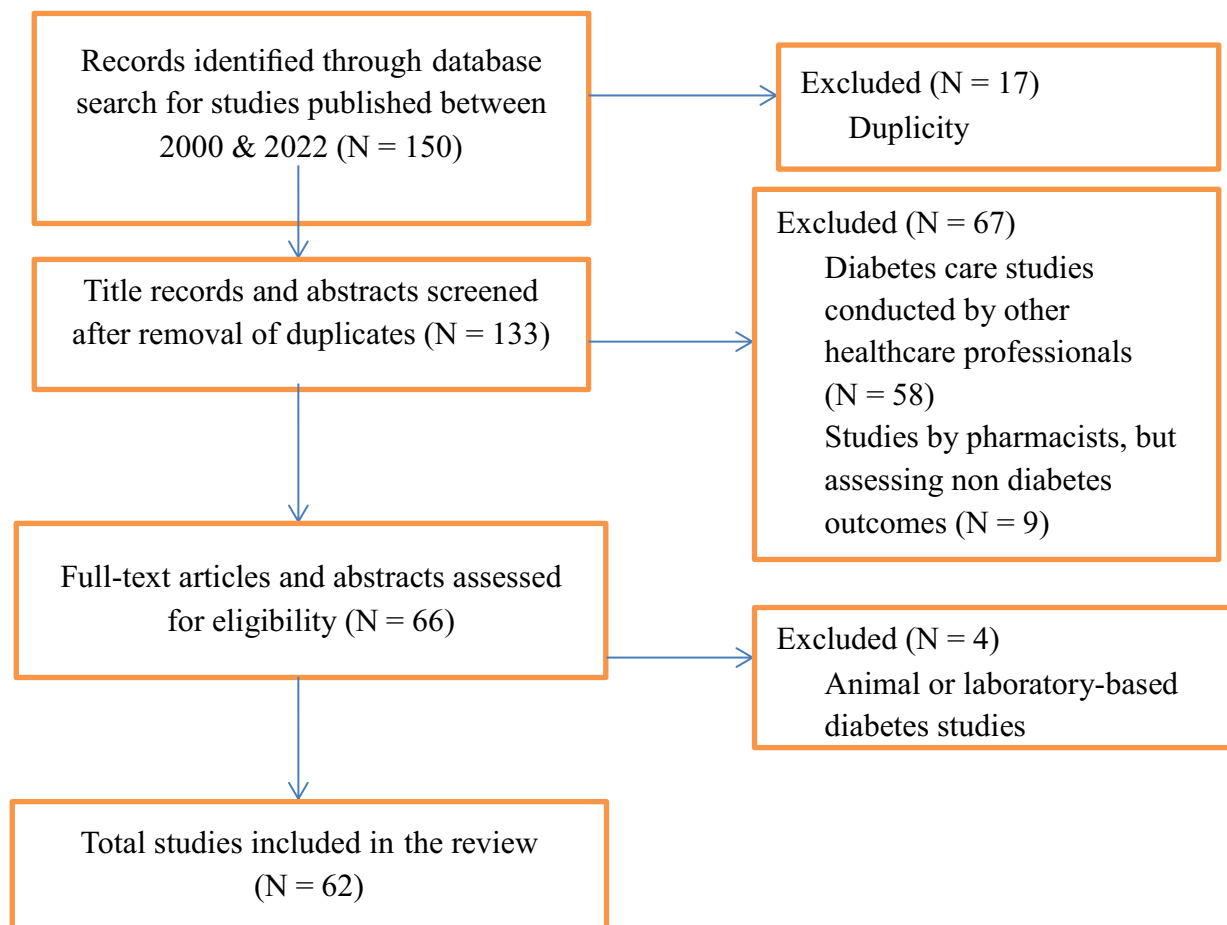
Figure 1: Systematic Review Flow Diagram

