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Availability, Accessibility and Affordability of Antimalarial Drugs in Benue State, North Central Nigeria

Paul Otor Onah[1*]

[1]Department of Clinical Pharmacy and Pharmacy Administration, Faculty of Pharmacy, University of Maiduguri, Borno State, Nigeria.

Author's contribution

The sole author designed, analyzed and interpreted and prepared the manuscript.

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ABSTRACT

Title: Availability, accessibility and affordability of antimalarial drugs in North Central Nigeria
Objectives: To assess the availability and affordability of antimalarial drugs in healthcare facilities as well as compare prices and affordability within and between sectors.
Background: Malaria is endemic in all parts of Nigeria and transmission occurs throughout the year. In north central Nigeria transmission is intense during the rainy season between April and October. Prevalence of malaria remains high; the prevention and treatment of clinical cases has been the focus of several ongoing interventions. The availability and affordability of recommended Artemisinin combination therapies (ACT) are both critical to the success of malaria control efforts.
Methods: This was a cross sectional healthcare facility study design in Benue State North Central Nigeria using WHO/HAI methodology. The study was carried out in three urban and three rural areas of the State between the rainy months of April and July.
Results: Artemisinin monotherapies and non artemisinin monotherapies accounted for the greater percentage of antimalarial medications recorded during the survey. Over 70% of both monotherapies and ACTs were found in private healthcare facilities. In-spite of the high availability

**Corresponding author: E-mail: onahpaul439@yahoo.com;*

of monotherapies, majority of patients purchased low priced generic versions of ACTs indicating increasing awareness and improvement in the implementation of antimalarial treatment policy at healthcare facility level. Innovator brands of antimalarial drugs were more than 200% more expensive compared to their low priced generic versions making them less affordable.
Conclusion: Monotherapies remain highly available in private healthcare facilities compared to ACTs; this poses serious challenge to the success of antimalarial treatment policy. Innovator brands of antimalarial drugs which are still widely available are less affordable than their low priced generic version. This has the potential to reduce financial access in areas where options are limited.

Keywords: Antimalarial drugs; availability; affordability; ACTs.

1. INTRODUCTION

Nigeria is among six countries of sub Saharan Africa where malaria is endemic and transmission occurs throughout the year. The disease remains a major public health burden in most parts of the country; pregnant women and children less than five are the most affected segment of the population. Majority of the population are at risk of infection throughout the year, only about 3% of the [1].

Recent reports by World Health Organization indicated that there has been a reduction in malaria prevalence and malaria - related mortality globally. In the 2010 – 2015 report malaria cases declined by 21% globally, mortality rates among at risk populations also declined by 29% and in children under five years 35% reduction was reported [2]. In sub Saharan Africa 90% of all malaria cases and 75% of malaria related mortality occur there. Nigeria is reported to account for 25% of malaria burden in Africa and 50% of malaria related deaths [3].

Plasmodium Fulciparum account for over 95% of all clinical cases and it's responsible for the most severe forms of the disease [4]. Malaria indicator survey report 2015 in Nigeria reported prevalence of between 22 – 58% across the country. The report also reported a 9.5% reduction in malaria prevalence over a five year period [1]. Several studies around the country reported malaria prevalence as high as 72%, 70.8%, 73.9% and 81.5% [5-8]. These results point to the fact that malaria prevalence in many local settings is much higher than the published national or regional average.

The current guideline for clinical case management of malaria requires the use of recommended artemisinin combination therapies. This decade old antimalarial treatment policy was predicated on the availability of recommended antimalarial drugs as well as their being accessible and affordable. The policy also de-emphasized the use of monotherapies; despite this, monotherapies are still widely available and used at almost all levels of healthcare system.

Some reports estimated that up to 60% of suspected cases of malaria are treated by profit - oriented private healthcare facilities [9]. This is primarily due to the fact that large segment of the population are under served by the few available government healthcare facilities and in some cases they are completely absent. The absence of public healthcare facilities is particularly acute for people living in remote rural areas and large urban slums. Availability of antimalarial drugs and access to healthcare facilities are critical for effective malaria case management. Several factors have been noted as key predictors of accessibility to healthcare services and they included distance to point of care [10] and working hours [11].

In Nigeria like in most developing countries expenditure on drugs can take 25 – 75% of all healthcare costs [12]. The absence of health insurance for most of the population coupled with absent medicine price control mechanisms and inefficient public healthcare system administration often means that most patients have to make out of pocket payment for drugs and other healthcare services [13]. Other complicating factors include wide price variability of medicine within and between sectors [14], which makes antimalarial drugs more expensive and prices unpredictable [15].

Furthermore, significant differences exist in the prices of the same product from manufacturers further compounding the unpredictability of antimalarial drug prices [16].

The low affordability of quality assured ACTs has been earlier reported [17]; however following the co-paid subsidy programme of the affordable medicines facility malaria (AMFm), prices of

ACTs covered under the programme has dropped significantly thereby improving access, availability and affordability.

National malaria treatment policy was anchored on prompt diagnosis and drug treatment of clinical cases. The continued sustenance of accessibility, availability and affordability of recommended ACTs is of critical importance in overall reductions in malaria related morbidity and mortality.

