

Electrocardiographic features in children with severe falciparum malaria at the University College Hospital, Ibadan

Akinkunmi B.F.¹, Ogunkunle O.O.², Akinbami F.O.³, Orimadegun A.E.⁴

Abstract

Introduction: The high burden of Malaria morbidity and mortality in children is due to its potential to cause multi-organ dysfunction. There is however limited information on the specific electrocardiographic features in falciparum malaria in paediatric age group.

Aim: To investigate the electrocardiographic (ECG) features in children with (complicated) severe falciparum malaria (SM) and acute uncomplicated malaria (AUM) at the University College Hospital, Ibadan.

Methods: This was a comparative cross-sectional study conducted among 398 children with symptomatic and confirmed Plasmodium falciparum malaria and apparently healthy controls. The frequencies of ECG features were described and compared among these children.

Results: The prevalence of ECG abnormality was 79.7% and 63.2% in Severe Malaria SM and Acute uncomplicated malaria AUM patients, respectively. Sinus tachycardia was significantly more frequent in SM than AUM and control groups ($p < 0.001$). The risk of an ECG abnormality was about three times higher in SM than healthy children ($p < 0.001$; OR=2.89; 95%CI[1.68,4.99]).

Conclusion: Severe malaria patients had significant ECG abnormalities (Sinus Tachycardia).

Keywords: Severe malaria, electrocardiography, sinus tachycardia.

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Caractéristiques électrocardiographiques chez les enfants atteints de paludisme à falciparum sévère dans l'hôpital du Collège Universitaire, Ibadan

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Résumé

Introduction: Le fardeau élevé de la morbidité et de la mortalité du paludisme chez les enfants est dû à son potentiel de provoquer un dysfonctionnement de plusieurs organes. Il existe cependant des informations limitées sur les caractéristiques électro cardiographiques spécifiques du paludisme à falciparum dans le groupe d'âge pédiatrique.

Objectif de l'étude: Étudier les caractéristiques électro cardiographiques (ECG) chez les enfants atteints de paludisme à *falciparum sévère (compliqué)* et de paludisme aigu non compliqué (AUM) dans l'hôpital du collège universitaire d'Ibadan.

Méthode de l'étude: Il s'agissait d'une étude transversale comparative menée auprès de 398 enfants atteints de paludisme à plasmodium falciparum symptomatique et confirmé et de témoins apparemment sains. Les fréquences des caractéristiques ECG ont été décrites et comparées chez ces enfants.

Résultat de l'étude: La prévalence des anomalies de l'ECG était de 79,7 % et 63,2 % chez les patients atteints de paludisme grave SM et de paludisme aigu non compliqué AUM, respectivement. La tachycardie sinusale était significativement plus fréquente dans les groupes SM que dans les groupes AUM et témoin ($p < 0,001$). Le risque d'anomalie de l'ECG était environ trois fois plus élevé chez les SM que chez les enfants sains ($p < 0,001$; OR=2,89 ; IC95 % [1,68, 4,99]).

Conclusion: les patients atteints de paludisme grave présentaient des anomalies significatives de l'ECG (tachycardie sinusale)

Mots- clés: Paludisme grave, électrocardiographie, tachycardie sinusale.

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INTRODUCTION

Malaria is a prevalent parasite illness despite improvements in worldwide control and elimination attempts. Malaria was responsible for around 228 million infections and 405,000 fatalities globally in 2018, responsible for an estimated 18% of deaths among children less than 5 years worldwide. (1) More than 80% of these deaths occur in sub-Saharan Africa. (1) Malaria continues to be a substantial burden on local health systems in low- and middle-income nations, necessitating frequent hospitalizations and increasing morbidity. (2) Though malaria morbidity has declined in many countries due to the implementation of some malaria interventions, including insecticide treated bed nets and effective medicines, the burden of malaria in Nigeria is still high, accounting for about 30% of childhood mortality, 11% of maternal mortality and about 30% to 40% of outpatient clinic consultations. (3) Malaria accounted for 12.4% of all paediatric deaths with an estimated overall case fatality rate of 9.6% in University college Hospital Ibadan. (4)

Malaria sickness manifests itself in a range of clinical ways, varying in pattern and severity from uncomplicated to complicated or severe malaria. The WHO defines severe malaria as having life-threatening manifestations such as cerebral malaria, hypoglycaemia, severe anaemia, haemoglobinuria, hyperbilirubinaemia, metabolic acidosis, recurrent seizures, prostration, and bleeding disorders. (5) *Plasmodium falciparum* malarial illnesses adversely affect all organs in children, including the heart.

