BEST JOURNAL 20(1): 52 - 63
Date received: 14/01/2023
Date accepted: 16/04/2023

HAEMATO-BIOCHEMICAL ALTERATIONS IN EXPERIMENTAL WISTAR RATS EXPOSED TO PYRETHROID-BASED MOSQUITO COILS AND LOCAL MOSQUITO REPELLANTS SMOKE

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ABSTRACT

This study assessed the sub-acute toxicity of inhaling pyrethroid–based mosquito coil smoke and locally made mosquito repellents on the haematological indices, liver and kidney enzymes in experimental wistar rats. Fifteen (15) rats with mean weight of 150.5 g were randomly divided into five (5) groups. Group I were considered as negative control while group II, III, IV and V were exposed to mosquito coil (super kill), mosquito incense stick (shooter), orange peels and Eucalyptus leaves respectively 8 h daily for 21 days. They were kept in fabricated fly wood cages of 45x70cm = 315 sqcm^2, mean room temperature 27.6 °C and a relative humidity of about 40% with 12 h light/dark cycle. Laboratory analysis in blood samples were carried out using standard procedure. The results obtained indicated significant decrease in weight in all the experimental rats compared with control. Red blood Cells (RBCs) count, haemoglobin (Hb) concentrations and packed cell volume (PCV) of the experimental rats reduced significantly ($p<0.05$) when exposed to group II mosquito smoke, compared to the control group. The white blood cell (WBC) mean corpuscular haemoglobin (MCH), mean corpuscular volume (MCV) and mean corpuscular haemoglobin concentrations (MCHC) in the experimental rats of group III, II, IV and V were significantly higher ($p<0.05$) than that of the control. It was observed that the activities of the liver enzymes, alanine aminotransferase (ALT), aspartate aminotransferase (AST) and alkaline phosphatase (ALP) increased significantly ($p<0.05$) in in the entire experimental rats when compared with the control. The urea and creatinine concentrations increased significantly ($p<0.05$) in all the experimental group compared with the control with the exception of total protein which decreased in the same trend. From the present finding it revealed that inhaling mosquito coil smoke and locally made mosquito repellents have the potential to stimulate varying pathological effect with tissue toxicity in the long run. It is recommended that, emphasis should be directed in regulating their indoor utilization in malaria control activities.

Keywords: Biochemical changes, mosquito coil smoke, repellants, pyrethroids, wistar rats

INTRODUCTION

Malaria is considered to be one of the most severe infectious diseases worldwide, causing about half a million deaths every year, primarily in the developing world (WHO, 2016). Fifteen countries mainly in sub-Saharan Africa, accounted for 80 % of cases and 78% of deaths globally in 2015 (WHO/UNICEF, 2017). Prevention of malaria is best achieved by vector control, which today in Africa relies on the use of insecticides (Karim *et al*., 2020). The mosquito coils are slow-burning products widely used as mosquito repellent which releases smoke containing one or more insecticides (Abdullah *et al.*, 2017).

