

A Nationwide Survey of Parkinson's Disease Medicines Availability and Affordability in Nigeria

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Abstract: Background and Objectives: Limited access to medicines can impact negatively on outcomes in people with Parkinson's disease (PD). The study objectives were to determine the availability and assess the affordability of antiparkinsonian medications in pharmacies across Nigeria.

Methods: This was a cross-sectional nationwide study utilizing the World Health Organization/Health Action Initiative methodology. Strategically selected private- and public-sector pharmacies in the six geopolitical zones of Nigeria were surveyed for availability of medicines for management of early and advanced PD. The nine categories were: levodopa/peripheral decarboxylase inhibitors, dopamine receptor agonists, monoamine oxidase type B inhibitors, anticholinergics, catechol-o-methyl transferase inhibitors, atypical antipsychotics, antidepressants, antidementia drugs, and miscellaneous (e.g., drugs for orthostatism, urinary incontinence, and sleep disturbance). Unaffordability was defined as paying more than 1 days' wages (>N600 or > US\$1.67) for a standard 30-day supply.

Results: One hundred twenty-three pharmacies were surveyed (62 private [50.4%] and 61 public sector [49.6%]; range of 15–25 pharmacies in each geopolitical zone). Private exceeded public-sector availability across all nine categories of PD medicines ($P < 0.05$). The most available medicines were dopamine receptor agonists (68.3%; predominantly ergot-derived bromocriptine), anticholinergics (56.1%; mainly trihexyphenidyl), and L-dopa formulations (48%; mainly 250/25 L-dopa/carbidopa). Only two medications (trihexyphenidyl tablets and biperiden injection) were affordable. The average number of day's minimum wages for a 30-day supply of PD medicines was 41.3 days (range, 1–371).

Conclusions: PD medicines access is limited in Nigeria. Strategies, including engagement of stakeholders to consider interventions to improve and prioritize PD medicines access, are urgently warranted.

Parkinson's disease (PD) is one of the top 10 neurological diseases encountered in primary care in Africa and the sixth-most frequent neurological disease in specialist care.¹ The Global Burden of Disease Study 2015 ranks PD 11th globally and in most of Africa with respect to attributable burden measured using age-standardized disability rates.² The number of persons with PD in developing countries is projected to increase from 2.37 to 3.08 million between 2015 and 2030.³ Data from the

United Nations (UN) indicate that more than half of the global population growth between 2015 and 2030 will be from Africa.⁴ This population growth is attributed to projected prolonged life expectancy and aging of the population. Nigeria currently has the seventh-largest population in the world, and is the most rapidly growing, with its population expected to surpass that of the United States by 2050, at which time it would become the third largest in the world.⁴ Given that PD affects approximately 1% of

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persons aged 65 to 85 years, and 4.3% of those > 85, considering the projected population expansion and survival into old age in Nigeria, the burden of PD will certainly become more immense in the near future.⁵

In spite of the growing numbers of people with PD globally, access to health care in general, and medications in particular, remains problematic. The UN Development Group (2003) defines access as “having medicines continuously available and affordable at public or private health facilities or medicine outlets that are within one hour’s walk from the homes of the population.”⁶ Access is a multidimensional concept that encompasses availability, acceptability, affordability, and accessibility. The second edition of the World Health Organization (WHO) Neurology atlas published in 2017 reported that drugs for PD were available to only 3% who needed them in primary care in Africa (in contrast to 69% in Europe and 34% global average).⁷ Pilot surveys suggest that there has been little or no change in PD medicines availability in most African countries, and wide intra- and intercountry variability is highly probable.^{8,9}

The Global PD Charter emphasizes this challenge, stating that “world governments and all healthcare providers should take strong and decisive action in making PD a public health priority area” and “ensure people with PD receive appropriate treatment.”¹⁰ In addition, the charter advocates for improved access to care across the full spectrum of PD.¹⁰ The present survey was aimed at investigating the availability and affordability of PD medicines in Nigeria, as part of a wider sub-Saharan Africa (SSA) initiative of the International Parkinson and Movement Disorder Society (MDS) Task Force on Africa to determine the status of access to PD medicines in Africa. The specific objectives were to determine the availability and assess the cost and affordability of antiparkinsonian medications in pharmacies across Nigeria. Such data are indispensable as an objective basis to inform policy change and advocate for improved access to medicines for people living with PD.