Although malaria mortality has declined significantly since 2000, there has been a concurrent increase from cardiovascular deaths in malaria-endemic area. (6) Children with severe malaria are in the class of critically ill patients because of the life-threatening features associated with the disease. (5)(6) The heart is one of the most heavily parasitized organs in severe *Plasmodium falciparum* infections. (7)(8) Despite prior evidence of linkages between parasite infections and cardiovascular disease, the link between malaria and cardiovascular disease has received little attention. (9). Abnormalities of cardiovascular function are not well described in children with severe malaria. (6) In spite of the fact that electrocardiography (ECG) has gained prominence in the care of critically ill patients who require close monitoring, reports on electrocardiography findings among Nigerian children with malaria

are scanty. (9,10) This study was therefore designed to determine the prevalence of ECG abnormalities in children with severe malaria, describe and compare ECG features in children with complicated and uncomplicated malaria and to determine the relationship between ECG changes and the outcome of severe malaria.

MATERIALS AND METHODS

Study Design and Setting

This was a comparative cross-sectional study that involved children with severe malaria as cases and acute uncomplicated malaria and a group of apparently normal children as control groups. The study was carried out at the Otunba Tunwase Children Emergency Ward (OTCHEW) and Children outpatient clinic (CHOP) and the Paediatrics wards of the University College Hospital (UCH) Ibadan in Nigeria. The OTCHEW is one of the six wards in the Department and has thirty-five bedspaces for admission. The average number of admissions per year is 2000. It has facilities for the care of childhood illnesses, a side-laboratory for basic investigations such as blood film microscopy, urinalysis, packed cell volume and cerebrospinal fluid protein estimation. The CHOP is open to all ill children from 8 am to 4 pm every day of the week except on weekends. It has a Malaria Research Laboratory where all children with fever are routinely screened for malaria parasites. On the average, 20-30 children are screened for *P. falciparum* infection daily. The University College Hospital (UCH) is a foremost tertiary referral 800-bed hospital located in Ibadan North Local Government Area of Oyo state, Nigeria. The Paediatrics Department admits about 3,000 children annually and about 11% of them are cases of severe malaria.

Sample size calculation

For this study, it was assumed that the prevalence of occurrence of at least one ECG abnormality is 15% among severe *falciparum* malaria cases as reported by Bethell et al. (11) Using the Stata/BE 17.0 for Windows option for calculating sample sizes for a two-sample proportions test, an estimated 113 patients will be required for each group, assuming the odds of ECG abnormality is 2.5 times higher in cases than controls, to achieve power of 80% at 95% level of confidence. Therefore, a total of 339 patients (113 in each group of complicated malaria, acute uncomplicated malaria and healthy control) were required as the minimum sample size.

Study Population and Sampling

The target population for this study were children aged 6 months to 15 years who presented with symptoms, signs, and evidence of malaria parasitaemia confirmed by microscopy as described by the World Health Organization (WHO). (1) During the study period, consecutive children who presented with fever at the OTCHEW and Children's Out-patient Clinics had peripheral blood film examinations for *Plasmodium falciparum*. Those with malaria parasitaemia were recruited; however children with other causes of fever were excluded. Cases were defined as *children with symptoms and sign of severe malaria as defined by WHO.*(1) This study adopted two controls, namely children with uncomplicated *P. falciparum* malaria who were symptomatic but had no life-threatening manifestations and children apparently healthy without symptoms and no malaria parasitaemia. Children who had haemoglobin genotype SS or SC, underlying cardiac disorders, and a history of symptoms suggestive of cardiac disorders were also excluded. Approval for the study was obtained from the University of Ibadan-University College Hospital Ethical Review Committee (UI/UCH Ethics committee Assigned Number: UI/EC/11/0033).