3.2 Outcomes Measures

3.2.1 Diabetes Knowledge and Self-care Practices: Ten studies[20,22,25,30,38,46,47,55,73,80] with a total of 2,066 participants reported different aspects of diabetes knowledge and self-care practices among diabetic patients, community pharmacists and pharmacists in the hospital practice setting. Majority of the patients reported family history of DM and had lived with diabetes for ≥ 1 year. Two studies[20,55] documented the level of physical activity among participants, while Aje and Adekoya[54] categorized patients' alcohol consumption rates and another author[20] reported that 26.6% discussed modalities to stop smoking with their healthcare team. The knowledge of DM varied among different study populations, ranging from 50% to 91.7%[47,80]. Two studies reported mean knowledge of DM self-care (DMSC) as 22.1%±3.0% and 39.5%±16.7%[38,80], while Anene-Okeke et al.[30] reported good knowledge of DMSC in 64% of the study population. Positive attitude (61%) and practice (76%) towards DMSC were reported in two studies[25,73], but other studies[38,80] recorded lower practice rates of 53.8% and 48.2%. Okunlola et al.[73] reported that marital status (P = 0.022), level of education (P = 0.000), employment status (P = 0.000) and family history (P = 0.012) were significantly associated with knowledge of DM and DMSC, while two studies[30,38] found that lack of motivation, inconveniences, low knowledge level were significantly associated with practice of DMSC (r=0.217; 95% CI = 0.02 – 0.39, P < 0.05).

3.2.2 Pharmaceutical Care Practice and Barrier:
Pharmaceutical care (PC) embodies a patient-centered and outcome-oriented pharmacy practice where pharmacists seek to optimise patients' treatment outcomes by ensuring effective, rational and safe use of medicines[82]. This review found twelve studies[21,23,26,28,29,36,37,39,45,68,69,75] comprising a total of 1,749 participants which published activities related to PC practice and barrier. The types of drug therapy problems observed in the studies were: the need for additional drug therapy, unnecessary drug therapy, dosage too high, dosage too low, interactions, adverse drug reactions, medication non-compliance or adherence. One study[23] reported several barriers to PC including poor pharmacists' attitude toward pharmaceutical care practice, resource-related constraints, system-related constraints, inter-professional obstacles and academic obstacles. One study[36] revealed that PC practice significantly improved patients' awareness of self-monitoring of blood glucose (SMBG) and adherence (p< 0.0001).

3.2.3 Drug Utilization Studies: Thirteen studies[31,40,43,44,48,49,57,58,59,60,65,71,79] reported drug utilization pattern among diabetic patients, with a total of 3,179 patients. Metformin was the most commonly prescribed OAHA[31,59,79], perhaps because of its weight loss advantage, tolerability, little or no hypoglycaemic effect and affordability[1] (ADA, 2019). The presence of comorbidity was reported in some of the studies including hypertension, overweight, stoke, retinopathy, neuropathy, nephropathy and dyslipidaemia[40,43,48,65,79], which further confirms the need for multiple medication utilization in patients with DM. One study[49] discussed drug or therapy brand switching. The study found that 38.6% of patients who experienced therapy switch had no knowledge of the substitution, 19.6% did not use drug after the switch, 35.6% rejected any substitution, 14.9% brand substitutions resulted in confusion for the patients and 24% substitution resulted in more side effects[49].

3.2.4 Quality of Life Studies: Three studies[27,42,57] reported health-related quality of life (HRQoL) among diabetic patients in Nigeria, with a total number of 697 participants. All three studies assessed physical, mental and emotional health domains including physical functioning (pain), mental health and emotional well-being, while two studies[27,57] reported that patients had significant improvement in their HRQoL following pharmacist intervention. Adibe et al.[27] carried out periodic follow-up intervention among patients with T2DM and found that the overall HRQoL of participants in pharmaceutical care (PC) arm was significantly improved at 6 months and 12 months compared to the usual care (UC) arm (0.79± 0.07 vs. 0.65 ± 0.05; P< 0.0001 and 0.86 ± 0.12 vs. 0.64± 0.10; P< 0.0001). A second study which involved 4 and 8 months follow-up[57] (Ojieabu et al., 2020) also reported significant improvement in the intervention group, except for pain domain (p< 0.001 vs p< 0.05).

3.2.5 National Health Insurance Studies among Diabetic Patients: Only one study[52] in this review examined the level of compliance to the National Health Insurance Scheme (NHIS) among patients with DM. The study had a total of 110 participants and approximately 50% received monthly salaries of more than #30,000.00. Slightly above one-third (44) participants admitted enrollment into the scheme and the study reported that the perception on drug availability and pharmacists' waiting time were significantly different among insured and uninsured enrollees (p < 0.001), such that while the insured

participants had positive perception about drug availability and pharmacy waiting time, the uninsured were negative.