Materials and Methods

Study Procedures

The study was a cross-sectional national survey utilizing an adaptation of the 2008 (2nd) edition of the World Health Organization (WHO)/Health Action Initiative (HAI) methodology.¹¹ In summary, the WHO/HAI document provides guidance for presurvey preparation, planning the survey, preparation for data collection, data collection in the field, data entry/analysis/interpretation, price components survey, and the data reporting/dissemination. Funding for the survey was provided by the MDS by its Task Force on Africa.

Nigeria is divided into six geopolitical zones, which include the 36 states and the Federal Capital Territory (FCT), Abuja. All six geopolitical zones were included in the survey. There are a total of 3,601 registered pharmacies in the country.¹²

Data were collected from pharmacists in registered pharmacies located in one state of each of the six geopolitical zones of the

country: North West (Kaduna, Kaduna State), North East (Yola, Adamawa State), North Central (Ilorin, Kwara State and Abuja, FCT), South West (Lagos, Lagos State), South South (Oghara, Edo State), and South East (Owerri, Imo State).

Each zone was coordinated by a neurologist, acting as zonal supervisor, and working at a major government tertiary health facility or teaching hospital. Data were collected by 12 trained data collectors (two per zone). Strategic sampling was utilized to ensure inclusion of pharmacies representing the public sector, private sector, and any other sector (e.g., mission) as defined by the WHO/HAI method.¹¹ For each zone, a minimum of five public sector hospital pharmacies (main one located in a federal or state teaching hospital located in a state capital and at least four others within the zone) and five private sector medicine pharmacies (randomly selected from pharmacies closest (within 5-km radius) to each public hospital as identified by the zonal coordinator), and at least 2 from another category (where available). Back-up pharmacies for each zone were identified for each pharmacy type at each site and were surveyed in the event of non-availability of 50% of the listed medicine categories at the primary pharmacy. An initial pilot survey at one public pharmacy was conducted in each zone, followed by the main survey (primary and back-up pharmacies) over a 4-week period. Medicines surveyed included medicines used across the spectrum of PD (early and advanced PD) and were categorized into nine groups as follows: levodopa/peripheral decarboxylase inhibitor formulations, dopamine receptor agonists (DRAs; ergot and non-ergot-derived), monoamine oxidase type B inhibitors (MAOIs), anticholinergics, catechol-*o*-methyl transferase (COMT) inhibitors, atypical antipsychotics, antidepressants, antedementia drugs, and miscellaneous (including medications for orthostatism, urinary incontinence, and sleep disturbance). Originator and generic brands availability, dosage strengths, quantity, and cost per defined pack and per unit tablet were determined. Availability was confirmed by physically sighting the medication in the pharmacy at the time of the survey.

Statistical Analysis

Data were analyzed using SPSS software (version 21.0; SPSS, Inc., Chicago, IL) and are presented using descriptive statistics. Availability of medications (major categories and all PD medicines) was calculated as a fraction of number of pharmacies surveyed overall and by geopolitical region. Availability in private versus public sector pharmacies was compared using chi-square test (with $P < 0.05$ statistically significant). Affordability is expressed as the number of days’ wages of the lowest paid unskilled government worker needed to purchase 30 days’ supply using standard treatment regimens. Unaffordability was defined as paying more than 1 days’ wages ($>N600$ or $>US \$1.67$) for a standard 30-day supply.¹³ The number of days wages required to pay for a 30-day supply of each medication was also calculated. At the time of the survey (August to September 2017), the national monthly minimum wage was N18,000 (18,000 Nigerian Naira, equivalent to \$50 United States Dollars or \$1.70 per day).¹⁴

