

# Toxicological Risk Assessment of Lead (Pb) Contamination in Public Water System in Lagos Metropolis, Nigeria

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## Abstract

**Study Background:** Lead continues to be a significant public health problem in developing countries, where there are considerable variations in the sources and pathways of exposure. **Aim:** This study investigates the level of lead in drinking water sources in Shomolu, Yaba and Bariga areas of Lagos State, Nigeria and the human risk exposure using a mice model. **Materials and Methods:** Water samples were collected in public water sources (borehole, sachet water, bottle water and tap water) and analyzed for lead using Flame Atomic Absorption Spectrophotometer (Varian model-AA240FS) equipped with a lead hollow cathode lamp. Contamination factor was determined. Healthy Mature female albino-mice, weighing  $25.3 \pm 2.5$  g were exposed to the contaminated drinking water for 28 days to the different concentrations of lead nitrate: 1 mg/l, 10 mg/l, 50 mg/l, 500 mg/l and 1000 mg/l. Blood and liver were collected for hematology liver function test and histopathology. **Results:** Lead concentrations in public water sources in Shomolu, Bariga and Yaba areas of Lagos State were below 5.0  $\mu\text{g/l}$  and contamination factor were less than 1.0. At 1.0 mg/l (1000  $\mu\text{g/l}$ ) Lead exposure, the relative weight increase in this group (as compared to the controlled group) was very slow, up to the 14<sup>th</sup> day (with weight loss of 3.17 g and relative weight loss of 23.1%), then increased up to the 28<sup>th</sup> day (with weight loss of 7.34 g, and relative weight gain of 18.4%). At 50.0 mg/l Lead exposure, there was a rapid weight decrease, a greater relative weight loss was experienced at the 14<sup>th</sup> day (weight gain, 1.36 g and 67.0% relative weight loss), then there was weight recovery at the 28<sup>th</sup> day (weight gain of 4.60 g, 25.8% relative weight loss). The 100.0 mg/l Lead exposed group showed steady decrease in weight, 14<sup>th</sup> day had a weight gain of 2.02 g and relative weight loss of 51.0% while the 28<sup>th</sup> day had 2.10 weight gain and 66.1% weight loss respectively. In the 500.0 mg/l Lead exposure group, a similar trend was observed as with 1.0 mg/l and 50 mg/l Lead

exposures, showing greater weight loss at the 14<sup>th</sup> day (2.14 g and 151.9% weight loss), as compared to the 28<sup>th</sup> day exposure (1.36 g and 121.9% weight loss respectively). Alanine aminotransferase (ALT) and Alkaline phosphatase (ALP) in the control group increased with time, but these had a different trend in the exposed groups. The RBC decreased with increase in concentrations from 1.0 mg/l to 50.0 mg/l Lead exposures, after which it increases at 100.0 mg/l, 500.0 mg/l and 1000 mg/l. The highest RBC was noticed at the highest exposure concentration at the 28<sup>th</sup> day with RBC, much higher than the control. The highest WBC was noticed at the highest exposure concentration at the 28<sup>th</sup> day with WBC,  $8.77 \pm 2.36 (\times 10^9/L)$  ( $p < 0.05$ ). The 28<sup>th</sup> day, 100.0 mg/L exposed mice's liver had cellular vacuolization and mild necrosis. At 14<sup>th</sup> and 28<sup>th</sup> day of exposure, the 500.0 mg/L and 1000.0 mg/L exposed mice had significant liver pathological alterations including the presence of polymorphic nuclei, blood vessel congestion, cellular vacuolization and severe necrosis. **Conclusion:** Lead induces hematological disturbances, liver histological alterations and change in weight in mice. These become obvious as exposure concentration increases with time. Continuous monitoring of municipal water pipeline reticulation should be ensured to prevent incidence of seepage of toxicants such as lead into domestic water sources.

## Keywords

Contamination, Lead, Hematology, Histopathology

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## 1. Introduction

Lagos, the most industrialized, populous and the fastest growing city in Africa, is currently facing a water management crisis [1]. Due to poor planning, lack of adequate infrastructure, insufficient funds, and a poor governance and regulatory framework, there is a vast demand gap of 330 MGD [1]. As such, only 10% of the population in Lagos is being served by the public water utility, Lagos Water Corporation [1]. The rest of the population gain access to water either from private boreholes or from informal private sector participants such as water vendors. This situation is further worsened by certain factors such as rapid population growth, corruption, climate change, unreliable electricity, inadequate enforcement, and water leakages and theft that cause 60% unaccounted-for-water losses. As a result, citizens experience water shortages, water pollution, inadequate sanitation and wastewater treatment, and water injustice and inequality. Due to high industrial and commercial activities and increasing population, pollution is often a major problem.

There has been a series of lead poisonings in Zamfara State, Nigeria, leading to the deaths of at least 163 people between March and June 2010, including 111 children [2]. Independent News Media [3] reported the health ministry figures as 355 cases, with 46 percent proving fatal [2]. This was due to unsafe mining and ore processing. Just five years later, in 2015, between April and May 2015, 28

children in Kawo and Magiro, two remote villages in Niger State, mysteriously died days after suffering symptoms of convulsions, insomnia and hallucinations, due to lead-rich gold mining [4]. Presently, heavy metals such as lead pose no health risk in Lagos State as compared to other states or regions, but if the right monitoring and management practices are not continually put in place, the case could be different [5]. However, if the concentration of these heavy metals surpasses the maximum admissible levels as stipulated by various organisations such as World Health Organization (WHO), American Public Health Association, then plant and animal health and developments may be affected because of malfunctions caused by bio-concentration of the heavy metals [6] [7].

