International Journal of Advances in Nephrology Research

4(1): 82-91, 2021; Article no.IJANR.74351

Evaluation of Endogenous Antioxidants and Kidney Function Indices in Albino Mice Infected with *Plasmodium berghei* and Treated with Sodium Bicarbonate

G. S. Haruna[1*], M. H. Abdullahi[1], H. S. Abdullahi[1], S. Usman[1], J. M. Egbaloshu[1], T. O. Bamidele[1] and M. Z. Zaruwa[1]

[1]Department of Biochemistry and Molecular Biology, Faculty of Natural and Applied Sciences, Nasarawa State University, Keffi, Nasarawa State, Nigeria.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

Editor(s):
(1) Prof. Darko Nozic, Clinics of Infectious and Tropical Diseases, Military Medical Academy, Serbia.
Reviewers:
(1) Soumya Sankar Rath, Utkal University, India.
(2) Harpreet Kaur, Kalpana Chawla Government Medical College, India.
Complete Peer review History: https://www.sdiarticle4.com/review-history/74351

Original Research Article

Received 05 August 2021
Accepted 10 October 2021
Published 15 October 2021

ABSTRACT

Malaria is an infectious disease that is transmitted through mosquito bites and is endemic especially in Sub-Saharan Africa. The current study aimed at evaluating the antioxidants and kidney function indices in albino mice infected with *P. berghei* and treated with sodium bicarbonate. Twenty mice were randomly divided into five groups of four mice each. Groups 1was the normal control, group 2 was infected with *P. berghei*, not treated groups (3, 4 and 5) were administered 84mg/kg b.w of sodium bicarbonate once, twice and thrice per day respectively for three days. Serum samples were collected and analyzed for MDA, GPx, SOD, CAT, GHS, Na^+, K^+, Cl^-, HCO_3^-, Urea and Creatinine following standard methods. MDA concentrations were significantly ($p<0.05$) higher in all the test groups compared to the control. GPx activity decreased significantly ($p<0.05$) in group 2 and increased significantly ($p<0.05$) in group 5 compared to the control group. SOD activity decreased significantly ($p<0.05$) in group 3 and increased significantly ($p<0.05$) in groups 2, 4 and 5 compared to the control. Catalase decreased significantly ($p<0.05$) in groups 2, 4 and 5

**Corresponding author: E-mail: sundayharuna@nsuk.edu.ng;*

compared to the control. GSH increased significantly ($p<0.05$) in all the test groups compared to the control. Sodium ion was significantly ($p<0.05$) higher in group 2,3 and 4 compared to the control. Potassium ion was significantly ($p<0.05$) higher in all the test groups compared to the control. Chloride ion increased significantly ($p<0.05$) in group 5 and decreased significantly ($p<0.05$) in group 3 and 4 compared to the control (75.37±0.707). Urea concentration increased significantly ($p<0.05$) in groups 2,4,5 and decreased significantly ($p<0.05$) in group 3 compared to the control (37.60±0.707). Similarly, creatinine increased significantly ($p<0.05$) in groups 2, 4 and 5 but decreased significantly ($p<0.05$) in group 3 compared to the control. This study revealed that infection of mice with *P. berghei* may have posed a massive metabolic stress on the kidney as indicated by elevated biochemical parameters although this could not be seen in the histological studies.

Keywords: Malaria; Sub-Saharan Africa; oxidative stress; Plasmodium berghei; sodium bicarbonate.

1. INTRODUCTION

Malaria is an infectious disease that is widespread in tropical and sub-tropical regions of the world. Many developing countries around the world are often mostly challenged with the scourge of malaria infection. Malaria has become one of the major health problems in developing countries of the world accounting for about 2-3 million deaths yearly. It is a tropical protozoan disease transmitted through female anopheles mosquitoes. It is mainly caused by various species of plasmodium parasite [1]. Four species of intracellular protozoa of the genus Plasmodium cause malaria infection in human beings and they include *P. falciparum, P. vivax, P. ovale, P. malariae. P. falciparum and P. vivax* cause the most serious forms of the disease [2]. *P. berghei* is the species that majorly infect rodents such as mice hence its suitability and common use in malaria model experiments. Blood is a tissue that circulates in a virtually closed system of blood vessels. It is composed of red and white blood cells, platelets, suspended liquids known as plasma and serum. Plasma is an extracellular fluid confined within the vascular system. The water and electrolyte composition of plasma is particularly the same as that of intracellular fluid, made up of water, electrolytes, metabolites, nutrients, proteins, enzymes and hormones [3], all playing vital roles towards survival of the cells.