Insect repelling products such as mosquito coil, liquid vaporizers, creams and aerosol sprays are used usually overnight to protect people from mosquito bites so as to prevent malarial attack (Hassan *et al.*, 2019). The common active ingredient in many mosquito coil are the piperonyl butoxide (PBO), aromatic, aliphatic hydrocarbons, pyrethrin and allethrin (Hassan *et al.*, 2019). The gas phase of the coil smoke contains mainly formaldehyde and acetaldehyde thereby causing irritation on the upper respiratory tract (Usman *et al.*, 2018). Allethrin insecticide acts on both on the peripheral and central nervous systems by affecting sodium channels causing delay in the inactivation of the Na^+ channels (increasing of sodium permeability across the channel) resulting in neuronal excitability and paralysis of insect's organs (Nafiu *et al*., 2020). Besides, pyrethroids have been reported to induce alterations in the liver enzymes and haematological indices dysfunction (Inyang *et al*., 2016). Mosquito coil upon burning, produces particulate matter equivalent to that of cigarettes in addition to the volatile organic compounds, free radicals, metal fumes among other gaseous pollutants such as polyaromatic hydrocarbons. The vapors from the smoke after inhalation reaches the alveolar region of lung and causing irritation of the upper respiratory tract and oxidative stress to the body cells/tissues (Niazi *et al*., 2012). Prolong exposure of mosquito smoke has been reported to correlate with asthma and persistent wheeze in human (Taiwo *et al*., 2008), along with focal declination and metaplasia in tracheal epithelium in rodents (Niazi *et al*., 2012). Allethrin insecticides along with other mosquito coil derived particulate matters have been reported to alter biochemical and haematological parameters (Abdullah *et al.*, 2017). Exposure of pyrethrin based mosquito smoke has been reported to significantly elevate white blood cell (WBC) counts in rat (Garba *et al*., 2007). On the other hand, information on the application of plant parts as insect repellents is a vital tool in ethnobotany new discoveries (Rice *et al*., 2020). It is regarded as a cheap and instant remedy to low income earners and most citizens mainly in the third world countries (Sani and Ibrahim, 2016). However, inhaling the unknown toxic particles present in plants could expose individuals to various health complications. In view of the above, this study aimed at assessing the toxicological effect of brands of mosquito coil smoke and locally made mosquito repellants on the haematology and biochemical parameters of experimental wistar rats.

MATERIALS AND METHODS

Test materials

Mosquito coil super kill brand manufactured by Hua Hui International Trading Company, LTD, Jaafar Street Sharada Phase II, Kano State and mosquito incense stick shooter were procured from Sabongari Market, Kano state. Super kill mosquito coil brand contained 0.05 % of Meperfluthrin and 0.1 % D-allethrin while mosquito incense stick shooter contained D-trans allerthrine 0.3 %. *Eucalyptus citriodora* leaves were obtained from Gezawa in Kano, Nigeria while the orange peels were sourced from orange vendors at Na'ibawa yanlemo Kano Nigeria. They were allowed to dry in a shade for eight days.

Fifteen (15) rats with mean weight (150.5 g) were randomly divided into five (5) groups in three (3) replicates. Group I were considered as negative control while group II, III, IV and V were exposed to mosquito incense stick shooter, super kill, orange peels and Eucalyptus leaves respectively 8 h daily for 21 days.

Table 1: commercial mosquito repellents and local mosquito repellents used for the research.

SN	Brand	Ingredients
1	Mosquito coil super kill	0.5% merperfluthrin and 0.1% D-allethrin
2	Mosquito incense stick (shooter)	0.3% D-trans allethrin: wood powder 99.2%
3	Orange peel	
4	*Eucalyptus citriodora* leaves	

Experimental Design and Procedure

The experimental rats were divided into groups I, II, III, IV and V they were kept in undisturbed locally fabricated plywood cages of 45 x 70 cm=315 sqcm^2, mean room temperature 27.6°C ± 0.45°C and a relative humidity of about 40 %. The cages were covered all round with a wire mesh and a window provided on top of the cages to allow for ventilations. Each group was kept in a different room. The rats in group group I, II, III and IV were expose to mosquito coil, mosquito incense stick shooter, orange peel, and *Eucalyptus citrodora* leaves, respectively for 21 days, while those in group 5 serve as a control were not exposed to any mosquito repellent. The rats were exposed for 8 h daily by allowing the repellant slowly on top of a mesh wire under which hot charcoal is provided throughout the research period in an attempt to minimize average period of time that the repellants are used by human at night. The rats in each group were examined for any clinical sign associated with the exposure to the different smoke as adopted by Muhammad and Yakasai et al. (2017).

Determination of Physical Change in Animal

The weight of experimental and control rats were taken before and after the research of any physical and behavioral changes such as; body weight changes, loss of hairs, coughing and sneezing as adopted by Muhammad and Yakasai (2017).

Blood Sample Collection

At the end of the exposure period of 21 days, the experimental rats were put to sleep with chloroform and blood samples were collected from prominent jugular vein of the challenged and control group using heparinized plastic syringe, fitted with 23 gauge hypodermic needle. Blood samples for biochemical analysis were placed in a lithium heparin bottles container while EDTA containers were used for heamatology analysis.

