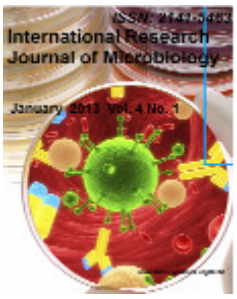

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Full Length Research Paper

Asymptomatic malaria (*Plasmodium falciparum)* in two villages receiving ivermectin treatment for onchocerciasis within Gurara River basin of Kaduna State, Nigeria

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Abstract

A spot survey to screen for malaria infection in two agrarian villages with an estimated population of 470 persons was undertaken. The two villages were enlisted in 1994 into the ongoing annual ivermectin (Mectizan®) mass distribution programme. Among the 73 volunteers screened, 15 (20.55%) with confidence interval (CI) of 9-24 (13-29%) were seropositive in the First Response® Malaria Antigen *Plasmodium falciparum* (HRP2) immunochromatographic card test (ICT). The microscopy of stained thin blood films showed 14 (19.2%) positive cases with CI of 8-22 (12-28%). The concordance between the two tests was 93.3%. The erythrocyte sedimentation rate (ESR) for the sample population was 2.9±1.1mm. There was a significant difference in PCV and ESR of the infected (n=15), 31.7±4.8 and 4.5±1mm compared to the uninfected (n=58), 37.2±6.8 and 2.5±0.6mm (P<0.05). The significant differences in quotients of participants PCV over ESR was capable of discriminating those that had malaria infection with low values from non-infected with higher values (P<0.05). The *P. falciparum* was chronic and asymptomatic infections in the study population (n=470). None of those infected showed any clinical evidence of infection. Malaria may be a cofactor that can reduce man-hour and productive capacity of farmers in these two villages. Absence of primary health care facilities could entrench treatments without medical supervision. Apparent drug abuse and under-dosage could lead to the development of drug resistance malaria in the study area. Control of malaria can take advantage of this ICT rapid screening kit. Importance of developing synergy between community-directed treatment of onchocerciasis and on-going Roll Back Malaria Programme to control and eradicate the disease was discussed.

Keywords: Malaria, *Plasomdium falciparum*, Card test, Incidence, Asymptomatic.

INTRODUCTION

Malaria is a vector borne mosquito transmitted parasitic disease. There are four different types of malaria caused by *Plasmodium falciparum*, *P. vivax, P. ovale and P. malariae.* Malaria is one of the neglected tropical diseases of poverty prioritized for control and eradication under the Millennium Development Goals (MDGs) objectives to improve health and wellbeing of citizens in developing world. The disease occurs in 90 countries with over 500 million clinical cases and 2.7 million malaria-related deaths are reported annually (WHO 1993). In Nigeria an estimated one million cases of malaria is reported. The disease is responsible for about 8-12 infantile deaths particularly of those under 5 years old. The situation is worsened by the emergence of drug resistance malaria parasites (Molta *et al*. 1993; Falade *et al.* 1997). It was the highest cause of mortality (92.1%) among migrant Fulani children less than 5 years old (Tidi

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et al. 2012). Research priorities in malaria in Nigeria include increased understanding of the nature of the disease, the burden it constitutes in the affected population and development of intervention for control. More importantly, there is no effective vaccine for malaria (Salako, 2006). It is a serious health problem causing infant mortality, complication with cerebral malaria in children and abortion, stillbirth, intra-uterine growth retardation, premature labour and sometimes death of the pregnant women (Kochar *et al*. 1999). Asymptomatic malaria has been reported among pregnant women in Lagos (Anorlu *et al*. 2001). Also, malaria is among the high risk of transfusing malaria infected blood to susceptible recipients (non-immune and immunocompromised) including transplacental transmission (Okon *et al*. 1993; Mbanugo and Emenalo, 2004; Nmore and Egwunyenga, 2004). This study was to determine the status of endemicity of malaria in two rural agrarian villages where attention to other endemic parasitic diseases (onchocerciasis, lymphatic filariasis and guinea worm) has been accorded community directed intervention (CDI).

