EVALUATION OF DRUG THERAPY PROBLEMS IN TREATMENT OF UNCOMPLICATED MALARIA AMONG PAEDIATRIC OUTPATIENTS AT A NIGERIAN TERTIARY HOSPITAL

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ABSTRACT

A drug-related problem (DRP) is an event or circumstance involving drug therapy that actually or potentially interferes with the desired health outcome. The paediatric population is easily affected by DRPs. This study aimed to evaluate Drug Therapy Problems (DTP) in prescriptions of children under 5 years with uncomplicated malaria at paediatric outpatient pharmacy of a Tertiary hospital in Kaduna state. Data were prospectively collected using the method adopted from the Pharmaceutical Care Network Europe (PCNE) version 8.02 from eligible patients' prescriptions attended the facility between the months of November 2018 and March 2019. The results showed that the majority of the patients (78.9%) were between the ages of 0 – 24 months, with half of them being males (53.7%). DTPs were found in 90.9% of prescriptions, with a higher percentage (79.9%) in infants aged 3 – 24 months. In conclusion, the study established that drug therapy problems were common among paediatric patients treated for uncomplicated malaria in Barau Dikko Teaching Hospital, Nigeria which was mostly due to incorrect prescription of ACT as a result of dose selection problem.

Keywords: Drug therapy problems, Paediatric, uncomplicated malaria, Pharmaceutical Care Network Europe (PCNE)

INTRODUCTION

According to world report by World Health Organization (WHO) world malaria report (WHO, 2017) malaria is a disease that may be prevented and treated, but it still kills about half a million people every year. Malaria kills a child every two minutes, with the majority of these deaths occurring in Africa and in children under the age of five, who accounted for 67% of all malaria deaths worldwide. As reported by World Health Organization (WHO) in a study on regional and global trends in malaria burden, 15 African nations and India accounted for about 80% of all malaria cases worldwide. Nigeria was accounted for nearly half of all global cases of malaria (WHO, 2018). Drugs are crucial for treating many diseases and improving health, but inappropriate use can cause drug-related problems (DTPs) (Suwitha *et al.*, 2020). Pharmaceutical Care Network Europe (PCNE) defines DTPs as undesirable events affecting health outcomes and requires professional judgment to resolve through careful assessment of patients, drugs, and disease information to determine the appropriateness of each medication regimen (PCNE, 2019). It is known in the literature that drug administration errors and drug-handling problems are more common in children and adolescents (Herziger *et al.*, 2022) which make them more susceptible to develop DTPs (Agazhi and Tigabu, 2018). This is considered a major concern because it may have a negative impact on the patients quality of life and health care budgets as a result of decreased effectiveness of therapy (Bekele *et al.*, 2021).In view of the forgone, this study was therefore aimed to evaluate drug therapy problems in the treatment of uncomplicated malaria at Baraud Dikko Teaching Hospital, BDTH Kaduna, Nigeria due to paucity of studies on the subject in the

research setting. The evaluation of drug therapy problems in pediatric patients is essential for ensuring safe and effective medication management. This process involves identifying and addressing issues such as inappropriate drug selection, dosage errors, adverse drug reactions, and drug interactions (Bizuneh *et al.*, 2020).

METHODS

Ethical Approval and Consent

Ethical clearance was collected from the Health Research Ethics Committee of Barau Dikko Teaching Hospital, Kaduna. An ethical clearance certificate identification number BDTH-HREC 16-00019 was issued. Caregivers gave their informed consent after the objective of the study was presented to them.

Study Population and Study Setting

The study was conducted among prescriptions of paediatric patients with uncomplicated malaria that visited the paediatric outpatient department of the facility within the period of the study.

Research Design

This was a prospective cross-sectional study carried out between the months of November 2018 to March 2019.

Sample Size and Sampling

To determine the appropriate number of patients for the study, the researcher utilized a formula based on a singular population proportion. Specifically, aimed to recruit 175 individuals from the paediatric outpatient pharmacy. This figure was arrived at by taking into account the previously reported statistic of 19.8% of antimalarial drug prescriptions having drug therapy problems, as found in a study conducted in Cote Di voire by (Abrogoua and Konan in 2016). To select participants, the researchers opted for a convenience sampling technique, which while convenient, carries a higher risk of sampling error due to its short duration.

Eligibility Criteria

The eligible study participants compromised children aged 3 to 59 months who were presented to the paediatric outpatient pharmacy unit with prescriptions of drugs for uncomplicated malaria during the study period.

