



Pharmacovigilance of Antimalaria Drug Treatment in Enugu State, Nigeria: Community and Health Workers' Perceptions and Suggestions for Reporting Adverse Drug Events

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Authors' contributions

This work was carried out in collaboration between all authors. Authors BSCU, MOA and ACN conceptualized the study. Authors MOA, CCO, ENO and AKU designed the study and wrote the protocol. All authors were involved in literature searches. Authors CCO, ENO and AKU did the statistical analyses. Authors MOA, ACN and ENO wrote the initial draft of the manuscript and revised by author BSCU. All authors read and approved the final manuscript.

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ABSTRACT

Aims: Aim of study was to determine the level of awareness of adverse drug reactions following treatment of malaria and the reporting systems available among community members and health workers and suggestions on how to improve the reporting system in Enugu state, Nigeria.

Study Design: This was a community based descriptive cross-sectional study.

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Place and Duration of Study: Enugu Metropolis Enugu State, Nigeria between February and April 2011.

Methodology: A three-stage sampling design was used to select 362 mothers/caregivers from five out of eight districts and 60 health workers from nine primary health centers in the study area. The respondents were interviewed using an adapted questionnaire. Data entry and analysis were done using Statistical Package for Social Sciences version 20. Student t test and Chi square test of statistical significance was used in the analysis.

Results: A higher proportion of the mothers/caregivers (97.2%) were aware of adverse drug reactions when compared with the health workers, (80%). The major source of information for adverse drug reaction for the mothers/caregivers was friends (43.5%). Majority of the them (54.7%) used chloroquine as first line drug for treatment of malaria. The most common adverse event observed by the respondents was itching (35.6%) mainly due to use of chloroquine. Among those that experienced an adverse reaction, majority (75.9%) did nothing about the adverse effect and only a minor proportion, (2.7%) reported to a doctor. The major reason for non reporting of adverse drug reaction was ignorance, (mothers/caregivers, 55.5% and health workers 75.0%) The suggestions for solving the problem of non reporting of adverse reactions were increased public awareness (mothers/caregivers 58.8% and health workers 83.3%), and provision of accessible health centers (mothers/caregivers, 23.2% and health workers 16.7%).

Conclusion: Knowledge of adverse events was high from the study but the major problems that affected the reporting of adverse drug events were ignorance and lack of funds. Information education and communication programmes in the communities and among the health workers should be improved. Funds should be made available to health workers to enable timely reporting of adverse drug events. Community surveillance is necessary to ensure timely reporting by members of the community.

Keywords: Pharmacovigilance; antimalaria; community; health workers; perception; Enugu State; Nigeria.

1. INTRODUCTION

Medicines, despite their benefits have been reported to have common adverse reactions that can cause morbidity, disability and mortality which are preventable [1]. These adverse drug reactions could be monitored and evaluated closely in order to guarantee safety of medicines for clinical use through pharmacovigilance. The World Health Organization (WHO) defines pharmacovigilance as the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem [2,3]. Adverse events refer to undesirable medical occurrences which develop following drug administration, regardless of the suspected relationship between the drug product and the event [4].

Malaria is a major health problem in Nigeria with high endemicity [5] and an approximate 50% of the populace suffer from malaria at least once annually [6]. Widespread resistance to older antimalarial drugs, has led to a change in antimalarial treatment, using newer Artemisinin Combination Therapies (ACTs), as first line drugs, [4,7] based on WHO recommendations in 2001 [8]. Many African countries including

Nigeria have adopted ACT as first line treatment for uncomplicated malaria [4,9]. This has made it necessary that a mechanism should be put in place for monitoring adverse drug reactions associated with use of ACTs with a reporting system in place through health facilities [10].

The national pharmacovigilance guidelines clearly addressed the issue of adverse drug reaction reporting and requires that all health workers and traditional medicine practitioners report all adverse drug reactions including those associated with orthodox medicines, vaccines, medical devices, herbal and traditional remedies. Nigeria also hopes to use pharmacovigilance as a tool to aid the fight against counterfeiting [11]. The voluntary reporting by patients to health workers of adverse drug reaction is not a valid way of maintaining pharmacovigilance system, even though it is useful and very affordable [12]. It is therefore necessary that patients and health workers should recognize these adverse events and be willing to report them spontaneously [13]. This is because spontaneous reporting has been the main data generating system of international pharmacovigilance and this relies on healthcare professionals (and in some places consumers) to identify and report any suspected adverse drug reaction to the national pharmacovigilance

centre or the manufacturer [14]. Reporting of adverse drug reactions is an essential component of the national healthcare delivery system. The national malaria treatment policy notes that information on use of antimalarial drugs should be updated, regarding efficacy and safety, including the assessment of adverse reactions [15].