MATERIALS AND METHODS

Study area/population

The two villages, Gidan Tama (9°43'1.84"N and 7°55'47.86"E) and Unguwar Shaho (9°42'46.13"N and 7°55'40.20"E) are situated about half a kilometer apart within an onchocerciasis meso-endemic focus (Osue, 1996). The study area is located within the Gurara River Basin with tributaries and rivulets. The people farm mainly Ginger as cash crop and yam, maize and millet as staple food. The village sample populations for G. Tama, 27 and U. Shaho, 46 were drawn from the study population of 260 and 210, respectively. Gender, age and ivermectin treatment information were obtained from individual participants.

Blood sample collection and test for malaria

Sterile hypodermic disposable syringes and needles were used for collecting 5ml of blood into ethylenediamine tetra-acetic acid (EDTA) containing bottle. The area was disinfected by swabbing with 70% ethanol prior to vein-section. Thin blood films were prepared; air dried, fixed with methanol and stained with 4% Giemsa stain. Slides were examined under microscope at x100 objective overlaid with immersion oil. A slide was considered positive only if any stage of the parasite was seen or negative where no parasite was seen after viewing at least 200 fields (Akambi *et al.* 2004). Examination of all the slides was done separately without the knowledge of the screening test result.

Immunochromatographic test

Patients' whole blood were tested with commercially available First Response® Malaria Antigen *Plasmodium falciparum* Histidine–Rich Protein 2 (HRP2) immunochromagraphic card test kit (Premier Medical Corporations Ltd, Daman, India and Transnational Technologies Inc., UK) following the manufacturer's instruction. The card contains a membrane strip, which is pre-coated with a monoclonal antibody (test line) specific to HRP2. The kit was developed for rapid qualitative determination of Malaria HRP2 in human blood as aid to diagnosis of malaria infection (Panton *et al*. 1989; Tjitra *et al*. 1999; Valecha *et al*. 2002). The test was regarded negative if only one colour band appeared at the control line 'C' and it was regarded positive if two colour bands appeared at the control line 'C' and test line 'T'. The result is invalidated if no colour band appears.

Packed cell volume (PCV) and Erythrocyte sedimentation rate (ESR)

Heparinized capillary tubes were filled with blood, one end sealed with plastiseal and centrifuged in a haematocrit centrifuge (Hawksley, England) at 10,000g for 5minutes. PCV was determined from a reader. Values of ESR attributed to different serum protein (Deegan *et al*. 1956) were determined in 1ml Wintrope or Westergreen tube (mm /hr). The relative blood density (RBD) was calculated by dividing the value of PCV by ESR (RBD=PCV/ESR). White blood cell (WBC) total ($x10^9$) and differential counts were done in improved Neubauer Chamber (Hawksley, London) and by enumeration of 100 cells in thin stained film.

RESULTS

Ivermectin treatment records

The two villages had received 11 rounds of treatment with ivermectin from 1994-2011. Albendazole distribution started in the area in 2005. The sample population had received a mean IVM of 4 treatment doses with the last dose in May 20011 before the study in August 2011.

Status of malaria

Incidence of malaria was recorded in male and female in both villages as shown on Figure 1. Two cases were detected out of the 3 females examined in U. Shao. There was no significant difference in infection between the two villages as shown on Table 1. Screening with First Response® Malaria Antigen *Plasmodium falciparum* (HRP2) Card Test kit showed 15 (20.5%) positive cases.