Lead continues to be a significant public health problem in developing countries, where there are considerable variations in the sources and pathways of exposure [7]. For example, in many Latin American countries, leaded paint is not a significant source of recurrent exposure, whereas lead-glazed ceramics are such a source [8]. Exposure attributable to miscellaneous sources may be even more significant than universal exposure associated with leaded petrol, especially for people living in poverty. Exposure to lead from lead mining, smelting, battery factories and cottage industries is a significant environmental hazard in developing countries [9]. Unlike overt lead toxicity, where there is usually one identifiable source, low-level environmental exposure to lead is associated with multiple sources (petrol, industrial processes, paint, solder in canned foods, water pipes) and pathways (air, household dust, street dirt, soil, water, food) [10]. Evaluation of the relative contributions of sources is therefore complex and likely to differ between areas and population groups. Where lead derived from petrol comprises the major part of atmospheric lead it is a significant contributor to the body lead burden and is the most widely distributed source of the metal in the environment [11]. It is thus desirable to phase out the use of lead additives in fuels as quickly as possible on the global scale.

Atmospheric lead that is deposited in soil and dust may then be ingested by children and may substantially raise their blood lead levels [8]. Signs of acute intoxication, include dullness, restlessness, irritability, poor attention span, headaches, muscle tremor, abdominal cramps, kidney damage, hallucinations, loss of memory and encephalopathy. These occur at blood lead levels of 100 - 120  $\mu\text{g}/\text{dl}$  in adults and 80 - 100  $\mu\text{g}/\text{dl}$  in children [12] [13]. Signs of chronic lead toxicity, including tiredness, sleeplessness, irritability, headaches, joint pain and gastrointestinal symptoms, may appear in adults at blood lead levels of 50 - 80  $\mu\text{g}/\text{dl}$  [10].

For the population at large, which is not occupationally exposed, food and water are important sources of baseline exposure to lead, in addition to atmospheric lead that is inhaled [11]. Even in countries where considerable efforts have been made to control lead, vast reservoirs of the metal still exist in soil, dust and house paint, and these sources will continue to affect populations for many years [10]. Lead exposure is clearly a global public health issue, but it is only just

being recognized as a potential problem in many developing countries, with studies only now being reported from Africa, Asia and South America [11].

The aim of this research was to identify levels of lead in drinking water sources in the environment and carry out the human risk assessment using a mice model.

## 2. Materials and Methods

### 2.1. Water Sample Collection

Water samples were collected in public water sources (borehole, sachet water, bottle water and tap water) in Shomolu, Yaba and Bariga areas of Lagos State.

#### *Pre-Treatment of Water Samples*

Water samples were digested according to APHA, 2005. Briefly, 1000 cm<sup>3</sup> of well mixed, acid preserved sample was transferred into a beaker. Exactly 50 cm<sup>3</sup> of conc HNO<sub>3</sub> was added and heated to boiling. This was then evaporated on a hot plate to 20 cm<sup>3</sup>. Heating and addition of conc. HNO<sub>3</sub> continued until after digestion was completed as indicated by a light colour, clear solution. The content was then transferred to 100 cm<sup>3</sup> plastic bottles, cooled and diluted to mark. Portions of the solution were used for Pb determination.

#### *Quantitative Determination of Lead in Water Samples*

In this work, flame atomic absorption spectrophotometer (Varian model-AA240FS) equipped with a lead hollow cathode lamp was used for quantitative determination of Pb in water samples. Standard calibration curve for the concentration range of 0.001 ppm<sup>-2</sup> - 2.000 ppm<sup>-2</sup> was used. This was linear with coefficient of determination of R<sup>2</sup> = 0.99.

#### *Contamination Factor (C.F) of Lead (Pb) in Water Samples*

The contamination factor (C.F) was calculated by dividing the concentration level of Pb in each water sample by the background value [14] [15]. In this study, the WHO [6] maximum limit for Pb in drinking water was selected as background level for the calculation of contamination factors of all the water samples.

### 2.2. Test Organism

The Test Organism used for the study was albino mice (*Mus musculus*). Fifty-four healthy Mature female albino-mice, weighing 25.3 ± 2.5 g were bred in the animal house unit of the Zoological Garden, University of Lagos for the study.

#### *Acclimatization*

The mice were acclimatized in the experimental setup environment for 14 days, before the commencement of the study.

#### *Housing and Feeding*

The mice used for the study were kept in plastic cages measuring 60 cm × 45 cm × 45 cm. Each cage was divided into 9 equal compartments. Each compartment was deemed to be spacious enough to house a female albino mice without

stressing out the animal. Thus, each cage contained 9 animals, and a total of 6 cages were used for the study. The cages were kept in the Zoological garden of the University of Lagos. The mean temperature of the surrounding area was  $28.0^{\circ}\text{C} \pm 2.0^{\circ}\text{C}$  and the relative humidity was  $58.0\% \pm 5.0\%$ . During the acclimatization as well as the experimental phase of the study, the test subjects were fed with standard mice feed purchased from the Nigerian Institute of Medical Research, Yaba. The constituents of the mice feed are shown in **Table 1**. The Mice were given Clean Water from the Zoological Garden tap, with a pH range of  $6.80 \pm 2.0$ , salinity index of 0.1% and a temperature range of  $22.0^{\circ}\text{C} \pm 5.0^{\circ}\text{C}$ .