Data Collection Procedure

The investigator interviewed all of the patients' carers using a structured proforma. If the patient was old enough (> 12year) to provide a credible history, history was gathered from caregivers and/or the patient. Each patient underwent a thorough physical examination The investigator noted all physical examination findings and other pertinent information, including the results of PCV, blood film for malaria, and parasite counts, in the validated structured questionnaire. For each patient, thick and thin films were prepared on the same slide, and a malaria parasite count was performed by an expert Microscopist using standard protocol. Electrocardiography was done for patients and controls following standard protocol using a 12-lead CMS-80A hand-held single-channel ECG machine CONTEC MEDICAL SYSTEMS CO. LTD, China). Patients with uncomplicated malaria were treated with Artemisinin-based combination therapy (ACT) in accordance with the National Malaria Treatment Guidelines. Patients with cerebral malaria were treated with intravenous Artesunate injections until they regained consciousness, at which point they were moved to oral ACT in accordance with the

National Malaria Treatment Guidelines. Other symptoms of severe malaria were appropriately treated in accordance with established protocol.

Data Management and Analysis

Categorical variables were compared using either the Chi square test while continuous variables were analysed using the Student t test or ANOVA. Continuous variable estimates were expressed as mean±SD or median while categorical variables were expressed in proportions, ratios, and percentages. Data were analysed using the SPSS 16.0 for Windows (SPSS Inc., Chicago IL, USA). Statistical significance level was set at $p < 0.05$.

RESULTS

Socio-demographic Characteristics of Study Participants

The study included 398 children, including 133 (33.4%) severe malaria cases, 133 (33.4%) children with uncomplicated malaria, and 132 (33.2%) who were apparently healthy. Overall, there were 209 (52.5%) males and 189 females (47.5%) and the median age of all participants was 48.5 months (range = 6 to 180 months). The number of male and female children enrolled in the severe malarial [male = 74 (55.6%); female = 59 (44.4%)], uncomplicated malaria [male = 67 (50.4%); female = 66 (49.6%)], healthy control [male = 68 (51.5%); female = 64 (48.5%)] groups did not differ significantly ($p = 0.664$). The two-third of the study participants (66.6%) were from the Yoruba language speaking tribe. Presenting symptoms other than fever among malaria patients are as shown in Table 1. The most common presenting complaint was vomiting (56%), followed by loss of appetite (44.4%), while yellowness of eyes (7.1%) was the lowest. Pallor, loss of appetite, irritability and convulsions were significantly more common at presentation among children with severe malaria than those with uncomplicated malaria.

ECG Findings in *P. falciparum* Malaria Patients and Healthy Control

Table 2 shows the ECG parameters of the study participants. The heart rates of the patients with malaria were faster than those of the healthy controls; those with severe malaria had faster heart rate (HR) than those with acute uncomplicated malaria ($p < 0.001$). Patients with uncomplicated malaria had a significantly higher mean P-wave amplitude compared to healthy controls and those with severe malaria ($p < 0.001$).

There was no significant difference in the mean P-wave duration for the different groups. The PR interval is shorter in cases of severe malaria compared to those of uncomplicated malaria and healthy children ($p < 0.001$). The mean QRS axis was similar in all three categories of the study participants, at approximately $+50$ degrees. The mean QRS duration and QTc intervals were also about the same in the 3 categories, approximately 0.06 s and 0.40 s, respectively. Patients with severe malaria had a higher mean R/SV1 compared to the uncomplicated and control groups. Whereas the healthy controls have a significantly higher mean R/SV6 compared to the patients with falciparum malaria ($P = 0.001$)

Pair-wise Comparison of Mean Values of ECG Parameters

Pair-wise comparison of mean values of ECG parameters among study participants were as shown in Table 3. The mean values of heart rate and P-wave amplitude were significantly higher in Acute uncomplicated malaria AUM and severe malaria SM than healthy children while mean QT interval, PR interval and R/S V6 were significantly higher in healthy children than in patients with AUM and SM. However, when AUM was compared with SM, only mean heart rate was significantly faster in SM than AUM while QT interval, PR interval and P-wave amplitude were significantly lower in SM than AUM

Specific ECG Abnormalities and Risk of at Least one ECG Abnormality

Table 4 shows the frequency of specific ECG abnormalities among the study participants. RVH was the commonest abnormality encountered in the whole group, while RAD was the least common. The only significant differences between the groups were sinus tachycardia (most common in patients with severe malaria) and LVH (most common in the healthy controls). Table 5 shows that although there was no statistically significant risk of at least one ECG abnormality among patients with acute uncomplicated malaria compared with healthy control (OR = 1.26; 95% CI = 0.77, 2.07). However, there was almost a threefold increase in odds of among at least one ECG abnormality among patients with severe malaria compared with healthy control (OR = 2.89; 95% CI = 1.68, 4.99). The prevalence of ECG abnormalities among children with severe malaria, acute uncomplicated malaria and the healthy control was 79.7%, 63.2% and 57.6% respectively