Malaria was the first parasitic infection to be clearly associated with glomerular diseases in tropical areas [4]. Severe malaria can cause disease in glomeruli, tubules and in the interstitial region. Kidney disease in malaria is primarily due to erythrocyte abnormalities. Parasitized red cells tend to adhere to healthy erythrocytes, blood platelets and capillary endothelium, leading to formation of rosettes and clumps, which impair microcirculation [5], and these events are probable contributing factors for kidney injury, in association with hemodynamic instability, including hypovolemia and shock. Endothelial activation leads to the release of several cytokines, including thromboxane, catecholamines, endothelin and other inflammatory mediators that are also implicated in the pathogenesis of malaria-associated kidney injury. Immune system activation in malaria can go through Th1 and Th2 response. When Th2 response prevails in the infection by *P. malariae*, complement activation occurs, with deposits of immune complexes leading to glomerulonephritis. Hemodynamic instability due to intense erythrocyte parasitism leads to acute tubular necrosis, as seen in the infection by *P. falciparum*. When Th1 response prevails, acute interstitial nephritis and acute glomerulonephritis can be seen. Cortical necrosis has also been described in malaria, characterizing a more severe kidney injury and generally associated with non-recovery of renal function and consequently development of end-stage kidney disease [6]. Several factors contribute to the occurrence of these complications, including hypovolemia, vasoconstriction, hemolysis (leading to hemoglobinuria), erythrocyte parasitemia, immune complexes deposition in glomeruli, microcirculation dysfunction (due to cytoadherence of parasite erythrocytes) and rhabdomyolysis (which is not common in malaria). Other contributing factor for kidney disease in malaria is hepatic dysfunction, with jaundice and hepatomegaly, through which hyperbilirubinemia can lead to cast nephropathy and acute kidney injury (AKI), and liver disease and its complications can also cause AKI (hepato-renal syndrome) [7-11]. The toxic effect of Plasmodium on the kidney could lead to increase in serum parameters such as urea and creatinine as well as an imbalance in the

concentrations of the electrolytes such as sodium ion, potassium ion, bicarbonate ion and chloride ion in malaria-infected persons which could then be harnessed as indicators for kidney dysfunction and as such critical factors to be managed during malaria-related episodes.

Sodium bicarbonate ($NaHCO_3$) solutions are sometimes administered to patients with metabolic acidosis who have both a low plasma HCO_3^- concentration, and a low plasma pH (< 7.2). Since this salt is for the most part completely dissociated in aqueous solution, Na^+, HCO_3^-, and H_2O are effectively added to the extracellular fluid (ECF) compartment. Since Na^+ molecules are being added without Cl^-, and since HCO_3^- has a tendency to displace Cl^- from the ECF compartment, both effects contribute to increase the "strong ion difference" (SID), thus causing 'alkalinization' of the system. The alkaline solution may also boost immune response amidst *P. berghei* infection [12]. In this study, we envisaged the possibility of sodium bicarbonate; an alkaline solution which safety has been authenticated and is been prescribed as a treatment for metabolic acidosis to interrupt the pathogenicity of *P. berghei* by posing an unfavorable pH to the parasite thereby ameliorating its damaging effect on the kidney, hence this study analyzed kidney function indices and histopathology following *P. berghei* infection and treatment with sodium bicarbonate.

2. MATERIALS AND METHODS

2.1 Materials

2.1.1 Experimental animals

Healthy albino mice of both sexes weighing between 20-33g each were used for the experiment. The animals were obtained from the Zoology Department, University of Jos Nigeria and transported to the Animal House, Department of Biochemistry and Molecular Biology, Nasarawa State University, Keffi, Nigeria and acclimatized for seven days before commencement of the experiment, they were fed with standard feed and water *ad libitum*. They were also maintained under standard conditions of humidity, temperature and 12 hours light/darkness cycle. Experiments were conducted in strict compliance with internationally accepted principles for laboratory animal use and care as contained in the Canadian council on animal care guidelines and protocol review [13].

2.1.2 Plasmodium Berghei

The plasmodium parasite; *P. berghei* NK 65 was used for the study. It was bought from National Veterinary Research Institute, Vom, Plateau State, Nigeria and kept alive by continuous intra peritoneal passage in mice every four days at the Department of Biochemistry and Molecular Biology, Nasarawa State University, Keffi, Nigeria according to Jigam [14].

2.1.3 Sodium bicarbonate

Sodium Bicarbonate injection (Pauco Sodium Bicarbonate; 8.4%w/v) was bought from a pharmaceutical shop in Keffi town, Nasarawa State, Nigeria and stored at between 8-25 ^{0}C in the laboratory at the Department of Biochemistry and Molecular Biology, Nasarawa State University, Keffi until commencement of the experiment.

2.2 Methods

2.2.1 Experimental design

A Simple randomized design was adopted where twenty mice were randomly divided into five groups of four mice per group. Groups 1 served as the normal control; not infected with the parasite and not treated with sodium bicarbonate and group 2 served as the positive control; it was infected with *P. berghei* but not treated with sodium bicarbonate while three other groups (3, 4 and 5) were assigned as test groups and administered 84mg/kg b.w of sodium bicarbonate injection once, twice and thrice per day respectively for three days.

