

Plasmodium Falciparum Clearance in Malaria Treated Children at Lake Alau Settlements, North Eastern Nigeria: Effects of Body Weight

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Abstract: The influence of body weights on *Plasmodium falciparum* clearance in malaria positive children was conducted using AT+SP and AQ+SP combination therapies, at the malaria holo – endemic and risk settlements of lake - alau, North Eastern Nigeria. A total of 313 children (6 - 59 months) were admitted into the study, to assess the efficacies of the combination therapies in children (6 - 59 months) using the effects of Body weights (kg) on parasite densities. Each child's weight was determined on days 0, 1, 2, 3, 4, 7, 14 and 28 during the follow up periods. The drugs were administered between 0-3 days. Finger prick and venipuncture (syringe) techniques were employed and blood was sampled by pricking using sterilized needle on days 0, 1, 2, 3, 4, 7, 14 and 28 for the assessment of parasite densities count (per μ l) while blood smear was prepared using Giemsa stained slides making thick and thin blood smears. The result shows body weight exerted negative effects on *Plasmodium falciparum* between the range of 71.63 to 96.0% for AT+SP and 87.79 to 96.38% for AQ+SP in the first three days of treatment. Furthermore, results showed for each kg gain in body weight there was a synchronous parasite clearance by 325.79 versus 1199.91/ μ , 16.621 versus 157.06/ μ , 17.445 versus 153.5/ μ for AT+SP versus AQ+SP on days 1, 2, and 3, respectively. The terminal results indicated a higher residual parasitaemia at the onset of late phase in children treated with AQ+SP (195.17 to 113.92/ μ) compared to AT+SP (182.48 to 25.531/ μ). The respective parasite densities clearance per kg body weight for days 7, 14 and 28 for AT+SP versus AQ+SP was 33.82 versus 35.887/ μ , 10.076 versus 29.578/ μ and 2.3548 versus 26.368/ μ respectively. Thus, on each of the late follow-up days, the rate of parasite depletion was higher in AQ+SP than AT+SP. *Corresponding Author: muskokoss@gmail.com

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I. Introduction

Malaria is one of the most important infectious parasitic diseases in the world and a leading cause of death of children in Africa [8]. Globally, an estimated five billion clinical cases known to occur annually, with more than ninety percent recorded in Africa, which remains a major cause of deaths and serious morbidities among younger children (\leq 59, months) and pregnant women [20] ; [22] . Malaria is a complex parasitic disease that varies widely in epidemiology and clinical manifestations in the different parts of the world [32] . These variability's could be due to factors like species difference of malaria parasites that occur in a given area at a point in time, their susceptibility to commonly used and available antimalarial drugs, their distribution, climatic factors as well as other environmental conditions and level of acquired immunity of the exposed human populations and respective body weights effects on course of treatments [36] ; [9] .

The emergence of drug resistance is one of the greatest challenges facing malaria control today and implicated in its spread and re-emergence in areas where the disease have been eradicated [19] . Despite a decision by many African countries to use Artemisinin based combination therapies Artemisinin combination therapies (ACTs) [4]. Most malaria cases are still treated with monotherapies and are bound to fail [34]; [2]; [9]. The combinations of drugs, rather than monotherapies are now considered the best option for treating malaria [29]; [30] and Artemisinin based are highly effective and reliable [4]; [17]. In areas with relatively low malaria transmissions, widespread use of ACTs has significantly reduced the burden of malaria by increasing faster parasite clearance [16]; [19]; [12]. Therefore, the control of malaria transmissions is challenged by increasing parasite resistance to monotherapies, particularly Chloroquine and Sulphadoxine - Pyrimethamine, which elicited the usage of the combination therapies against plasmodium species using the World Health Organizations protocols [30]. Thus, in endemic areas, effective anti-malarial case management and treatments depends on adequate case requires assessments of body weight categories management particularly critical in younger and lighter children, who are on course of acquiring partial immunity to malaria parasites which is characterized of acute clinical episodes that could progress rapidly to severe, life-threatening malaria be checked[30] .