1.1 Objectives

- To determine availability of antimalarial drugs across sectors
- To compare availability of monotherapies and ACTs in healthcare facilities
- To compare prices of antimalarial drugs within and between sectors
- To assess affordability of innovator brands and low priced generics

2. METHODS

2.1 Setting

Benue State is located in the North Central region of Nigeria and typically of woody savannah vegetation. The wet season occurs between April to October and annual rainfall is about 1270 mm. It has twenty three local government councils and the population is multi-ethnic, multi-religious with many languages spoken across the State. The State is host to two university teaching hospitals one of which is located in the State capital, general hospitals in some local government headquarters and primary health care centers in a few rural areas. In addition non-governmental organizations, religious institutions and appropriately qualified individuals operate hospitals, community Pharmacies, patent medicine stores and maternity homes across the State. Most public secondary and tertiary healthcare facilities are located in urban and semi urban areas while privately owned health care centre are largely concentrated in rural areas. All community pharmacies are located exclusively in urban areas, patent and proprietary medicine vendors are the major source of medications in the rural areas.

2.2 Study Design

This was a cross sectional survey design using methods validated by World health organization and Health Action International (WHO/HAI) [18].

2.3 Survey Areas

The State capital (Makurdi) was purposely selected along with Gboko and Otukpo (urban areas), while Oju, Yandev and Aliade represented rural areas. All selected areas were less than two hour drive from the State capital. In each selected urban area a public hospital was selected as the reference point and five other healthcare facilities within two kilometer radius were randomly selected for the survey. Where the number of health facilities was less than desired or consent was withheld, an additional facility was added from neighbouring area. The health facilities were marked and numbered and consent was sought and obtained from management of the facilities, approval was similarly obtained from back up health facilities in case the selected facilities decline consent.

2.4 Antimalarial Drug Selection

An official list of registered antimalarial drugs was obtained from the National Agency for Foods Drugs Administration and Control (NAFDAC), the agency responsible for registration of pharmaceutical products in Nigeria. Three community pharmacies were surveyed in each of the urban areas and using the result as a template, sixty six antimalarial drugs including ACTs and monotherapies were selected. Selection of antimalarial drugs was based on class, unique drug combination and brand; all drugs without official registration were not included.

2.5 Recruitment and Training of Data Collectors

A total of six data collectors including pharmacist and pharmacy assistants with adequate knowledge of the survey areas were recruited and trained for data collection. The training focused on data collection process, data entry into appropriate forms, data quality, data collection techniques, facility identification and how to secure cooperation from facility managers.

2.6 Informed Consent

Prior to data collection exercise, written approval was sought and obtained from the management

of healthcare facilities after written and verbal explanation of the purpose of study and data to be obtained. Healthcare facilities provided either oral or written consent before data collection exercise.

2.7 Data Collection

Pair of data collectors consisting of a pharmacist and pharmacy assistant upon locating pre-selected healthcare facility proceeds to validate prior informed consent before data collection exercise. Antimalarial data collected included name of drug, drug combination, brand name, pack size, quantity in stock, and quantity in stock in one month, cost price and selling price etc. Antimalarial drugs found in the facilities were checked against the survey list and data appropriately entered. Additional antimalarial drugs found were entered into a supplementary data form. Where the number of antimalarial drugs found in a facility was less than 50% of survey drug list, an additional back up facility was surveyed. At the end of data collection exercise, supervisors made random survey of healthcare facilities already surveyed and data obtained was compared with that collected by field workers so as to ensure data quality.

2.8 Data Analysis

The data were collated, checked for errors and entered into Microsoft excel workbook and then loaded into SPSS version 20 for descriptive and inferential analysis. The results were expressed as percentages, means, averages and standard deviation where applicable. P values ≤ 0.05 is considered statistically significant.

2.9 Ethical Issues

Ethical approval was sought and obtained from Health Research Committee of Benue State Ministry of Health.

3. RESULTS

3.1 Distribution of Surveyed Facilities

A total of forty four healthcare facilities were surveyed across the six survey areas. All private pharmacies and public hospitals but one was located in urban areas. On the other hand all private health facilities, patent medicine shops and facilities owned by faith based organizations were in rural areas (Fig. 1).