Bearing in mind the burden of malaria in Nigeria, presumptive treatment of fever using antimalarials without laboratory diagnosis is common practice [4]. Such widespread use of these drugs in this manner present problem of over or under dosing, inappropriate treatment and drug resistance which in effect worsens adverse drug events [16]. Furthermore, the Nigeria National Drug Policy is of the opinion that government should encourage the establishment of pharmacovigilance units nationwide to collect, evaluate and disseminate information on adverse drug reactions and poisoning [17]. Some studies have shown the relationships between malaria perception and treatment seeking behaviours in Nigeria. [5,18,19,20] but little is known about the community and health workers' perceptions of adverse drug reactions. This study sought to outline the practical challenges facing pharmacovigilance of antimalarial drug treatment and proposed approaches that could be adopted. It also determined the community and healthworkers perception of adverse drug reactions with anti-malarial treatments and suggestions for reporting such adverse events.

2. MATERIALS AND METHODS

2.1 Description of Study Area

The study was carried out in Enugu Metropolis in Enugu State, southeast Nigeria. It is made up of 3 Local Government Areas (LGAs) namely Enugu North, Enugu South and Enugu East LGAs and accounting for 22% of Enugu State population [21]. There are 23 government-owned primary health centers in the metropolis. All the health centers have drug dispensing units, but no laboratory facilities. Other complementary health providers in existence are some privately owned health facilities. There is an all-year high transmission rate of malaria in the study area.

2.2 Study Design

The study was a community-based descriptive cross-sectional study, however a comparison was made of community and health workers'

perceptions and suggestions for reporting adverse drug events.

2.3 Study Participants

The study population consisted of mothers/ caregivers from the community and health workers in the primary health centers selected for the study.

2.4 Study Instrument

The study instrument was a semi-structured questionnaire adapted from a similar study in Nigeria which focused on adverse drug reporting by Physicians [22]. Information obtained from the mothers included their socio-demographic characteristics and knowledge of adverse drug reactions of anti-malaria treatment, the source of information on adverse drug reaction, drug used for treatment of malaria and observed adverse events, action taken and suggestions on how to solve the problem of non reporting of adverse drug reactions. The questionnaire for the mothers was administered through trained research assistants. The research assistants reside in the selected districts and had completed at least senior secondary school education and were trained for two days by the researchers on data collection using the study instrument. The questionnaire for the health workers which was self-administered included questions on their socio-demographic characteristics, knowledge of adverse drug reactions and types of reporting system known and suggestions on how to solve the problem of non-reporting of adverse drug reactions.

2.5 Sample Size Determination

The minimum sample size for the study was determined by the formula used for single proportions [23]. A sample size of 362 mothers/caregivers was used in the study based on a type 1 error (α) of 0.05, a tolerable margin of error of 0.05 and an estimated knowledge of adverse drug events of 50%. All the sixty health workers working in the nine selected primary health centers were included in the study.

2.5.1 Sampling technique

A three-stage sampling technique was used for the study. In the first stage, a simple random sampling technique of balloting was used to select nine primary health centers from the list of 23 primary health centers and five districts from

among a list of eight districts in the metropolis. The population of Enugu Metropolis based on the 2006 national population census was 722,644 people and for the five selected districts 424,019 people [21]. The number of households in the selected five districts was estimated at 78, 667. In the second stage, 362 households were selected using the Primary Health Care house numbering system as a guide. This is a form of house census system utilized by National Primary Health Care Development Agency for primary health care activities in Nigeria. For each selected district, one household was randomly selected from a list of registered households in the primary health care house numbering system using a table of random numbers. The household forms the index household for the selected district. Households were selected if they had at least one child who is less than or equal to 5 years old. From each household, a woman or caregiver willing to participate was included in the study. Every twentieth house from the index household was selected on alternate street basis until the sample size was completed. A simple random sampling technique of balloting was used to select a single household from the number of households who met the inclusion criteria in each house. Each of the selected

district contributed a minimum of seventy participants to the study. All the health workers in the selected health centers who gave consent to participate were included in the study.

2.6 Data Analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS), statistical software version 20. Frequency tables and cross tabulations were generated and presented as tables. Continuous variables were summarized using mean and standard deviation and comparison of mean age was done using the Student t test. Categorical variables were presented as frequencies and proportions and comparison was made of community and health workers' perceptions and suggestions for reporting adverse drug events using Chi square test of statistical significance and level of significance was determined by a p value of <0.05.

