



Tissue Lead and Cadmium Levels and Associated Haematological Changes in Goats Slaughtered at The Bodija Abattoir, Ibadan

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ABSTRACT

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Heavy metal environmental contamination consequent of anthropogenic factors has become a global concern with cadmium and lead constituting a major public health, livestock and ecological threat. This study, therefore, uses goats (as sentinel animals) raised in 2 different regions based on their mining history (previous and existing) to evaluate exposure to cadmium and lead and their consequent toxicities and pathological changes. A total of 130 goats (composed of 88 goats which constitute the suspected exposure (SE) group and 44 goats, the suspected unexposed (SU) group) were sampled. Blood and tissue samples (liver, kidney and muscles) were analysed for lead and cadmium levels using Atomic Absorption Spectrophotometer along with the complete blood count analysis. The mean blood lead levels (BLLs) and cadmium levels (BCLs) in the goats from the SE groups were 14.59 and 3.12 µg/dl respectively, which were significantly higher than the SU groups (9.23 and 0.46 µg/dl respectively). A significantly higher frequency of goats in the SE (93.18%) also had an elevated BLLs compared to the SU group (78.57%). The levels of tissue lead and cadmium in both the SE and SU groups were found significant and higher than the FAO/WHO maximum limits. The packed cell volume, red blood cell count, and haemoglobin concentration were found significantly lower, and the platelet count and some leucocyte parameters (total white blood cell, neutrophil, eosinophil, and monocyte count) were found significantly higher in the SE group. The elevated cadmium and lead level in both groups further highlight the ubiquitous spread of cadmium and lead environmental contamination in both study regions and the direct risk of exposure to human and animals in Nigeria. The relative differences in the observed pathological changes in the two study groups also suggest the influence of the environmental heavy metal pollution and exposure levels on health.

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Introduction

Heavy metals are ubiquitous naturally occurring metals (with high atomic weight and density of more than 5g/cm³) with diverse industrial, agricultural, medical, commercial, technological and domestic applications. These metals (such as aluminium, arsenic, cadmium, chromium, lead, mercury, nickel) have been associated with widespread distribution in the environment consequent of their naturally occurring status and diverse utilization (Järup, 2003; Tchounwou et al., 2012; Jaishankar et al., 2014). Some heavy metals (such as zinc, copper) in trace amount have also been associated with important biochemical and physiological roles in the body. Despite their wide applications, some have non-physiological function in the body of living organisms and are associated with diverse

systemic toxicities and harmful environmental effects (Alissa and Ferns, 2011; Patra, Rautray and Swarup, 2011; Tchounwou et al., 2012). These toxicities and pathological changes have been attributed to the cumulative impact of the interference with normal physiological and biochemical mechanism, chronic degenerative changes, teratogenicity and carcinogenic effects (García-Lestón et al., 2010; Alissa and Ferns, 2011; Jaishankar et al., 2014). As a result, environmental heavy metal contamination has become an important global concern with increased interest in the public health and ecological impact of these heavy metals and their toxicity. (Järup, 2003; Tchounwou et al., 2012; Omonona et al., 2016). More so, the spate of industrialization, urbanization and anthropogenic activities

(such as mining, smelting, paint production, incineration, agriculture, fossil fuel combustion), and natural events (such as weathering, erosion, volcanic eruptions) has resulted in an increase in the severity of environmental heavy metal pollution and exposure (He, Yang and Stoffella, 2005; Patra et al., 2007; Nagajyoti, Lee and Sreekanth, 2010; Chen, Chen and Dong, 2012; Tchounwou et al., 2012). However, anthropogenic activities contribute the highest source of environmental contamination (Mensah et al., 2009; Tchounwou et al., 2012; Jaishankar et al., 2014) as illustrated by the role of mining activities in the Zamfara state (Nigeria) lead poisoning (Burki, 2012) and the Toyama Prefecture (Japan) Itai-Itai disease (cadmium poisoning) incidence (Kaji, 2015). With the impact of both heavy metals widely recognised globally as the most prevalent environmental contaminants with far-reaching toxicity effects.

Lead (Pb) is an extremely toxic heavy metal with a wide range of industrial and domestic application. This metal is found in nature in ores such as galena while anthropogenic process such as domestic and industrial activities constitute important sources of exposures and environmental contamination (Needleman, 2004; Mañay, Cousillas and Heller, 2011; Tchounwou et al., 2012). Lead exposure in humans and animals is primarily through inhalation of lead-laden dust particles, and ingestion of lead-contaminated food and water (Tchounwou et al., 2012).

Cadmium (Cd) is an equally important heavy metal with profound industrial and manufacturing application (and often found as a co-contaminant with lead contamination). Cadmium toxicity is of important concern due to its major occupational and environmental risk and public health concern even at a low dose of exposure and risk of chronic exposure (Davison et al., 1988; Tchounwou et al., 2012). Different route of cadmium exposure abounds viz inhalation (such as airborne cadmium fume and cigarette smoking being a major source of exposure), skin absorption (though rare) and ingestion of cadmium contaminated food (Davison et al., 1988; Järup, 2003; Tchounwou et al., 2012).