2.2.2 Parasite inoculation

The method described by Kabiru [15] was used for the inoculation of parasite into experimental animals. The inoculums consisted of 5x107 of *P. berghei* parasitized erythrocytes per ml. This was done by first determining the percentage parasitaemia and then the erythrocytes count of the donor mouse. The blood was diluted with phosphate buffer saline in proportions indicated by both determinations. The Albino mice were inoculated intraperitoneally, with 0.2 ml of the already infected blood.

2.2.3 Determination of percentage parasitaemia

To obtain the percentage parasitaemia, thin blood smears were made from the tail of each mouse, fixed with methanol and stained with 10% Giemsa stain. The parasitaemia level was determined by counting the number of parasitized erythrocytes out of 100 erythrocytes in random 8 fields of microscope. Parasitaemia was calculated by light microscopy by using the 100× objective lens and the following equation was used

$$\% \text{ Parasitemia} = \frac{\text{Number of Parasitized RBC}}{\text{Total Number of RBC Counted}} \times 100$$

2.2.4 Determination of MDA and Antioxidant status

MDA concentration was measured spectrophotometrically as described by Wallin [16].

The principle for the estimation is based on the fact that thiobarbituric acid (TBARS) reacts with malondialdehyde (MDA) to give a red or pink colour, which absorbs maximally at 532 nm.

Glutathione peroxidase (GPx) activity was assayed spectrophotometrically according to the method described by Ursini [17]. The Cayman chemical glutathione peroxidase assay kit measures glutathione reductase activity indirectly by a coupled reaction with GPx. Oxidized glutathione GSSG, produced upon reaction with an organic hydroperoxide by GPx is recycled to its reduced state by glutathione reductase and NADPH. The oxidation of NADPH to $NADP^+$ is accompanied by a decrease in absorbance at 340 nm. The rate or decrease in A_{340} is directly proportional to the GPx activity in the sample.

Superoxide dismutase, (SOD) activity was assayed spectrophotometrically according to the method of International Federation of Clinical and Applied Chemistry IFCC, [18] as outlined in the RANDOX manual for SOD estimation. The role of SOD is to accelerate the dismutation of toxic superoxide radical (O_2^-), produced during oxidative energy processes, to hydrogen peroxide and molecular oxygen. This method employs Xanthine and Xanthine oxidase (XOD) to generate superoxide radical which react with 2-(4-iodophenyl)-3-(4-nitrophenol)-5-phenyltetra-zolium chloride (I.N.T) to form a red formazan dye. The SOD activity is that which causes a 50% inhibition of the rate of reduction of I.N.T under the conditions of the assay.

Assay of catalase activity was carried out according to the method of Aebi [19]. The ultraviolet absorption of hydrogen peroxide can be easily measured at 240 nm. On the decomposition of hydrogen peroxide with catalase, the absorption decreases with time and from this decrease, catalase activity can be measured.

Determination of Glutathione (GSH) concentration was done based on the method of Jollow *et al,* [20]. Reduced glutathione (GSH) forms the bulk of non-protein sulfhydryl groups. This method is based on the formation of relatively yellow coloration when Ellman's reagent is added to a sulfhydryl compound.

2.2.5 Determination of Kidney function markers

Sodium Ion concentration was determined using the method of Trinder [21] and Maruna [22] as outlined in Teco Kits. Sodium is precipitated as the triple salt, sodium magnesium uranyl acetate with the excess uranium then being reacted with ferrocyanide, producing a chromophore whose absorbance varies inversely as the concentration of sodium in the test specimen.

Potassium ion concentration was determined using the method of Terri and Sesin, [23] as described in Teco diagnostic kits. The amount of potassium was determined by using Sodium tetraphenylboron in a specifically prepared mixture to produce a colloidal suspension, the turbidity of which was proportional to potassium concentration in the range of 2-7 mEq/L.

Serum chloride concentration was determined using the titration method of Schales and Schales [24]. The method is based on the precipitation of chloride ions in serum using mercuric nitrate. When chloride ion is titrated with standard solution of mercuric ion, undissociated but soluble mercuric chloride, $HgCl_2$, is formed. The excess mercuric nitrate reacts with diphenylcarbazone to produce a violet colour.

Titration method of Van Slyke and Neil [25] was employed in determining the concentration of bicarbonate ion in sera samples. The method is based on the release of carbon dioxide from bicarbonate ion in serum with dilute hydrochloric acid. The excess acid was then titrated

with sodium hydroxide using phenol red as indicator.

Urea concentration was determined using the method of Bartels and Bohmer [26] as described in Randox Kit. Urea in serum is hydrolyzed to ammonia in the presence of urease. The ammonia is then measured spectrophotometrically.

The serum creatinine was determined using the method of Bartels and Bohmer [26] as outlined in the Randox kit.