Outcomes of Severe Malaria

Of the 133 children with severe malaria, 4 died, thus the case fatality rate was 3.0%. One hundred and six of these 133 children had at least one ECG abnormality (including the 4 mortalities). Table 6 shows the specific ECG abnormalities noted among those who died were sinus tachycardia (100.0%), right ventricular hypertrophy (75.0%), and left atrial hypertrophy (25.0%). Notably, none of these patients had potentially lethal ECG features such as arrhythmias, prolonged PR interval or prolonged QTc. Thus, the cause of their death could not have been their ECG abnormalities. Three of these patients had severe metabolic acidosis and 2 had elevated serum urea. Two of the mortality cases had cerebral malaria, two had severe malaria anaemia and one of the patients had haemoglobinuria along with acidosis and cerebral malaria. One of the patients with severe malaria (cerebral malaria, haemoglobinuria, and seizures) also developed neurologic sequelae of spastic hemiparesis, and visual, hearing and speech impairment, but these all resolved completely before discharge from the hospital.

DISCUSSION

This study was carried out with the aims of describing the electrocardiographic (ECG) features in children with severe falciparum malaria compared with the findings with those of uncomplicated malaria as well as healthy children. The prevalence of ECG abnormalities among children with severe malaria, acute uncomplicated malaria and the healthy children in the study was 79.7%, 63.2%, and 57.6%, respectively. Specific leading ECG abnormalities included: right ventricular hypertrophy sinus tachycardia, Prolonged QTc and left ventricular hypertrophy. However, there was no potentially lethal ECG abnormality recorded in any of the malaria patients.

This study has revealed that the odds of having an ECG abnormality among children with severe malaria are 2.29 times more than uncomplicated malaria cases and 2.89 times more than control. The prevalence of ECG abnormalities (79.7% and 63.2% for severe and uncomplicated malaria respectively) found in this study are higher than previous values reported by Franzen *et al*(12) (22.3%) and Bethel *et al*. (11) (31.0%) and Günter *et al*, (13) (14.3%). There are a few reasons for these disparities. First, the settings and designs of these earlier studies compared with the present study are evidently different. Both Bethel *et al* (11) Günter

et al. (13) reviewed case records of malaria patients in a settings not stated in their publications. Second, their sample sizes were considerably lower than the number of malaria patients recruited in the present study. Third, participants in the present study were children while those of the past studies involved both adults and children. While there are controversies about how prevalent ECG abnormalities might be among children with malaria, the high prevalence observed in the present study suggests that abnormal ECG findings may be a common feature in during malaria episodes and it may require the attention of paediatricians, especially in those with complicated malaria.

Another ECG finding in this study is the evidence of atrial hypertrophy, but the frequency was not significantly different between severe malaria and uncomplicated groups. The observed atrial hypertrophy in this study is unexpected because malaria being an acute febrile illness is unlikely to be the cause. It is therefore likely that these children had background atrial hypertrophy prior to malarial illness. The occurrence of first-degree heart block among the study participants was also not uncommon as previous studies have demonstrated the same finding. In studies by Gunther *et al* (13) and Ogunkunle *et al* (14) similar first-degree heart blocks were reported. Berg *et al* (15) have also reported AV block in an 18year boy with severe malaria. Other reports on the occurrence of AV block were in studies which evaluated the cardiac effects of antimalarials.(16) Though malaria patients in the present study were treated with either ACTs and/or intravenous artesunate, it is somewhat difficult to compare the data with studies which primarily set out to evaluate effects of drugs because this was not part of the objectives. Therefore, the findings of first-degree heart block in those who participated in the present study needs to be view against the lack of data evidence on the contributions of antimalarial therapies given before and during hospitalisation in the study centre.