3.2.6 Medication Adherence Studies: Medication adherence is a key strategy that ensures therapy optimisation, but many studies have reported poor medication adherence among people with DM. Ten studies[33,50,51,54,59,60,61,70,71,77] reported pharmacists' activities with regards to adherence among patients with DM. The studies were mostly cross-sectional, with a total of 1,761 participants. The mean duration of DM reported among the participants ranged between 6.3±5.6 years and 9.65 ± 8.62 years[59,61,77], with majority using OAHAs and few on insulin therapy[50,60]. The prevalence of non- or poor adherence found in this review was between 27.5% and 77.1%[59,60] and factors associated include financial constraint/cost of medication, forgetfulness, age, drug out-of-stock, long waiting time at the clinic or pharmacy, insufficient information on medication, complexity of dosage regimen, lack of family support, busy work schedule, medication side effects and non-response after taking medication[54,59,60,61,70,77]. Adisa *et al*.[59] categorized the reasons for medication non-adherence as intentional and unintentional. The reasons for intentional non-adherence include side effects or deliberate dosage omission due to fear associated with daily medication ingestion, inconveniences of taking medications outside the home, fear of taking too many drugs at a time, too busy work schedule and unpleasant taste of drugs. The reasons for unintentional non-adherence include forgetfulness or difficulty in filling prescription due to cost of medication, inability to get medication refill at nearby pharmacy and scarcity of prescribed medication(s). Two studies[71,77] reported that the factors significantly associated with medication adherence includes educational qualification, gender, income and belief in the efficacy of medication (p<0.05). This review also revealed that most patients do not disclose their non-adherent status to their healthcare providers due to short consultation period and lack of privacy[50].

3.2.7 Treatment Outcomes: A total of nine studies[25,32,34,35,56,76,78,79,81] focused on glycaemic control and other treatment outcomes among diabetic patients. The study participants were 1,861 and three studies[35,56,76] showed that the provision of drug therapy counseling, education and follow-up text messages (electronic intervention) significantly reduced glycated haemoglobin (A1C) concentrations and fasting blood glucose (p<0.05) levels in patients with uncontrolled DM. Furthermore, blood pressure, body mass index (BMI), clinic attendance, diet,

exercise and adherence to medications were also improved in patients who received pharmacists' intervention[35,56,76]. Adamu *et al*.[81] reported that gender, use of fixed-dose combination, physical activity were associated with greater odds of good glycaemic control, while the presence of diabetic foot ulcer or more than one complication lowers the odds of achieving good glycaemic control.

3.2.8 Pharmacoeconomic Outcomes Studies: Pharmacoeconomics is a relatively new area in clinical pharmacy practice, especially in Nigeria. It has great potential to improve pharmacists' self-image, relevance and attract reimbursement in the near future. As the transition in modern pharmacy practice continue to evolve toward providing services and playing greater roles in health promotion, disease prevention, medication therapy management and PC provision (in addition to the long-established traditional roles of preparation, dispensing and supply of medicines), the need to estimate the economic benefits of pharmacists' contributions to patient care is increasingly getting apparent. This review found six studies[26,41,53,59,61,65] which covered different aspects of pharmacoeconomics, with a total of 676 participants and an inter-facility based study[72]. Five studies[26,41,53,61,65] reported the annual cost of illness among people with diabetes, the mode of payment adopted by patients for their medication and other healthcare consumptions[61] and the impact of pharmacist-led care on pharmacoeconomic parameters[26], while a study[59] estimated the annual cost of managing the comorbidity of DM and tuberculosis (8,604,819). The annual cost of illness for diabetic patients in Nigeria ranges between #194,067.66 and 268,572.81, while majority (80.8%) practiced out-of-packet mode of payment and there was significant correlation between age and cost of illness (p< 0.05). In a randomized controlled pharmacist intervention study, Adibe *et al*.[26] reported a positive improvement in incremental cost effectiveness ratio (ICER) value of #10,623 with a corresponding 0.12 quality adjusted life years (QALY) gained. The improvement was associated with an ICER of #88,525, while the net monetary benefit expressed in willingness to pay went from zero to #450,000. In the inter-facility based study, Osuafor *et al*.[72] reported the availability of originator brands (OBs) and low priced generics (LPGs) in the public hospital pharmacies, private pharmacies and private hospital pharmacies. The study assessed percentage price difference between procurement prices and patients' prices for OBs and LPGs across the three categories of pharmacies and found that no OBs were affordable, while LPGs were sold at 49.4% mark-

up in public hospital pharmacies, 51.4% in private pharmacies, and 323% in private hospital pharmacies.