2.2.6 Histological studies of Kidney sections

Histopathological studies of the kidney sections were carried out as described by Bancroft and Stevens, [27]. At the end of the experiment the liver from the various groups of rats were collected for histopathology after which they were fixed in 10% formal saline and dehydrated in ascending grades of ethanol. Thereafter, the tissues were cleared in chloroform overnight, infiltrated and embedded in molten paraffin wax. The blocks were later trimmed and sectioned at 5 – 6 microns. The sections were deparaffinized in xylene, taken to water and subsequently stained with Haematoxylin and Eosin (H and E) for light microscopy.

2.7 Statistical Analysis

The data obtained were analyzed using one-way Analysis of Variance (ANOVA) in SPSS version 23.0 and expressed as mean ± SD. Tests of statistical significance were carried out using the Duncan test. P values < 0.05 were considered statistically significant.

3. RESULTS AND DISCUSSION

3.1 Results

3.1.1 Changes in MDA concentration and endogenous antioxidants in *P. berghei* infected mice treated with sodium bicarbonate

MDA concentrations were significantly ($p<0.05$) higher in all the test groups; 2 (3.80±0.070), 3 (4.06±0.007), 4 (4.11±0.007) and 5 (4.25±0.070) when compared to the control (3.64±0.007). GPx activity decreased significantly ($p<0.05$) in group 2 (42.64±0.70) and increased significantly ($p<0.05$) in group 5 (67.29±0.70) while the activities in groups 3 (50.47±0.70) and 4 (50.47±0.70) were not significant ($p>0.05$) when compared to the control (50.47±0.70) group. SOD activity decreased significantly ($p<0.05$) in group 3 (0.08±0.007) and increased significantly ($p<0.05$) in groups 2 (1.12±0.009), 4 (1.12±0.007) and 5 (1.13±0.007) when compared to the control (1.09±0.007). Catalase activity decreased significantly ($p<0.05$) in groups 2 (1.32±0.007), 4 (1.07±0.007) and 5 (0.97±0.007) while the activity was non-significantly ($p>0.05$) higher in group 3 (1.76±0.007) when compared to the control. GSH concentrations increased significantly ($p<0.05$) in all the test groups; 2 (3.23±0.007), 3 (3.430±0.007), 4 (3.43±0.007) and 5 (3.74±0.007) when compared to the control (3.17±0.007).

3.1.2 Changes in kidney function indices in albino mice infected with *P. berghei* and treated with sodium bicarbonate

The concentration of sodium ion was significantly ($p<0.05$) higher in group 2 (101.89±0.707), 3 (103.86±0.007) and 4 (103.86±0.007) but the value was statistically not significant in group 5 (100.08±0.070) when compared to the control (100.08±0.0070). Potassium ion was significantly ($p<0.05$) higher in groups 2 (3.028±0 .011), 3 (2.96± 0.004), 4 (3.15±0.007) and 5 (100.08±0.070) when compared to the control (2.91±0.707) group. Chloride ion concentration increased significantly ($p<0.05$) in group 5 (77.44±0.707) and decreased significantly ($p<0.05$) in group 3 (71.48±0.707) and 4 (74.07±0.707) but the value was non-significant ($p>0.05$) in group 2 (75.18±0.707) when compared to the control (75.37±0.707). No significant difference ($p>0.05$) was observed in bicarbonate ion concentration in all the test groups; 2 (21.63±0.707), 3 (22.34±0.707), 4 (21.31±0.707) and 5 (21.39±0.707) when compared to the control (22.100±0.707). Urea concentration increased significantly ($p<0.05$) in groups 2 (40.00±0.707), 4 (40.00±0.707) and 5 (43.73±0.707) and decreased significantly ($p<0.05$) in group 3 (36.00±0.707) when compared to the control (37.60±0.707). Similarly, creatinine concentration was observed to increase significantly ($p<0.05$) in groups 2 (1.45±0.007), 4 (1.45±0.007) and 5 (1.59±0.123) but decreased significantly ($p<0.05$) in group 3 (1.24±0.089) when compared to the control group (1.36±0.007).

Table 1. Changes in MDA concentration and endogenous antioxidants in *P. berghei* infected mice treated with sodium bicarbonate

Treatment Group	MDA and Antioxidant Indices				
	MDA Conc. (mg/dl)	GPx Activity (IU/L)	SOD Activity (IU/L)	Catalase (IU/L)	GSH Conc. (mg/dl)
Group 1	3.64±0.007[a]	50.47±0.70[a]	1.09±0.007[a]	1.72±0.007[a]	3.17±0.007[a]
Group 2	3.80±0.070[b]	42.64±0.70[b]	1.12±0.009[b]	1.32±0.007[b]	3.23±0.007[b]
Group 3	4.06±0.007[c]	50.47±0.70[a]	0.08±0.007[c]	1.76±0.007[a]	3.430±0.007[c]
Group 4	4.11±0.007[c]	50.47±0.70[a]	1.12±0.007[b]	1.07±0.007[d]	3.43±0.007[c]
Group 5	4.25±0.070[d]	67.29±0.70[c]	1.13±0.007[d]	0.97±0.007[e]	3.74±0.007[d]