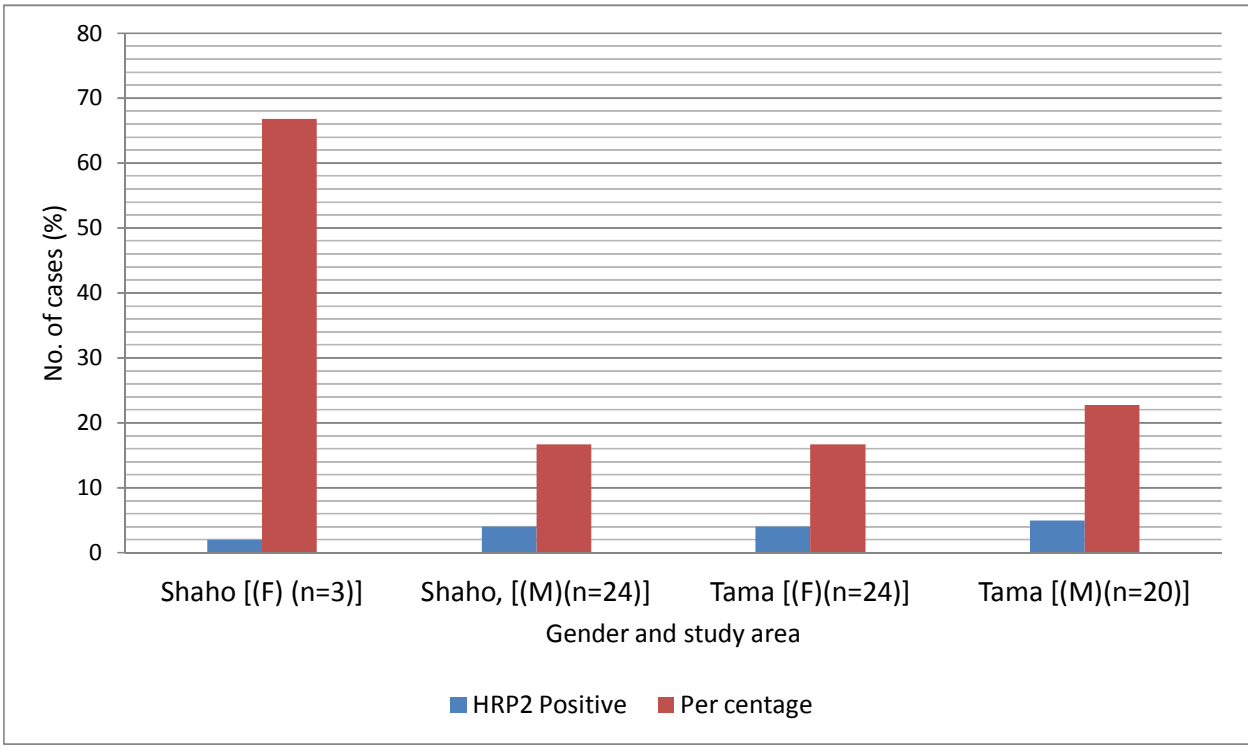

Figure 1. Prevalence of *Plasmodium falciparum* by gender and village (F= female; M=male).

Table 1. Prevalence of *Plasmodium falciparum* and haematological status in study villages.

S/No.	Study area	Age (years)	Packed cell volume (PCV) (%)	White Blood Cells (WBC) Count (10^9)	Histidine-Rich Protein 2 (HR2P) CAT Positive	Erythrocyte Sendimentation Rate (ESR) (mm)
1.	Ungwar Shaho (mean, n=27)	45.5±17.7	36.8±6.8	4.8±2.0	22.2%	3±1.1
	Range	18-80	20-50	2.2-6.6	n=6	2.0-5.0
2.	Gidan Tama (mean, n=46)	39.3±13.5	35.8±7.0	4.7±1.3	19.6%	2.9±1.1
	Range	15-70	29-53	2.0-10.6	n=9	2.0-6.0

CAT= card agglutination test

Stained thin film microscopy identified 14 (19.2%) parasitological positive cases. Concordance between ICT and microscopy was 93.3%.

PCV, ESR and RBD

Overall, there was no significant difference in the incidence of malaria, PCV, ESR and WBC counts in the sample population of both villages as shown on Table 1. The difference in PCV of infected group (n=15) with 31.7±4.8 compared to that of the uninfected group (n=55) with 37.2±6.8 was statistically significant, $P<0.05$) as shown on Table 2. Similarly, the difference in ESR of infected 4.5±1 and uninfected 2.5±0.6 groups was statistically significant, $P<0.05$. The ratios of PCV to ESR

Table 2. Comparing some haematological indices of those with or without *Plasmodium falciparum* infection