Haematological Analysis

The blood samples collected were analyzed using automated hematology analyzer (SK 9000 Model) at Haematology Laboratory Aminu Kano Teaching Hospital Kano. The blood sample was analyzed for packed cell volume (PCV), haemoglobin, (Hb) Red Blood Cells (RBCs) and White Blood Cells (WBC) count. Red blood indices such as Mean Corpuscular Haemoglobin Concentration (MCHC), Mean Cell Volume (MCV) and Mean Corpuscular Haemoglobin (MCH) were calculated as follows.

$$\text{MCHC (g/dl)} = \frac{Hb\left(\frac{g}{dl}\right) x\ 100}{PCV\ (\%)}$$

$$\text{MCH (pg/cell)} = \frac{Hb\left(\frac{g}{dl}\right) x\ 10}{RBC\ \left(\frac{1012 \text{cells}}{\text{L}}\right)}$$

$$\text{MCV (fl/cell)} = \frac{PCV\ (\%) x\ 10}{1012\ \text{cells/L}}$$

Biochemical Analysis

The blood samples were collected in lithium heparin bottles container for biochemical analysis. Serum obtained by centrifugation at 5000 rpm for 4mins was used to analyze aspartate aminotransferase (AST), alkaline phosphatase (ALP), alanine aminotransferase (ALT) activities using randox kits as adopted by Ezenwaji *et al.* (2013).

Determination of Total Protein

This was carried out by the method of George (2009). Three (3) test tubes were marked as Blank (B) Standard (S) and Test (T). Exactly 0.5 ml each of distilled water, protein standard and serum were added in blank, standard and serum tubes respectively. This was followed by the addition of 1ml Biuret reagent into each of the test tubes and incubated at 37°C for 10 minutes. The absorbance of the standard and test were measured against the blank within 1hour.

$$\text{Total protein (g/dl)} = \frac{Absorbance\ T \times 8}{Absorbance\ S}$$

Determination of Creatinine

This was carried out according to the procedure of Bartel and Bohmer (1972). Three test tubes were labelled test (T), standard (S) and blank (B). One thousand microliter (1000 µl) of working reagent was pipette followed by addition 100 µl of serum, standard and distilled water to the respective tubes. Contents were well mixed and incubated for 30 seconds and the absorbance of the standard and samples were measured and measurements repeated after two minutes at 492 nm.

$$\text{Creatinine in serum (mg/dl)} = \frac{Absorbance\ sample \times 2.04}{Absorbance\ Standard}$$

Determination of Urea

Determination of urea in serum was carried out as modified by Sood (2006). Three clean and dry test tubes, labelled Blank (B), Standard (S) and Test (T), were used. To the three test tubes, 100 µl of reagent 1 was pipette followed by 10 µl of serum, and distilled water. The contents were mixed and incubated at 37°C for 10 min. Two thousand five hundred microliter (2500 µl) of reagent 2 and 3 were added to all the tubes. After mixing and incubation at 37°C for 15 min, the absorbance of the test (A Test) and standard (A Standard) was measured against the reagent blank at 546 nm.

$$\text{Urea (mg/dl)} = \frac{Absorbance\ sample \times 80.35}{Absorbance\ Standard}$$

Statistical Analysis

Statistical analysis was conducted using SPSS (Version 23.0). Data from the 3 replicates of the experiment was subjected to one-way Analysis of Variances of (ANOVA). Treatment means was separated using LSD at 5 % probability level. Probability level of less than 5 % ($p < 0.05$) was considered significant.

RESULTS

Toxicological implication of inhaled local and commercial mosquito repellants on Mean Body Weight.

During the study period, there was significant changes in the mean body weight of the rats challenged with local and commercial mosquito repellants smoke when compared to the control group which recorded increase in weight (Table 2). Highest weight gain of 10.8 g was recorded among control group while group III had the highest weight loss of -22.8g. However, after 2 weeks exposure, feeding habit decreased with irregular sneezing, coughing and body weakness which continued for the remaining period of exposure. None of the above behavioral changes was observed in the control group.