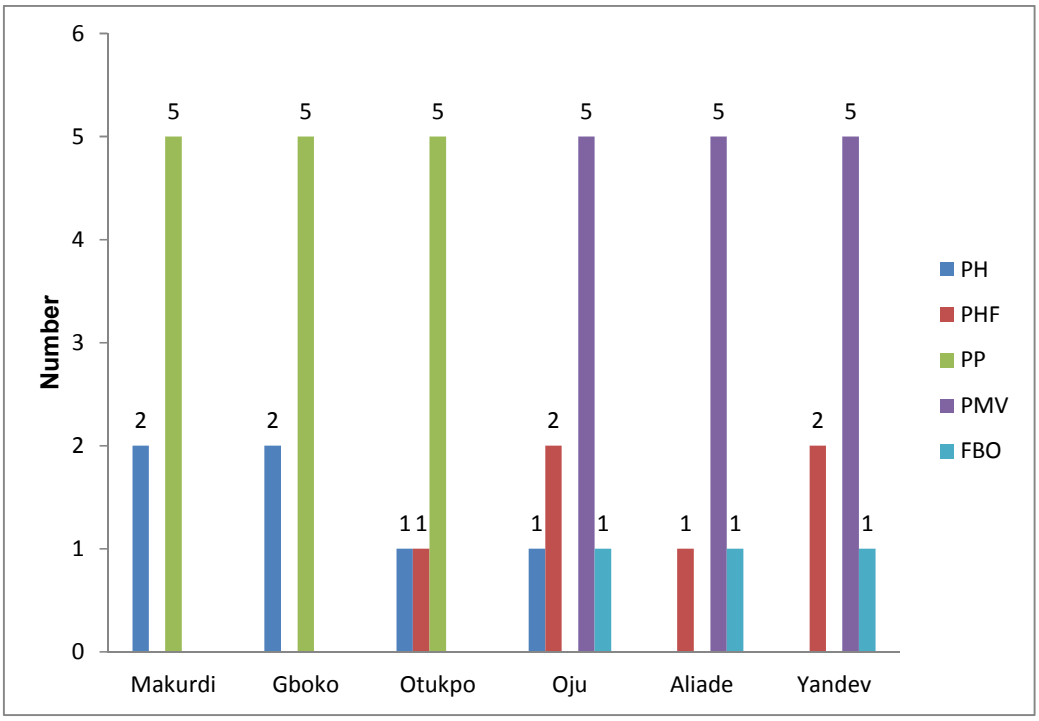

Fig. 1. Health facilities per survey areas

Key: PH = Public hospitals, PHF = Private health facilities, PP = Private pharmacies, PMV = Patent medicine vendors, FBO = Faith based organizations

3.2 Distribution of Classes of Antimalarial Drugs

A total of eighteen thousand and thirty nine full course doses of various antimalarial drugs were recorded during the survey out of which 44.3% were ACTs (Artemisinin combination therapies) (n = 7996). Non artemisinin monotherapies accounted for 42.4% of antimalarial drugs (n = 7658), while artemisinin monotherapies accounted for 13.3%. The distribution per survey areas indicated that ACTs were found in higher percentages in urban areas (16.5 – 48%) compared to 2 – 6.7% in rural areas. This highlighted huge disparity in availability and accessibility of quality assured ACTs in rural areas (Fig. 2).

3.3 Availability of ACTs

Distribution of ACTs across survey areas indicated that a large percentage of them were found in private healthcare facilities in both urban and rural areas. For instance, 19 – 24% of ACTs were found in public healthcare facilities in urban areas compared to 8 – 13% availability in rural areas. This clearly point to problem of low availability of quality assured ACTs in public health facilities (Fig. 3).

3.4 Availability of Monotherapies

Artemisinin and non Artemisinin monotherapies remain widely available in private health facilities across urban and rural areas accounting for 70 – 91% of all monotherapies. About 8- 28% of monotherapies were still being found in public health facilities (Fig. 4).

3.5 Distribution of Brands of Antimalarials

The availability of low priced generic antimalarial drugs appeared to be higher across all categories of healthcare facilities but one. About 20.3% of antimalarials found in private pharmacies were low priced generics; other facilities had less than 10% of these brands. The same pattern was observed for innovator and most sold generics brands across the other health care facilities. For instance private pharmacies had in stock 11.9% of all antimalarial drugs as innovator brands compared to 6%, 4.9% and 2.9% in patent medicine shops, private health facilities and public hospitals respectively (Fig. 5).

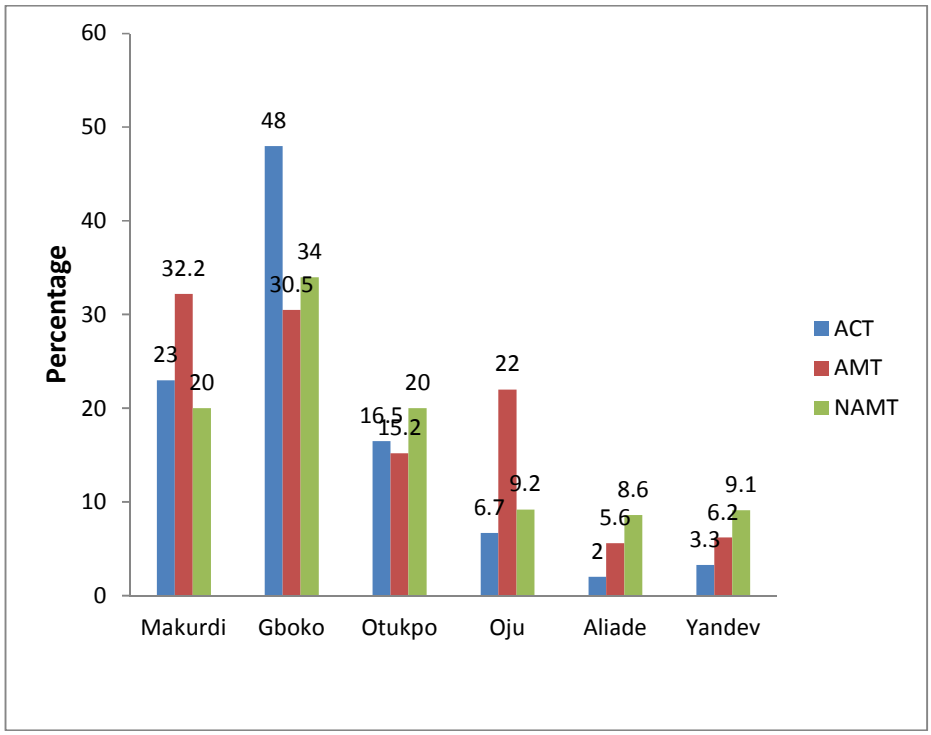

Fig. 2. Antimalarial drug classes available per survey area

Key: ACT = Artemisinin combination therapy, AMT = Artemisinin monotherapy, NAMT = Non Artemisinin monotherapy