Lead and cadmium toxicity have been associated with a broad systemic interaction and alteration of the normal physiological and biochemical processes in humans and animals. These toxicities have been associated with biochemical mechanisms such as alteration of the antioxidant system and interaction with the toxic oxidative changes, alteration of enzymatic and biochemical processes with resultant pathological consequences and associated impact on the physiological mechanism (Koedrith and Seo, 2011; Patra, Rautray and Swarup, 2011; Jaishankar et al., 2014; Sharma, Singh and Siddiqi, 2014). These changes have been reportedly more profound in the nervous, cardiovascular, respiratory, gastrointestinal, hepatic, renal, hematopoietic, endocrine and immunological systems in animals (Inoue, 2011; Lehmann, Sack and Lehmann, 2011; Jaishankar et al., 2014; Sharma, Singh and Siddiqi, 2014). Similar pathological consequences have also been reported in plants along with residue formation in both plants and animals thus making it a significant food safety and public health threat (Nagajyoti, Lee and Sreekanth, 2010; Otitoju et al., 2014). Furthermore, lead and cadmium (like many

other heavy metals) have also been associated with many genotoxic effects, mutagenicity, teratogenicity and carcinogenic properties (Serpe et al., 2012; Koedrith et al., 2013; Jaishankar et al., 2014; Jubril, Fagbohun and Adekola, 2017; Jubril, Omadevuaye and Adekola, 2017). All these along with long environmental persistence and bioaccumulation in the ecosystem and food chain has made cadmium and lead toxicity a recurring livestock and public health risk with potential impact on the ecosystem. Consequent of these, the impact of these toxicities on wildlife conservation, ecology, public health and livestock production has further underscored the importance of the evaluation of these heavy metals and their residue analysis in soil, food, plants and animals (Van der Oost, Beyer and Vermeulen, 2003; Nagajyoti, Lee and Sreekanth, 2010; Akoto et al., 2014; Omonona et al., 2016). This has thus made the evaluation of the heavy metal (blood and tissue residue) along with the observed pathological changes and biomarkers in sentinel animals important in the evaluation of the extent of exposure, risks and as a tool for remediation programmes impact assessment (Mañay, Cousillas and Heller, 2011; Reif, 2011; Serpe et al., 2012).

In Nigeria, lead and cadmium are of profound importance due to the abundant reports of environmental contamination, and toxicity incidence in plants, humans and animals (Otitoju et al., 2014; Izah, Chakrabarty and Srivastav, 2016). For instance, the Zamfara state lead poisoning incidence due to the illegal artisanal mining has been reported as the worst case of acute lead poisoning in human history (Burki, 2012; Medecins Sans Frontieres, 2012; Orisakwe et al., 2017). However, while efforts have been focused on the impact of this environmental pollution in the affected region, the indirect exposure (through exposed animals and food contamination) in distant areas are rarely explored. This, has thus, necessitated the evaluation of the biomarkers of exposure (blood and tissue lead and cadmium levels) and effects (haematological changes) (Mañay, Cousillas and Heller, 2011) in animals transported from these affected regions for slaughtered in Ibadan, Southwestern Nigeria as a crucial approach in the evaluation of this indirect impacts.

This study explores the evaluation of lead and cadmium levels in goats (due to be slaughtered in Ibadan) transported from selected Northern Nigeria states that constitute the major source of small ruminant production in Nigeria and with previous documented heavy metal contamination cases (Reynolds, 1986; Ajala, Lamidi and Otaru, 2008). A comparison of the cadmium and lead levels (tissue and blood) and the associated haematological changes in goats in the two study groups as also conducted.

Materials and Methods

Study Area and Animal Selection

Goat sample selection for this study was conducted at the Bodija Municipal abattoir, Ibadan, Oyo State, Nigeria with full collaboration with the butcher and animal dealers. Based on the record obtained from the animal dealers, goats meant to be slaughtered at the abattoir acquired mainly from Zamfara state (Orisakwe et al., 2017) and other Northern Nigerian states (Kaduna, Kano, Sokoto, Niger) with recorded major incidences of heavy metal poisoning (Jagun, Olopade and Taiwo, 2013; Otitoju et al.,

2014; Izah, Chakrabarty and Srivastav, 2016; Jubril, Fagbohun and Adekola, 2017) were selected for this study. This group constituted the “Suspected Exposed (SE)” goats’ group. A comparison “Suspected Unexposed (SU)” group was also selected from Apete (7.4493° N, 3.8721° E), a residential community in Ibadan, Oyo state with no previous documented major incidence of heavy metal pollution.

A total of 130 goats (mainly Sokoto Red, West African Dwarf goats and crosses) were randomly sampled from goats due to be slaughtered at the abattoir with 88 goats in the suspected exposed group and 42 in the suspected unexposed group.

Antemortem examination was conducted for all the sampled goats to evaluate the health status and check for other presenting clinical manifestations of ill-health.

Sample Collection

Blood Collection

Blood was collected by venepuncture of the jugular vein (4mls) from the goats to obtain whole blood samples prior to slaughter, while, 2mls each of the collected blood samples were dispensed into heparinized tubes for haematological analysis while the remaining 2mls were preserved and stored for the blood lead and cadmium evaluation.