TABLE 1 Distribution and types of pharmacies surveyed by geopolitical zone

Geopolitical Zone	Population of Zone (2006 Census)	Population of Zone (Current Estimate)	No. of Pharmacies Surveyed n (%)	Private Sector n (%)	Public Sector n (%)
North Central	20,339,956	26,073,790	19 (15.4)	11 (57.9)	8 (42.1)
North East	18,984,299	24,335,973	20 (16.3)	10 (50.0)	10 (50.0)
North West	35,915,467	46,040,037	15 (12.2)	7 (46.7)	8 (53.3)
South East	19,710,428	25,266,798	20 (16.3)	10 (50.0)	10 (50.0)
South South	21,044,081	26,976,407	25 (20.3)	13 (52.0)	12 (48.0)
South West	27,722,432	35,537,386	24 (19.5)	11 (45.8)	13 (54.2)
All zones	143,716,663	184,230,391	123 (100)	62 (50.4)	61 (49.6)

Results

Baseline Population Information for Included Zones

The population information for the surveyed zones is provided in Table 1. This includes the population size of the geopolitical zone, state selected for survey within the zone, and town within which the primary pharmacies were located.

Description of Pharmacies Surveyed

Table 1 describes the pharmacy types and number of pharmacies surveyed in each geopolitical zone. In all, 123 pharmacies were surveyed, categorized as public sector (61; 49.6%) and private sector (62; 50.4%). The pattern of pharmacy types did not differ significantly across the zones (Pearson $\chi^2 = 0.89$; $P = 0.54$).

Availability of Medicines for Management of PD

Availability profile for each of the nine categories of PD medicines is provided in Table 2. For the “Miscellaneous” category, availability of each listed medicine is stated in the footnotes. For the other categories, availability overall and for specific categories of medicines is shown, including private- and public-sector pharmacy availability.

Affordability of Available Medicines for Management of PD

The cost of the PD medicines included in the survey, and the price for the estimated 30-day requirement, is shown in Table 3. Prices for originator and generic formulations are shown where available, and affordability, based on the relationship of cost to daily minimum wage (as per the definition in the methodology), is also indicated. Only two of the medications (trihexyphenidyl tablets and biperiden injection) were affordable. The average number of a day's minimum wages for a 30-day supply of PD medicines overall was 41.3 days (range, 1–371).

Discussion

This is the first study reporting the status of access to medicines for the management of PD from Nigeria, and provides the “best scenario” from a nationwide perspective. The major methodological strengths are the nationwide coverage of the survey (which included all the six geopolitical zones) and utilization of the highly recommended WHO/HAI methodology to characterize and select the pharmacies surveyed, ensuring that those most likely to stock specialized medicines were included. Furthermore, the zonal coordinators were all practicing neurologists conversant with the region and able to determine and include pharmacies that, in their experience, were most likely to stock

TABLE 2 Availability of medicines for treatment of PD in 123 pharmacies surveyed

Category	Availability N = 123 (%)	Availability (Private Sector) n = 62 (%)	Availability (Public Sector) n = 61 (%)	P Value
L-dopa formulations	59 (48.0)	47 (75.8)	12 (19.7)	0.000
DRAs	84 (68.3)	56 (90.3)	28 (45.9)	0.000
MAOIs	10 (8.1)	9 (14.5)	1 (1.6)	0.02
COMT inhibitors	3 (2.4)	2 (3.2)	1 (1.6)	1.00
Anticholinergics	69 (56.1)	48 (77.4)	21 (34.4)	0.000
Atypical antipsychotics	22 (17.9)	17 (27.4)	5 (8.2)	0.009
Antidepressants	3 (2.4)	3 (4.8)	0 (0.0)	0.24
Antidementia	41 (33.3)	35 (56.5)	6 (9.8)	0.000
Miscellaneous	See footnote	See footnote	See footnote	See footnote
Overall* (at least one category)	93 (75.6)	59 (95.2)	34 (55.7)	0.000

Footnote: Miscellaneous medications: fludrocortisone (1; 0.8%; private; $P = 1.00$), oxybutynin (26; 21.1%; private 24; $P = 0.000$), melatonin (13; 10.6%; private 12; $P = 0.002$), amantadine (4, 3.3%; private; $P = 0.12$), midodrine (0), apomorphine injection (0). P value comparing availability in private versus public pharmacy types. Atypical antipsychotics: clozapine, quetiapine, aripiprazole. Antidementia: memantine, donepezil, rivastigmine, galantamine. Antidepressants: nortriptyline, desipramine, imipramine.