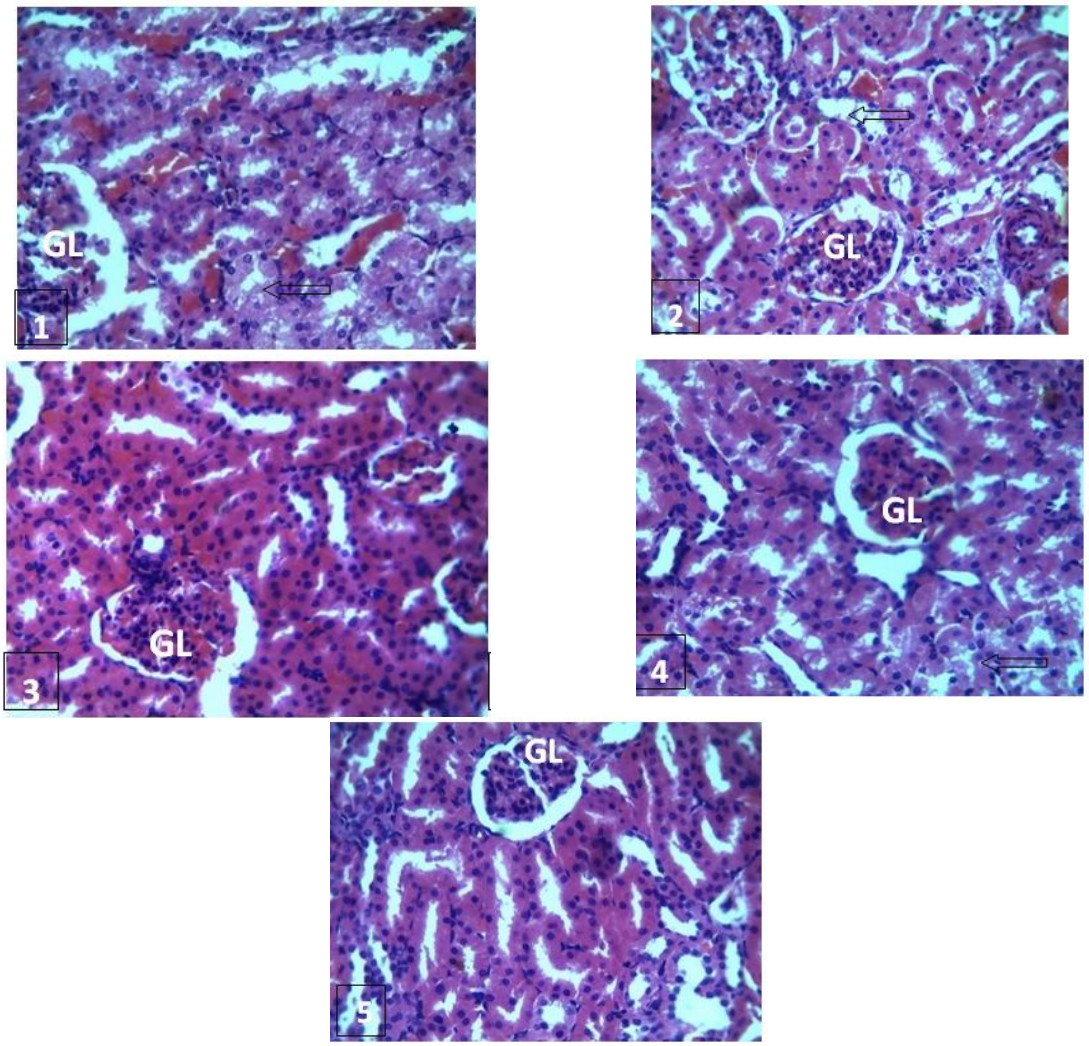
Results are expressed in Means ± SD (n = 4), Mean values with different letters as superscripts across the columns are considered significant at p < 0.05

Table 2. Changes in kidney function indices in albino mice infected with P. berghei and treated with sodium bicarbonate

Group	Na^+	K^+	Cl^-	HCO_3^-	Urea	Creatinine
	(mmol/L)	(mmol/L)	(mmol/L)	(mmol/L)	(mg/dl)	(mmol/L)
Group 1	1.36±0.007[a]	100.08±0.0070[a]	2.91±0.707[a]	75.37±0.707[a]	22.100±0.707[a,b]	37.60±0.707[a]
Group 2	1.45±0.007[b]	101.89±0.707[b]	3.028±0 .011[b]	75.18±0.707[a]	21.63±0.707[a,b]	40.00±0.707[b]
Group 3	1.24±0.089[c]	103.86±0.007[c]	2.96± 0.004[c]	71.48±0.707[b]	22.34±0.707[b]	36.00±0.707[c]
Group 4	1.45±0.007[b]	103.86±0.007[c]	3.15±0.007[d]	74.07±0.707[c]	21.31±0.707[a]	40.00±0.707[b]
Group 5	1.59±0.123[d]	100.08±0.070[a]	3.16±0.1009 [d]	77.44±0.707[d]	21.39±0.707 [a,b]	43.73±0.707[d]