S/No.	Statistical analysis	Age	PCV (%)	WBC (10^9)	HR2P CAT Positive	ESR (mm)
1.	Negative, n=58 (mean±StDev)	38.9±14.7	37.2±6.8	4.7±1.7	0	2.5±0.6
	Range	15-80	20-53	2.2-6.6		2.0-5.0
2.	Positive, n=15 (mean±StDev)	48.5±17	31.7±4.8	4.58±1.2	15 (20.5%)	4.5±1
	Range	19-70	20-39	2.0-10.6		2.0-6.0
3.	Sample size (n=73)	40.9±15.6	36.10±6.8	4.70±1.6	15 (20.5%)	2.9±1.1
	Range	15-80 yrs-o	24-53	1.4-10.6	na	2.0-6.0

were overall 14.1±5.3 (range, 4-26.5), positive subgroup (n=15), 7.5±3.1 range, 4- 17) and negative subgroup, 15.8±4.4 (range, 8-26.5). A case of ICT positive and parasitological negative had PCV of 31%, ESR of 5mm/hr and PCV/ESR value of 6.2.

DISCUSSION

In the present studies, incidences of malaria caused by *P.falciparum* in two agrarian villages have been established. The disease was found among residents participating in impact assessment of mass drug administration for the control of onchocerciasis and lymphatic filariasis using IVM and Albendazole, respectively. The participants had not shown any clinical evidence of the disease at the time of screening. This was a clear indication of asymptomatic nature of malaria infection as observed in pregnant women (Okon *et al*. 1993; Anorlu *et al*. (2004; Chimere *et al*. 2009). As residents had received doses of both IVM and albendazole just few months prior to this study, the drugs would appear not to confer any curative or protection against malaria infection. One of the documented additional clinical benefits from IVM treatment is the expulsion of intestinal worms (Whitwort *et al.* 1991).

A strong concordance of the two tests confirmed the manufacturers claim. Explanation for the subject that was ICT positive and parasitologically negative may be attributed to having taken treatment prior to sampling. It has been documented that most treatments at home were without medical supervision (self-medication) a common practice (Deressa *et al*. 2003; Yeung and White, 2005). Epidemiological situation like this cannot be regarded as false positive. The manufacturer had recommended that a definitive clinical diagnosis should not be based on a single test, but should be made by the physician after clinical and laboratory findings have been evaluated. The HRP2 ICT will be valuable tool for attaining WHO (2005) objective of home management of malaria treatment strategy.

Anaemia measured by PCV was moderate with a range, 20-39 compared to the standard range of 35-45. Setting the cut-off point at 10, the ratio of PCV to ESR could serve as a simple indication of chronic status of infection. It can be performed in rural setting as means to assess severity of anaemia where determination of haemoglobulin cannot be performed due to cost and lack of facility.

Incidence of malaria (20.5%) will contribute to loss in gross domestic product (GDP) estimated at 1-5% (FMOH, 1993). It is imperative that the disease will lead to reduction in man hour in these two agrarian communities. Ongoing Roll Back Malaria Programme of the World Health Organization supporting free diagnosis and treatment can be strengthened and made more effective by keying it into existing community directed treatment intervention (CDTI) using triple approach. This includes the adoption of free distribution of FRHRP2 ICT kit to PHC at the district health level, anti-malaria drugs for mass treatment with suitable drug and insecticide impregnated bed nets to remote and often inaccessible rural settlements without any primary health care facility. Anti-malaria drugs are available for treatment of uncomplicated malaria (Molta *et al*. 1993). These drugs meet the criteria of efficacy, safety, and tolerability for use in mass drug administration and can be used alternatively where drug resistance becomes apparent (Molta *et al*. 1993; Agomo *et al.* 2008). Evidence-based decision using surveillance will be needed to achieve effective malaria control. We advocate adoption of Yeung and White, (2005) recommendation for community malaria control programme with training of community Health Workers in Nigeria.

Similar to what obtains in onchocerciasis, mathematical model projection (Poolman and Galvani, 2006) suggested treatment coverage of 65% will be adequate to achieve a break in transmission of the disease. A five year biannual national mass drug treatment programme for malaria could bring the disease to a sustainable level of control. This will require strong political and administrative support and commitment at all

tiers of government. Community awareness and participation and ownership will ensure sustainability and treatment compliance.

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