* Availability of at least one of the categories of medicines.

TABLE 3 Cost and affordability of average 30-day supply of available medications for treatment of PD in Nigeria

Medication	Originator or Generic	Dosage Strength (mg)	Presumed Monthly Need	Price per Tablet (N) (Mean ± SD)	Cost per 30-Day Supply (₦/US\$)*	No. of Day's Wages for 30-Day Supply [†]	Affordability (30-Day Cost > N600) [‡]
l-dopa/carbidopa 250/25	Originator	250/25	90 tablets	173.7 ± 69.8	15,633 (43.4)	26	No
l-dopa benserazide 250/25	Originator	250/25	90 tablets	139.4 ± 51.0	12,546 (34.9)	21	No
l-dopa/carbidopa CR 100/25	Originator	100/25	90 tablets	181.3 ± 14.0	16,320 (45.3)	27	No
l-dopa/carbidopa CR 200/50	Originator	200/50	60 tablets	163.5	9,810 (27.2)	16	No
l-dopa/carbidopa/entacapone	Originator	100/25/200	90 tablets	877.0	78,930 (219.2)	132	No
Bromocriptine	Generic	2.5	90 tablets	83.4 ± 14.1	7,506 (20.9)	12.5	No
Bromocriptine	Originator	2.5	90 tablets	124.6 ± 37.4	11,214 (31.2)	19	No
Pramipexole	Originator	0.18	90 tablets	176.9 ± 8.1	15,921 (44.2)	26	No
Ropinirole	Originator	2	60 tablets	113.2	6,794 (18.9)	11	No
Ropinirole XL 2 mg	Originator	2	60 tablets	481.4	28,886 (80.2)	48	No
Rotigotine	Originator	30 patches	30 patches	7,416	222,500 (618)	371	No
Selegiline	Generic	5	60 tablets	100 ± 8	6,000 (16.7)	10	No
Rasagiline	Originator	5	30 tablets	145.7 ± 19.6	8,742 (24.3)	15	No
Entacapone	Originator	200	90 tablets	122.7 ± 85.8	11,043 (30.7)	18	No
Trihexyphenidyl	Generic	5	90 tablets	8.2 ± 9.1	738 (2.1)	1	Yes
Trihexyphenidyl	Originator	5	90 tablets	40.4 ± 48.5	3,636 (10.1)	6	No
Biperiden (injection)	Originator	5 mg/1 mL	1 vial	788.3 ± 462.0	788 (2.2)	1	Yes
Amantadine	Generic	100	90 tablets	445.3 ± 376.1	40,077 (111.3)	67	No
Amantadine	Originator	100	90 tablets	1,091.1	98,199 (272)	164	No
Clozapine	Generic	100	30 tablets	132.5 ± 17.5	3,975 (11.0)	7	No
Clozapine	Originator	100	30 tablets	211.5 ± 109.8	6,345 (17.6)	11	No
Quetiapine	Generic	100	30 tablets	40.4 ± 4.3	1,212 (3.4)	2	No
Quetiapine	Originator	100	30 tablets	307.5 ± 42.5	9,225 (25.6)	15	No
Nortryptilline	Generic	25	60 tablets	254.8 ± 239.1	15,288 (42.5)	26	No
Memantine	Originator	10 mg	60 tablets	546.4 ± 484.4	32,784 (91.1)	54.6	No
Rivastigmine	Originator	1.5	60 tablets	759.5 ± 527.8	45,570 (126.6)	76	No
Donepezil	Generic	5 mg	30 tablets	87.3 ± 69.9	2,619 (7.3)	4	No
Donepezil	Originator	5 mg	30 tablets	216.1 ± 22.7	6,483 (18.0)	11	No
Fludrocortisone	Originator	0.1 mg	60 tablets	411.0	24,660 (68.5)	41	No
Oxybutinin	Generic	2.5	60 tablets	75.1 ± 90.8	4,506 (12.5)	7.5	No
Melatonin	Generic	3 mg	30 tablets	50.8 ± 47.4	1,524 (4.2)	2.5	No
Imipramine	Originator	25 mg	30 tablets	37.5	1,125 (3.1)	2	No
Aripiprazole	Originator	10 mg	30 tablets	2,250	67,500 (187.5)	112	No

