



Research Article

Effect of Exercise on Malaria and some Biochemical Parameters

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ABSTRACT

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Resistance to antimalarial drugs is increasing day by day, suggesting the importance of discovering new techniques to mitigate the effects of malaria. The current study assesses the effect of exercise on parasitemia and liver function in asymptomatic malaria-infected subjects at Yobe State University, Damaturu. Forty (40) adult patients presenting to the University clinic with uncomplicated malaria comprising 23 males and 17 females were used in this study. The subjects were grouped into four with 10 subjects in each group. Group I served as control; they were malaria-infected but not subjected to exercise. Group II, Group III and Group IV were malaria-infected; and placed on regular exercise of 20, 40 and 60 minutes respectively daily for 9 days. Blood samples were collected on day 3, 6, and 9 respectively for percentage parasitemia determination while liver function indices were analyzed at the end of the study (i.e. at day 9). The total number of red blood cells and average number of infected red blood cell were counted and the percentage of parasitemia were calculated using the data. Significant ($p < 0.05$) reduction was observed in parasitemia level as a result of the exposure of infected subjects to exercise in a dose-dependent pattern compared to control groups. Liver function analysis revealed a slight decrease in the activity of enzymes (AST, ALT and ALP) direct and total bilirubin in patients subjected to exercise in dose dependent pattern compared to control group. However, no significant difference was seen in Albumin and total proteins between non-exercise and exercise groups. Within the scope and limit of this research, it can be concluded that exercise plays a significant role in ameliorating malarial complications, and encouraging exercise in malaria-endemic regions as a primary means to minimize symptoms and complications should be adopted.

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INTRODUCTION

Malaria is a dangerous disease mainly found in tropical nations, it is both preventable and curable. However, without prompt diagnosis and effective treatment, a case of uncomplicated malaria can progress to a severe form of the disease, which is often fatal without treatment (World health organization, 2023).

Malaria is not communicable and cannot spread from one person to another; the disease is transmitted through the bites of female *Anopheles* mosquitoes. Although there are over 400 different species of *Anopheles* mosquitoes and around 40 of them known as vectors of the disease, only five species of parasites can cause malaria in humans and 2 of these species, i.e. *Plasmodium falciparum* and *Plasmodium vivax* pose the greatest threat (Fujioka and Aikawa, 2002).

Malaria is a major global public health dilemma that exerts a high mortality and morbidity in many countries, particularly in resource-poor countries across Sub-Saharan Africa, South East Asia and Latin America, and probably contributes to keeping these countries in poverty (Roll Back Malaria, 2020). According to the latest world malaria report published in December 2022, malaria claimed an estimated life of 619,000 in 2021, compared to 625,000 in 2020 (WHO, 2022).

Malaria disease occurs mainly in tropical and subtropical regions. The vast majority of malaria cases and deaths were reported from WHO African region, with majority of cases caused by *Plasmodium falciparum* parasite. This parasite is also reported to be dominant in other malaria hotspots, including the WHO regions of Southeast Asia, Eastern Mediterranean and Western Pacific. However, In the WHO Region of the Americas, *Plasmodium vivax* parasite was

reported as the predominant malaria causing parasite (WHO, 2023).

The threat posed by malaria is highest in sub-Saharan Africa, with 4 countries accounting for nearly half of all malaria deaths worldwide in 2021: Nigeria (26.6%), the Democratic Republic of the Congo (12.3%), Uganda (5.1%), and Mozambique (4.1%). Nigeria suffers from the world's greatest malaria burden with approximately 51 million cases and 207 000 deaths reported annually while 97% of the total population (approximately 173 million), is at risk of infection (WHO, 2023).

Various drugs were used for management of malaria. These include quinine (QN), chloroquine (CQ), amodiaquine, piperazine (PPQ), mefloquine (MQ), lumefantrine (LUM), pyrimethamine (PYR), proguanil, sulfadoxine, atovaquone, primaquine, and artemisinin and its derivatives (ART) (Gorobets *et al.*, 2017). Artemisinin-based combination therapies (ACTs) are now recommended worldwide for treatment of *P. falciparum* infections (Phillips *et al.*, 2017).

Exercise is a subset of physical activity that is planned, structured, and repetitive and has as a final or an intermediate objective, i.e the improvement or maintenance of physical fitness (Dishman *et al.*, 1985).

Exercise is reported to increase the body demand for oxygen. At rest, our nervous system maintains a parasympathetic tone, which affects the respiratory rate, cardiac output, and various metabolic processes. Exercise stimulates the sympathetic nervous system and will induce an integrated response from the body. This response works to maintain an appropriate level of homeostasis for the increased demand in physical, metabolic, respiratory, and cardiovascular efforts (Craemer *et al.*, 2019).