3. RESULTS

Table 1 shows the socio-demographic characteristics of community respondents and health workers.

Table 1. Socio-demographic characteristics of residents of a community and health workers

Variable	Community respondents n=362 N (%)	Health workers n=60 N (%)	χ^2	p value
Age (years)				
Mean (\pm SD)	25.6 \pm 5.4	30.7 \pm 5.5	4.674**	<0.001
Age groups				
16-20 years	70 (19.3)	0 (0.0)		<0.001
21- 25 years	109 (30.1)	12 (20.0)		
26- 30 years	126 (34.8)	20 (33.3)		
31-35 years	39 (10.8)	12 (20.0)		
>35 years	18 (5.0)	16 (26.7)		
Gender				
Male	19 (5.2)	29 (48.3)	94.778	<0.001
Female	343 (94.8)	31 (51.7)		
Educational attainment of respondents				
No formal education	5 (1.4)	NA	NA	
Primary education	102 (28.2)			
Secondary education	26 (7.2)			
Tertiary education	229 (63.3)			
Designation				
Medical officer	NA	6 (10.0)	NA	
Nurse		13 (21.7)		
Community health officer/ Community health extension worker		41 (68.3)		

** Student t test; NA: Not applicable

Table 2. Knowledge of adverse drug reactions of residents of a community and health workers

Variable	n=362 (Frequency)	Percent (%)
Community respondents		
Source of knowledge of adverse drug reaction		
Friends	153	43.5
Doctor	106	30.1
Television	89	25.3
Radio	4	1.1
Nil	10	
Episode of malaria among respondents		
Yes	362	100
No	0	0.0
Drug used for treatment of malaria		
Chloroquine	198	54.7
Sulfadoxine-pyrimethamine	103	28.5
Artemisinin combination therapy	58	16.0
Halofantrine	3	0.8
Adverse drug reaction experienced following ingestion of anti malaria		
Itching	129	35.6
Headache	38	10.5
Abdominal pain	35	9.7
Blurred vision	6	1.7
Rashes	6	1.7
Fainting	6	1.7
Nausea	4	1.1
Never noticed any adverse reaction	138	38.1
Action taken by respondents on the adverse drug reactions		
Nothing was done	170	75.9
Stopped the drug	39	17.4
Took other drugs	9	4.0
Visited a doctor	6	2.7
Reason for doing nothing for adverse drug reaction		
Lack of funds	66	38.8
Ignorance	62	36.5
Stress	38	22.4
Lack of accessible health centre	4	2.3
Health workers		
	n=60	Percent (%)
Type of reporting system known to health workers		
Spontaneous reporting	48	80.0
Nil	12	20.0
Reports of adverse drug reaction to anti-malarial drug received in past one year		
None	22	36.7
1	26	43.3
2	8	13.3
3	3	5.0
4	1	1.7
Reporting system used		
Spontaneous reporting	n= 48	
	48	100.0

The mean age/standard deviation of the health workers was 30.7±5.5 years and this was significantly higher than that of the mothers/

caregivers which was 25.6±5.4 years, (p<0.001). Majority of the mothers/caregivers (94.8%) and health workers, (51.7%) were female and the

difference in proportions was found to be statistically significant, ($p < 0.001$). Also, majority of the community respondents, (63.3%) had post secondary education while majority of the health workers, (68.3%) were Community health officers/ Community health extension workers.

Table 2 shows knowledge of adverse drug reactions of community respondents and health workers. Among the mothers/caregivers, the major source of information on adverse drug reactions was friends, (42.2%). Chloroquine was the first line of treatment for malaria among the respondents and itching was the most common adverse reaction noticed. A higher proportion of the respondents, (47.0%) did nothing for the adverse reaction, mainly due to lack of funds (38.8%). The spontaneous reporting system was the only reporting system known to the health workers and the one practiced by them.

Table 3 shows the community respondents and health workers' awareness and perceptions for non-reporting of adverse drug reactions. A significantly higher proportion of the community respondents (97.2%) were aware of adverse drug reactions when compared with the health workers, 80.0%, ($p < 0.001$). The major reason for non-reporting of adverse drug reactions among the two study groups was ignorance, (community, 55.5% and health workers 75.0%) followed by lack of funds, (community, 26.2% and health workers 6.7%) and the difference in

proportions was found to be statistically significant, ($p < 0.001$). Also, a significantly higher proportion of the health workers, (83.3%) perceived increased public awareness as the main solution to non reporting of adverse drug reaction when compared with the mothers/ caregivers. 58.8% ($p < 0.001$).