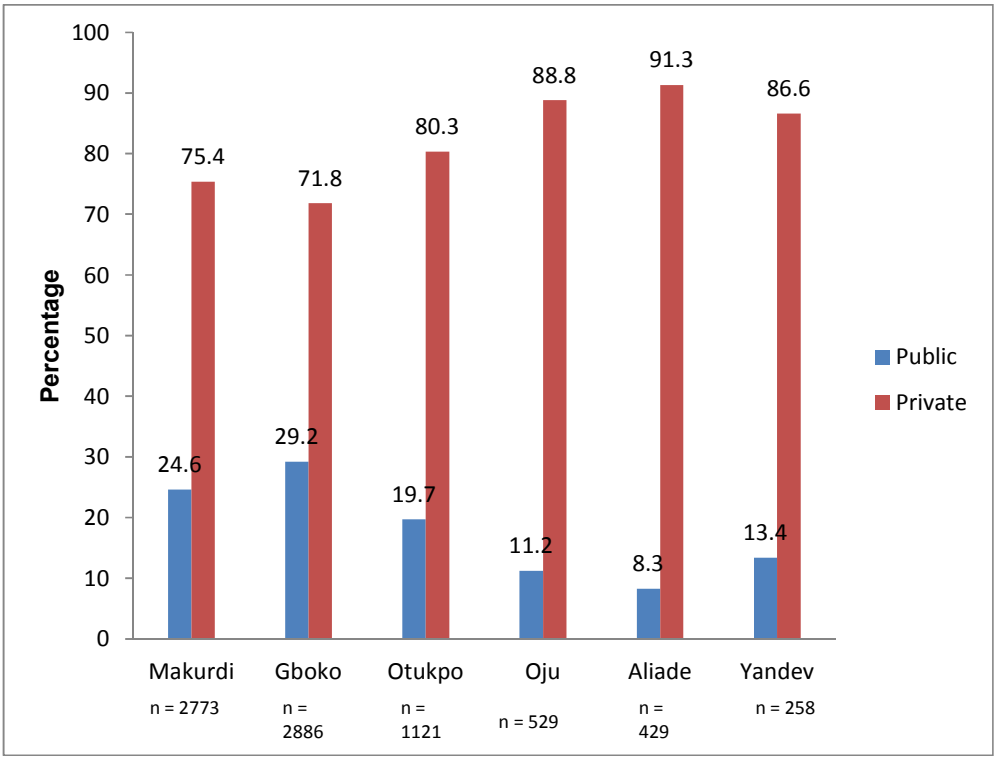

Fig. 3. Availability of ACTs in public and private health facilities
Key: n = treatment units of ACTs

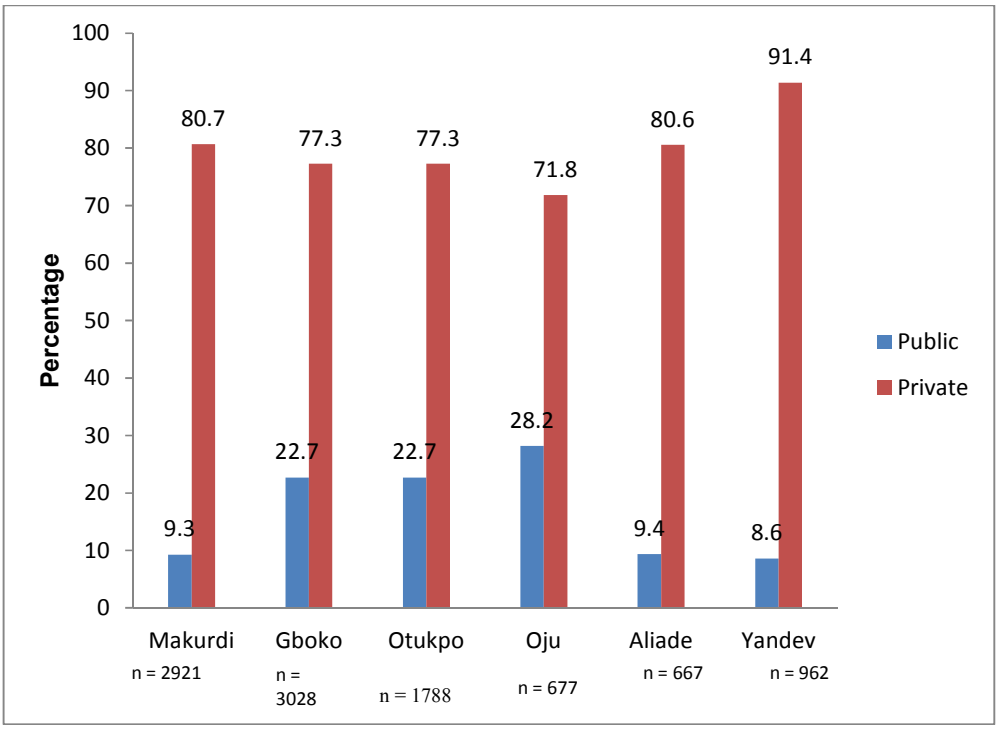

Fig. 4. Availability of monotherapies in public and private health facilities
Key = treatment units of monotherapies