Results are expressed in Means ± SD (n = 4), Mean values with different letters as superscripts across the columns are considered significant at p < 0.05

3.1.3 Photomicrograph of kidney sections



Figs. 1-5. Photomicrograph of kidney sections from experimental groups 1; normal control, group 2; infected with *P. brerghei* and not treated, group 3; infected with *P. berghei* and treated with 84 mg per kg body weight of sodium bicarbonate once per day, group 4; infected with *P. brerghei* and treated with 84 mg per kg body weight of sodium bicarbonate twice per day and group 5; infected with *P. brerghei* and treated with 84 mg per kg body weight thrice per day showing normal glomerulus (GL) and tubules (arrows) H and E X 400.

3.2 Discussion

Lipid peroxidation involves the formation and propagation of lipid radicals, the uptake and propagation of lipid radicals, the uptake of molecular oxygen and arrangement of double bonds in the unsaturated lipids and eventually their destruction with subsequent production of a variety of breakdown products, including alcohols, ketones, aldehydes and ethers [28]. Malondialdehyde (MDA) is a reliable and commonly used marker of overall lipid peroxidation levels and the presence of oxidative stress [29]. Lipid peroxidation product accumulation in human tissues is a major cause of tissue and cellular dysfunction that plays a major role in ageing and most age-related and oxidative stress-related diseases [30]. In this study, results showed that serum MDA level in the treated groups increased significantly when compared to the untreated control. The increase reduction in MDA level observed in this study shows that infection of the mice with *P. berghei* may have induced lipid peroxidation in the vulnerable organs leading to its leakage from those organs in to the main blood circulatory

system and sodium bicarbonate administered once, twice and thrice respectively in subsequent groups may not have reversed the adverse situation by not been able to inhibit lipid peroxidation in the treated animals implying that it may not possess antioxidant capacity. The increased lipid peroxidation amidst *P. berghei* and sodium bicarbonate as noticed in the present study may be due to the inefficient antioxidant system due to the presence of the parasite. In this study, treatment with sodium bicarbonate did not reduce the lipid peroxidation in the treated group compared to the control. Thus, in broad sense, complications associated with oxidative stress such as cancer, arthritis, cardiovascular diseases among others during plasmodium infection may not be ameliorated by sodium bicarbonate.

Glutathione peroxidase (GPx) is an enzyme that is responsible for protecting cells from damage due to free radicals like hydrogen and lipid peroxides. The result showed significant elevation in the activity of GPx of the rats infected and treated with 84 mg/kg body weight sodium bicarbonate thrice per day compared to that of the control group. This may be due to the fact that the administered dose stimulated the activity of GPx to detoxify hydrogen and lipid peroxides.

Superoxide dismutase (SOD) is an antioxidant enzyme that protects the cells from superoxide radical (O_2-). Under the action of SOD, O_2- is transformed into hydrogen peroxide (H_2O_2) and hydroxyl radical (OH^-) [31]. The increase in the activity of SOD in the untreated group could be attributed to its role in trying to combat the free radicals generated during the infection. Treatment with sodium bicarbonate twice and thrice per day was able to restore the SOD activity implying that the observed lipid peroxidation marked by high MDA may have been due to other mechanisms.

Catalase is an essential enzyme in the decomposition of intracellular hydrogen peroxide (H_2O_2) [32]. This study revealed a decrease in catalase of the treated animals compared to the control animals. The decrease in the level of catalase of the treated animals showed that sodium bicarbonate was not able to restore the activity of catalase utilized to degrade hydrogen peroxide. Non-restoration in the activity of the antioxidant enzymes could be related to its inability to scavenge ROS, thus not preventing further damage to cell membrane lipids. Therefore, the non-antioxidant potential of sodium bicarbonate may have resulted in the non-recoupment in the activity of catalase.

Glutathione is one of the most important and popular antioxidants that plays a vital role in maintaining the redox state of living cells [33]. The increase in the level of GSH in the treated group compared to the control animals showed that sodium bicarbonate may boost the antioxidant system of the host organism via the glutathione recovery pathway.