Table 2: Mean Weight of Experimental Rats before and after Exposure with Mosquito Incense Sticks Smoke

Group ID	Mean weight before exposure	Mean weight after exposure	Mean weight gain/loss after exposure
Group 1(Control)	212.5±2.46	293.32±2.64	10.8±1.81
Group 2	166.40±1.50	147.50±3.64	-18.9±0.31
Group 3	155.36±3.00	133.18±1.92	-22.8±0.52
Group 4	141.50±1.85	120.66±1.33	-20.5±1.43
Group 5	127.13±1.11	113.38±1.46	-14.13±0.81

Haematological Indices

Effect of mosquito coil smoke and locally made mosquito repellents inhalation on haematological indices is presented in Table 3. During the study period, the mean MCV, MCH and MCHC values of the experimental rats increased from group II to V when compared with control. (Table 3). The RBC indices did not differ significantly between the experimental groups ($p>0.05$) and the control. The lowest value of RBCs (5.18 mm^2) was obtained in group V while the highest value was recorded in the control of 8.60±0.02 $x10^6/mm^2$. Furthermore, the hemoglobin concentrations and PCV of the experimental rats significantly reduced ($P< 0.05$) in all the treated group when compared with control (Table 3).

Table 3: Effect of Mosquito coil and locally made mosquito repellents Smoke Inhalation on Haematological Indices in Albino Wister Rats

Parameters	Group I	II	III	IV	V
Hb (g/dl)	17.67±0.12 [a]	15.27±0.13 [b]	15.60±0.25 [b]	15.40±0.10 [b]	14.58±1.43 [b]
RBC ($10^6/mm^2$)	8.60±0.02 [b]	6.10±0.12 [a]	7.70±0.08 [a]	6.90± 0.07 [a]	5.18±0.64 [a]
PCV (%)	53.00±0.17 [a]	46.00±0.40 [a]	42.13±1.23 [a]	43.45±0.51 [a]	43.00±3.47 [a]
MCV (fl)	98.67±0.20 [a]	101.40±0.67 [a]	96.70±0.86 [a]	98.35±1.05 [a]	96.21±1.88 [a]
MCH (pg)	34.38±0.56 [a]	31.33±0.32 [a]	34.00±0.60 [a]	31.73±0.58 [a]	29.17±1.29 [a]
MCHC (g/dl)	34.00±0.33 [a]	32.67±0.37 [a]	32.67±2.17 [a]	31.00±0.45 [a]	31.33±0.06 [a]

Note: values are means and SD, means with the same superscript in a row are not significantly different ($P>0.05$)

During the study period, the mean lymphocytes, neutrophils and platelet values increased at 21 days when exposed to different mosquito coil and locally locally made mosquito repellents smoke (Table 4). The lowest value of lymphocytes (16.33 %), neutrophils (35.67 %) and platelet (397.07 x 10^3/ul) were obtained in the control group while the highest values were recorded in group III (19.00 %), IV (45.67 %) and V (423.83 x 10^3/ul) respectively (Table 3). Statically, mean values between control and experimental samples differ significantly ($P<0.05$). Furthermore, the WBCs, monocytes and eosinophils count of the experimental rats reduced significantly ($p< 0.05$) when compared with the treated group of 5.15 x $10^3/mm^3$, 24.58 % and 3.33 % in group V and II, respectively (Table 4).

Table 4: Effect of Mosquito coil and locally made mosquito repellents Smoke Inhalation on White Blood Cells counts in Albino Wister Rats

Parameters	Group I	II	III	IV	V
WBCs (10^3/mm^3)	7.27±0.29^b	6.33±0.21^a	7.60±0.36^b	6.00±0.45^a	5.15±0.45^a
Lymphocytes (%)	16.33±0.91^b	18.10±0.48^a	19.00±0.90^b	16.67±0.01^a	18.50±0.92^a
Monocytes (%)	38.67±1.41^a	35.00±0.90^a	30.67±0.51^a	27.00±0.73^a	24.58±1.83^a
Neutrophils (%)	35.67±0.35^a	36.50±0.10^a	39.03±0.46^a	45.67±0.44^a	7.87±1.15^a
eosinophils (%)	4.33±0.12^a	3.33±0.07^a	4.00±0.27^a	5.33±0.12^a	6.00±1.92^a
Platelets (10^3/ul)	397.07±8.02^a	421.00±4.52^a	412.33±5.03^a	407.73±3.00^a	423.83±5.80^a