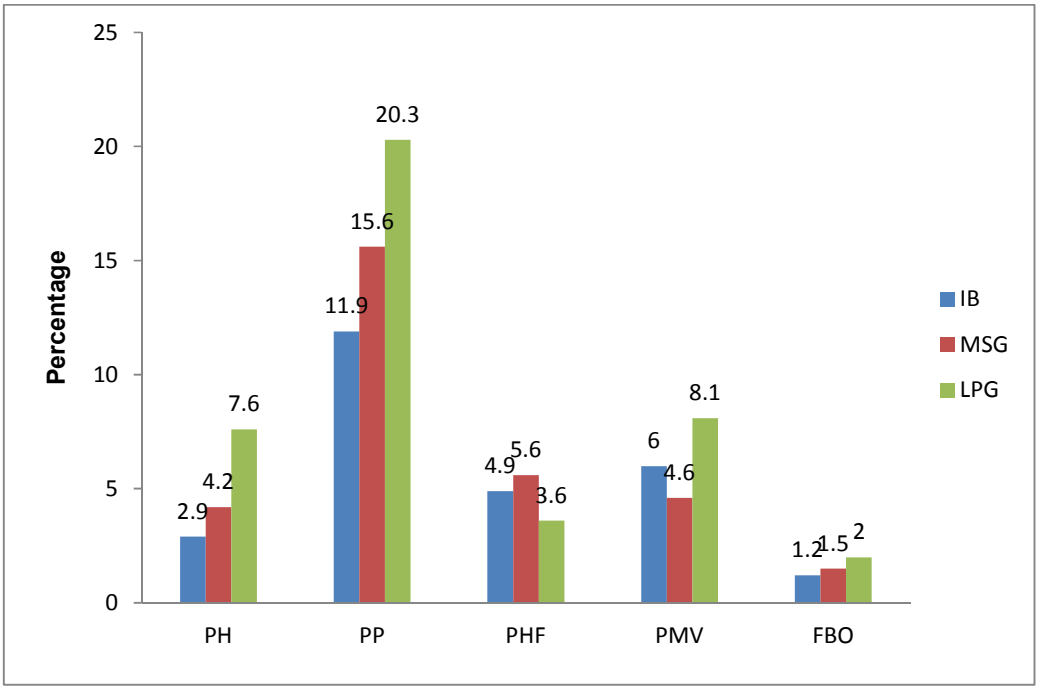

Fig. 5. Percentage of antimalarial drug brands across sectors

Key IB = Innovator brands. MSG = most sold generic version. LPG = low priced generics

3.6 Antimalarial Drug Class Dispensed

The overall use of quality assured ACTs within the study period ranged between 31 – 76% across survey areas though rates were much higher in urban areas. In urban areas 65 – 76% of antimalarials dispensed were ACTs compared to 31 – 46% in rural areas. Conversely, the use of Artemisinin and non Artemisinin monotherapies in rural areas was more than double the rates in some urban areas. These classes of antimalarial drugs though not recommended any longer, they remain widespread in most healthcare facilities (Fig. 6).

3.7 Median Price of Antimalarial Drugs

The median price of full treatment course of antimalarials drugs indicated that quality assured cost of ACTs ranged between 1 – 3 USD, while most monotherapies cost less than 1USD. The exceptions were Halofantrine and Arteether injection both of which cost above 4 USD per treatment course. The median prices of these monotherapies are relatively high because they are mostly available as innovator brands (Fig. 7)

3.8 Median Price Ratios of Antimalarial Drugs

A comparism of median price ratios of innovator and low priced generic versions of antimalarial drugs indicated that price differences between these brands can be as high as 200 – 445%. This is a clear indication of wide variability of prices between various brands of antimalarial medications (Table 1).

3.9 Comparism of Median Price Ratios within Sector

There are significant differences in median price ratios of the same antimalarial drug within the same sector. Apart from Arteether injection (P= 0.106), Artemether/Amodiaquine (P= 0.126) and Chloroquine (P=0.129) other drugs had wide price variability which makes malaria treatment cost highly unpredictable (Table 2).

3.10 Comparism of Median Price Ratios Across Sectors

The median prices of antimalarial drugs are not significantly different across sectors (P>0.05). The median prices of innovator brands and other brands are not significantly different indicating

that price gap between brands is rapidly closing up (Table 3).

3.11 Antimalarial Drug Affordability

Affordability which is defined as the number of days the least paid public sector worker needs to work to be able to afford antimalarial drugs is low for innovator brands. It would cost more than a day's wages to pay for innovator antimalarial drugs as against low price generics which would cost less than one day wages which makes them affordable (Table 4).

4. DISCUSSION

A total of forty four healthcare facilities consisting of primary, secondary and tertiary levels were surveyed across the State. Government owned facilities including tertiary and secondary healthcare facilities were largely located in urban areas, while privately owned facilities were spread across the survey areas. However privately owned pharmacies and hospitals were all located in urban areas and patent medicine vendors were the main providers of antimalarial drugs to the rural population (Fig. 1).