Footnote: ₦ = Nigerian Naira; US\$ = U.S. dollar.

* 30-day cost calculated as price per tablet × presumed monthly need.

† Calculated based on 30-day cost/daily minimum wage of ₦600.

‡ Affordability based on cost of monthly supply not exceeding 1 day's minimum wage (₦600); average number of day's minimum wages to purchase 30-day supply = 41.

PD medicines. The present study aligns with the recommendations from the WHO Global Action Plan for the Prevention and Control of Non Communicable Diseases 2013–2020 (GAP) by considering both availability and affordability of PD medicines and core concepts of the multidimensional model of access.¹⁵ Availability and affordability are closely intertwined and, in our setting, where purchase is predominantly by out-of-pocket expenditure, are regarded as inextricable.¹⁵ Bearing in mind that PD is a progressive neurodegenerative disorder requiring lifelong and consistent treatment, we explored access to medicines used across the spectrum of disease severity, providing a robust and comprehensive perspective.

Our data show that, for the majority of PD medication categories, availability was limited and did not attain the WHO benchmark of 80%. Only one of the nine medication categories (DRAs) was available as defined, and in private-sector pharmacies only. Consistently, private-sector pharmacy availability was higher than that in the public sector for all medication categories. In their study assessing achievement of WHO target for availability of essential medicines to treat noncommunicable diseases (NCDs; principally medications for cardiovascular diseases, diabetes, chronic obstructive pulmonary diseases, and central nervous system [CNS] conditions), Ewen and colleagues reported that median availability of generics for NCDs did not exceed 80% for any of the therapeutic groups in the public sector, and private-sector availability exceeded that of the public sector.¹³ Their data also showed that in the private sector, medicines for CNS conditions were the least available of the lowest-priced generics in all three country income groups.¹³

The top three medications stocked by the private- and public-sector pharmacies respectively were DRAs (90.3% and 45.9% availability), anticholinergics (77.7% and 34.4%), and L-dopa formulations (75.8% and 19.7%). It is instructive that the most frequently stocked medications had other indications necessitating their availability. For instance, the most frequently stocked DRA was the ergot-derived bromocriptine, used in obstetrics for hyperprolactinemia causing infertility, hence its widespread availability. The anticholinergic drug, trihexyphenidyl, is also frequently used as an adjunct to antipsychotic medications in psychiatry and thus frequently stocked for this purpose. Specific L-dopa formulations varied in their availability, with the 100/25 and 200/50 formulations being least available despite being the better formulations used in developed countries (and listed on the WHO Essential Medicines List 20th edition, 2017).¹⁶ The implication of the latter is that the majority of patients would have to be treated with formulations accompanied by a considerably higher side-effect profile. Nonmotor symptoms and complications of dopamine replacement therapy (such as dyskinesias) impact negatively on quality of life in PD, and availability of medications to address them is an important issue. The medicines for treatment of the nonmotor symptoms of PD were scarcely available. Our data clearly demonstrate one of the major constraints (nonavailability) to providing high-quality care along the continuum of severity and symptomatology of PD in our practice environment. In a comparative study of Cameroonian (central African) and Spanish (European) PD cohorts, Cubo and colleagues made the salient observation that the Cameroonian

patients received treatment only intermittently, had a trend of receiving lower doses of L-dopa, less frequently used dopaminergic agonists (and, when used, ergot derivatives were the norm), and more frequently took anticholinergics instead.¹⁷ Their conclusion was that this translated to significantly more-severe impairment in motor function and cognitive status and a higher burden of anxiety, depression, psychosis, somnolence, fatigue, pain, caregiver burden, and quality-of-life impairment.¹⁷