Values are means & S.D, means values with the different superscript alphabet in a row differed significantly (P<0.05)

Biochemical Analysis

The mean liver AST of the experimental rats increased at 21 days when expose to the varying mosquito coil and locally made repellant smoke (Table 5). Lowest activity was obtained in the control group of 34.60 U/L and the highest of 58.37 U/L was obtained in group III. The AST activity between control and exposed group differed significantly (P<0.05). The activity ALT had the highest activity of 48.09 U/L among group III exposed rats while the lowest was recorded among control group of 38.67 U/L and the mean values differed significantly between the groups (P<0.05).The serum ALP activity had its highest value among group V rats of 43.78 U/L, followed by the Group IV with 37.91 U/L, group III (36.09 U/L) and Group II 35.67 U/L against the lowest value from the control group of 31.78 U/L. The mean values obtained differed significantly (P<0.05).

Table 5: Mean Concentrations of Biochemical Indices of Experimental Rats Exposed to mosquito coil and locally made repellant Smoke

Group/parameters	AST (U/L)	ALT (U/L)	ALP (U/L)
GROUP 1(control)	34.60 ±1.19^a	38.67±1.51 ^{a}	31.78±1.50^b
GROUP II	48.49±0.92^b	46.87 ±1.09^a	35.67±1.02^a
GROUP III	58.37±1.03^a	45.51±2.41^a	36.09±0.60^b
GROUP IV	42.74±0.86^a	48.09±1.02^a	37.91±2.10^a
GROUP V	52.16±1.03^b	39.60±0.01^a	43.78±1.10^a

Note: values are means and SD, means with the same superscript in a row are not significantly different (P>0.05)

Highest protein content was recorded in the control group of 73.37 g/l, followed by group 4(53.47 g/l), group III (52.35 g/l), group II (49.54 g/l) and group V (43.59 g/l). Statistically, the mean protein content differed significantly (p<0.05) between group V and control. Serum urea in the experimental rats had its highest values of 5.84 µmol/l in the control rats while the lowest of 2.94 µmol/l was recorded in group IV. The urea concentrations between control and group IV differed significantly (P<0.05). Highest creatinine activity was recorded in group V of 0.79 µmol/l, followed by g roup IV (0.75 µmol/l), group II 0.73µmol/l) and the lowest among the control group of 0.41 µmol/l.

Table 6: Mean Concentrations of Biochemical Indices of Experimental Rats Exposed to mosquito coil and locally made repellant Smoke

Group/parameters	TOTAL PROTEIN (59-86g/l)	Urea (2.1-6.9 µmol/l)	Creatinine (0.3-1.3 µmol/l)
GROUP 1(control)	73.37 ±0.29[a]	2.84±0.12 [a]	0.41±0.01[a]
GROUP 2	49.54±1.69[a]	3.47 ±0.01[b]	0.73±0.10[a]
GROUP 3	52.35±1.37[a]	3.56±0.04[a]	0.75±0.01[a]
GROUP 4	53.47±1.71[b]	4.94±0.15[a]	0.74±0.01[a]
GROUP 5	43.59±0.93[b]	4.43±0.19[b]	0.79±0.10[a]

Means with same superscripts in a column did not differ significantly (p>0.05).

DISCUSSION

The study was design to assess the noxious implication of Mosquito coil inhalation and locally made repellent on experimental rats. The mean body weight of the exposed rats upon exposure decrease significantly. Decrease in the mean body weight observed upon inhalation of the smoke, is in consistent with the body weight decline trend reported by Garba *et al*. (2007) and Karim *et al*. (2020). The body weight decline examined in the exposed rats might be associated to the immunosuppression and loss of appetite by inhaling the smoke containing pyrethrin, D-allethrin and meperluthrin based- insecticides. The decrease in the mean body weight by the exposed groups attributed to the effect of smoke components which could disrupt metabolism of nutrients which is vital for healthy living as reported by Cheng *et al*. (2008).This imply that inhalation of the insecticide smoke affected the wellbeing of the experimental rats.