II. Materials and Methods

2.1. Study site and patient's recruitment procedure

The study took place at the Lake - alau settlements of Konduga Local Government Area of Borno State, North Eastern Nigeria, it is located at (Lat: 12⁰N and 13⁰N; Long: 11⁰E and 13⁰E). The lake and other water bodies surrounding the settlements make a serious malaria holo-endemic environment which disposes the inhabitants to incessant and consistent epidemics all the year round while the peak of transmissions are during the rainy season (July - December).

2.2. Ethical clearance:

Prior to the commencement of this experiment, ethical clearance was sought from the Konduga Local Government Health Authorities through Borno State Ministry of Health, Nigeria. Then a letter of consent was served to all the affected villages and district heads units and their affected leaders and settlers who were mobilized on the study protocols [29].

2.3. Inclusion and exclusion criteria:

Individuals were admitted into the study using [29] guideline for evaluating anti-malarial drugs in children between 6 - 59 months. Complete physical examination was performed and full medical record was obtained by qualified nurses and medical personnel. Detailed information's concerning the history of present illness; past drug histories such as hypersensitivity reaction to drugs like 4- aminoquinolines together with other similar clinical ailments observed were noted and recorded into the case record form (CRF). An informed consent must was provided by the patients or parents/guardians [28] . Furthermore, children with clinically apparent and uncomplicated malaria, devoid of danger signs like inability to drink or breast feed, vomiting with recent history of convulsions, lethargy, unconsciousness and general body weakness or inability to sit or stand up. Others are mono-infection with only *Plasmodium falciparum* positive with slide-confirmed asexual blood stage with parasitaemia on day 0/ initial enrollment with parasite density requirements of > 2,000 asexual parasites/ μ l of blood. Complete absence of complications such as concomitant infections and severe malnutrition as defined by [30].

2.3. Procedures for physical parameters: The Body weight (kg) of each child was determined and recorded using weighing machine per kilogram on days 1, 2, 3, 4, 7, 14 and 28 during the follow up days [29].

2.4. Laboratory procedures

2.4.1. Blood Sampling

Finger prick and venipuncture (syringe) technique [28] was employed. The blood was sampled by pricking the lateral side of the third phalanx with a sharp sterile needle after cleaning with spirit-moistened cotton. The blood was sampled on days 0, 1, 2, 3, 4, 7, 14 and 28 for the assessment of parasite densities.

2.4.2. Thin film:

The procedures of [13] were adopted for thin film preparation. A drop of blood sample, equivalent to 1.5 μ l and 3 - 4 mm in diameter, was collected on one end of a slide. The edge of a second slide, held at an angle of 45⁰ with the first slide was then used to spread the blood thinly on the other slide.

2.4.3. Thick film: The procedures of [13] were adopted in the preparation of thick blood film. Three drops (4.0 μ l) of blood sample was used for the preparation of the thick film. Three triangular blood drops were placed on the slide which was then gently mixed for 20-30 seconds using the corner of a second slide then defibrinated the blood to a round smear of about 1 cm in diameter on the slide.

2.5. Parasite density count (per μ l): Thick blood samples on slides were examined using objectives of a research microscope (x100) asexual parasites were counted alongside with 200 leukocytes. In an even that parasite count was < 10 parasites/200 leukocytes; count was continued per 500 leucocytes. The parasite density was expressed as the number of asexual parasites per ml of blood by assuming a mean normal leukocyte count of 8000/ μ l of blood [29].

2.6. Randomization and treatment allocation: After satisfying the inclusion criteria children were randomly assigned into two groups. The drug dosages were prescribed using body weights of patients by medical personels [28]; [29].