Other ECG findings in this study are evidence of right ventricular hypertrophy (RVH), prolonged QTc, and elevated ST segment but the frequencies were not significantly different among control, severe malaria, and uncomplicated malaria groups. Malaria, being an acute illness is not expected to cause cardiac chamber hypertrophy or enlargement which is a manifestation of a chronic insult on the heart. The reason for the finding of RVH might be due to the criteria used to diagnose RVH in this study. The

presence of upright T wave in the right precordial leads V1, V2 in children less than the pubertal age and the present of neonatal RS progression pattern in children greater than 5 years or persistence of infantile RS progression pattern after the age of 18 months as described in previous studies.(17)

The observed ST segment elevation in one child in the control group and two patients with severe malaria is suggestive of myocardial infarction which is rather a rare finding in children. ST segment elevation occurs in pericarditis and myocarditis suggesting the possibility of malaria causing myocarditis. Mohsen *et al.* (18) and Costenaro *et al.* (19) have reported cases of malaria associated myocarditis. However, the prevalence of ST segment abnormalities in this study is considerably lower than those reported by Gunther *et al* (13). The reason for the relatively low prevalence might be due to the fact that ST segment abnormalities occur less frequently in children than adults, which constituted the majority of the study participants in those reports.

Children with severe malaria and acute uncomplicated malaria who had prolonged QTc in the present study but it was lower than those of healthy controls, this is similar to report by other researchers(14,20,21, 22) have also observed prolonged QTc to be a frequent finding during malaria illness. The mortality rate in this study is lower than 9.6% reported in the same centre about a decade earlier by Orimadegun. *et al.*(4) It is also lower than the 17% reported by Bethel *et al.*(11) The reason for this relatively low mortality rate might be as a result of improvement in treatments of severe malaria in recent years with introduction of newer, more potent and effective antimalarials (in this case ACT).

It is worth noting that all the children who died during the conduct of the study had either metabolic acidosis or arrhythmias or both. All the deaths had sinus tachycardia. However, none of these patients had potentially lethal ECG features like conduction abnormalities (prolonged PR interval or prolonged QTc). Thus, it is unlikely that the cause of death were ECG abnormalities alone. Furthermore, the only child with neurologic deficit, a (7 years old girl with cerebral malaria) had left spastic hemiparesis, visual, hearing and speech impairment. Apart from sinus tachycardia she had no ECG abnormality. She however had a complete resolution of these complications before discharge from the hospital.

CONCLUSION

This study has shown that patients with severe malaria have higher prevalence of ECG abnormalities compared to children with acute uncomplicated malaria and apparently healthy children. Electrocardiographic abnormalities do occur more frequently in children suffering from severe and uncomplicated malaria than in healthy children. Children with severe malaria are twice more likely to have ECG abnormalities than those with uncomplicated malaria. All cases of severe malaria deserve thorough cardiovascular evaluation (including an initial ECG). Patients with severe malaria with ECG abnormalities should have a repeat study at follow up to rule out a possible underlying cardiac problem

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Table 1: Presenting Symptoms other than Fever among Malaria Patients

| | Malaria cases (N = 266) | | AUM (N=133) | | SM (N = 133) | | P |
|--------------------------|----------------------------|------|----------------|------|-----------------|------|--------|
| | n | % | n | % | n | % | |
| Weakness/Lethargy | 99 | 37.2 | 0 | 0 | 99 | 73.9 | - |
| Pallor | 79 | 29.7 | 6 | 4.5 | 73 | 54.9 | <0.001 |
| Difficult/Fast breathing | 44 | 16.5 | 0 | 0 | 44 | 33.1 | - |
| Loss of appetite | 118 | 44.4 | 48 | 36.4 | 70 | 52.2 | 0.009 |
| Cough | 58 | 21.7 | 33 | 24.8 | 25 | 18.7 | 0.223 |
| Chills/Rigors | 60 | 22.6 | 29 | 22.0 | 31 | 23.1 | 0.820 |
| Vomiting | 149 | 56.0 | 74 | 55.6 | 75 | 56.4 | 0.902 |
| Body pains/aches | 69 | 25.8 | 34 | 25.6 | 35 | 26.1 | 0.917 |
| Irritability | 37 | 13.9 | 5 | 3.8 | 32 | 23.9 | 0.000 |
| Diarrhoea | 35 | 13.1 | 19 | 14.3 | 16 | 11.9 | 0.570 |
| Yellowness of the eyes | 19 | 7.1 | 0 | 0 | 19 | 14.4 | - |
| Coma | 44 | 16.5 | 0 | 0 | 44 | 32.8 | - |
| Convulsions | 86 | 32.2 | 13 | 9.8 | 73 | 54.5 | <0.001 |
| Passage of dark urine | 52 | 19.5 | 0 | 0 | 52 | 38.8 | - |