The average number of day's wages to purchase a 30-day supply of PD medicines surveyed was 41.3 (range, 1–371). This is further compounded by the fact that a significant proportion of the population with PD live below the minimum wage that forms the basis for defining affordability, and even the lowest-cost generic medicines are unaffordable to such patients in any case. Nigeria has the second-largest population of poor worldwide (86 million as at 2013 estimates), with 53.5% of the population living below the \$1.90-a-day poverty line (close to the minimum wage of \$1.67 per day).¹⁸ This challenge is further pronounced because median age of onset coincides with the retirement period for the majority of patients, and those still in active service have difficulty retaining employment because of the disability associated with PD, creating a vicious cycle resulting in loss of work and wages. In Nigeria, the majority of the population do not have health insurance, and expenses are paid out of pocket. Despite the establishment of a National Health Insurance Scheme in 2005, as a universal social health insurance model, the scheme has only achieved less than 5% coverage.¹⁹ There are major challenges to access to health care in Nigeria. Physician density is 0.38 per 1,000.²⁰ Health care provision is by three tiers (primary, secondary, and tertiary) in the public and private sectors. Although the government funds public health care (infrastructure, salaries, and some medications), private spending as a percentage of total health expenditure in Nigeria is around 63.3%, 95.4% of which is out-of-pocket payments by individuals.²¹ Medications provided publicly at no cost to the majority are those for infectious diseases (malaria, tuberculosis and HIV/AIDS, and childhood immunizations). No medicines for NCDs (including PD) are free.¹²

For medications that had both generic and originator formulations available, the originator was also consistently higher priced than the generic. This pattern is not unique to this study and underscores the drive to promote use of quality-assured generics that meet regulatory standards, where feasible. This includes strengthening generics substitution policies and enhancing regulations that ease the importation and/or local production of high-quality generics.²²

The data from the present study expose the challenge that limited access poses to the management of PD in Nigeria and reflects the scenario in most SSA countries. We acknowledge that demographic, social, political, economic, cultural, and technological constraints are persistent obstacles to realizing full, equitable access to medicines for treatment of PD in SSA. It is also clear that competing health agenda and perceived priorities as well as health systems inadequacies (including drug supply-chain management failures and human capacity insufficiency) are a reality of our health care system. In spite of these, in fact, on

account of these, the status calls for deliberation and concerted sustainable action to ensure that the World PD Charter declarations are implemented in SSA. These should include strategies to encourage governments to make PD a public health priority in the face of other health challenges that seem to constantly be on the front burner. Borrowing from experience gained in improving medicines access for other NCDs, a multisectorial approach (engaging governments and fostering partnerships with pharmaceuticals and civil society, and enhancing universal health coverage) is required.¹³

There are limitations to our study. Firstly, the data represent the best-case scenario regarding both availability and affordability and should be evaluated in that context. We surveyed pharmacies that were most likely to stock medications, and this would greatly enhance the indices measured. Also, we utilized the national minimum wage to define affordability as prescribed by the WHO, whereas in reality, a large proportion of the population live below the minimum wage, and PD patients particularly are more likely to be either retired or out of employment on account of the disability. Our study did not consider patient opinions and experiences regarding availability and affordability, and we acknowledge that this perspective would be beneficial in improving our understanding of the challenges faced by people with PD in our environment.

Author Roles

1. Research Project: A. Conception, B. Organization, C. Execution; 2. Statistical Analysis: A. Design, B. Execution, C. Review and Critique; 3. Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

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Disclosures

Ethical Compliance Statement: Ethics approval was obtained from the Health Research Ethics Committee of the Lagos University Teaching Hospital (LUTH HREC), Idi Araba, Lagos State, Nigeria (National Health Research Ethics Committee Registration Number 19/12/2008a). The LUTH HREC assigned study number is ADM/DCST/HREC/APP/1628 (Notice of exemption). We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

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