### 2.3. Experimental Setup

The experiment was setup to compare the histological, liver function enzyme and hematological parameters of mice exposed to Lead with those mice that had no form of exposure to lead, while keeping every other variable constant. For the study, Lead exposure was in form of lead nitrate dissolved in the drinking water fed to the mice. Lead nitrate salt was gotten from the Chemistry Department of the University of Lagos. The salt was dissolved into five (5) concentrations to give a lead concentration exposure of: 1 mg/l, 10 mg/l, 50 mg/l, 500 mg/l and 1000 mg/l. The controls were not given any water contaminated with dissolved Lead nitrate.

Thus, the experimental subjects were classified based on the concentration of their exposure: 0% (Control) group, 1 mg/l group, 50 mg/l group, 100 mg/l group, 500 mg/l group and 1000 mg/l group. Each experimental group was made up of 9 animals that were placed in the same cage that has been meticulously compartmentalized. The test subjects were exposed to the contaminated drinking water for 28 days according to the different concentration group they belonged to.

#### *Test Solution*

The various lead exposure concentrations (1 mg/l, 50 mg/l, 100 mg/l, 500 mg/l and 1000 mg/l) were prepared from lead nitrate using the following formula:

**Table 1.** Component of the mice feed used for the study.

S/N	Components	Composition
1	Soya Beans Meal (44% Protein)	52.5%
2	Fish Meal	15.5%
3	Distillers Dried Soluble	7.5%
4	Wheat Shafts	5.0%
5	Animal Fats	3.0%
6	Pellet	2.5%
7	Di-Calcium Phosphate	0.5%
8	Coated Vitamin C	0.057%
9	Trace Mineral Mix	0.075%

$$\text{Number of moles} = \frac{\text{Mass (x)}}{\text{Molar mass}}$$

$$\text{Molarity} = \frac{\text{Number of Moles}}{\text{Volume (L)}}$$

### ***Sample Collection from Test Subjects***

3 mice from each group were sacrificed on day 0, 14 and 28 of the study respectively. 2 ml of blood was collected from the eye region for each mouse using heparinised haematocrit tubes and transferred into properly labelled ethylene diamine tetra-acetic acid (EDTA) anti-coagulant bottles. Also the sacrificed mice were dissected after which liver samples were then collected from each mouse. Each harvested organ was kept in a universal bottle and transported into the laboratory for analysis.

### **2.4. Determining Difference in Physiological Weight and Relative Weight**

The physiological weight before exposure (day 0) and after exposure were determined. Then the difference in these weights were obtained (Initial weight of the mice- $W_i$  and final weight- $W_f$ ). While, the relative weight change was obtained as the rate of change of the physiological weight in comparison with the control group. This is given with the formulae below:

$$\text{Relative weight (\%)} = \{ \text{Experimental group (} W_f - W_i \text{)} / \text{Control group (} W_f - W_i \text{)} \} * 100$$

### **2.5. Hematological Studies**

To investigate the effect of lead exposure on the haematological parameters of the mice, their, Platelet (PLT), Red Blood Cell (RBC), White Blood Cell (WBC) and Packed Cell Volume (PCV) indices were estimated using electronic counters. Blood-filled heparinized micro-haematocrit capillary tubes were centrifuged at 12,000 for 5 min using a micro-haematocrit centrifuge and the haematocrit (Hct) values were read directly. The haemoglobin concentration was measured by the cyan-methaemoglobin method at a wavelength of 540 nm. Concurrently, the Total Red Blood Cell (RBC) was obtained by employing the methods described by Oluah and Ulasi [16]. Mean cell haemoglobin concentration (MCHC), mean cell volume (MCV), and mean cell haemoglobin (MCH) were calculated using the following equations:  $MCHC = (Hb/PCV) \times 100$ ,  $MCH = (Hb/RBCC) \times 10$  and  $MCV = (PCV/RBCC) \times 100$  (11).

The activities of the liver enzymes; Alanine Aminotransferase (ALT), Aspartate Aminotransferase (AST), and Alkaline Phosphatase (ALP) were determined using the blood sample. The blood was centrifuged at 5000 rpm for 5 minutes; the plasma sample was then collected and kept at 20°C. The enzymes activities were determined by colorimetric method. The enzymes were then assayed using reagents obtained from enzyme assay kits.

## 2.6. Histopathology Procedure

To investigate the effect of lead exposure on the tissues of the mice, the histopathology of liver was studied. After each tissue sample had been properly labelled, they were cut and placed inside a tissue embedding cassette. The tissue samples were then processed using a 24 hours automatic tissue processor for a time ranging from 17 - 19 hours. The tissue processor completely fixed the tissue in 10% formal saline, after which the tissue was dehydrated using isopropyl alcohol. After dehydration, the tissue processor cleared the dehydrating agents using xylene L and H and then the tissue was cast in molten paraffin at the end of the 19 hours cycle.

After the tissue samples were removed from the tissue processor, they were embedded in molten paraffin wax that was contained in a plastic disposable embedding mould. The mould was then left to cool to room temperature. The embedded samples were then cut using a microtome and the cut sections were placed on a grease free slide. The slides were in turn placed on a hot plate for 30 minutes to enhance the tissues' adherence to the slides. The slides were then stained using the H and E staining method and then slides were there after viewed under the microscope.

## 2.7. Statistical Analysis

The values for the liver function enzymes, weight and hematological parameters of the control and various treatment groups were compared using SPSS 20.0 version.