4. DISCUSSION

From the results of this study, a significantly higher proportion of the respondents in the community (97.2%), were aware of adverse drug reactions when compared with the health workers, (80%). This is despite the training of the health workers and the possibility of additional information on adverse drug reactions they could have received from some pharmaceutical companies on pharmacovigilance, [24]. This finding is not encouraging bearing in mind the need for increased awareness of adverse drug events in Nigeria of which the health workers will have an increased role. It is however important to note that most of these antimalarial drugs could have been procured without prescription and so the resultant adverse events may not be brought to the attention of the health workers. Also, in health facilities, health workers in their interactions with patients may be more concerned with the diseases the patient present with which they may perceive as serious rather than focus on complains of side effects of drugs. Based on this finding, there is the need for specific training of health workers on

Table 3. Comparison of community and health workers' perceptions for non-reporting of adverse drug reactions and suggestions to solving the problem

Variable	Community respondents n=362	Health workers n=60	χ^2	p value
Awareness of adverse drug reaction				
Yes	352 (97.2)	48 (80.0)	30.949	<0.001
No	10 (2.8)	12 (20.0)		
Reasons for non-reporting of adverse drug reaction				
Ignorance	201 (55.5)	45 (75.0)	25.836	<0.001
Lack of funds	95 (26.2)	4 (6.7)		
No accessible health center	54 (14.9)	9 (15.0)		
Self medication	12 (3.3)	0 (0.0)		
Stress	0 (0.0)	2 (3.3)		
Suggestions to solving the problem of non reporting of adverse drug reaction				
Increase public awareness	213 (58.8)	50 (83.3)	25.562	<0.001
Provision of accessible health centers	84 (23.2)	10 (16.7)		
Provision of free treatment for malaria	50 (13.8)	0 (0.0)		
Prevention of self medication	15 (4.1)	0 (0.0)		

pharmacovigilance and also increased public enlightenment on the subject with emphasis on the need to recognize and promptly report adverse drug events. This will increase public awareness on pharmacovigilance as demonstrated by the results from a study in Tanzania [25].

The reporting system known by most of the health workers was the spontaneous reporting system. None of the health workers was aware of cohort studies, case control study, case (anecdotal) study and intensive hospital reporting. This is probably because spontaneous reporting system is the commonest and simplest form of adverse drug reporting. This is similar to a finding from a study in northern Nigeria where the health workers reported adverse events in their normal daily reporting books and not with the conventional yellow forms [26]. This has made it necessary that other systems of adverse drug reactions reporting are made known to the health workers so as to improve on the quality and reliability of the adverse drug reaction database.

The most common source of information on adverse drug reactions for the mothers/caregivers was from friends. This was closely followed by doctors and to an extent, it portrays the fact that doctors are not adequately carrying out the function of passing information to clients and patients on adverse drug reactions. This was also reflected in the results of this study in which the mothers/caregivers were more aware of adverse drug reactions than the health workers. One of the risk minimization strategies for adverse drug reactions is the passing of information to physicians by the pharmaceutical companies on side effects of their products, [24] and this is expected to have increased the knowledge of health workers on adverse drug reactions. Other similar studies in Nigeria revealed that most doctors were unaware of the available reporting systems for reporting adverse drug reactions [26,27,28,29]. These results apart from revealing the lack of knowledge of adverse drug reactions by medical practitioners also point to the fact that underreporting of adverse drug reactions is a major problem in Nigeria, [26] hence the need for training of health workers on pharmacovigilance. The least common source of awareness on adverse drug reaction was from the electronic media especially the radio. Utilizing the radio will help increase the awareness of the populace of adverse drug reaction and also bring the relevance of the exercise to the people.

Of importance is that all the mothers/caregivers have had at least one episode of malaria in the last one year showing the high endemicity of malaria in Nigeria [5]. This reveals the necessity for an established pharmacovigilance system in the country. The antimalarial drug used most by the respondents when they had malaria was chloroquine. This was followed by sulfadoxine-pyrimethamine. The choice of these drugs for treatment of malaria may be because they are relatively cheaper than the recommended ACT. Despite the recommendation of the World Health Organization to African countries on the use of Artemisinin based Combination Therapy (ACTs) as the first line of treatment for uncomplicated malaria, it appears there is no full compliance to this rule. Studies in Nigeria show that chloroquine is still the most frequently used first line drug for treatment of uncomplicated malaria [30,31,32]. This may be because the ACTs are expensive in these countries as demonstrated by the result of a study in Sudan [33]. It has been reported that the implementation of the use of ACT has been affected by the limited availability of the drugs, its high cost and the problem of sustainability [34,35].