2.6.1. Group one; - Artesunate + Sulphadoxine- Pyrimethamine (AT+SP). Each child in this group orally received 4 mg/kg body weight Artesunate daily for three days and a combined 25 mg/kg body weight Sulphadoxine and 1.25 mg/kg body weight Pyrimethamine as single oral dose on the first day of treatment.

2.6.2. Group two; Amodiaquine + Sulphadoxine –Pyrimethamine(AQ+SP). Each child in this group orally equally received 10 mg/kg body weights of Amodiaquine daily for three days and also a combined 25 mg/kg body weight Sulphadoxine and 1.25 mg/kg body weight Pyrimethamine as a single oral dose on the first day of treatment.

2.7. Data and statistical analysis

Data collected were subjected to statistical analysis using the analytical software Staistix Version 8.0 (Microsoft, 2003) to determine percentages and correlation coefficients using regression analysis on the effects of body weights categories on parasite densities patterns during follow up period.

III. Results

The study enrolled a total of 313 children with 149 (47.6%) males and 164 (52.4%) females. The mean age of the children was highly dispersed between 8 - 59 months from the mean of 43.3 ± 14.4 months. Body weight was equally diverse (3.0 - 50.0 kg) with mean value of 18.4 ± 8.5 kg. There was significant ($P = 0.01$) positive correlation ($r = 0.4258$, $df = 311$) between body weight and age of the children studied. The mean parasite count on admission was highly dispersed (2304 - 36800/ μ l) from the mean of 20820 ± 5277.7 / μ l (Table 1). Results on Fig. 1 indicates the influence of body weight on parasite clearance rate as negatively affected *Plasmodium falciparum* clearance between the range of 71.63 to 96.0% for AT+SP compared to 87.79 to 96.38% for AQ + SP in the first three days of treatment and in quantitative terms each kg gain in body weight and there was a simultaneous parasite clearance by 325.79 versus 1199.91/ μ , 16.621 versus 157.06/ μ , 17.445 versus 153.5/ μ for AT+SP versus AQ+SP on days 1, 2, and 3, respectively. The results in Fig. 2 shows a late phase body weight response to parasitaemia in children treated with AQ+SP (195.17 to 113.92/ μ) and AT+SP (182.48 to 25.531/ μ). The respective parasite clearance per kg body weight for AT+SP versus AQ+SP for the late phase was, 33.82 versus 35.887/ μ , 10.076 versus 29.578/ μ and 2.3548 versus 26.368/ μ on days 7, 14 and 2 respectively (Fig. 1 and 2).

IV. Discussion

The effects of body weights on parasite clearance from the peripheral circulation is normally affected by the cumulative effects of drug's, host immunity, as well as age and the respective body weights categories of patients [18]: [15]. Conversely, parasitological recovery could be viewed as the clearance of parasites from peripheral blood smears in which parasites are generally cleared to the lowest below detectable limits of 10 – 50 parasites/ μ l [22]. However, the results of the present study on fig.- 1 shows that body weight succeeded in exerting negative effects on *Plasmodium falciparum* parasitaemia between the range of 71.63 to 96.0% for AT+SP and 87.79 to 96.38% for AQ+SP in the first three days of treatment (early phase). This result infer that the response of AQ+SP was more body weight dependent than AT+SP, but in either of the treated group, there was a speedy parasites clearance within the first three days in respect to the body weights categories, these results on cognate relationship between parasite clearance and body weight of malaria treated children is in concordance with [5]; [11]; [1]. The results further explained the impacts of host body weights on acute uncomplicated *Plasmodium falciparum* parasitaemia in children malaria. Reference could be made to the predictive parameters in the endemic areas that shows the pre-treatment weights are significantly lower than the 14 to 28-days post-treatment weights ($P = 0.0001$) linking body weights to parasite burden and drug efficacies in malaria infected children. The fractional fall in body weight exceeded 4.9% which equally correlated negatively with age and body weight ($P = 0.014$ and 0.0001 , respectively) [18]. Similarly, results shows that the mean daily parasite density as affected by each kg gain in body weight showed a simultaneous parasite clearance by 325.79 versus 1199.91/ μ , 16.621 versus 157.06/ μ , 17.445 versus 153.5/ μ for AT+SP versus AQ+SP on days 1, 2, and 3, respectively (fig - 1), indicating faster parasite clearance by AQ+SP on daily bases compared to AT+SP in the early period (1 – 3 days)(fig 1). In summary, both combination therapies performed creditably in parasite clearance in the early days clearance of the parasites in respect to body weights categories [23]. The results further revealed the trends of relationships at the terminal end (Fig. 2) showing a relatively higher residual parasitaemia at the beginning of late phase in children treated with AQ+SP (195.17 to 113.92/ μ) than AT+SP (182.48 to 25.531/ μ)(fig 2).