## 3. Results and Discussion

### 3.1. Lead Concentration in Public Water Source in Shomolu, Bariga and Yaba Areas of Lagos

The major sources of lead exposure in some parts of Nigeria according to [5] are from vehicular pollution from leaded gasoline use, industrial pollution from mining, consumption of Nigerian leaded salt, drinking water absolutely obtained from wells. In this study, lead (Pb) concentrations in milligram per liter measured from public tap water, bore-hole, industrially produced bottle water and sachet water in Shomolu, Bariga and Yaba areas of Lagos State however, showed values below 5.0 µg/l and contamination factor less than 1.0 (Table 2). Unlike cases of lead poisoning in Zamfara and Niger States, there has not been reported

**Table 2.** Lead concentration in public water source in Shomolu, Yaba and Bariga areas of Lagos.

Location	Tap water		Bore hole		Bottle water		Sachet water	
	Conc. (µg/l)	C.F						
Shomolu	2.60	<1.0	4.24	<1.0	0.32	<1.0	2.25	<1.0
Bariga	2.10	<1.0	3.91	<1.0	0.53	<1.0	2.02	<1.0
Yaba	1.80	<1.0	4.02	<1.0	0.45	<1.0	1.58	<1.0

C.F—Contamination factor; WHO, 2011 estimated maximum lead concentrated limits; 3.8 µg/l/day for an infant to 10 µg/l/day for an adult.

case of lead poisoning in Lagos State.

### 3.2. Changes in the Physiological Weight of the Experimental Mice during Exposure to Lead

Lead poisoning can have significant effects on human and animals. One of these effects is gradual or rapid weight loss or rapid weight gain/obesity. **Table 3** shows the changes in physiological weight of the mice exposed to varying concentrations of lead for 14 days and 28 days compared to the pre-treatment period (0 day). There was a steady increase in weight in the controlled group; Mean  $\pm$  SD, 0 day, 23.06 g  $\pm$  1.46 g,  $p < 0.01$ , 14<sup>th</sup> day, 27.18 g  $\pm$  1.45 g,  $p < 0.01$  and 28<sup>th</sup> day, 29.26 g  $\pm$  0.72,  $p < 0.01$ . At 1.0 mg/l Lead exposure, the weight also increased as the control but the relative increase (as compared to the controlled group) was very slow, up to the 14<sup>th</sup> day (with weight loss of 3.17 g and relative weight loss of 23.1%), then increased up to the 28<sup>th</sup> day (with weight loss of 7.34 g, and relative weight gain of 18.4%).

At 50.0 mg/l Lead exposure, there was a rapid weight decrease, a greater relative weight loss was experienced at the 14<sup>th</sup> day (weight gain, 1.36 g and 67.0% relative weight loss), then there was weight recovery at the 28<sup>th</sup> day (weight gain of 4.60 g, 25.8% relative weight loss). 100.0 mg/l Lead exposure showed steady decrease in weight, 14<sup>th</sup> day had a weight gain of 2.02 g and relative weight loss of 51.0% while the 28<sup>th</sup> day had 2.10 weight gain and 66.1% weight loss respectively. 500.0 mg/l Lead exposure had a similar trend as 1.0 mg/l and 50 mg/l Lead exposures, showing greater weight loss at the 14<sup>th</sup> day (2.14 g and 151.9% weight loss), as compared to the 28<sup>th</sup> day exposure (1.36 g and 121.9% weight loss respectively) (**Table 3**).

About 70% of Nigerian children have blood lead levels of about 10  $\mu\text{g}/\text{dl}$  [17]. According to the Centers for Disease Control and Prevention [18], the unborn child, bottle-fed babies, preschool children, and occupants of older houses are susceptible to lead from diverse sources. In this study, there was a steady increase in weight in the control group as compared to the exposed. The highest concentration of exposure (1000.0 mg/l) which is a 100 fold of the WHO guideline [6], showed a different trend; there was little or no increase or loss in weight, up

**Table 3.** Changes in the weight of the experimental albino mice (*Mus musculus*) during exposure to lead (n = 3).

Conc (mg/l)	Weight (g) Mean $\pm$ Standard Deviation (Weight gain or loss,% diff. from control)( $\Delta W$ )		
	0 day	14 <sup>th</sup> day	28 <sup>th</sup> day
0.00	23.06 $\pm$ 1.46**	27.18 $\pm$ 1.45** (4.12, 0.0%)	29.26 $\pm$ 0.72** (6.20, 0.0%)
1.00	27.70 $\pm$ 3.79**	31.68 $\pm$ 3.17** (3.17, -23.1%)	35.04 $\pm$ 1.36** (7.34, +18.4%)
50.00	27.14 $\pm$ 3.27**	28.50 $\pm$ 3.84** (1.36, -67.0%)	31.74 $\pm$ 2.08** (4.60, -25.8%)
100.00	26.12 $\pm$ 3.08**	28.14 $\pm$ 2.86** (2.02, -51.0%)	28.22 $\pm$ 1.81** (2.10, -66.1%)
500.00	29.02 $\pm$ 4.13**	26.88 $\pm$ 2.32** (-2.14, -151.9%)	27.66 $\pm$ 3.26* (-1.36, -121.9%)
1000.00	27.14 $\pm$ 1.69**	27.12 $\pm$ 1.53** (-0.02, -1.0%)	23.34 $\pm$ 3.01* (-3.80, -161.3%)

\*\*Signifies mean is significant at 0.01 level ( $p < 0.01$ ) and \*Signifies mean is significant at 0.05 level ( $p < 0.05$ ).

to the 14<sup>th</sup> day, after which the weight loss became very rapid, with the highest relative weight loss of 3.80 g and 161.3% respectively (**Table 3**). This is in strong agreement with the study of Allouche *et al.* [19], who reported that the long-term exposure to low lead concentration might lead to high weight gain and obesity risk. Likewise, Brunton [20], reported common symptoms of acute lead poisoning as gastrointestinal problems, such as constipation, diarrhea, poor appetite, and weight loss. Absorption of large amounts of lead over a short time could cause shock (insufficient fluid in the circulatory system) due to loss of water from the gastrointestinal tract [19].