Electrolytes such as sodium, potassium, chloride and bicarbonate ion imbalances in the body may serve as an indicator of renal failure and this has been indicated in malaria-infected individuals [34]. The result of the electrolytes (potassium and sodium ions) revealed that there was a significant increase ($p<0.05$) in the concentrations of sodium and potassium ions in the infected and sodium bicarbonate treated groups. Thus sodium bicarbonate was able to restore the levels of these electrolytes in the system [35] also reported a decrease in electrolytes in the infected but untreated group of mice treated with synthetic drugs [36] reported that there is an increase in the level of Sodium, potassium, bicarbonate, and in the control group than in malaria infected children which is in line with this study although the bicarbonate in this study decreased. Elevated potassium ion is associated with renal failure, hence its importance in checking the integrity of the kidney [23]. A decrease or increase in the serum sodium level will have an effect on the plasma osmolality and this can have deleterious effects on the whole body, particularly, the central nervous system [37].

Urea concentration was found to be significantly ($p<0.05$) higher than control group at in the group infected, not treated and the groups infected and treated with sodium bicarbonate twice and thrice indicating that the parasite may have stimulated protein metabolism leading to high release of the nitrogenous waste products which is released into the bloodstream and is transported to the kidneys for excretion. An elevated concentration may overwhelm the kidney. The elevation in creatinine levels of the infected and treated animals compared to the control reveals that sodium bicarbonate is not capable of maintaining the integrity of the kidney. Elevated creatinine and urea levels signified a possible impaired kidney function. Impairment of the kidney leads to rise in creatinine level in the blood [38]. A

situation that was not reversed by the administered sodium bicarbonate.

The histological examination of the kidney sections did not present any remarkable change, indicating that the parasite did not invade the kidneys hence the kidney may not play a direct role in the proliferation of the parasite and that the administered sodium bicarbonate may not have posed nor exacerbated a remarkable histological damage on the kidneys of mice that were infected and treated differently.

4. CONCLUSION

The outcome of this study showed that infection of albino mice with *P. berghei* may have impaired kidney functions due to elevated concentrations of some of the metabolites usually excreted by the kidneys such as urea, creatinine and electrolytes such as sodium, potassium and chloride ions. The lipid peroxidation product MDA was also high amidst elevated endogenous antioxidant markers such as GPx, SOD and GSH. The administration of sodium bicarbonate could not be said to have ameliorated the stress posed on the kidneys, Histological studies however did not review any remarkable injuries on the kidneys as both the glomerulus and tubules appeared normal.

ETHICAL APPROVAL

Animal Ethic committee approval has been taken to carry out this study.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Kamble P, Bhagwat V, Trivedi DJ, Bargale A. Comparative study of free radical activity in Plasmodium falciparum and Plasmodium vivax malaria patients. Int J Pharm Bio Sci. 2011;2(4):99-102.
2. Akaninwor JO, Essien EB, Chikezie PC, Okpara RT. Haematologic and biochemical indices of Plasmodium falciparum infected inhabitants of Owerri, Imo State, Nigeria. Glob J Med Res Dis. 2013;13(4):20- 28.
3. Chidoka CP, Tochukwu OR. Haematologic and biochemical indices of Plasmodium falciparum infected inhabitants of Owerri, Imo State, Nigeria. J Med Lab Diagn. 2013;4(3):38-44.
4. Barsoum RS. Malarial acute renal failure. J Am Soc Nephrol. 2000;11:2147–2154.
5. Kute VB, Trivedi HL, Vanikar AV, Shah PR, Gumber MR, Patel HV, et al. Plasmodium vivax malaria–associated acute kidney injury, India, 2010–2011. Emerg Infect Dis. 2012;18:842–845.
6. Naqvi R. Plasmodium vivax causing acute kidney injury: a foe less addressed. Pak J Med Sci. 2015; 31:1472–1475.
7. Saravu K, Rishikesh K, Parikh CR. Risk factors and outcomes stratified by severity of acute kidney injury in Malaria. PLoS One. 2014;9:e90419.
8. Elsheikha HM, Sheashaa HA. Epidemiology, pathophysiology, management and outcome of renal dysfunction associated with plasmodia infection. Parasitol Res. 2007;101:1183–1190.
9. Gomes AP, Vitorino RR, Costa AP, Mendonça EG, Oliveira MG, Siqueira-Batista R. Malária grave por Plasmodium falciparum. Rev Bras Ter Intensiva. 2011;23:358–369.
10. Koopmans LC, van Wolfswinkel ME, Hesselink DA, Hoorn EJ, Koelewijn R, van Hellemond JJ, et al. Acute kidney injury in imported Plasmodium falciparum malaria. Malar J. 2015;14(523)
11. Mohapatra MK, Behera AK, Karua PC, Bariha PK, Rath A, Aggrawal KC, et al. Urinary bile casts in bile cast nephropathy secondary to severe falciparum malaria. Clin Kidney J. 2016;9:644–648.
12. Haruna GS, Enemali MO, Achimugu II, Isah R, Miftah M. Effect of Sodium Bicarbonate on Haematological Parameters and Differential Cells in Plasmodium Berghei-infected Albino Mice, International Journal of Pathogen Research. 2021;7(2):1-8.
13. Canadian Council of Animal Care (CCAC) Guidelines and Protocol; 1997.
14. Jigam AA, Usman TA, Halima AM, Tijani FO. Efficacy of thonningia sanguine Vahl root extract against Plasmodium inflammation and nociception in mice. Journal of Applied Pharmaceutical Science. 2012;2(01):47-51.
15. Kabiru AY, Okolie NL, Muhammad HL, Ogbadoyi EO. Preliminary studies on the antiplasmodial potential of aqueous and methanol extracts of camaldulensis. Asian

