Knowledge, Attitudes and Perception of Artemisinin- based Combination Therapy in Malaria treatment in Yenagoa, Bayelsa state, Nigeria

[1]Okolie Justine,U.,[2]Onyenwe Nathaniel,E.,[3] Uzoechi Anslem, U. [4]Echeta, Maryrose, O.[1]Dozie, I.N.S.

[1] Department of Public health Technology, Federal University of Technology Owerri
[2] Department of Pharmaceutical Microbiology, University of Ibadan, Nigeria
[3] Department of Medical Laboratory Science, Imo state College of Nursing and Health Sciences.
[4] Department of Microbiology, Imo State Polytechnic, Umuagwo.
o_nathejik@yahoo.com,Tel: 08037797813

Abstract: The emergence of drug resistance *in Plasomidum falciparium* has significantly undermined malaria-control programs in countries it is endemic especially Nigeria, thus to ensure high cure rates and to combat this threat, the World Health Organization recommended the use of Artemisinine-Based Combination Therapy (ACT). Based on this fact, investigation using a simple random techniques were adopted to distribute 500 questionnaires following a descriptive survey method. The survey revealed that a total of 200(76.9%) respondents were treated with Artemisinine Based Conbination Therapy (ACT). While a total of 95(36.5%) respondents were untreated with ACT's, 155(66.67%) respondents stated that they have no knowledge about ACT's, but may have been treated with ACT's unknowingly to them. The ages between 31-40 years were the highest age range with 64(32.0%) treated with ACT's, indicating a high acceptance ratio. The indigene and non-indigenes that accepted the Artemether/Lumefantrine to other ACT'S showed a slightly significant effect across the female and male indigene and non–indigenes as relates to the used of ACT's as reported by the respondents. From the study the ACT's were more preferred to other single dose therapy in Yenagoa, Bayelsa state, Nigeria. Chi-square test statistics and Analysis of variation (ANOVA) shows that, the frequency at which these ACT anti malaria drugs were used for treatments is significant, and that the Knowledge, Attitudes and Perception of the ACT's by the female and male indigenes and non-indigenes is highly significant at probability level of $\alpha < 0.05$ respectively, thereby making the artemisine–based combination therapy a perfect treatment for malaria endemic areas like Yenagoa. Thus, today, to adequately treat malaria, the drug of choice must be fast acting, highly potent against asexual blood stage infection as in the combination therapy of Artemether/Lumefantrine, which have minimal toxicity and are affordable to residents in endemic regions of Bayelsa in Nigeria.
[Okolie Justine, U., Onyenwe Nathanie l,E., Uzoechi Anslem, U. Echeta, Maryrose, O. Dozie, I.N.S.. **Knowledge, Attitudes and Perception of Artemisinin- based Combination Therapy in Malaria treatment in Yenagoa, Bayelsa state, Nigeria.** *Nat Sci* 2014;12(9):55-60]. (ISSN: 1545-0740). http://www.sciencepub.net/nature. 9

Introduction

Malaria is a life threatening parasitic disease transmitted by mosquitoes. Today approximately 40% of the world's population mostly those living in the world's poorest countries are at risk of malaria (WHO 2006). Malaria is Africa's leading cause of under-five mortality (20%) and constitutes 10% of the continent's overall disease burden. It accounts for 40% of public health expenditure, 30-50% of in-patient admissions and up to 50% of out-patient visits in areas with high malaria transmission. *Plasmodium falciparum* accounts for up to 98% of malaria cases in Nigeria (FMOH 2005, Abeku, 2004).

According to Greenwood*, et al.,* (2008), more than 2 billion people are at risk of malaria which primarily affects poor populations in tropical and subtropical areas, where the temperature and rainfall are most suitable for the development of the malaria causing Plasmodium parasites in *Anopheles* mosquitoes. It is estimated that malaria kills a child in Africa every 30 seconds. Pregnant women and their unborn children are also particularly vulnerable to malaria, which is a major cause of prenatal mortality, low birth weight and maternal anemia (WHO 2006). The World Health Organization now considers it mandatory that replacement of antimalarial therapies be deployed as combination therapies (Hastings, and Ward, 2005) and those combination therapies containing artemisinin derivation are currently among the most popular.