Tissue Collection

Liver, kidney and muscle tissue samples weighing approximately 5 grams were collected post-mortem from each slaughtered goat. These samples were appropriately labelled in tissue sample bags before being transported in cold packs to the laboratory for storage and onward analysis.

Sample Analysis

Blood and Tissue Heavy Metal Analysis

One millilitres of blood and 1g of the collected tissue samples were digested using the wet digest. The collected blood and tissue digest were measured via Atomic Absorption Spectrophotometer, (Alpha 4, and CHEMTECH 4200, Chem. Tech. Analytical Co. England) with graphite furnace and background correction (SR-BDG). Signals were read at 283.3 nm with background Zeeman correction for the determination of heavy metal (lead and cadmium) levels using the method described by Das and Choudhury (Das and Choudhury, 2016) with slight modifications. Standards and samples were both diluted (1:10) with an aqueous matrix modifier solution (containing 0.2% HNO₃, 0.5% Triton X-100, and 0.2% NH₃H₂PO₄).

All blanks, standards, and samples were analysed in duplicates. The calibration curve gave a linear response across this range with a correlation coefficient of 0.999. The averages of the duplicate values were taken for statistical analysis.

The blood and tissue levels of lead and cadmium were computed for the estimation of the mean level and the evaluation of the maximum levels in each group. The blood lead level (BLL) was used to further divide based on the WHO/CDC blood lead level classification to delineate the goats in the exposure groups into those with normal BLL range (<10 µg/dl) while those with BLLs ≥10 µg/dl were

classified as above normal range (Lubran, 1980; Dapul and Laraque, 2014).

Haematology

The qualitative evaluation of the erythrocyte parameters (Red blood cell count, packed cell volume, haemoglobin concentration) along with the calculation of the erythrocyte indices (mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration). The leucocyte count (total white cell and the absolute leucocyte count) and the platelet count were also quantified (Jain, 1986; Latimer et al., 2011).

Statistical Analysis

The collected data were inputted and collated using Microsoft Excel. Statistical analysis was carried out using IBM SPSS for Windows v.24 (IBM Corporation, 2016). Data obtained were expressed as mean and standard deviation (SD).

The quantitative data collected were expressed as means with the appropriate standard deviation (Mean±SD). The comparison of the means was done using t-test. Qualitative variables relating to the categorization of the groups based on the elevated blood lead level were expressed as frequencies with the appropriate calculation of the odds ratio (OR). A binary logistic regression was performed to determine the differences in the frequency of elevated blood lead levels in the 2 study groups with the appropriate odds ratio and confidence intervals. All variables with a probability level (P<0.05) were accepted as statistically significant.

Results

Antemortem Examination

The antemortem examination of the goats revealed a variety of clinical presentation including severe emaciation, dehydration (along with prominent sunken eyes, and loss of skin turgor), ocular discharge, listlessness, rough hair coat, and poor body condition. This was more prominent in the Suspected exposed (SE) goats group compared to the Suspected unexposed (SU) goat groups (Figure 1).



Figure 1. Figure showing severe emaciation and loss of body condition in the exposed goat group compared to the unexposed goat group.

Heavy Metal Analysis

The mean blood levels of cadmium and lead in the sampled goats are as shown in Table 1. The mean BLLs and BCLs in the goats from the suspected exposed groups (14.59

and 3.12 µg/dl respectively) were significantly higher than the values reported in these groups (9.23 and 0.46 µg/dl respectively). The reported mean BLLs and BCLs values in the SU group were also significantly higher than the tolerable WHO/CDC blood levels for lead and cadmium (10 µg/dl and 0.5 µg/dl respectively). The highest BCLs and BLLs values in both the SE and SU groups were also significantly higher than the WHO/CDC tolerable blood levels.

As shown in Table 2 and Figure 2, the percentage of subjects with elevated blood lead levels in the SE group (93.18%) was significantly higher (P=0.02) compared to the SU group (78.57%). A significantly higher percentage of the goats with normal BLLs were reported in the SU groups (21.43%) compared to the SE groups (6.82%)

As shown in table 2, the odds ratio (OR) of having elevated BLLs in the goats was 3.73 (CI: 1.23±11.30; P = 0.02). From the odds ratio, we can imply that the odds of the goats from the SE population having an elevated/abnormal BLLs was 3.73 times higher compared to the SU group. This is significant (P<0.05) and we can be 95% confident that the OR represents a true higher risk of exposure in the SE region compared to the SU region in this study.

As shown in Table 3, the tissue (kidney, liver and muscles) lead and cadmium levels in both the SE and the SU goat groups were significantly higher than FAO/WHO (2000) maximum limits with the levels in the SE group being significantly (P<0.05) higher than the levels in the SU groups.