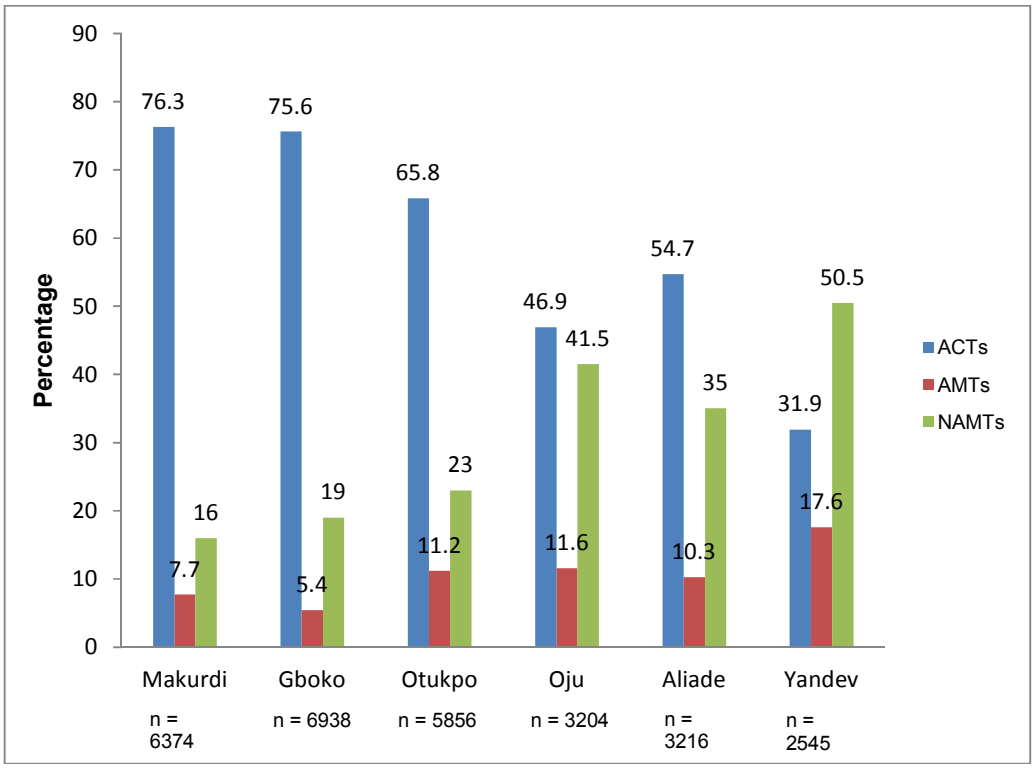

Fig. 6. Antimalarial drug classes dispensed in survey areas

Table 1. Median price ratio of innovator and low priced generic versions

	Innovator brand (IB)	Low price generic (LPG)	Ratio. IB : LPG
Artemether/Lumefantrine	2.27	0.51	445%
Dihydroartemisinin/Piperaquine	0.92	0.52	200%
Artemether/ Amodiaquine	2.15	1.32	200%
Artesunat	0.42	0.23	200%
Sulfadoxine/Pyrimethamine	3.52	1.60	250%
Artemether injection	1.75	0.57	300%
Quinine injection	2.92	1.57	200%
Chloroquine	5.98	1.49	400%
Proguanil	0.75	0.42	200%