### 3.3. Liver Function Enzyme Responses to Varying Concentrations of Lead for 14 and 28 Days

The results of the present experiment clearly indicate that acute and long-term exposure to lead nitrate causes significant biochemical alterations, which increases with exposure concentrations and time. **Table 4** shows the responses of the liver function enzymes to varying concentrations of lead for 14 and 28 days. The liver function enzymes in the blood; alkaline phosphatase (ALP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are indicators of stress condition of the liver. Changes in any of these enzymes relative to the control indicate alteration from normal or health condition.

Alkaline phosphatase (ALP) in the control group increased with time, 14<sup>th</sup> day,  $32.99 \pm 3.11$  g ( $p < 0.01$ ), 28<sup>th</sup> day,  $34.24 \pm 5.00$  g ( $p < 0.05$ ). The trend was slightly different in the exposed groups. Specifically, for those exposed to 1.0mg/l, the values were  $43.39 \pm 1.16$  g ( $p < 0.05$ ) and  $5.75 \pm 0.76$  g ( $p < 0.05$ ) by day 14<sup>th</sup> and 28<sup>th</sup> of exposure respectively. For the 50.0 mg/l exposure group, ALP was  $35.18 \pm 1.12$  g ( $p < 0.01$ ), and  $11.4 \pm 0.55$  g ( $p < 0.01$ ) after 14 and 28 days exposure respectively. In the 100.0 mg/l group, it changed from  $20.76 \pm 0.73$  g ( $p < 0.01$ ) at day 14 to  $9.40 \pm 2.05$  g ( $p < 0.05$ ) by day 28<sup>th</sup>. For those exposed to 500.0 mg/l, the values were  $23.76 \pm 0.73$  g ( $p < 0.01$ ) and  $11.37 \pm 0.93$  g ( $p < 0.011$ ) by day 14<sup>th</sup> and day 28<sup>th</sup> of exposure respectively, while in the 1000.0 mg/l exposure group, the value was  $58.46 \pm 1.46$  g ( $p < 0.01$ ) on day 14<sup>th</sup> and 8.44

**Table 4.** Hepatic antioxidant enzyme responses to varying concentrations of Lead for 14 and 28 days.

Conc. (mg/l)	ALP ( $\mu$ /l) (Mean $\pm$ SD)		AST ( $\mu$ /l) (Mean $\pm$ SD)		AL T ( $\mu$ /l) (Mean $\pm$ SD)	
	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day
0.00	$32.99 \pm 3.11^{**}$	$34.24 \pm 5.00^*$	$29.01 \pm 3.89^*$	$12.15 \pm 2.89^{**}$	$2.44 \pm 0.53$	$3.12 \pm 0.53^*$
1.00	$43.39 \pm 1.16^{**}$	$5.75 \pm 0.76^*$	$27.11 \pm 1.08^{**}$	$13.62 \pm 0.36^{**}$	$18.17 \pm 1.90^{**}$	$3.95 \pm 0.11^{**}$
50.00	$35.18 \pm 1.12^{**}$	$11.4 \pm 0.55$	$37.53 \pm 1.36^{**}$	$41.32 \pm 5.02^{**}$	$4.63 \pm 1.49^*$	$4.13 \pm 0.38^{**}$
100.00	$20.76 \pm 0.73^{**}$	$9.40 \pm 2.05^*$	$26.15 \pm 1.45^{**}$	$36.69 \pm 4.76^{**}$	$4.17 \pm 0.25^{**}$	$3.78 \pm 0.65^*$
500.00	$23.76 \pm 0.73^{**}$	$11.37 \pm 0.93^{**}$	$27.15 \pm 0.32^*$	$38.24 \pm 1.86^{**}$	$28.57 \pm 1.50^{**}$	$4.60 \pm 0.65^{**}$
1000.00	$58.46 \pm 1.46^{**}$	$8.44 \pm 1.91^*$	$38.13 \pm 1.09^{**}$	$35.21 \pm 3.04^{**}$	$23.29 \pm 2.13^*$	$3.01 \pm 0.10^{**}$

\*\*Signifies the mean is significant at 0.01 level ( $p < 0.01$ ) and \*Signifies mean is significant at 0.05 level ( $p < 0.05$ ). AST—Aspartate aminotransferase; ALT—Alanine aminotransferase; ALP—Alkaline phosphatase.

$\pm 1.91$  g ( $p < 0.05$ ) on day 28<sup>th</sup> (Table 4).

Alanine aminotransferase (ALT) in the control group also increased with time, 14<sup>th</sup> day,  $2.44 \pm 0.53$  g ( $p < 0.01$ ), 28<sup>th</sup> day,  $3.12 \pm 0.53$  g ( $p < 0.05$ ). The trend in the exposed groups was different. For those exposed to 1.0 mg/l, the values were  $18.17 \pm 1.90$  g ( $p < 0.01$ ) and  $3.95 \pm 0.11$  g ( $p < 0.01$ ) by day 14<sup>th</sup> and 28<sup>th</sup> of exposure respectively. For the 50.0 mg/l exposure group, ALT was  $4.63 \pm 1.49$  g ( $p < 0.05$ ), and  $4.13 \pm 0.38$  g ( $p < 0.05$ ) after 14 and 28 day of exposure respectively. In the 100.0 mg/l it changed from  $4.17 \pm 0.25$  g ( $p < 0.01$ ) at day 14<sup>th</sup> to  $3.78 \pm 0.65$  g ( $p < 0.05$ ) by day 28<sup>th</sup>. For those exposed to 500.0 mg/l, the values were  $28.57 \pm 1.50$  g ( $p < 0.01$ ) and  $4.60 \pm 0.65$  g ( $p < 0.01$ ) by day 14<sup>th</sup> and 28<sup>th</sup> of exposure respectively, while in the 1000.0 mg/l exposure group, the value was  $23.29 \pm 2.13$  g ( $p < 0.01$ ) on day 14<sup>th</sup> and  $3.01 \pm 0.10$  g ( $p < 0.05$ ) on day 28<sup>th</sup> (Table 4).