Table 1. Blood heavy metal levels in the exposed and unexposed goat samples

Heavy Metal	Group	N	Mean level (µg/dl)	Highest value (µg/dl)	WHO/CDC Tolerable Blood Levels (µg/dl)
Lead (Pb)	Suspected Exposed	88	14.59	52.81	10*
	Suspected Unexposed	42	9.23	36.15	
Cadmium (Cd)	Suspected Exposed	88	3.12	9.62	0.5*
	Suspected Unexposed	42	0.46	3.07	

Key: N = Number Source: *Tolerable Blood Lead Level (Lubran, 1980; Dapul and Laraque, 2014) *Tolerable Blood Cadmium Level (WHO, 2000)

Table 2. Percentage of goats based on the blood lead levels and the logistic regression analysis of elevated BLLs frequency in the two study groups

Group	Blood Lead Levels (BLLs)		Odds Ratio	Confidence Interval		P-value
	Above normal range (%)	Within normal range (%)		Lower Limit	Upper Limit	
Suspected Exposed (n = 88)	82 (93.18)	6 (6.82)	3.73	1.23	11.30	0.02
Suspected Unexposed (n = 42)	33 (78.57)	9 (21.43)	-	-	-	-
Total	115 (88.46)	15 (11.54)				

Where; n= number of goats, Using normal range = 10, µg/dl where above normal range (≥10 µg/dl), within normal range (<10 µg/dl)

Table 3. Tissue heavy metal levels in the different groups compared with international maximum tolerable standards

Tissue	Tissue Lead Levels (mg/kg)			Tissue Cadmium Levels (mg/kg)		
	Suspected Exposed (n=88)	Suspected Unexposed (n=42)	FAO/WHO Maximum Levels*	Suspected Exposed (n=88)	Suspected Unexposed (n=42)	FAO/WHO Maximum Levels*
Kidney	59.41±29.20	12.63±8.25	0.50 [†]	5.06±1.20	1.48±0.13	1.00
Liver	63.81±13.64	9.36±2.11	0.50 [†]	4.54±1.53	1.12±0.13	0.50
Muscle	59.76±23.51	14.84±6.36	0.10	3.50±3.85	0.38±0.27	0.05

*Source: (FAO/WHO, 2000) Reference to the FAO/WHO maximum offal lead level

Table 4. Haematological Parameter Differences (Mean±S.D) between the Suspected Exposed and Suspected Unexposed Goat Groups

Parameters	Exposed n = 88	Unexposed n = 42	p-value
PCV (%) [*]	29.38±5.68	33.77±7.88	0.002
RBC (×10 ³ /µl) ^{**}	8.86±2.77	10.47±1.81	0.001
HB (g/dl) [*]	9.80±1.97	11.16±3.21	0.0035
MCV (fl)	55.43±79.59	31.19±6.21	0.0051
MCHC (pg)	33.33±1.46	32.88±2.02	0.1508
Platelet Count (x10 ⁵ /µl) ^{**}	1.70±0.41	1.14±0.30	< 0.0001
WBC (x10 ³ /µl) ^{**}	9.80±2.2	7.3±1.7	< 0.0001
Neutrophil count ^{**}	4.1±1.9	1.6±1.4	< 0.0001
Eosinophil count (×10 ³ /µl) ^{**}	0.5±0.3	0.2±0.2	< 0.0001
Lymphocyte count (×10 ³ /µl)	4.9±1.5	5.3±1.9	0.1954
Monocyte count (×10 ³ /µl) ^{**}	0.3±0.1	0.2±0.2	< 0.0001

PCV= Packed Cell Volume; HB = Haemoglobin Concentration; RBC= Red Blood Cell count; MCV = Mean Cell Volume, MCH = Mean Cell Haemoglobin, MCHC = Mean Cell Haemoglobin Concentration; WBC= White Blood Cell Count. Asterisk superscript (*) and (**) indicate significant differences between suspected exposed and suspected unexposed group where * indicate significance at probability level (P<0.05) and ** indicate significance at probability level (P<0.001)

A comparison of the lead tissue levels in the SE goat group revealed the highest concentration was detected in the liver (63.81 ± 13.64 mg/kg) while the lowest concentration was detected in the kidney (59.41 ± 29.20 mg/kg). This contrasts with the levels in the SU groups in which the highest concentration was detected in the muscle (14.84 ± 6.36 mg/kg). The tissue cadmium level in the SE group was also significantly higher compared to the levels in the SU group with the highest concentration reported in the kidney while the lowest levels were detected in the muscle in both the SE and SU groups.

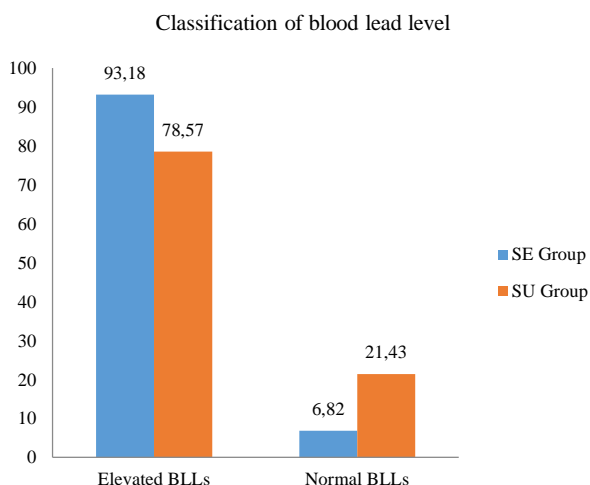


Figure 2. Figure showing the frequency of elevated and normal BLLs in the different exposure groups

Haematology

The haematological parameters in the SE and SU goats were summarized as shown in Table 4 below. The erythrocyte parameters (including the packed cell volume, red blood cell count, and haemoglobin concentration) were significantly lower ($P < 0.05$) in the SE group compared to the SU group. The platelet count in the SE group was also significantly higher ($P < 0.05$) than the level in the SU group. Conversely, the leucocyte parameters (total white blood cell, neutrophil, eosinophil, and monocyte count) in the SE group was significantly higher compared to the level observed in the SU group.