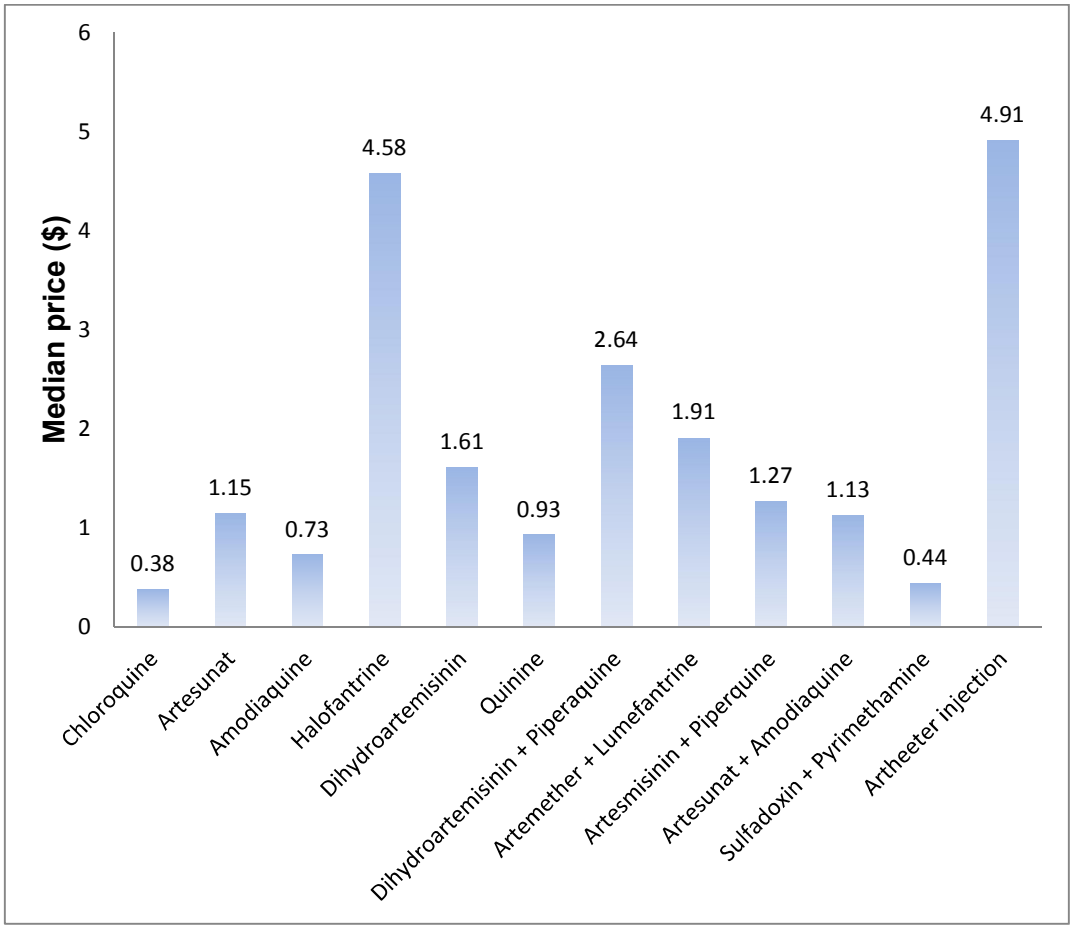

Fig. 7. Median prices of antimalarial drugs
One USD is equivalent to 315 naira

Table 2. Median price ratio across private pharmacies

Drug		Pharmacy 1	Pharmacy 2	Pharmacy 3	P value
Artemether/Lumefantrine	IB	2.02	2.28	2.44	0.003
	LPG	0.42	0.59	0.51	
Dihydroartemisinin/	IB	0.99	0.85	0.92	0.019
Piperaquine	LPG	0.46	0.52	0.59	
Sulfadoxine/Pyrimethamine	IB	4.01	4.49	3.52	0.011
	LPG	1.60	1.28	1.44	
Artesunat	IB	6.53	5.53	5.02	0.028
	LPG	2.51	3.01	2.81	
Artemether injection	IB	1.52	1.77	1.69	0.106
	LPG	1.16	0.37	0.34	
Artemether/Amodiaquine	IB	1.92	2.15	2.48	0.126
	LPG	1.16	1.49	1.65	
Chloroquine	IB	73.18	58.55	48.79	0.129
	LPG	29.27	19.52	39.03	

Availability of antimalarial drugs showed that all facilities surveyed had at least one artemisinin combination therapy (ACT), though overall availability of pre-selected drugs was less than 50%. In urban areas availability of ACTs was more than fifteen times of that in the rural areas

(Fig. 2). The same pattern was observed for monotherapies where availability in urban areas was three times of that in rural areas. Generally the higher availability of antimalarial drugs in urban areas was driven by demand, easy access to public hospitals and private healthcare facilities that are highly patronized by the well-educated and economically well off. Majority of patients obtained their antimalarial medications from private sector healthcare facilities similar to conclusions from a previous study [19]. This report further noted that only 4% of

Table 3. **Median price ratio between innovator brands and others**

Drug	Type	PF	PP	PHF	PMV	P value
Artemether/ lumefantrine	IB	2	2.3	2.7	2.2	0.082
	LPG	0.5	0.6	0.7	0.5	
Dihydroartemisinin/Piperaquine	IB	0.8	1.2	1.3	0.8	0.283
	LPG	0.6	0.7	0.9	0.4	
Dihydroartemisinin	IB	1.3	1.5	2	1.2	0.137
	LPG	0.5	0.8	0.9	0.4	
Artemether/Mefloquine	IB	1.6	1.8	2.2	2.1	0.083
	LPG	0.6	0.7	0.9	0.6	
Artemether/ Amodiaquine	IB	0.9	1.3	1.4	1.1	0.118
	LPG	0.6	0.7	0.8	0.7	
Artesunat	IB	0.8	1.1	1.2	0.7	0.179
	LPG	0.5	0.6	0.7	0.4	
Artemether/Piperaquine	IB	1.2	1.5	1.6	1.3	0.086
	LPG	0.6	0.8	0.8	0.6	
Sulfadoxine/Pyrimethamine	IB	0.3	0.5	0.5	0.4	0.098
	LPG	0.2	0.1	0.2	0.1	

Key: PF = Public facilities, PP = Private pharmacies, PHF = Private health facilities, PMV = Patent medicine vendors

Table 4. Mean affordability of antimalarial drugs

Drug	Brand	PF	PP	PH	PMV	Mean number of days
Artemether/ Lumefantrine	IB	2	2.3	2.7	2.2	2.3
	LPG	0.5	0.6	0.7	0.5	0.6
Dihydroartemisinin + Piperaquine	IB	0.8	1.2	1.3	0.8	1.0
	LPG	0.6	0.7	0.9	0.7	0.6
Dihydroartemisinin	IB	1.3	1.5	2	1.2	1.5
	LPG	0.5	0.8	0.9	0.4	0.6
Artemether + Mefloquine	IB	1.6	1.8	2.2	2.1	1.9
	LPG	0.6	0.7	0.9	0.6	0.7
Artemether + Amodiaquine	IB	0.9	1.3	1.4	1.1	1.2
	LGP	0.6	0.7	0.8	0.7	0.7
Artesunat	IB	1.2	1.5	1.6	1.3	1.4
	LPG	0.6	0.8	0.8	0.6	0.7
Arteether injection	IB	2.5	3	3.5	2.7	2.9
	LPG	1.5	1.7	2	-	1.3
Artemether injection	IB	2	2.6	3	-	1.9
	LPG	0.6	0.7	1.1	0.5	0.7
Sulfadoxine/Pyrimethamine	IB	0.3	0.5	0.5	0.4	0.4
	LPG	0.2	0.1	0.2	0.4	0.2