The emergence of drug resistance *in Plasomidum falciparium* has significantly undermined malaria-control programs in countries it is endemic (Price and Nosten, 2001). To ensure high cure rates and to combat this threat, the World Health Organization (WHO) has recommended the use of Artemisinine-Based Combination Therapy (ACT), although debate regarding the most suitable combination and how ACTs should be deployed and funded still continues.

In Nigeria, in an attempt to reduce the incidence of relapse and treatment failure due to large scale resistance to existing drugs, the World Health Organization advocated the use of Artemisinin-based combination therapy (ACT) for the treatment of malaria. Also, due to the increasing resistance of malaria caused by *Plasmodium falciparum* to antimalarial drugs and the major threat it is posing to the global effort to "Roll Back Malaria". Chloroquine and Sulfadoxine–pyrimethamine (SP) are being rendered increasingly ineffective, resulting in increasing morbidity, mortality, economic and social costs. However, the cost of these combinations is higher than most of the currently used monotherapies and alternative non Artemisinin-Based Combinations Therapy in Nigeria. In a bid to actualize these objectives of the roll back malaria project in Nigeria, especially in Bayelsa state, which is now part of the area for National Policy on malaria treatment (FMOH, 2005). Bayelsa State is endemic for malaria and has a water- logged environment that supports the sustained breeding of mosquitoes. Thus, there is an important need to appreciate the use of Artemisinine-Based Combination Therapy (ACT) in the management of this disease. Based on these facts, the aim of the present study was designed to determine the knowledge, attitudes and perception, as regards the use of Artemisinine-Based Combination Therapy in malaria treatment in Yenagoa, Bayelsa state, Nigeria.

Materials and Methods
Study area
The study area is Yenagoa, which is the capital city of Bayelsa State in southern Nigeria, known as the core Niger Delta region. It is bordered in the north by Delta State, in the south by creeks and rivers spreading through the Atlantic Ocean and in the east by Rivers State. The language spoken here is Ijaw language. Others dialects are Nembe, Atissa, Akassa, Ogbia, etc. However, like the rest of Nigeria, English is the official language. The geographical constraints imposed by the limited dry land for settlements and agricultural practices, extensive mangrove swamps, excessive rainfall, prolonged and disastrous floods, creek erosion, among others, underscore the population distribution pattern in the state. People are thinly scattered among "floating" settlements of villages and towns. However, the geography of the state as regards its flooded nature encourages the breeding of mosquitoes making residents prone to malaria infection hence the need for the use of ACTs for treatment.
Study population
According to 1999 Nigeria population census, Yenagoa had a population of about 112,169 people scattered among the two towns namely, Atissa and Epie. The population of this study includes both the male and female indigenes and non-indigenes residing in Yenagoa L.G.A, Bayelsa state**.** The local populations engage on a subsistence fishing, farming and to some extent commercial. Bayelsa state is a riverine and estuarine settlement. A lot of her communities are almost completely surrounded by water.

Research Design
A pre-survey advocacy visit was made to the paramount rulers, the community development chairmen and heads of managements of the healthcare centres of the study communities. The purpose of study was carefully explained to them and they responded well by accepting for the research to be carried out in their community. Ten health centres in the two towns that make up Yenagoa L.G. A**.** were randomly selected and community health workers were educated on how to distribute the questionnaires.
Instrument for Data collection and Sampling Techniques
descriptive survey was adopted for this study. The questionnaires were first pretested in a small health centre in Agudama and some deficiencies were observed and corrected. Then 500 self structured questionnaires were distributed to 10 health centres in Yenagoa L.G.A,; 5 health centres's each from the two towns namely Epie and Atissa. The 5 health centre's in Epie town includes Igbogene, Agudama, Opolo, Amarata and Azikoro health centres. And The 5 health centers in Atissa town include Akaba, Ogu, Famgbe, Obogoro and Swali health centers. The community health workers randomly distributed the questionnaires to one out of every three indigenes and non-indigenes above 10 years, that visited the health centers. After distributing the questionnaires, the questions were answered individually based on their knowledge of ACTs, their acceptability and usage of the drugs.
Statistical Analysis and Computation of the Result
The analysis of Variance (ANOVA) and percentage prevalence were used to analyze the results of the questionnaires retrieved.