AUM =Acute uncomplicated malaria, SM= Severe malaria

Table 2: Comparisons of Mean Values ECG Parameters in Study Participants

| ECG parameters | HC | AUM | SM | P |
|------------------------------|-------------|--------------|---------------|-------|
| Heart Rate, HR (beat/minute) | 103.7±23.6 | 126.1±25.6 | 148.7±25.7 | 0.000 |
| P-wave amplitude (mm) | 1.3 ± 0.42 | 1.6 ± 0.50 | 1.4 ± 0.5 | 0.000 |
| P-wave duration (s) | 0.08 ± 0.01 | 0.079± 0.011 | 0.078 ± 0.015 | 0.372 |
| PR interval (s) | 0.14 ± 0.02 | 0.13 ± 0.023 | 0.11 ± 0.023 | 0.000 |
| QRS axis (°) | 51.2 ±27.3 | 51.6 ± 25.0 | 53.5 ± 26.6 | 0.742 |
| QRS duration (s) | 0.06± 0.02 | 0.06± 0.02 | 0.05± 0.02 | 0.371 |
| QT interval (s) | 0.32±0.036 | 0.29±0.049 | 0.26± 0.038 | 0.143 |
| QTc (s) | 0.41±0.033 | 0.41±0.047 | 0.401±0.038 | 0.105 |
| R/S V1 | 0.76±0.66 | 0.78±0.57 | 0.86±0.56 | 0.338 |
| R/S V6 | 9.3±6.8 | 6.3±4.5 | 6.7±4.1 | 0.001 |

AUM =Acute uncomplicated malaria, SM= Severe malaria, HC = Healthy control

Table 3: Pair-wise comparison of mean values of ECG parameters among Study Participants

| ECG parameters | HC versus AUM | | | HC versus SM | | | AUM versus SM | | |
|--|---------------|--------------|-------|--------------|--------------|-------|---------------|--------------|-------|
| | Mean diff.* | 95% CI | P | Mean diff.* | 95% CI | P | Mean diff.* | 95% CI | P |
| Heart Rate, HR (beat/minute) | -22.4 | -29.8, -15.0 | 0.000 | -44.9 | -52.3, 37.6 | 0.000 | -22.5 | -29.9, -15.2 | 0.000 |
| QT interval (s) x 10 ⁻¹ | 0.31 | 0.19, 0.43 | 0.000 | 0.59 | 0.47, 0.71 | 0.000 | 0.23 | 0.16, 0.40 | 0.000 |
| PR interval (s) x 10 ⁻² | 1.03 | 0.33, 1.73 | 0.001 | 2.18 | 1.49, 2.89 | 0.000 | 11.58 | 0.46, 18.6 | 0.000 |
| P-wave amplitude(mm) | -0.31 | -0.45, -0.18 | 0.000 | -0.18 | -0.32, -0.04 | 0.006 | 0.14 | 0.27, 0.00 | 0.049 |
| QTc (s) x 10 ⁻² | -0.41 | -1.60, 0.80 | 1.000 | 0.63 | -0.55, 1.80 | 0.600 | 1.04 | 0.13, 2.20 | 0.100 |
| R/S V1 | -0.02 | -0.16, 0.20 | 1.000 | -0.13 | -0.28, 0.08 | 0.491 | -0.08 | -0.26, 0.09 | 0.810 |
| QRS duration (s) x 10 ⁻² | 0.35 | -0.18, 0.89 | 0.341 | 0.58 | 0.13, 1.12 | 0.028 | 0.23 | -0.30, 0.80 | 0.990 |
| R/S V6 | 2.91 | 0.84, 5.01 | 0.002 | 2.51 | 1.46, 4.60 | 0.035 | -2.45 | -3.24, 1.66 | 1.000 |
| P-wave duration (s) x 10 ⁻² | 0.16 | -0.22, 0.54 | 0.937 | 0.22 | -0.16, 0.60 | 0.523 | 0.06 | -0.43, 0.32 | 1.000 |
| QRS-T angle | -1.69 | -7.53, 4.16 | 1.000 | -2.62 | -8.53, 3.30 | 0.862 | -0.93 | -6.76, 4.89 | 1.000 |
| QRS axis | -0.46 | -8.23, 7.30 | 1.000 | -2.33 | -5.41, 10.09 | 1.000 | -1.88 | -9.61, 5.86 | 1.000 |