Discussion and Conclusion

Lead and cadmium contamination has been an attendant consequence of many anthropogenic activities with mining and many industrial activities being a major source (Patra, Rautray and Swarup, 2011; Izah, Chakrabarty and Srivastav, 2016). This has resulted in major toxicity outbreaks in various places in Nigeria with other salient impact not directly evident. The cohabitation of animals in these polluted regions with humans make them of direct importance due to the impact of this toxicity on their health and productivity. They are also of indirect impact to public health due to the effect of tissue residues in meat and other animal products consequent of the bioaccumulation and biomagnification of these heavy metals (EFSA, 2010; Meltzer et al., 2013; Fustinoni et al., 2017).

As a direct consequence of heavy metal toxicity in this study animals, the observed antemortem changes observed in this study animals had the highest prevalence in the exposed group. This is similar to the observation of similar signs of ill-health in small ruminants and animals reared in close proximity and in communities with mining activities and heavy metal toxicity incidence in China and Ghana (Liu, 2003; Akoto et al., 2014).

The mean lead and cadmium blood levels observed in the SE groups in this study were significantly higher than the WHO/CDC level blood levels for lead and cadmium ($10 \mu\text{g/dl}$ and $0.5 \mu\text{g/dl}$ respectively). This is similar to previous studies in which elevated heavy metal levels were reported in animals from regions with previous mining activities and reported heavy metal contamination. More so, the significantly higher percentage of animals with elevated BLLs and the significantly lower mean lead and cadmium levels in the SU goats compared to those from the SE regions can be ascribed to the relative difference in environmental contamination in the different regions (Okada et al., 1997; Liu, 2003; Tchounwou et al., 2012; Akoto et al., 2014; Orisakwe et al., 2017). This further supports the relevance of environmental contamination as a potential source of heavy metal exposure as highlighted by previous toxicological studies.

The elevated lead and cadmium tissue levels observed in both the SE and SU goat groups in this study highlights the report by previous studies about the detection of elevated heavy metal levels in animals. This also further stresses the consideration of environmental heavy metal contamination with lead and cadmium as a ubiquitous epidemic in Nigeria. This is also crucial as it stresses the need for adequate measures necessary for the mitigation of the impact, remediation of affected area and institution of policies aimed at reducing environmental pollution and their adverse consequences. The comparative difference between the two study regions stresses a geographical pattern in the severity of the environmental pollution and exposure of the sample goats. This finding also ties to the regional difference in the activities in the study region (with higher mining activities being reported in the northern regions selected as the exposed group (Jagun, Olopade and Taiwo, 2013; Orisakwe et al., 2017).

Inhalation of lead and cadmium-laden dust particles has been ascribed as a major source of exposure in both humans and animals (Mensah et al., 2009; Tchounwou et al., 2012) with a high temperature, low moisture and relative humidity being an important factor encouraging dust particle detachment, dispersal and risk of exposure (Csavina et al., 2011, 2012, 2014). This is important in the context of the regions in this study as the higher temperature and relative lower humidity and rainfall in the northern region (lying in the Sahel and Sudan Savannah agro-ecological zone) compared to the tropical wet and Guinea savannah climate in the SU group region (Aregheore, 2009; Adefisan and Abatan, 2015) increases the risk of particle inhalation and dispersal. This could be adduced as a key factor responsible for the observed difference, and severity of the biomarkers of exposure (blood and tissue lead and cadmium levels) and resultant biomarkers of effect (antemortem observation and haematological changes) difference between the two regions.

Our report of elevated tissue lead levels was found to be highest in the liver in the exposed group compared to the kidney and muscle. This report is similar to previous studies in which the mean lead concentration was found to be highest in the liver (Swaileh et al., 2009; Ihedioha and Okoye, 2012; Magwedere et al., 2013) compared to the kidney as reported by other studies (Liu, 2003; Adetunji, Famakin and Chen, 2014). The observation of high lead levels in both the kidney and the liver however is consistent with the relevance of these organs as important site of metal accumulation due to their role as portal of metabolism and excretion (Liu, 2003; Serpe et al., 2012; Akoto et al., 2014) and their total rank score (TRS) based on their ability to concentrate metals (Swaileh, Hussein and Abu-Elhaj, 2003; Swaileh et al., 2009). The lead level detected in the muscle and the viscera in this study were similar to the previous elevated levels range reported in cattle and other livestock reared in lead-contaminated gold mine in Nigeria (Ihedioha and Okoye, 2012; Jubril, Fagbohun and Adekola, 2017; Orisakwe et al., 2017), Ghana (Akoto et al., 2014) and China (Liu, 2003).