Results
Table 1 shows the total number of respondents that were treated with Arthemisinine-Based Combination Therapy (ACT) based on the age range of individual. The result shows that the ages between 31-40 years old were the highest age range with 64 respondents that were treated with ACT's, followed by 21-30 years with 57 respondents and 51-60 years being the third highest respondents with 31 respondents. Similarly, a total of 95 respondents were

untreated with ACT's, while a total of 155 respondents stated that they have no knowledge about the Arthemisinine-Based Combination Therapy, but may have been treated with it unknowingly to them.

Though the age range between 61- above were those that have the highest number of respondents having no knowledge of ACT's, but may have been treated with it.

Table 1: Respondents using Arthemisinine-based Combination Therapies (ACT's) in Bayelsa state

Age range	No(%)treated with ACT's	No(%)untreated with ACT's	No(%)without knowledge of ACT's
10-20	10(5)	22(23.2)	20(12.9)
21-30	57(28.5)	20(21.1)	19(12.3)
31-40	64(32)	50(52.6)	17(11)
41-50	18(9)	1(1.1)	29(18.7)
51-60	31(15.5)	0(0)	15(9.7)
61& above	20(10)	2(2.1)	55(35.5)
Total number	**200**	**95**	**155**

Table 2: Respondents with side effect after treatment with other ACT's and specific combination of Arthemether/ Lumefantrin in Bayelsa.

TYPES OF SIDE EFFECTS COMPLAINED BY PATIENTS				
Type of Drug combination	Head ache / GIT Disturbance(%)	Nausea/ Vomitting(%)	Dizzinness/ Blurredvision(%)	Patience without Notable side effects (%)
Arthemether/ Lumefantrin	44 (36.7)	12(27.3)	10 (23.8)	14(25.9)
Other ACT'S	76 (63.6)	32(72.7)	32 (76.2)	40(74.1)
Total	**120**	**44**	**42**	**54**

Table 4: Preference of Artemether/ Lumefantrin to other ACT's by respondents in Bayelsa state.

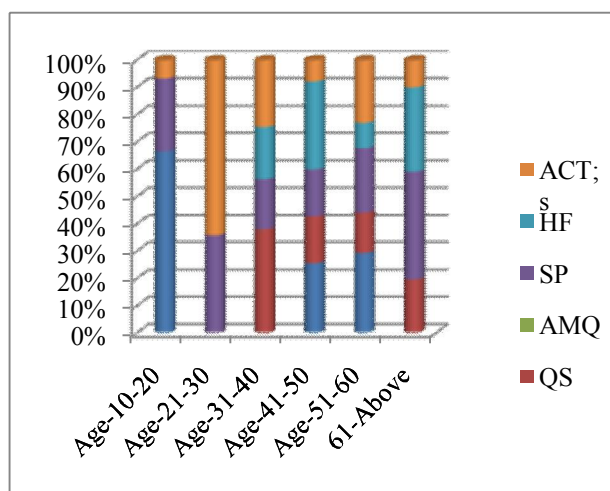| Act's type	female indigene	male indigene	female non-indigene	male non-indigene
Arthemether/Lumefantrin	100(50.0%)	65(76.5%)	85(80.9%)	37(61.7%)
Arthemether/ Amodiaquine	20(10.0%)	6(7.06%)	2(1.9%)	5(8.3%)
Arthemether/Mefloquine	15(7.5%)	2(2.4%)	1(0.95%)	3(5.0%)
Dihydro-arthemisinine/ Piperaquine	40(20.0%)	10(11.8%)	15(14.3%)	12(20.0%)
Artesunate/Sulphodoxine pyrimitamine	25(12.5%)	2(2.4%)	2(1.9%)	3(5.0%)