Research has shown that exercise, in conjunction with other lifestyle

modifications, can reduce the risk of hypertension regardless of inherent genetic predispositions; also, exercise has been shown to increase insulin sensitivity in the management approach to diabetes (Kordonouri and Riddell, 2019; Young *et al.*, 2019).

Resistance to current treatment options has been reported from nearly all the malarial regions. Efforts are being made to discover new strategies to prevent rather than cure malaria cases. This research was instigated to establish the role of regular exercise in ameliorating malaria complications in malaria-prone area

MATERIALS AND METHODS

Materials

Study Area

The research was carried out at Yobe State University, Damaturu. The state is located in savannah region of northeastern Nigeria between latitudes 10.00°N to 11.30°E and longitude 12.00°E and 11.50°E. It shares boundaries with four states; Jigawa to the west, Bauchi to the south, Borno to the east, and Adamawa to the north. The state is recognized as one of the poorest states in the country with the majority of the population illiterate to western education (Oruonye, 2009).

Data Collection instrument

Consent forms and questionnaire were given to participating subjects who have met the inclusion criteria.

Exclusion and Inclusion Criteria

Asymptomatic individuals infected with malaria who were confirmed by the

Group I: Malaria infected; no exercise

Group II: Malaria infected; placed on regular exercise of 20 minutes daily for 9 days

Group III: Malaria infected; placed on regular exercise of 40 minutes daily for 9 days

Group IV: Malaria infected; placed on regular exercise of 60 minutes daily for 9 days

Blood samples were collected on day 3, 6, and 9 respectively for percentage parasitemia

laboratory analysis and gave consent were used as the study subjects while individuals confirmed by laboratory analysis to be negative of malaria parasite as well as subjects with other ailments like diabetes, hypertension, and HIV were exempted.

Methods

Sample Collection

5mL of blood was collected from each participant's into appropriately labeled EDTA and plain containers for microscopy and biochemical tests respectively.

Plasmodium falciparum using Microscopy

The method adopted was as described by Cheesbrough (2005). A drop of each blood sample was placed at the center of a clean glass slide at least 2mm from one end. Smears were made by moving the coverslip forward on each glass slide. The thin smears were immersed in methanol contained in a petri dish for about 15 minutes. They were then placed in a petri dish containing Geimsa's stain for about 10 minutes, followed by washing of the excess stains with clean tap water. The smears were dried in the air by hanging the glass slides inverted in a rack. Each dried smear was microscopically observed under high power objectives (x100) using oil immersion. An average parasitemia was determined using the reading of 3 microscopic fields

Experimental Design

Forty subjects were used for the study; they were then grouped into four groups of 10 participants each.

determination while liver function indices were analyzed at the end of the study (i.e. at

day 9). The average number of infected (uncleared) RBC, as well as total RBC, was

$$\% \text{ Parasitemia} = \frac{N_X \times 100}{N_T}$$

N_X = Average number of parasitized RBC

N_T = Average number of both parasitized and cleared RBC (Mukhtar *et al.*, 2006).

Aspartate aminotransferase (AST) and Alanine Aminotransferases Assay (ALT) were assayed using Reitman and Frankel (1957) method, Alkaline Phosphatase (ALP) activity was assayed using the method developed by Roy (1970), Bilirubin by method of Molley and Evolyn (1937), and Total protein was determined by Biuret method (1995).

Statistical Analysis

Results were expressed as mean \pm standard deviation and analyzed using analysis of variance with p value <0.05 considered significant followed by Tukey's post hoc test. GraphPad InStat3 Software version 3.05 by GraphPadInc was used for the analysis.

Consent

The research protocol for patient participation and collection of blood samples for laboratory analysis was approved by the

University's ethical committee. Participants were informed about the objectives of the research, the voluntary nature of their participation, their right to refuse or withdraw from the study at any point as well as potential benefit of participation in the study. Upon accepting the conditions and statements, participants were given the questionnaire.

RESULTS

The socio-demographic features of the respondents were presented in table 1. A total of 40 subjects were selected randomly for the research. It was observe that the mean age of the respondents is 22.3 years while the minimum age is 15 years and maximum is 46 years. More than 50% of the respondents do not exercise regularly while only 5% of the respondents exercised for about 1 hour daily.