The mean tissue cadmium level in this study was higher in the kidney than in the liver and consistent with the observation of other previous studies (Santos et al., 2002; Gasparik et al., 2004; Ihedioha and Okoye, 2012; Magwedere et al., 2013; Adetunji, Famakin and Chen, 2014; Gašparik et al., 2017). The cadmium levels observed in this study were also above the FAO/WHO Codex Alimentarius maximum level in both the exposed and the unexposed group. The comparatively higher concentration of cadmium in the liver and the kidney compared to the muscle is associated with the established higher turnover and concentration of cadmium in these two organs (Nordberg, Fowler and Nordberg, 2014). The significantly high levels reported in this finding for both the exposed and the suspected unexposed groups were similar to report of manifold elevated cadmium levels in muscle and edible offal slaughtered in Nigeria above the FAO/WHO maximum level (Ihedioha and Okoye, 2012; Adetunji, Famakin and Chen, 2014). This is however contrary to previous reports in which the levels of cadmium reported in tissues of meat slaughtered in Nigeria (Bala et al., 2012) and other places were below the maximum level (Jorhem et al., 1991; Miranda et al., 2001; Magwedere et al., 2013).

Blood lead level (BLLs) has been reported as the most reliable biomarker of recent environmental lead exposure with relevant biomonitoring, diagnostic and screening applications (Mañay, Cousillas and Heller, 2011; Rao, 2016). This has thus made the evaluation of BLLs in animal (considering their sentinel roles and application) in ecotoxicological evaluation a veritable tool for the evaluation of ongoing heavy metal contamination and evaluation of the impact along with the assessment of remediation programmes (Rabinowitz et al., 2008; Reif, 2011; Jubril, Omadevuaye and Adekola, 2017). As reported in this study, the BLLs and BCLs were significantly higher in the SE group than the SU group and the WHO tolerable BLLs levels. These levels were also higher than the levels reported from previous studies.

As indicated by the odds ratio in this study, there is a positive association between the risk of elevated BLLs with the suspected level of heavy metal contamination in the sampling region. This further stress the role of

environmental factors and level of contamination as a predictor of blood lead level exposure in the inhabitants (Mañay, Cousillas and Heller, 2011; Magwedere et al., 2013; Plumlee et al., 2013; Jaishankar et al., 2014). The relative difference in the BLL compared to the tissue levels can be adduced to the relative ease of lead clearance from the blood compared to the tissue residue (Department of Primary Industry and Fisheries, 2016).

The haematology in this study showed a significant reduction ($P<0.05$) in the erythrocyte parameters (including PCV, RBC and Hb) while significantly higher mean values were observed in the platelet count and in some leucocyte parameters (viz WBC, neutrophil, eosinophil and monocyte count) in the SE compared to the SU group. This is an important indicator of the pathological role of elevated heavy metal exposure on the haematological parameters. This finding is consistent with previous report of profound alteration of the haemopoietic mechanism consequent of lead and heavy metal exposure (Mañay, Cousillas and Heller, 2011; Patra, Rautray and Swarup, 2011; Flora, Gupta and Tiwari, 2012). An important mechanism of action attributed for many heavy metal toxicities in animals and human is their profound interaction with the enzymatic processes and their consequent alteration of physiological functions. While the full mechanism of the interaction of heavy metals in the production of their toxicities has not been fully elucidated, the concomitant impact of free radical generation, alteration of antioxidant mechanism, and enzymatic processes has further stressed the significant deleterious effect of heavy metal mixture exposures and toxicity (Inoue, 2011; Patra, Rautray and Swarup, 2011; Koedrith et al., 2013; Sharma, Singh and Siddiqi, 2014). For instance, alteration of the δ -aminolevulinic acid dehydratase (δ -ALAD) regulatory mechanism by lead binding proteins (consequent of lead exposure) and metallothionein (consequent of cadmium exposure) has been adduced as a potential synergistic mechanism for the observed cadmium-induced renal injury and δ -ALAD inhibition associated with combined cadmium and lead toxicity (Goering and Fowler, 1985; Goering, Mistry and Fowler, 1986; Koedrith et al., 2013). This synergistic mechanism of heavy metal toxicity has thus been implicated in the observed pathological changes seen in the haematological parameters of heavy metal exposed animals and humans.

An important finding in this study is the comparatively high prevalence of samples with elevated blood lead and tissue heavy metal levels in the two study groups for this study. This highlights the ubiquitous spread of heavy metal contamination in Nigeria outside regions where major mining activities are presently (and have previously been) operated and in residential regions. This is a crucial finding as it stresses (using these animals as sentinels for the detection of heavy metal environmental contamination) the direct risk of exposure to humans and the impact of this exposure on the health of both humans and animals in the affected areas. This is important as it underscores the need for further surveys to evaluate the extent of environmental contaminations, research on environmental remediation to reduce the scourge of heavy metal pollution, and the need for policies and interventions stemmed at mitigating further exposure.