Data Collection Instrument

DRP- registration fornV8.02 PCNE classification (PCNE, 2019) was used for data collection. It is standardized tool for DTP developed by Pharmaceutical Care Network Europe foundation. The tool has 3 primary domains for the "Problem", 8 primary domains for "Causes" and 5 primary domains for "Interventions" and 4 primary domains for "Outcomes" (PCNE, 2019). All identified DTPs were classified using a modified version of PCNE classification V 8.02. The modifications to the PCNE classification included changes to the cause category as DTPs due to dispensing causes (C5 of PCNE V8.02), the use of drugs [drug use process (C6)], which were removed. These were limitations of our study as errors due to dispensing and use of drugs and administration of medications were not observed during this study mainly due to the fact that it will be difficult to observe these in outpatients.

The addition of necessary information not provided, which was categorized under dispensing (C6) of PCNE V8.02 was included in our study to explore frequency of incomplete prescriptions, which may lead to DTPs. Under the intervention category, no interventions were done at prescribers' level as prescribers were not involved in this study. Interventions were only done at patient's and drug levels

Data Collection

The study collected data from patients with uncomplicated malaria at the paediatric outpatient Pharmacy Unit of BDTH between November 2018 and March 2019. The researcher assessed potential drug-to-prescription (DTP) using Pharmaceutical Care Network Europe (PCNE) version 8.02 developed by and the National Malaria

Treatment Guidelines (FMoH, 2015). The accuracy of Artemisinin-based combination therapy, ACT doses was assessed based on body weight of patients, type, and composition of the ACT. Medscape online drug interaction checker available on https://reference.medscape.com/drug-interactionchecker was used to identify drug-drug interactions. The rate of DTPs was estimated by calculating the number of DTPs per individual patient. Interventions were carried out at both patient and drug levels since the intervention by default did not necessary require the prescriber's approval.

Statistical Analysis

A descriptive analysis was conducted on patient demographics, DTP causes, intervention types, and outcomes. Results were presented in charts and tables. Non-parametric Spearman's correlation and Pearson's Chi square analysis were used to determine statistical relationships between drug therapy problems, patient variables, and ACT prescribed type a *p* value (<0.05).

RESULTS

The patients included in the study consist of (53.7%) males and (46.3%) females. Most children between 19 and 24 months old, comprising over half of the population, weighed between 6 and 10kg, with 56.6% falling in this range. Additionally, around half of the children, specifically 54.9%, fell within this weight range. A total of 246 causes of DTPs were identified across the seven categories of Cause of DTP domain in the tool. The highest was dose selection 184 (74.8%) in which dose timing instruction wrong, unclear or missing accounted for 58.9%, drug dose too high accounted for 5.7%, drug dose too low 6.5%, and dosage regimen too frequent 3.7%. Drug form is the least encountered cause of DTPs (2.4%) (Table 1). A significant statistical association existed between the presence of DTPs with number of patients with DTP per age group and number of DTP based on types of ACT (p<0.001) (Table 2). A total of 363 interventions were done by the pharmacist of which half of the interventions were carried out at the drug level (52.7%). Almost all the DTPs identified were resolved (Table 4).

Table 1: Causes of Drug Therapy Problems Among Patients with Uncomplicated Malaria Observed in This Study, N=175

Cause and subcategories of DTPs	frequency	
	N	%
Drug selection	44	
Inappropriate drug combination		17.9
Drug form		
Inappropriate drug form	6	2.4
Dose selection		
Drug dose too high	14	
Drug dose too low	16	
Dose timing instruction wrong, unclear or missing	145	74.8
Dosage Regimen too frequent	9	
Treatment Duration		
Treatment Duration too long	12	4.9

A total of 246 causes of drug-related problems (DTPs) were identified. One DTP may have up to three causes

Table 2: Chi Square Test of Association Between Patient Variables and DTPs Identified Among Prescriptions of Children with Uncomplicated Malaria n= 246

Characteristics	Frequency n (%)	P- Value
Number of patients with DTP	159 (90.9)	
Number of patients with DTP per gender		
Male	88 (55.3)	
Female	71(44.7)	
Number of patients with DTP per age group		$P < .0001^*$
< 1 year	67(42.1)	
1-2 years	60(37.7)	
2-3 years	13(8.2)	
3-4 years	14(8.8)	
4-5 years	5(3.2)	
Number of patients with DTP per weight		
1-5 kg	14(8.8)	
6-10 kg	87(54.7)	
11-15 kg	42(26.4)	
16-20 kg	14(8.8)	
21-25 kg	2(1.3)	
Number of DTP based on types of ACT		$P < .0001^*$
Artermether/lumefantrine	140 (88)	
Artesunate/Amodiaquine	14(8.8)	
Dihydroartemisinin/piperaquine	5(3.2)	

Level of Significance* *P* <0.0001*, DTP Drug Therapy Problem, ACT- Artemisinin Combination Therapy

Table 3: Drug Therapy Problems Identified from Prescriptions of Paediatric Patients With Uncomplicated Malaria N= 246