Table 1: Socio-demographic Features of the Participants

Parameters	Total (%)
<i>Gender of participants</i>	
Males	23(57.5)
Females	17(42.5)
<i>Age group</i>	
15-24	16(40)
25-34	12(30)
35-44	09(22.5)
45-54	03(7.5)
<i>Level of Exercise</i>	
Do not exercise at all	21(52.5)
Exercised for 10-20 minutes daily	05(12.5)
Exercised for 21-40 minutes daily	12(30)
Exercised for 41-60 minutes daily	02(5)

Table 2 present the percentage parasitemia of the various groups at day 3, 6 and 9 of the study. A significant decrease ($p < 0.05$) in

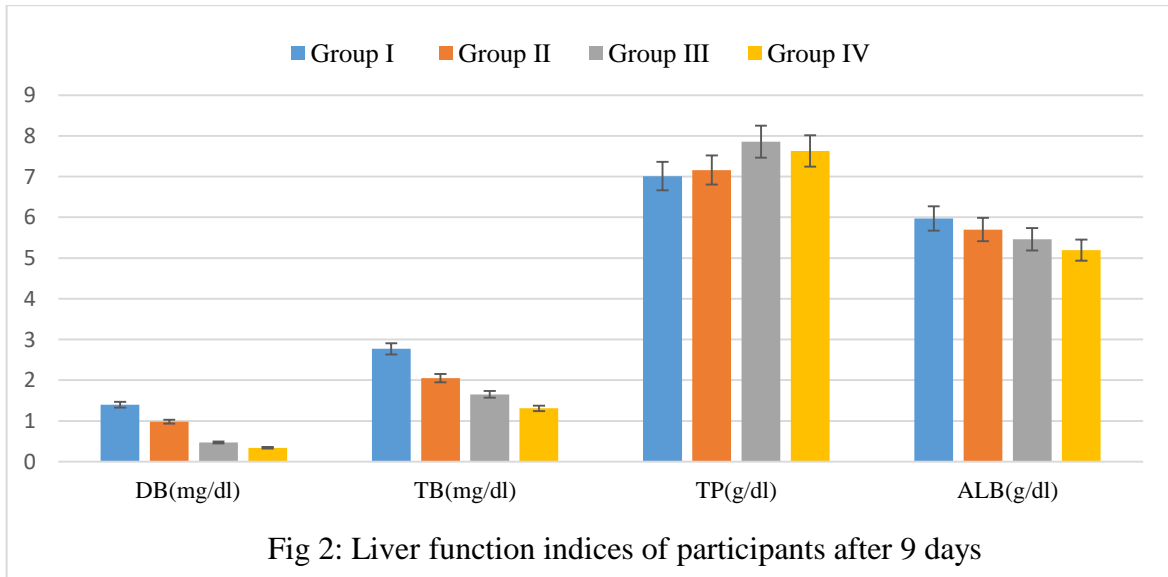
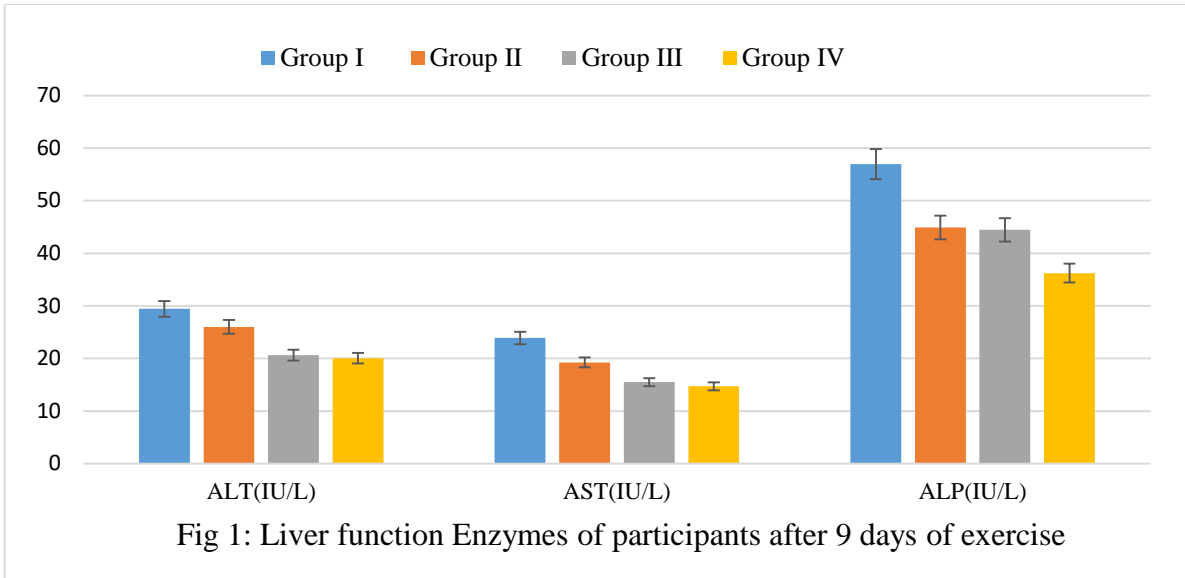
parasitemia in exercise time-dependent pattern on days 3, 6 and 9 respectively