Recommendation

This research was designed using an epidemiological approach in the assessment of the heavy metal pollution crisis in different geopolitical zones associated with small animal ruminant production and previous history of heavy metal contamination. The stack difference in the heavy metal level in the SE group animals and the comparison SU group animals further extend the potential for the far-reaching impact of heavy metal residues and pollution across different geopolitical zones. This, therefore, highlights the importance of the institution of holistic interventions aimed at both regions with previous mining activities, heavy metal contamination incidence and regions not affected, to mitigate direct exposures and those potentially at risk of indirect exposures due to contact with contaminated fomites, livestock, and food items.

This further highlight the need for analysis of soft tissue Pb and Cd concentrations in the food chain to identify the risk from environmental exposure to the animal and the public health implication consequent of direct exposure to environmental heavy metal contamination and food safety implication consequent of heavy metal tissue residues.

Limitations of Study

Fewer goats from the unexposed region selected for this study were slaughtered at the abattoir compared to those from the Northern regions selected as the suspected exposed region. Consequent of this, the exposed cases in this study were more than the sampled control (unexposed). The animals transported from the Northern regions were markedly dehydrated upon arrival and slaughter at the abattoir. This could be due to the poor conditions they were subjected to during transportation which explains the marked antemortem features of dehydration observed in the SE group compared to the SU group. This transportation stress, however, cannot explain the significant emaciation and poor body score of the animals in the SE compared to the SU group as those features are typical of a chronic stress and exposure which could not arise from the acute effect of transportation (Gerdin et al., 2016). In addition, the evaluation of the environmental heavy metal levels in the different areas from which the animals were reared was not sampled. This would have been vital in the evaluation of the precise level of environmental exposure the study animals in the different groups were exposed to and helped in the correlation of the observed blood and tissue residue in the goats from the different groups with their background exposure levels. The significant difference in the cadmium and lead biomarker of exposure (blood and tissue levels) in SE group areas and the reflection on the observed pathological biomarkers of exposures (post-mortem findings and haematological changes) however stresses the difference in contamination level and toxicity impact in the two study areas.

Conflict of Interests

The authors would like to declare that there is no conflict of interest.

Authors' Contributions

AJJ did the study conception and design, acquisition of funding, analysis and interpretation of data, drafting of the manuscript and critical revision. AES contributed to the field data acquisition, fund acquisition, data compilation and initial draft of the manuscript. AAA contributed to the research study design, data analysis, manuscript draft and critical revision. ALA contributed to data analysis and interpretation, manuscript draft and review.

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References

- Adefisan E, Abatan A. 2015. Agroclimatic Zonning of Nigeria Based on Rainfall Characteristics and Index of Drought Proneness. *Journal of Environment and Earth Science*, 5(12): 115–128
- Adetunji VO, Famakin IO and Chen J. 2014. Lead and cadmium levels in cattle muscle and edible tissues collected from a slaughter slab in Nigeria. *Food Additives and Contaminants: Part B Surveillance*, 7(2): 79 – 83. doi: 10.1080/19393210.2013.848942
- Ajala MK, Lamidi OS and Oturu SM. 2008. Peri-urban small ruminant production in Northern Guinea Savanna, Nigeria. *Asian Journal of Animal and Veterinary Advances*, 3(3): 138 – 146. doi: 10.3923/ajava.2008.138.146
- Akoto O, Bortey-Sam N, Nakayama SMM, Ikenaka Y, Baidoo E, Yohannes YB, Mizukawa H and Ishizuka M. 2014. Distribution of Heavy Metals in Organs of Sheep and Goat Reared in Obuasi: A Gold Mining Town in Ghana. *International Journal of Environmental Science and Toxicology*, 2(4): 2315–9927
- Alissa EM and Ferns GA. 2011. Heavy metal poisoning and cardiovascular disease. *Journal of Toxicology*. Hindawi, p. 870125. doi: 10.1155/2011/870125
- Aregheore EM. 2009. Country Pasture / Forage Resource Profiles: NIGERIA. Rome
- Bala A, Saulawa M, Junaidu A, Salihu M, Onifade K, Magaji A, Anzaku S, Faleke O, Musawa A, Mohammed M, Muhammad L, Ubangari M and Ifende V. 2012. Detection of Cadmium (Cd) Residue in Kidney and Liver of Slaughtered Cattle in Sokoto Central Abattoir, Sokoto State. *J. Vet. Adv*, 2(Cd): 168–172
- Burki TK. 2012. Nigeria's lead poisoning crisis could leave a long legacy. *The Lancet*: 792. doi: 10.1016/S0140-6736(12)60332-8
- Chen C-W. 2012. Chen CF and Dong CD Distribution and Accumulation of Mercury in Sediments of Kaohsiung River Mouth, Taiwan. *APCBEE Procedia*, 1: 153 – 158. doi: 10.1016/j.apcbee.2012.03.025
- Csavina J, Field J, Félix O, Corral-Avitia AY, Sáez AE. and Betterton EA. 2014. Effect of wind speed and relative humidity on atmospheric dust concentrations in semi-arid climates. *Science of the Total Environment*. NIH Public Access, 487(1): 82 – 90. doi: 10.1016/j.scitotenv.2014.03.138
- Csavina J, Field J, Taylor MP, Gao S, Landázuri A, Betterton EA and Sáez AE. 2012. A review on the importance of metals and metalloids in atmospheric dust and aerosol from mining operations. *Science of the Total Environment*. NIH Public Access: 58–73. doi: 10.1016/j.scitotenv.2012.06.013