These findings suggest that AQ+SP that trailed behind in the early phase were left in arrears with more parasite load to clear in the late phase. Conversely, the combination therapies normally rely on components like Sulphadoxine - Pyrimethermine which has longer half life will have greater effects on parasite clearance at the later phase [4]. Reports indicated that the antifolates such as Sulphadoxine-Pyrimethamine arm of the combination exerts little or no effect on the parasites during the first 24 h of their life cycles despite its longer half life, but acts gradually over time[35]; [31] but at the late phase it affects the activities of the dividing forms of *Plasmodium* species due to its persistence (Schizonts) [34]. Previous reports indicated higher influence of body weights on parasite clearance due to antimalarial drug efficacies in treatments [6]; [3]; [12]. In

endemic areas, treated children with lower body weights ($\leq 5 - 10\text{kg}$) are more particularly vulnerable to slower parasite clearance as compared to older with higher weights ($15 - 25\text{kg}$) [21]; [30]. This is because the younger or lighter body weights may not have acquired protective immunities by then as compared to the older/heavier children, as a result there may be higher tendencies for higher residual parasites remaining as was observed in the present study, that is why the trend lines (figs 1 and 2) showed a downwards pattern of parasite reduction with the increase in body weights, these findings concurs with [24]; [25]; [26]; [7] and [11].

V. Conclusion

The present result clearly showed that both drugs were efficacious against *Plasmodium falciparum* infections in children and was enhanced by body weight, which however, decreased over time. However, body weight elicited more response in AT+SP patients in the first three days of drug administration, but due apparently to the higher residual parasitaemia in AQ+SP which accrued higher response in the late phase of treatment.

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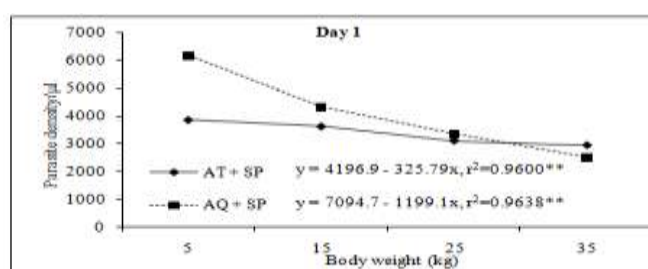
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Table 1. Baseline Characteristics of Patients at Enrollment

Parameter	Baseline data
1. No. enrolled (N)	313
2. Gender (No. /%)	
Male	149 (47.6)
Female	164 (52.4)
3. Age (months)	
Mean ± SD	43.3 ± 14.4
Range	8 - 59
4. Body weight (kg)	
Mean ± SD	18.4 ± 8.5
Range	3.0 - 50.0
5.. Parasite count (µl)	
Mean ± SD	20820 ± 5277.7
Range	2304 - 36800