Detailed classification of Drug therapy problem	Frequency (%)
Treatment Effectiveness	
Effect of the drug not optimal	53 (21.6)
Treatment Safety	
Adverse drug reaction possible to occur	48(19.6)
Other	
Incomplete prescription	145(58.9)

* One patient may have encountered more than one DTP, where the same DTP type or more than one DTP type may be experienced by the same patient. Thus, total DTPs (and percentages) do not add up to the total number of patients with DTPs reported

Table 4: Interventions implemented to resolve the identified DTPs N= 363

Intervention	Frequency, n (%)
At patient level	
Patient counselling	174 (47.3)
At Drug level	
Dosage changed	23 (7.6)
Formulation changed	5(1.4)
Instruction for use changed	161 (43.8)

One DTP may have up to 3 interventions

DISCUSSION

Most children that were being treated for uncomplicated malaria were infants and toddlers (0-24months) which is consistent with the report that children within such age group are more vulnerable to childhood diseases such as malaria, pneumonia and diarrhea (UNICEF, 2020). The study shows that there is a high prevalence of DTPs in prescriptions of children under 5 years treated for uncomplicated malaria. However, prescriptions of patients aged less than 1 year to 2 years revealed the occurrence of more DTPs than other age groups which is similar with the findings of Nguyen *et al.,* (2021), this implies that there is need for careful attention to their medication due to the increased likelihood of drug therapy problems. In addition, this study could help

healthcare providers to improve the quality of care provided to children under 5 years treated for uncomplicated malaria.

The study discovered that a significant number of young patients (under 5 years old) who were prescribed antimalarial drugs also had drug therapy problems (DTPs). In fact, the majority of these patients had at least one DTP, which is much higher than a similar study in Cote D'Ivoire (Abrogoua *et al*., 2016) that found only 19% had DTPs. This high prevalence of DTPs suggests noncompliance with guidelines and may be a contributing factor to the growing problem of drug resistance and ineffective treatment of malaria in this at-risk group. The WHO emphasizes the importance of complete compliance with malaria treatment policies by clinicians, program officers, and patients to

prevent the emergence and spread of drug resistance (WHO 2018)

Furthermore, the study reported a high quantum of dose selection on drug therapy problem in Barau Dikko Teaching Hospital (BDTH). This could be attributed to the fact that physicians do not adhere to the standard treatment guideline and could also be due lack of sufficient knowledge especially among house officers about the appropriate way of prescribing ACTs. A study by (Abrogoua *et al*, 2016) reported a similar trend for a study conducted in Cote D'ivoire indicating incorrect doses and drug-drug interactions in management of uncomplicated malaria in a peadiatric ward. However, the findings in this study was higher than which was reported by (Birarra *et al.*, 2018) and (Suwitha *et al.*, 2020) that found out that dosing problem was the most frequent DTPs with a 43% rate all in general peadiatric ward.

Additionally, roughly half of the pharmacist's interventions involved modifications to medication usage instructions at the drug level. This indicates that the clinical pharmacist was able to resolve identified drug therapy problems (DTPs) without necessarily consulting with the prescriber, which aligns with previous research (Indermitte *et. al,* 2007; Lyra et al., 2004). These studies demonstrate that pharmacists are capable of addressing a variety of DTPs without requiring input from other healthcare providers. This finding supports other research that highlights the role of clinical pharmacists in identifying and solving drug therapy problems. For example, clinical pharmacists were able to intervene in 49% to 89.3% of cases depending on the problem (Guignard *et.al*, 2015; Mekonnen *et al*., 2013).

The practical significance of this discovery is that clinical pharmacy services offered in the paediatric outpatient clinic of BDTH help to detect and solve drug therapy problems. This could be used to establish an antimalarial stewardship program aimed at reducing treatment failure and drug-resistant parasites.

Nevertheless, some limitations exist in this study. Previous studies of DTPs involved the collaboration of physicians, with pharmacists, which was not possible in this study. This would have been beneficial for better quantification of the DTPs found. Collaboration between prescribers and pharmacists may be considered in future DTP studies, which has the potential to eliminate biasness that may stem from a study fully conducted by pharmacists. Considering that severity and preventability of DTPs as well as cost savings and appropriate interventions to improve prescribing practice for pediatric patients in Nigeria were not covered in this study, these are potential areas to focus on in future studies. Such studies would elucidate the significance of DTP occurrences from a different angle.

CONCLUSION

The study established that drug therapy problems were common among paediatric patients treated for uncomplicated malaria in Barau Dikko Teaching Hospital, Nigeria which was mostly due to incorrect prescription of ACT as a result of dose selection problem. The involvement of clinical pharmacists in pediatric patient units is very important to reduce DTPs and they should work in collaboration with other health care professionals.

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