Physiological status and environmental conditions have been reported to affect haematological parameters of organisms (Pierre *et al.*, 2017). Heamatological investigation characterizes the elevated WBC and it may be the result of immune response against toxic smoke. The mean WBCs, MCV, MCH and MCHC values of the experimental rats increased at 21 days when exposed to brands of mosquito coil smoke and locally made repellant. The elevated value for WBCs, MCV, MCH and MCHC recorded may associated to the noxious effect of active ingredients or other compounds present in mosquito coil and incense sticks which interfere with the body metabolism of the exposed rats. Similar observations were recorded by Idowu *et al*. (2013), Nafiu *et al*. (2020).

Fluctuations in RBCs indices such as MCV, MCH and MCHC observed in the present finding corroborates with RBCs count, PCV and Hb count. The fluctuations in the parameters indicates the current condition of the experimental rats' homeostatic system (Hassan *et al.*, 2019). Significant decline in PCV, RBCs and Hb was recorded in the experimental rats exposed to group III, IV and V insecticides when compared with control. The decline observed in the exposed rats might be due to damage of RBCs shape and concentration which ultimately leads to anaemic condition (Sani and Ibrahim, 2016). The anaemic condition observed in the exposed group to different mosquito coil and locally made repellant is attributed to the liver cells disruption on the course of RBCs transformation which ultimately alter the haem-synthesis (Idowu *et al*., 2013). The decline in Haemoglobin concentrations indicates anaemic conditions in the exposed rats, which could be attributed the stress-caused by RBCs haemolysis and erythropenia as reported by Usman *et al*. (2018).

Sani and Ibrahim (2016) also attributed decline in RBCs, PCV and Hb in rabbits challenged to mosquito repellents with bone marrow cell apoptosis and degeneration of haematopoietic growth factors. The decrease in RBCs count in the present study might be due to the inhibitory effect of the noxious compounds in the mosquito coil smoke on the enzyme system responsible for haemoglobin (Taiwo *et al.*, 2008). Active ingredients in mosquito coil such as synthetic pyrethrin has been reported to facilitate rat's immunological response with acute inflammatory effect to hepatic or pulmonary irritation (Uthman *et al.* 2016).

White blood cells count protects cells against infectious agents caused by toxicants (Abdul-Majid *et al.*, 2014). In the present finding WBCs count elevated with among the exposed experimental rats compared with control samples. The elevated WBC count is attributed to the stimulation of immune system due to cellular/tissue dysfunction or due to the activation of the experimental rats' defense mechanism (Niazi *et al*., 2010). The trend of response for elevated WBC count could be attributed to the toxin-induced cellular alterations and the effect of non-specific immune system causing elevated WBC count (Usman *et al*., 2018). Lymphocytes and monocytes count decline among the treated rats relative to the control. The decline in lymphocytes and monocytes might be due to the interactive effect of mosquito coil smoke active ingredients which have been reported to affect metabolic activities in the rats' lymph tissues (Yuonis *et al*., 2015).The decrease in lymphocytes and monocytes could also be due to the effect of active ingredient in the pesticide which stimulates cellular oxidative damage and ultimately the decrease in lymphocytes and monocytes (Ullah *et al.*, 2019).

There was an increased in the neutrophils and eosinophils count when compared with the control experimental rats. The elevated level in the neutrophils and eosinophils count examined might be due to the detoxifying effort against the pesticides-induced toxicity on the WBCs indices (Yuonis *et al*., 2015). An increase in neutrophils and eosinophils might be due to the lipophilic nature of pyrethroids insecticide on biological membrane cells where they are readily absorbed, causing induced-oxidative stress in the tissues and stimulate in the neutrophils and eosinophils count as reported by Fayinminnu *et al.* (2017) in wistar rats exposed to Chlorpyrifos.