Aspartate aminotransferase (AST) in the control group decreased with time, 14<sup>th</sup> day,  $29.01 \pm 3.89$  g ( $p < 0.05$ ), 28<sup>th</sup> day,  $12.15 \pm 2.89$  g ( $p < 0.05$ ). The trend was however irregular in the exposed groups. For those exposed to 1.0 mg/l, the value decreased from  $27.11 \pm 1.08$  g ( $p < 0.01$ ) at day 14<sup>th</sup> to  $13.62 \pm 0.36$  g ( $p < 0.01$ ) by day 28<sup>th</sup>. There was an increase in value for those exposed to 50.0mg/l from  $37.53 \pm 1.36$  g ( $p < 0.01$ ) on day 14<sup>th</sup> to  $41.32 \pm 5.02$  g ( $p < 0.05$ ) by day 28<sup>th</sup>. In the 100.0 mg/l exposure group there was also an increase in value from  $26.15 \pm 1.45$  g ( $p < 0.01$ ) at day 14<sup>th</sup> to  $36.69 \pm 4.76$  g ( $p < 0.01$ ) by day 28<sup>th</sup>. For those exposed to 500.0 mg/l the values were  $27.15 \pm 0.32$  g ( $p < 0.05$ ) and  $38.24 \pm 1.86$  g ( $p < 0.01$ ) by day 14<sup>th</sup> and 28<sup>th</sup> of exposure respectively, while in the 1000.0mg/l exposure group, there was a decrease from  $38.13 \pm 1.09$  g ( $p < 0.01$ ) on day 14<sup>th</sup> to  $35.21 \pm 3.04$  g ( $p < 0.01$ ) by day 28<sup>th</sup> (Table 4).

These results in this study, are in agreement with the work of Bharali [15], but not with Allouche *et al.* [19]. Bharali [21] reported that increased lead concentrations caused increase in serum level of ALT enzyme and caused imbalance of the oxidant status of the cells, which is reflected in the rising level of liver tissue MDA level. Allouche *et al.* [19] reported that no evident disturbance of serum biochemical liver parameters was observed after long-term lead exposures. The author discounted the incrimination of the long-term lead exposure to risk of atherosclerosis or impairment of liver function.

In this study, alanine aminotransferase (ALT) and alkaline phosphatase (ALP) in the control group increased with time, but these had different trend in the exposed groups. ALT is commonly measured clinically as a part of a diagnostic evaluation of hepatocellular injury to determine liver health. Significantly elevated levels of ALT and ALP often suggest the existence of health problems such as viral hepatitis, diabetes, congestive heart failure, liver damage, bile duct problems, infectious mononucleosis, or myopathy.

### 3.4. Changes in Hematological Parameters in Mice Exposed to Varying Concentrations of Lead for 14 and 28 Days

The effects of lead exposure could further be seen in the hematological param-

ters as changes in the red blood cell counts, white blood cell count, mean hemoglobin volume and concentration, mean corpuscular volume and concentration and so on. **Table 5** and **Table 6** show changes in hematological parameters in mice exposed to varying concentrations of Lead for 14 and 28 days.

The Red blood cells (RBC) decreased with increase in concentrations from 1.0 mg/l to 50.0 mg/l Lead exposures, after which it increases at 100.0 mg/l, 500.0 mg/l and 1000 mg/l. The highest RBC was noticed at the highest exposure concentration at the 28<sup>th</sup> day with RBC,  $10.43 \pm 1.46$  (g/dL) ( $p < 0.01$ ) much higher than the control. The white blood cells (WBC) took a different trend compared with the RBC, there were steady increase at 1.0 mg/l, 50.0 mg/l, 100.0 mg/l, 500.0 mg/l and 1000.0 mg/l. The highest WBC was noticed at the highest exposure concentration at the 28<sup>th</sup> day with WBC,  $8.77 \pm 2.36$  ( $\times 10^9/L$ ) ( $p < 0.05$ ) much higher than the control  $2.27 \pm 0.81$  ( $\times 10^9/L$ ) ( $p < 0.05$ ). The Mean Corpuscular Volume (MCV) (fL) decreased with increase in concentrations from 1.0 mg/l to 1000.0 mg/l Lead exposures. The lowest MCV was noticed at the highest exposure concentration at the 14<sup>th</sup> and 28<sup>th</sup> day with MCV,  $35.17 \pm 0.91$  (fL) ( $p < 0.05$ ) and  $40.50 \pm 1.37$  (fL) ( $p < 0.01$ ) respectively, much lower than the controls  $39.67 \pm 0.76$  (fL) ( $p < 0.05$ ) and  $42.73 \pm 0.91$  (fL) ( $p < 0.01$ ) respectively (**Table 5**).