4. Discussion

The impact of pharmacist-led care/programs on treatment outcomes of patients with DM is globally proven using RCTs[8,9], but the evidence is scanty in Nigeria. The results showed that over 50% (36 out of 62) of the studies were conducted between 2015 and 2022 and approximately 98% (61 out of 62) between 2008 and 2022. This suggests that pharmacist-led diabetes care research has significantly increased in the recent past. Study distribution is skewed in favor of the southern zone of the country, which accounts for 82% of the studies included in this review. This is similar to the reports of other Nigerian diabetes-based reviews published in the past[13,14]. The reviewers observed that most of the studies were cross-sectional surveys aimed to assess outcomes such as patients or pharmacists' knowledge of DM, attitude and practice regarding DM management, knowledge of, practice and barriers related to pharmaceutical care, DMSC, prevalence of DM, pharmacoeconomic evaluations, glycaemic control, adherence to DM medications and lifestyle recommendations[21,22,30,33,39,42,47,59,79]. Other outcomes include assessment of HRQoL and drug therapy problems[27,68]. Therefore, the level of evidence provided by these studies was rated low, which is supported be earlier reviews[13,14]. The review found ten (10) studies of moderate to high quality ratings (3 quasi randomized studies and 7 RCTs) conducted by pharmacists among people with DM in Nigeria[25,27,28,35,36,56,57,61,67,76]. Most of the studies sought to estimate the impact of pharmacists' intervention and pharmaceutical care service delivery on treatment outcomes, while some assessed the effect of pharmacists' intervention on patients' adherence to medication[61] and the cost utility for providing Pharmaceutical care[28]. On the zonal distribution of the moderate and high quality studies; four (4) studies were conducted in South-West[57,61,67], three (3) in South-East[25,27,28], two (2) in South-South[35,36] and one (1) in North-East[76] geo-political zones respectively. In the 7 RCTs and 3 quasi randomized studies, the addition of pharmacist-provided care resulted in significant improvement in treatment outcomes and adherence. This is a positive development and it demonstrates that pharmacists in Nigeria are beginning to take their place as critical stakeholders in the delivery of quality healthcare to the public and optimizing drug therapy outcomes through the provision of pharmaceutical care services. However, it is lamentable that despite the overwhelming evidence of positive outcomes previously reported[9] and observed in this review, only a single RCT has been conducted in the whole of northern Nigeria[75]. Furthermore, both the cross sectional surveys and RCTs conducted by pharmacists with regards to diabetes care, the north accounts for barely 17.7% (11 out of 62), with the North-East contributing 54.6% (6 out of 11) of the northern studies and 9.7% (6 out of 62) of the entire country. The observation in this review is therefore a wakeup call to all pharmacists in Nigeria and especially in the northern region of the country to take pragmatic steps towards bridging the gaps and dearth of pharmacist-led involvement in diabetes care.

5. Limitation

Although an extensive literature search was conducted to ensure the inclusion of all published articles between January, 2000 and June, 2022, it is still possible that articles not archived in PubMed/Medline, African Journal Online (AJOL), Clinical Trials Registrar and Google Scholar repositories may be missing in this review. Nevertheless, the databases used for article search makes up the largest and most patronized medical and healthcare data repositories in the world. Thus, the outcome of this review may not be negatively affected in anyway.

6. Conclusion

According to this review, the contribution of Nigerian pharmacists in diabetes care has greatly improved over the last decade. However, majority of the studies were conducted in the country's southern region, and only 7 were randomized controlled trials (high quality studies), with evidence of positive outcomes in patients who received pharmacist intervention. Well-designed, high-quality facility-based pharmacist-led interventional research is recommended at local government, state, regional, and national levels, to provide more home-grown data to policymakers on the importance of including pharmacists in diabetes care teams across the country and employing more pharmacists in public health institutions for optimal care delivery.

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