Key: *Daily minimum wage for least paid government worker = $1.9*

The Price calculation was based on adult equivalent treatment dose- which is the amount of active ingredient need to treat a 60kg person. This is to allow for comparism between antimalarial drugs of diverse classes, dosage forms and different courses of treatment

antimalarial drugs were found in public healthcare facilities, although the figure from this study appears to be much higher. In terms of availability of quality assured ACTs all the healthcare facilities surveyed had at least one in stock compared with just half in a previous report [19] (Fig. 3). This improvement in availability of ACTs may be largely due to the Co-paid AMFm initiative that made available and increased access to cheap generic versions of quality assured ACTs, although availability of monotherapies remains unaffected (Fig. 4).

In a recent review of ACT availability data clearly showed that availability increased up to 80% in public and private sectors with pharmacies accounting for much of the increase [20], however the findings of this study showed availability to be just under 50% in urban areas and just 2% in rural areas. Herein lies the problem of availability of ACTs in rural areas; low availability of ACTs may be partly responsible for increased use of monotherapies including Sulfadoxine/Pyrimethamine.

Analysis of the volume of antimalarial drugs dispensed within the study period showed that twice as much of artemisinin monotherapies and non artemisinin monotherapies dispensed in rural areas compared to urban areas (Fig. 6). In contrast ACTs accounted for two thirds of all dispensed in urban areas of which more than half was Artemether/Lumefantrine. In rural areas over 90% of all monotherapies consist of Sulfadoxine/Pyrimethamine and Quinine similar to other reported studies [9]. These trends reflect the demand dynamics in urban and rural areas, educational level of patients, presence of qualified healthcare personnel and quality of healthcare services all of which generally favour urban residents. Most rural dwellers would patronize cheap and popular monotherapies in patent medicine shops as opposed to urban residents who would typically consult qualified healthcare provider.

About two thirds of all monotherapies were dispensed in private healthcare facilities and half of them were sold in rural areas [21], where patent medicine vendors and poorly functional primary healthcare centers' are apparently the only sources of antimalarial drugs (Fig. 4). The continuous use of these monotherapies is sure to increase the likelihood of malaria treatment failure and increase the risk of resistance development [22]. Similar findings have been reported earlier [23,24], though the expectation that improved availability, accessibility and affordability following ACT subsidy programme would encourage their greater use appear not to be the situation [25]. Other studies similarly reported high availability of monotherapies [26,27] and low availability of ACTs [28,29], although there has been significant improvement recorded in this study.

The popularity of monotherapies among rural dweller is that treatment is sought in patent shops [30], other factors include quality of health education of retail drug sellers [31], Cost of drugs [32] and transport to point of care [33]. Despite recent similar studies confirming improved availability of quality assured ACTs [4,34], availability of Artemisinin monotherapies and non Artemisinin monotherapies continue to remain unacceptably high across all level healthcare services. The availability of monotherapies appear to decline in areas where penetration of subsidized ACTs is high [34], however this finding is not replicated across rural and urban settings.

The median prices of ACTs found in this study remain high making them 3 – 7 times more expensive compared to monotherapies (Fig. 7). This is similar to recent reports [20], though some newer generation monotherapies are still highly expensive. Prices of antimalarial drugs also depend on whether they are innovator brands or low priced generics. The median price ratios of innovator brands are 200 – 400% higher than prices of their low priced generic versions with no significant prices differences across sectors (Table 1). The prices of ACTs are 5 – 24% more costly than the popular monotherapies (Chloroquine and Sulfadoxine/Pyrimethamine) [35] which are comparable to this study, though the margin is far less. Furthermore, prices of ACTs were higher in private healthcare facilities compared to public health facilities [36]

Prices of antimalarial drugs have a direct impact on ability of patients to pay for both antimalarial drugs and associated treatment services. Affordability which is defined as the number of days an unskilled public employee needs to work to purchase a full course of therapy may be influenced by brand and the type of healthcare facility providing the service. Overall innovator brands of antimalarial drugs are generally unaffordable costing up to 2-3 days of wages (Table 1). While antimalarial drug median price variability is significant between community

pharmacies (Table 2), price variability between sectors was not significant (Table 3). The affordability of innovator antimalarial drugs found in this study is similar to 3.2 days wages earlier reported [35] (Table 4). This clearly confirmed that most innovator brands of antimalarial drugs are not affordable across all sectors [17] (Table 4). There have been appreciable reduction in cost of ACTs since subsidy programme was introduced; there is still ongoing concern that in rural areas and urban slums with limited choice of antimalarial drugs and healthcare facilities, the benefits may be far from optimized. The combined factors of low availability and poor accessibility of affordable low priced generic versions of quality assured ACTs can impede the progress of roll back malaria programmes in these settings.

5. CONCLUSION

Availability of quality assured ACTs is low in the State and the problem is particularly acute in rural areas. The combination of low availability of low priced generic version of ACTs and high availability of monotherapies have the potential to reduce the progress of malaria control programmes in the State. Most generic versions of ACTs are generally accessible and affordable and thus offer an opportunity to dramatically scale up availability and use of recommended ACTS in both public and private healthcare facilities.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the author(s)

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the author(s).

COMPETING INTERESTS

Author has declared that no competing interests exist.

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