More than one third of the mothers/caregivers (38.1%) did not notice any adverse drug reaction after the ingestion of antimalarial drugs which may be an indication that so many adverse drug reactions go unnoticed. It is also important to note that therapeutic ineffectiveness is also a reportable event in pharmacovigilance [36]. The most common adverse drug reaction that was noticed by the respondents after an antimalarial treatment was itching, and this might be because most of the respondents used chloroquine. Itching/pruritis has been known to be one of the worrisome side effects of chloroquine [37]. The other side effects noticed were headache, abdominal pain, nausea, blurred vision, rashes and fainting. Known adverse effects of ACT include among others anorexia, fatigue, headache, dizziness, palpitations, cough, nausea, vomiting and diarrhea [9].

For the mothers/caregivers who experienced adverse drug reactions in the use of antimalarials, majority of them (75.9%) did nothing about it. This is an indication that ignorance or lack of knowledge about adverse drug reaction could be a contributory factor to the gross under-reporting of adverse drug event of drugs. This was corroborated by the results of other studies [26,37]. It is important to know that only a minor proportion of the respondents

(2.7%), visited a doctor to receive appropriate advice based on the reaction experienced. The common reasons why the respondents did nothing with regard to the adverse drug reactions they experienced was lack of funds and ignorance. This was similar to a finding from a study in Uganda [13].

A minor proportion of the health workers (36.7%) did not witness any reporting of adverse drug reaction in their various health facilities in the past one year. Of the proportion that reported adverse drug reaction due to use of antimalarials this was done via the spontaneous reporting system. This confirms that adverse drug reaction reporting system is low in Nigeria and this is supported by the finding that Resident Doctors in Nigeria have inadequate knowledge about the reporting of adverse drug reactions [29]. Our study thus reveals that there is a high knowledge of adverse drug reactions by the respondents but very few of them report these adverse reactions to antimalarials to the appropriate authorities. This has also been confirmed by the result of another study [28]. In the spontaneous reporting system, the responsibility of reporting actually lies on the patient and most are ignorant on the importance of reporting.

Majority of the health workers (75%) were of the opinion that the problem affecting reporting of adverse drug reactions was due to ignorance followed by lack of funds. Interestingly, among the mothers/care givers, ignorance was also recognized as the major reason for the non reporting of adverse drug reactions due to use of anti malarial drugs. Also, in a study in Uganda, even though the awareness of adverse drug reactions was high as was observed in this study, these events were hardly reported mostly due to ignorance and lack of funds [13]. This stresses the need for adequate public education on the need to report adverse drug reactions to the appropriate authorities. This was aptly captured by the suggestions by both the health workers and the mothers/caregivers on how to solve the problem of non reporting of adverse drug events in which case, emphasis was on increased public awareness. This has made it necessary to initiate public enlightenment campaigns using the mass media especially the radio in order to increase the awareness of the populace on the need for timely reporting of adverse drug events.

The lack of funds as reason for non reporting of adverse drug events which was mentioned by both the mothers/caregivers and the health

workers as one of the problems that affect reporting of adverse drug reactions suggests that incentives could be used as a way to stimulate adverse drug reaction reporting [38]. It is important to note that there is a tendency that this might lead to over-reporting of these events. However a study in Iran showed that considerable remuneration might encourage reporting of unimportant reactions while lesser remuneration would not increase or add any value to reporting rate [39].

5. CONCLUSION

Knowledge of adverse events was high from the study but the major problems that affected the reporting of adverse drug events were ignorance and lack of funds. Information education and communication programmes in the communities and among the health workers should be improved. Funds should be made available to health workers to enable timely reporting of adverse drug events. Community surveillance is necessary to ensure timely reporting by the community. Adverse drug reaction guidelines can be put up as posters in reader-friendly formats in the health facilities and at strategic places in the communities as a way of increasing public awareness of adverse drug reactions. The media can also be adequately mobilized for this exercise.

ETHICAL APPROVAL

Ethical approval for the study was obtained from the Health Research and Ethics Committee of University of Nigeria Teaching Hospital Ituku-Ozalla, Enugu. All respondents were required to sign an informed consent form before the interview and the nature of the study and their level of participation were well explained to them. Participation in the study was voluntary and participants were assured that all information as would be provided in the questionnaire will be treated confidentially.

DISCLAIMER

This manuscript title was presented in the conference.

Conference name: "Third international Conference for Improving Use of Medicines. Informed Strategies, Effective Policies, Lasting Solutions".

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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