**Table 5.** Mean values and standard deviation of the blood parameters of mice exposed to lead.

Conc (mg/l)	RBC (g/dL)		WBC ( $\times 10^9/L$ )		MCV (fL)	
	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day
0.00	$9.17 \pm 0.06^{**}$	$8.43 \pm 1.23^{**}$	$2.27 \pm 0.81^*$	$2.77 \pm 1.10^*$	$39.67 \pm 0.76$	$42.73 \pm 0.91^{**}$
1.00	$7.02 \pm 0.03^{**}$	$7.91 \pm 0.76^*$	$3.77 \pm 0.85^*$	$5.00 \pm 3.61^*$	$39.20 \pm 0.79^{**}$	$43.13 \pm 0.59^{**}$
50.00	$6.92 \pm 0.10^{**}$	$5.67 \pm 0.55^{**}$	$3.93 \pm 0.32^*$	$5.93 \pm 0.25^{**}$	$38.37 \pm 0.71^*$	$45.07 \pm 0.16^{**}$
100.00	$7.05 \pm 0.16^{**}$	$6.40 \pm 1.35^*$	$3.73 \pm 0.57^{**}$	$6.70 \pm 0.56^{**}$	$37.27 \pm 0.42^{**}$	$44.77 \pm 1.06^{**}$
500.00	$7.09 \pm 0.14^{**}$	$6.70 \pm 1.45^{**}$	$4.93 \pm 1.27^*$	$7.60 \pm 2.09^*$	$36.30 \pm 0.72^{**}$	$40.47 \pm 0.40^{**}$
1000.00	$7.15 \pm 0.11^{**}$	$10.43 \pm 1.46^{**}$	$5.83 \pm 1.21^*$	$8.77 \pm 2.36^*$	$35.17 \pm 0.91^*$	$40.50 \pm 1.37^{**}$

\*\*Signifies the mean is significant at 0.01 level ( $p < 0.01$ ) and \*Signifies mean is significant at 0.05 level ( $p < 0.05$ ). RBC—Red Blood Cell (g/dL); WBC—White Blood Cell ( $\times 10^9/L$ ); MCV—Mean Corpuscular Volume (fL).

**Table 6.** Mean values and standard deviation of the blood parameters of mice exposed to lead.

Conc (mg/l)	MCH (Pg)		MCHC (g/dL)		HCT (%)	
	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day	14 <sup>th</sup> day	28 <sup>th</sup> day
0.00	$15.13 \pm 0.61^{**}$	$14.87 \pm 0.16^{**}$	$35.83 \pm 0.21^*$	$35.07 \pm 0.16^*$	$37.23 \pm 0.76^*$	$38.63 \pm 0.35^{**}$
1.00	$15.17 \pm 0.75^{**}$	$14.27 \pm 0.12^*$	$30.43 \pm 1.40^{**}$	$33.90 \pm 0.50^{**}$	$35.93 \pm 1.06^{**}$	$35.60 \pm 1.37^{**}$
50.00	$14.88 \pm 0.63^{**}$	$14.30 \pm 0.10^{**}$	$29.00 \pm 0.46^*$	$31.45 \pm 0.25^{**}$	$34.60 \pm 0.72^{**}$	$43.07 \pm 0.15^{**}$
100.00	$14.77 \pm 0.42^{**}$	$14.17 \pm 1.11^*$	$28.47 \pm 1.66^{**}$	$32.77 \pm 0.15^{**}$	$33.53 \pm 0.94^{**}$	$36.97 \pm 5.78^*$
500.00	$14.42 \pm 0.14^{**}$	$14.87 \pm 0.46^{**}$	$27.27 \pm 1.31^*$	$35.77 \pm 0.16^{**}$	$32.37 \pm 1.31^{**}$	$34.90 \pm 1.83^{**}$
1000.00	$14.13 \pm 0.12^{**}$	$15.13 \pm 0.61^{**}$	$25.67 \pm 0.97^{**}$	$36.13 \pm 0.88^{**}$	$30.43 \pm 1.31^*$	$32.20 \pm 0.36^{**}$

\*\*Signifies the mean is significant at 0.01 level ( $p < 0.01$ ) and \*Signifies mean is significant at 0.05 level ( $p < 0.05$ ). MCH—Mean Corpuscular Hemoglobin (Pg); MCHC—Mean Corpuscular Hemoglobin Concentration (g/dL); HCT—Hematocrit (%).

The Mean Corpuscular Hemoglobin (MCH) (Pg) decreased very slowly at 1.0 mg/l, 50.0 mg/l, 100.0 mg/l, 500.0 mg/l and 1000.0 mg/l except for the 28<sup>th</sup> day 500.0 mg/l and 1000.0 mg/l exposures, where there were increase in MCH much greater than the control. The lowest peak was at the 28<sup>th</sup> day 100.0 mg/l exposure,  $14.17 \pm 1.11$  (Pg) ( $p < 0.05$ ) and the highest MCH was at the 28<sup>th</sup> day 1000.0 mg/l exposure,  $15.13 \pm 0.61$  (Pg), ( $p < 0.01$ ) compared to the control,  $14.87 \pm 0.16$  (Pg), ( $p < 0.01$ ). The Mean Corpuscular Hemoglobin Concentration (MCHC) (g/dL) had similar trend as the MCH, decreased at 1.0 mg/l, 50.0 mg/l, 100.0 mg/l, 500.0 mg/l and 1000.0 mg/l except for the 28<sup>th</sup> day 500.0mg/l and 1000.0 mg/l exposures, where there were increase in MCHC much greater than the control.