Fig 1: The age-related and preference of ACT's to single dose therapy
Key: Chloroquine = CQ, Quinine- Sulphate =QS, Amodiaquine = AMQ, Sulphodoxine/ pyrimethamine= SP, Halofantrine = HF, Artemisinine combination therapy = ACT's

Table 5: Rate of acceptability of ACT's to other single dose therapy in Bayelsa state

drug treatment	No of people treated (%)	number untreated (%)	unaware of drug treated with (%)
ACT'S	200(76.9)	95(36.5)	50(66.67)
Chloroquine	9(3.46)	5(4.35)	10(13.33)
Quinine Sulphate	10(3.84)	2(1.74)	5(6.67)
Amodiaquine	0(0.0)	1(0.87)	2(2.67)
Sulphodoxine/ pyrimethamine	25(9.61)	12(10.43)	5(6.67)
Halofantrine	16(6.15)	0(0.0)	3(4.0)

Table 6: Analysis of variance

Source of variation	Degree of freedom	Sum of square	Mean of square	F-value
Blocks	4	2245	561.25	5.28*
Treatments	3	12588	4196	39.47**
Error	12	1276	106.3	
Total	19	16109		

Key: * = Significant, **= Highly significant

Discussion

Since the Global Malaria Eradication programme ended, the burden of malaria has increased substantially in many parts of the world especially in Yenagoa, Bayelsa state, Nigeria. Due to the evolution of widespread resistance to chloroquine and sulfadoxine pyrimethamine in Africa (Abeku, 2004), it has been mandatory to require the urgent introduction of new antimalarial therapies as stated by Hastings, and Ward,(2005) In this study it was discovered that Artemisinine-Based Combination therapy (ACT) was more preferred to other single those therapy as reported by the respondents in yenagoa, Bayelsa state. The survey shows a total of 200 respondents were treated with Artemisinine-based Combination Therapy (ACT). Based on this survey, it shows that the people are responding positively to ACT'S drugs in the treatment of malaria in Yenagoa, Bayelsa State. From the study, it was also revealed that the age range between 31-40 years had 64(32.0%) in terms of usage for Artemisinine-Based Combination Therapy drugs. Followed by 21-30 years that had 57(28.5%), 51-60 years having 31(15.5%), 61-above had 20(10.0%), 41-50 had 18(19.0%) and the least 10-20 years having 10(5.0%) usage for the ACT's drugs(fig.1). While other antimalarial's such as Chloroquine, Halofantrine, Quinine Sulphate, Amodiaquine, and Sulphadoxine/ pyrimethamine had less usage by the respondents in terms of acceptability(tab.5). Based on these respondents, which correlates with the work of Prince, *et.al.*,(2006), when they stated that Artemether-Iumefantrine is currently the only combination therapy widely available that is manufactured to Good Manufacturing Practices and standards in a fixed-dose preparation (each table contains 20 mg of artemether and 120 of Lumefantrine). The fixed dose regimen ensure that malaria parasites always encounter artemether and metabolites in the presence of Lumefantrine and provides protection against the emergence of resistance to both components, but absorption of the lipophilic Iumefantrine is erratic, and the drug needs to be administered twice per day (Ezzet, *et. al.*, 2000). Although in some countries, for example In Thailand, according to Roberts *et.al.*,(2000) transmission has continued to decline in parallel with economic development, improved health infrastructure, and continued anti-vector measures (Roberts *et.al.*, 2000).