Pacific Journal of Tropical Disease. 2012;S809-S814.
16. Wallin B, Rosengren B, Shertzer HG, Camejo G. Lipoprotein oxidation and measurement of TBARS formation in single microlitre plate; It's use for evaluation of antioxidants. Analytical Biochemistry. 1993;208:10-15.
17. Ursini F, Mariorino M, Brigelius-Flohé R, Aumann KD, Roveri A, Schomburg D, Flohé L. Diversity of glutathione peroxidase. Methods in Enzymology. 1995;252:38–53.
18. International Federation of Clinical and Applied Chemistry, I.F.C.C. primary reference procedure for the measurement of catalytic activity concentrations of enzymes at 37ºC, Journal of Clinical Chemistry Laboratory. 2002;40(60):643-648.
19. Aebi HE. Catalase. In "Method of Enzymatic Analysis", VCH, Weinheim, Germany-Deerfield, F.L. 1983;**3**:273-286.
20. Jollow DJ, Michell JR, Zampaglionic, Gillete JR. Bromobenzene-induced Liver necrosis: Protective role of glutathione and evidence for 3,4-Bromobenzene oxide as hepatotoxic metabolite. Pharmacology. 1974;11:151-169.
21. Trinder P. Colorimetric Determination of Sodium. Analyst. 1951;76:596
22. Maruna RFL. Colorimetric determination of sodium. Clinical Chemistry. 1958;2:581
23. Terri AE, Sesin PG. Colorimetric Determination of Potassium. American Journal of Clinical Pathology. 1958;29:86.
24. Schales O, Schales SS. A Simple and Accurate Method for Determination of Chloride in Biological Fluids J. Biol. Chem. 1941;140 (5):879 - 882.
25. Van Slyke DD, Neil FM. The Determination of Gases in Blood and other Solutions. J. Biol. Chem. 1924;6(6):523.
26. Bartels H, Bohmer M. In vitro Determination of Creatinine and Urea. Clinical Chemistry. 1972;2:37-193
27. Bancroft JD, Stevens A. Theory and Practice of Histological Techniques. Churchill Livingstone, Edinburgh. 1977;16-64.
28. Soumen Bhattacharjee. Membrane lipid peroxidation and its conflict of interest: the two faces of oxidative stress. Current Science. 2014;107 **(**11):10.
29. Kayar A, Dokuzeylul B, Kandemir FM, Kirbas A, Bayrakal A, ME. Or Total oxidant and antioxidant capacities, nitric oxide and malondialdehyde levels in cats seropositive for the feline coronavirus. Veterinarni Medicina. 2015;60(5):274–281.
30. Anne NS, Auge N, Ayala V, Basaga H, Boada J, Brenke R, Chapple S, et al. Pathological aspects of lipid peroxidation. Free Radical Research. 2010;44(10): 1125–1171
31. McCord JM, Fridovich I. Superoxide dismutase: the first twenty years (1968-1988). Free Radical Biology and Medicine. 1988;5:363-369.
32. Alberts B, Johnson A, Lewis J, Raff M, Roberts K, Walter P. Peroxisomes" Molecular Biology of the Cell(4th ed.). New York: Garland Science; 2002.
33. Matill HA. Antioxidants. Annual Review Biochemistry. 1947;16:177-92
34. Kirk K, Horner HA. Novel anion dependence of induced cation transport in malaria-infected erythrocytes. Journal of Biological Chemistry. 1995;270:24270-24275.
35. Ime AU, Itam AH, Nzekwe NN. Electrolytes Changes in Malaria Infected Albino Mice Treated With Selected Artemisinin Based Combination Therapies (Acts). World Journal of Pharmacy and Pharmaceutical Sciences. 2016;5(8):243-252.
36. Olusegun Matthew Akanbi. The influence of malaria infection on kidney and liver function in children in Akoko area of Ondo state, Nigeria. Journal of Parasitology and Vector Biology. 2015;**7**(8):163-168.
37. Ashish KD, Pushpa Y, Agarwal AK, Rewari BB. Clinical Approach to Altered Serum Sodium levels. Journal, Indian Academy of Clinical Medicine. 2006;7(2):91-103.
38. Shemesh O, Golbetz H, Kriss JP, Myers BD. Limitations of creatinine as a filtration marker in glomerulo-pathic patients. Kidney Integrity. 1985;28(5):830-838.

Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle4.com/review-history/74351