The Hematocrit (HCT) (%) at the 14<sup>th</sup> day exposure, decreased steadily at 1.0 mg/l, 50.0 mg/l, 100.0 mg/l, 500.0 mg/l and 1000.0 mg/l. The highest exposure concentration had the lowest HCT,  $30.43 \pm 1.31$  (%) ( $p < 0.01$ ), much lower than the control,  $37.23 \pm 0.76$  (%) ( $p < 0.05$ ). At the 28<sup>th</sup> day, the hematocrit, initially decreased at 1.0 mg/l, then increased at 50.0 mg/l, before decreasing at 100.0 mg/l, 500.0 mg/l, and 1000.0 mg/l. The highest exposure concentration had the lowest HCT,  $32.20 \pm 0.36$  (%) ( $p < 0.01$ ), much lower than the control,  $38.63 \pm 0.35$  (%) ( $p < 0.01$ ) (**Table 6**).

These results are in agreement with the study of Oluah and Ulasi [16], that reported increased erythropoiesis in *Clarias gariepinus* exposed to lead poisoning. The highest WBC was noticed at the highest exposure concentration at the 28<sup>th</sup> day with WBC, much higher than the control. Both the red blood cells and white blood cells increased with concentration at 28 day exposure, this also agrees with [16].

Erythropoiesis is stimulated by decreased oxygen in circulation, which is detected by the kidneys, which then secrete the hormone erythropoietin [22]. This hormone stimulates proliferation and differentiation of red cell precursors, which activates increased erythropoiesis in the hemopoietic tissues, ultimately producing red blood cells. Lead poisoning could be associated with hematopoietic toxicity as this occurs as a result of enzymatic inhibition and damage to the barrier between the blood and bone marrow [22]. Increased lead concentrations will directly inhibit certain enzymes including heme synthetase, aminolevulinic acid dehydrogenase, ferrochelatase, 5<sup>th</sup> nucleotidase, and coproporphyrinogenase. Enzymatic inhibition results in an increase in the concentration of heme precursors (protoporphyrins), metarubricytosis, basophilic stippling, and erythrocytes that are more susceptible to physical damage [22] [23].

### 3.5. Histopathological Responses to Varying Concentrations of Lead Exposed Mice for 14 and 28 Days

The acute and long-term lead exposure can cause significant and irreversible pathological alterations. This was only observed in the liver. Histological examination showed significant alteration in the liver (**Table 7**). The liver sample from the control group, the 14<sup>th</sup> and 28<sup>th</sup> day 1.0 mg/L and 50 mg/L exposed groups

**Table 7.** Hepatic histopathological responses to varying concentrations of Lead exposed mice for 14 and 28 days.

Exposure Conc (mg/L)	Alteration		Polymorphic Nuclei		Vessel congestion		Vacuolization		Mild Necrosis		Severe Necrosis	
	14 day	28 day	14 day	28 day	14 day	28 day	14 day	28 day	14 day	28 day	14 day	28 day
Control	No	No	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs
1.0 mg/L	No	No	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs
50.0 mg/L	No	No	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs	Abs
100.0 mg/L	No	Yes	Abs	Abs	Abs	Abs	Abs	Pres	Abs	Pres	Abs	Abs
500 mg/L	Yes	Yes	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres
1000.0 mg/L	Yes	Yes	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres	Pres

Abs—absent, Pre—Present.

and 14<sup>th</sup> day 100.0 mg/L exposed mice had no significant alterations. By the 28<sup>th</sup> day of exposure to 100.0 mg/L, the mice liver had cellular vacuolization and mild necrosis. In addition, by the 14<sup>th</sup> and 28<sup>th</sup> day of exposure to both 500.0 mg/L and 1000.0 mg/L of lead, the mice had significant liver pathological alterations, which include the presence of polymorphic nuclei, blood vessel congestion, cellular vacuolization and severe necrosis.

This was reported by Bharali [21] as shown in this study. Bharali [21] reported 24 hour acute post exposure and also hepatocytes surrounding centrilobular area of liver displayed increased apoptotic morphology and cytoplasmic vacuolation. In this study, the hepatocytes of the control group, the 14<sup>th</sup> and 28<sup>th</sup> day 1.0 mg/L and 50 mg/L exposed groups and 14<sup>th</sup> day 100.0 mg/L exposed mice had no significant alteration. By the 28<sup>th</sup> day, 100.0 mg/L exposed mice had cellular vacuolization and mild necrosis. At 14<sup>th</sup> and 28<sup>th</sup> day of exposure, the 500.0 mg/L and 1000.0 mg/L exposed mice had significant liver pathological alterations including the presence of polymorphic nuclei, blood vessel congestion, cellular vacuolization and severe necrosis.

#### 4. Conclusion

In view of these results, it appears that lead induces hematological disturbances, liver histological alterations and change in physiological weight in mice. These become obvious as exposure concentration increases with time. Continuous monitoring of municipal water pipeline reticulation should be ensured to prevent incidence of seepage of toxicants such as lead into domestic water sources. The heavy metal, lead, which is known for these effects, is particularly dangerous to human health and is present in the air, soil, public water system and in food chain. To put an end to cases of lead poisoning in Nigeria, the right monitoring and management practices are necessary. Artisanal ore mining which often releases lead into surrounding environments as seen in the Zamfara State and Niger State case studies of lead poisoning should be discouraged across the Nation. Continuous monitoring of municipal water pipeline reticulation should be ensured to prevent incidence of seepage of toxicants such as lead into domestic

water sources.

### Conflicts of Interest

None of the Authors have conflict of interest.

### Availability of Data

Raw data is available on request at the Department of Zoology Archive, University of Lagos.

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