In this study, it has been deduced that Artemisine-Based Combination Therapy has been highly accepted by the people in Yenagoa in Bayelsa State, as has been recommended by World Health Organization (WHO). Analysis also revealed that the artemether/Lumefantrine is the most accepted

ACT'S, followed by Dihydroartemisine/piperaquine, before artemether/amodiaquine etc.(tab.4). From the reports of the respondents in this study, most people prefers the 6-dose regimen of artemether/lumefantrine because of the few side effects observed when compared to other ACT's together, as responded by the people taking the drug from the questionnaire issued. The percentage side effects of Artemether/lumefantrine were compared to other ACT's together and the respondents showed that gastroenteritis and headache were reported by the people in which artemether/lumefantrine were administered to be 36.7%, nausea/vomiting 27.3%, dizziness, blurred vision 23.8% and those without notable side effects were observed to be 25.9%.(tab.2). Though the acceptability ratio of the ACT's were higher than the single dose therapy as reported by the respondents, the use of ACT's for the treatment of malaria is higher when compared to all the single dose regimen like Chloroquine, Quinine sulphate, Amodiaquine, Sulphadoxine and Halofantrine at every age range sampled(tab.5). Though from the reports of the respondents not all the people could ascertain the type of malaria drugs used during their treatment of malaria, as a total number of 155 people reported that they don't have the knowledge of the type of antimalarial drugs they were treated with, while a total of 95 respondents were not treated with ACT's at all. A total of 200 people reported to have been treated with one ACT's or the other at any range sampled as earlier reported in this survey. According to Staedke, *et.al.*(2001) in their report, that the fixed combination of sulphadoxine and pyrimethamine which are inhibitors of two foliate pathway enzyme has been chosen to replace Chloroquine as first line therapy for uncomplicated falciparium malaria in several African countries. It has been reported also in this study to be highly accepted with 9.61% prevalence rate of acceptability after the ACT's (76.9%) as shown in the analysis, than Chloroquine (3.46%). This report shows that since the introduction of ACT's in the country, Sulphadoxine/pyrimethamine still continues to wax strong because of its advantages of low cost, simple dosing and few toxic effects. Though, the therapeutic life span of Sulphadoxine/pyrimethamine is limited by the rapid emergence of Sulphadoxine/pyrimethamine resistance parasites (Staedke, *et. al.*,2001). The acceptability ratio of ACT's as compared to the other single dose therapy have agreed with the reports of Staedke, *et. al.*, (2001), that the strategy of combining drug with different modes of action and mechanism of resistance, is a standard approach as in the treatment of tuberculosis and HIV infection, now being advocated as a way to improve antimalarial

therapeutics effectiveness and to delay the emergence of drug resistance. Nevertheless, most people prefer both the combined and single dose therapy as reported in the respondents' questionnaires. This study showed that most people take their drugs with foods as stated by Ezzat, *et.al*.,(2000) and the age group is not a factor in determining the acceptability of these drugs, but from the analysis lack of education was observed as a predisposing factor in ACT'S acceptance and because of this factor, most of the people do not complete the dose of the drugs (Artemisine Based Combination Therapy) after symptoms have subsided within two days of administration despite the facts that most of the people (respondents) prefer the 6-dose regimen of I tablet, morning and night (twice daily).

According to the reports of Greenwood, *et. al*., (2008), most countries in the world has now switched to an official policy of using an ACT's as the first-line treatment. Thus, in this study, most of the people have decided to be administering these ACT's without even the doctor's prescriptions. At least 50% (male) of the retrieved questionnaires from the respondents stated so. Though most of the female (especially the pregnant women) do not take the ACT's unless prescribed by the doctor, because most of them prefer staying or sleeping under the mosquitoe treated net in as much as some of the ACT's are cheap. Thus the statistical analysis using analysis (ANOVA) shows that the level of knowledge and perception of the ACT's by the female and male indigenes and non-indigenes is highly significant at probability level of $p<0.05$, thus making the Artemisine-Based Combination Therapy a perfect choice for treatment of malaria in endemic areas like Yenagoa.