Elevated activity of these hepatic enzymes is strongly correlated with hepatic injury (Idowu *et al*., 2013). It is either due to the direct effects of allethrin on the membrane phospholipids of hepatocytes and/or indirect effects caused due to the by-product derived from pyrethroid metabolism. Allethrin is membrane active materials, which acts upon membrane phospholipids and facilitates membrane fluidity and leading to leak out cellular enzymes in extracellular matrix ultimately elevating the transaminases activity in blood. An increase in transaminase level has been reported previously by Karthikeyan *et al*. (2006) in mice, exposed to mosquito repellent vapor. During the present research, important liver biomarkers such as AST, ALT and ALP in the blood of all the experimental rats elevated significantly when exposed with mosquito coil smoke (Ugwu *et al*., 2013). Increased activity of these hepatic enzymes when compared with control could be associated with hepatic damage as reported by Abdullah *et al*. (2017) and Nafiu *et al*. (2020). This might be due to the effect of active ingredient in the mosquito coil smoke allethrin or its by-product pyrethrum derived from pyrethroid metabolism on the membrane phospholipids of hepatocytes as obtained in group III incense sticks.

In the present study, increase in the activity of ALT, AST and ALP in the exposed rats to mosquito coil smoke specifically group III, IV and V might be associated to hepatic injury, myocardial infarction and cardiovascular diseases (Ugwu *et al*., 2013). This is in consistent with the observation of Abubakar and Hassan (2007) who reported an increase in liver enzymes (ALT, AST and ALP) due to exposure to different brands of mosquito coil (Swam, Rambo and Cork) smoke. Mossa *et al.* (2013) depicted that increased level of serum enzymes (ALT, AST and ALP) were due to exposure to pyrethriod-based insecticides and combination of different pyrethriod-based insecticides (Tetramethrin and Sumithrin). The elevated activity of liver enzymes in the experimental rats exposed to group II, III, IV and V could be due to the presence of toxic chemicals in the smoke that interfere with catalytic interconversion of amino acids and α-ketoacids by amino group in ALT as reported by Pierre *et al.* (2017). The increment of these enzyme levels is not due to elevated rate of biosynthesis, rather the alterations of these enzymes from cytosolic damaged hepatic cells into the blood stream (Usman *et al*., 2018). The exposure of mosquito coil smoke resulted in a dose dependent depletion and total protein activity in all inhaled rats (Uthman *et al*., 2016). Plasma concentration of Creatinine and Urea could be used as indicators of Nephrotoxicity (Inyang *et al*., 2017). Metabolic indices such as creatinine and urea can be used as a biomarker for assaying the physiological function of kidney. An increase in urea concentrations recorded in the experimental group relative to the control is an indication that that the smoke in the coil is lethal by disrupting the physiological functions of the organs responsible for the regulation of urea levels in the experimental rats. The large quantity of waste generated (urea) is liberated in response to low metabolic process taking place as a result of the toxicant effect Inyang *et al*. (2016). Creatinine is a nitrogenous waste product derived from the metabolism of creatinine in the skeletal muscle. It has been known to diffuse freely throughout the body fluid (Inyang *et al*., 2017). It is filtered from the extracellular fluid by the kidney and excreted in the urine. The high values recorded in the experimental group could be due to diminished impairment of the kidneys to filter wastes resulting in low creatinine and urea liberation in the urine (Upadhyay *et al*. 2017). The mosquito coil smoke has previously been reported to reduce serum total protein activity both in rodent animal and human subject. Higher protein degradation with subsequent reduction of total protein activity of blood in smoke inhaled subject has also been confirmed by marked increase of plasma free amino acid levels (Mahmood *et al*., 2018). Similar observation was reported by Abdulla *et al*. (2017).The blood concentration of excretory urea and creatinine are vital biomarkers in determine the functional intergrity of the kidney (Abdulla *et al*., 2017). The present finding revealed elevated urea level in the experimental rats compared to control. This could be due to the high level of catabolism of blood protein as reported by Inyang *et al*. (2016). An increased level urea in the serum might be associated to the hepatotoxic effect of chlorine which is known to be an inert ingredient of mosquito coil (Samanta *et al*., 2014).

Conclusion and Recommendations

From the present finding it can be concluded that inhaling smoke from burning of mosquito coil and locally made mosquito repellent for long term may not be safe as it revealed different haematological and biochemical implications in the exposed rats. It is therefore recommended that further study should be carried out to determine the mechanism of toxicity of the repellants. It is therefore recommended that, emphasis should be made in regulating their indoor application during malaria control program.

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