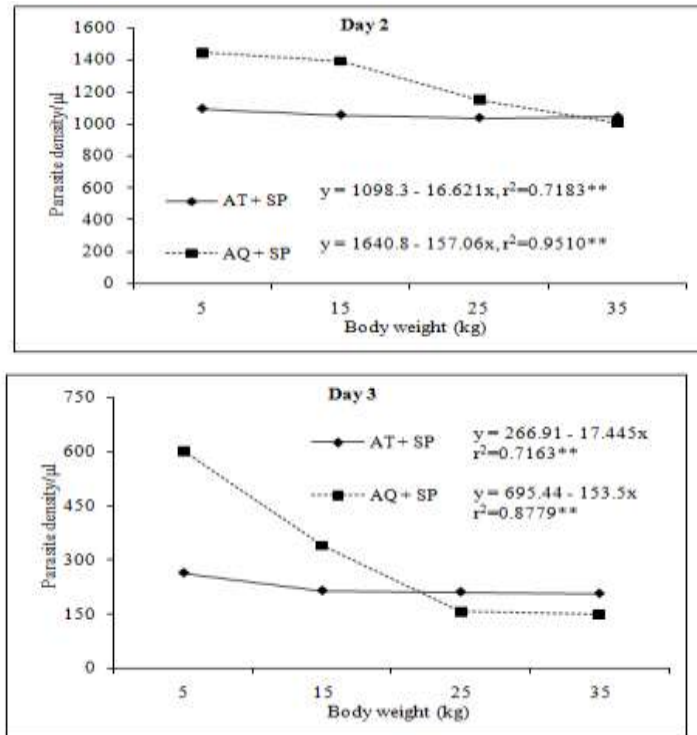


Fig. 1: Effects of body weight on parasite density on early follow-up days for a) AT + SP and b) AQ + SP

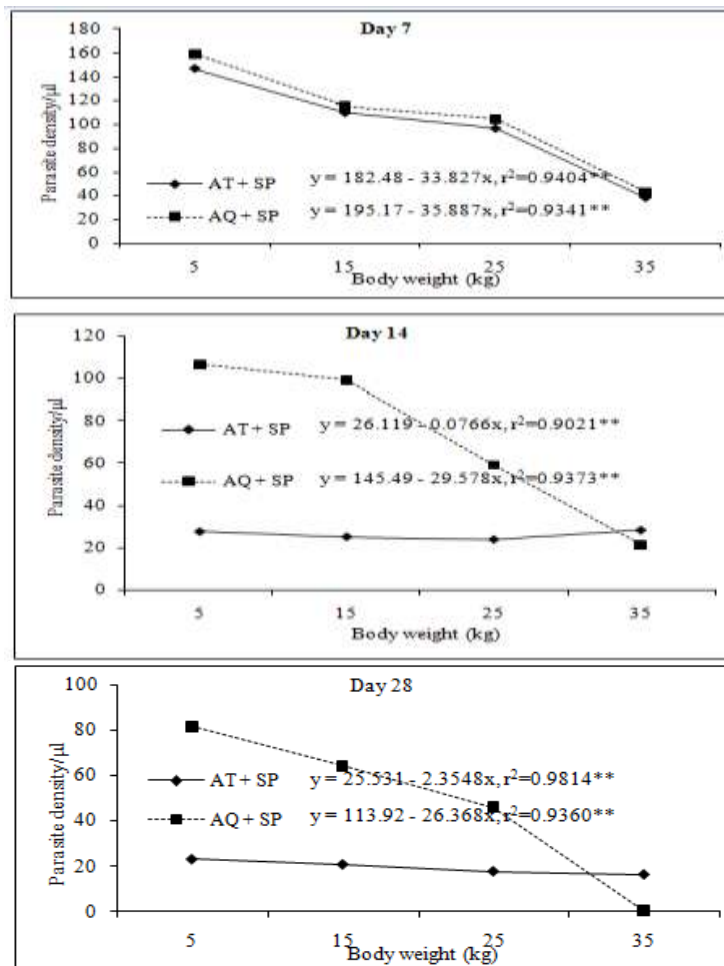


Fig. 2: Effects of body weight on parasite density at late early follow-up days for a) AT + SP and b) AQ + SP