Conclusion
In Nigeria today, to adequately treat malaria, the drug of choice must be fast acting, highly potent against asexual blood stage infection, minimal toxicity and affordable to residents in endemic regions. These study survey that was carried out in Yenagoa has justified the efforts of World Health Organization in the fight against malaria and the use and acceptability of an effective combination therapy such as the Artemisine-Based Combination Therapy in eradication of these global 'bug' called plasmodium. Thus current effort are therefore focused on evaluating the impact of other ACT'S, including artemether/lumefantrine,dihydroartemisinine/piperaq uine and artesunate/amodiaquine, when they are deployed as new first line treatments (Greenwood, *et.al.*, 2008). Nevertheless it is also advised to

comply with the dose regimen supplied in any of these areas in Yenagoa and adequate use of the long lasting Mosquitoes treated nets for complete eradication of Plasmodiasis in Bayelsa State, Nigeria.

Corresponding author:
Onyenwe, Nathaniel, E.
Department of Pharmaceutical Microbiology
Faculty of Pharmacy,University of Ibadan
E-mail: o_nathejik@yahoo.com,

References
1. Ezzet f, Van Vugt, M, Nosten, F, Looareesuwan, S, White NJ. Pharmacokinetics and Pharmacodynamics of lumefantrine (benflumetol) in acute falciparum malaria. Antimicrob Agents Chemother. 2000; 44:697 – 704.
2. Federal Ministry of Health. National malaria control programme in Nigeria. Annual Report. Abuja Nigeria. 2005.
3. Greenwood, B, Mutabingwa, T, Malaria in 2002. Nature. 2002; 415: 670-672.
4. Greenwood, BM, Fidock, DA, Kyle, DE, Kappe, SHI, Pedro, L, Alonso, PL, Collins, FH, and Duffy, PE, Malaria: Progress, Perils, and Prospects for eradication. J Clin Invest. 2008; 118(4): 1266 – 1276.
5. Hastings, IM, and Ward, SA, Coartem (Artemether-lumefantrine) in Africa: The beginning of the end. Journal of infectious diseases. 2005; 5:1-5.
6. Prince, RN, and Nosten, F, Drug resistant falciparum malaria: clinical consequences and strat6egies for prevention. Drug Resist Update. 2001; 4:187 -96.
7. Prince, RN, Uhlemann, AC, Vugt, MV, Brockman, A., Hutagalung, R, Nair, S, Denae, N, Singhasivanon, P, Anderson, TJC, Krishna, S, White, NJ, Nosten, F, Molecular and Pharmacological Determinants of the Therapeutic Response to Artemether-Lumefantrine in Multidrug-Resistant Plasmodium falciparum Malaria. Clinical infectious Disease. 2006; 42:1570 – 7.
8. White, NJ, Nosten, F, Molecular and Pharmacological Determinants of the

Therapeutic Response to Artemether-Lumefantrine in Multidrug-Resistant Plasmodium falciparum Malaria. Clinical infectious Disease. 2006; 42:1570 – 7

9. Roberts, DR, mangiun, S, mouchet, J, DDT house spraying and re-emerging malaria. Lancet. 2000; 356:330-332.

10. Staedke, SG, Kamya, MR, Dorsey, G, Gasarira, A, Ndeeze, G, Charlebois, ED, Rosenthal, PJ, Amodiaquine, salfadoxine/pyrimethamine, and combination therapy for treatment of uncomplicated falciparun malaria in Kampala, Uganda: a randomized trial. The Lancet. 2001; 358 – 374.

11. World Health Organisation, Position of WHO's Roll Back malaria Department on malaria treatment policy. Available at *http//www.who.int/malaria/docs/who_apt_position.htm.* 2006.

12. Abeku, TA. Malaria epidemic early warning and detection in African highlands. Trends parasitol. 2004; 20: 400 – 405.

8/21/2014