Table 2: Effect of exercise on percentage parasitemia

Groups	% parasitemia Day 3	% parasitemia Day 6	% parasitemia Day 9
Group I	36.45±4.34 ^{x,y,z}	27.67±3.16 ^{x,y,z}	30.46±5.20 ^{x,y,z}
Group II	28.33±3.13 ^x	20.82±3.22 ^x	19.29±3.88 ^x
Group III	23.08±4.20 ^y	16.45±2.20 ^y	14.53±3.16 ^y
Group IV	21.56±3.23 ^z	15.06±3.43 ^z	9.03±2.34 ^z

Values are expressed as Mean ± Standard deviation, (n=10). Value with the same superscripts in a column are significantly different compared to each other ($P < 0.05$). The effect of exercise on liver function parameters in malaria individuals are presented in Figures 1 and 2 below. A

decrease in the activity of the enzymes (AST, ALT and ALP) direct and total bilirubin were observed in exercise exposed subjects compared to non-exercise exposed subjects. However, no significant difference was seen in Albumin and Total Proteins



DISCUSSION

The role of exercise malaria parasites on asymptomatic patients was observed during the nine days of the experiment and parasitemia counts on interval of 3 days was recorded. Exposure of research subjects to exercise resulted in an exponential

decrease in parasite count as the days and intensity of exercise increased. Although studies there are limited studies of such kind, similar results were reported for the positive effect of exercise on cardiovascular diseases, cancer and diabetes Mellitus (Berger, 2019; Grimmett *et al.*, 2019).

The exact mechanism by which exercise causes a decrease in parasitemia level is unclear. However, during exercise, RBCs that have been in circulation for a long time tend to be less compliant than younger RBCs, meaning that during exercise, older RBCs can be hemolyzed intravascularly when passing through capillaries in contracted muscles. This activity leads to an average decrease in RBC age since the younger RBCs have more favorable rheological properties. This clearance of older RBCs that are infected with the parasite might lead to a decrease in parasitic load as observed.

The liver is an important body organ and is central to many metabolic pathways (Meyer and Kulkarni, 2001). Hepatic injury due to either chemicals or infectious agents is associated with distortion of these metabolic functions and may lead to progressive loss of liver architecture and ultimately liver failure. Several studies have reported a positive correlation between parasitemia and liver functions (Mohamed *et al.*, 2016; Kayode *et al.*, 2011 and Oyewole *et al.*, 2010). Infection of kupffer cells by the sporozoites form of *Plasmodium falciparum* can cause organ congestion, sinusoidal blockage, and cellular inflammation. These changes in hepatocytes can lead to the leakage of localized parenchymal enzymes of the liver to the circulation. Hence, the observed increase in liver enzymes (AST, ALT, and ALP) in malaria-infected patients. Studies also demonstrated that serum activities of liver enzymes increased with the increase in

malarial parasite density (Onyesom, 2012; Baheti *et al.*, 2003).

The observed fall in these enzymes in malaria-infected asymptomatic exercise groups might not be unconnected with the replacement of older infected RBCs with young non-infected RBCs. It was also observed that exercise increases erythropoietin levels, which causes an increase in RBC production. Thus reversing the earlier sinusoidal blockage and cellular inflammation and restoring the hepatic architecture (Ibeneme *et al.*, 2019).

Direct and total bilirubin also shows similar results with the liver enzymes. Malaria can cause hemolysis, leading to increased bilirubin levels due to the release of hemoglobin. The severity of this increase can differ based on various factors, including the individual's immune response, the strain of malaria parasite, and the presence of complications (Bjørke, 2019).

CONCLUSION

Based on the findings of the study, it was concluded that exercise significantly reduces parasitemia level in malaria infected subjects.

CONFLICT OF INTERESTS

The authors declare no conflict of interest.

AUTHORS' DECLARATION

The authors hereby declare that the work presented in this article is original and that any liability for claims relating to the content of this article will be borne by them.

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