AUM =Acute uncomplicated malaria, SM= Severe malaria, HC = Healthy control

Table 4: Frequency of specific ECG abnormalities among Study Participants

| ECG abnormalities | Total | | Control | | AUM | | SM | | P |
|-------------------------------|-------|------|---------|------|-----|------|----|------|-------|
| | N | % | N | % | N | % | N | % | |
| Right ventricular hypertrophy | 139 | 34.9 | 37 | 28.0 | 47 | 35.3 | 55 | 41.4 | 0.075 |
| Sinus tachycardia | 83 | 21.0 | 3 | 2.3 | 16 | 12.0 | 64 | 48.1 | 0.000 |
| Prolonged QTc | 38 | 9.5 | 14 | 10.6 | 16 | 12.0 | 8 | 6.0 | 0.424 |
| Left ventricular hypertrophy | 31 | 7.8 | 17 | 12.9 | 4 | 3.0 | 10 | 7.5 | 0.011 |
| Biventricular hypertrophy | 20 | 5.0 | 6 | 4.5 | 7 | 5.3 | 7 | 5.3 | 0.954 |
| First degree heart block | 37 | 9.3 | 14 | 10.6 | 12 | 9.0 | 11 | 8.2 | 0.490 |
| Left atrial hypertrophy | 11 | 2.8 | 5 | 3.8 | 2 | 1.5 | 6 | 4.5 | 0.145 |
| Right atrial hypertrophy | 6 | 1.5 | 1 | 0.8 | 4 | 3.0 | 1 | 0.8 | 0.447 |
| Sinus arrhythmia | 3 | 1.0 | 1 | 0.8 | 1 | 0.8 | 1 | 0.8 | 0.779 |
| Myocardial ischaemia | 4 | 1.0 | 1 | 0.8 | 1 | 0.8 | 2 | 1.5 | 0.779 |
| Left axis deviation | 6 | 1.5 | 0 | 0.0 | 1 | 0.8 | 5 | 3.8 | 0.368 |
| Right axis deviation | 1 | 0.3 | 1 | 0.8 | 0 | 0.0 | 0 | 0.0 | NC |

AUM = Acute uncomplicated malaria, SM = Severe malaria,

P<0.05 indicate statistically significant difference, NC = Not calculated

Table 5: Risk of at least one ECG abnormalities among Study Participants

| Diagnosis | Abnormal ECG | | Normal ECG | | P | OR (95% CI) |
|-----------|--------------|------|------------|------|----------|-------------------|
| | N | % | N | % | | |
| Control | 76 | 57.6 | 56 | 36.8 | - | 1 |
| AUM | 84 | 63.2 | 49 | 36.8 | 0.353* | 1.26 (0.77, 2.07) |
| SM | 106 | 79.7 | 27 | 20.3 | <0.001** | 2.89 (1.68, 4.99) |

*Compares AUM with Control **Compares SM with Control

Comparing SM with AUM, OR = 2.29 (95% CI: 1.32, 3.97)

AUM = Acute uncomplicated malaria, SM = Severe malaria HC – Healthy control

Table 6 Mortality among children with severe malaria

| S/N | Age (month) | Sex | Temp (°C) | PCV (%) | Parasite count/ μ l | Electrolyte Derangement | ECG Abnormality |
|-----|-------------|-----|-----------|---------|-------------------------|-------------------------------|-----------------------------|
| 1 | 43 | F | 39 | 18 | 92313 | * | Sinus Tachycardia, LAH, RVH |
| 2 | 71 | M | 36.5 | 18 | 108 | HCO ₃ 15, Urea 255 | Sinus Tachycardia, RVH |
| 3 | 64 | M | 36.8 | 23 | 22200 | HCO ₃ 14, Urea 185 | Sinus Tachycardia, RVH |
| 4 | 19 | F | 36.3 | 15 | 543366 | HCO ₃ 5 | Sinus Tachycardia |