- Csavina J, Landázuri A, Wonaschütz A, Rine K, Rheinheimer P, Barbaris B, Conant W, Sáez AE and Betterton EA. 2011. Metal and metalloids contaminants in atmospheric aerosols from mining operations. *Water, Air, and Soil Pollution*. NIH Public Access, 221(1–4): 145 – 157. doi: 10.1007/s11270-011-0777-x
- Dapul H and Laraque D. 2014. Lead Poisoning in Children. *Advances in Pediatrics*. Mosby: 313 – 333. doi: 10.1016/j.yapd.2014.04.004
- Das S and Choudhury S. 2016. Analysis of heavy metals from water, sediment, and tissues of Labeo angra (Hamilton, 1822), from an Ox-box lake- a wetland site from Assam, India. *Journal of Environmental Science and Health, Part A*, 51(1): 21–33. doi: 10.1080/10934529.2015.1079102
- Davison AG, Newman Taylor AJ, Darbyshire J, Chettle DR, Guthrie CJG, O'Malley D, Mason HT, Fayers PM, Venables, KM, Pickering CAC, Franklin D, Scott MC, Holden H, Wright AL and Gompertz D. 1988. Cadmium fume inhalation and emphysema. *The Lancet*, 331(8587): 663 – 667. doi: 10.1016/S0140-6736(88)91474-2
- Department of Primary Industry and Fisheries. 2016. Lead poisoning- information for livestock owners. Northern Territory, Australia: 1 – 2
- EFSA. 2010. Scientific Opinion on Lead in Food, *EFSA Journal*. doi: 10.2903/j.efsa.2010.1570
- FAO/WHO. 2000. Report of the 32nd session of the codex committee of the food additives contaminants; March 20–24. Beijing, People's Republic of China
- Flora G, Gupta D and Tiwari A. 2012. Toxicity of lead: A review with recent updates. *Interdisciplinary toxicology*. Slovak Toxicology Society, 5(2): 47–58. doi: 10.2478/v10102-012-0009-2
- Fustinoni S, Sucato S, Consonni D, Mannucci PM and Moretto, A. 2017. Blood lead levels following consumption of game meat in Italy. *Environmental Research*, 155: 36 – 41. doi: 10.1016/j.envres.2017.01.041
- García-Lestón J, Méndez J, Pásaro E and Laffon B. 2010. Genotoxic effects of lead: an updated review. *Environment international*, 36(6): 623 – 36. doi: 10.1016/j.envint.2010.04.011
- Gašparik J, Binkowski ŁJ, Jahnátek A, Šmehýl P, Dobiaš M, Lukáč N, Błaszczuk M, Semla M and Massanyi P. 2017. Levels of Metals in Kidney, Liver and Muscle Tissue and their Influence on the Fitness for the Consumption of Wild Boar from Western Slovakia. *Biological Trace Element Research*. Springer, 177(2): 258 – 266. doi: 10.1007/s12011-016-0884-z
- Gasparik J, Massanyi P, Slamecka J, Fabis M and Jurcik R. 2004. Concentration of Selected Metals in Liver, Kidney, and Muscle of the Red Deer (*Cervus elaphus*). *Journal of Environmental Science and Health, Part A*, 39(8): 2105 – 2111. doi: 10.1081/ESE-120039378
- Gerdin JA, McDonough SP, Reisman R and Scarlett J. 2016. Circumstances, Descriptive Characteristics, and Pathologic Findings in Dogs Suspected of Starving. *Veterinary Pathology*, 53(5): 1087 – 1094. doi: 10.1177/0300985815575049
- Goering PL and Fowler BA. 1985. Mechanism of renal lead-binding protein reversal of d-aminolevulinic acid dehydratase inhibition by lead. *Journal of Pharmacology and Experimental Therapeutics*, 234(2)
- Goering PL, Mistry P and Fowler BA. 1986. A Low Molecular Weight Lead-Binding Protein in Brain Attenuates Lead Inhibition of d-Aminolevulinic Acid Dehydratase: Comparison with a Renal Lead-Binding Protein. *The Journal of Pharmacology and Experimental Therapeutics*, 237(1): 220 – 225
- He ZL, Yang XE and Stoffella PJ. 2005. Trace elements in agroecosystems and impacts on the environment. *Journal of Trace Elements in Medicine and Biology*, pp: 125 – 140. doi: 10.1016/j.jtemb.2005.02.010
- IBM Corporation: IBM SPSS Statistics for Windows. Armonk NY. 2016. IBM Corp
- Ihedioha JN. and Okoye COB. 2012. Cadmium and lead levels in muscle and edible offal of cow reared in Nigeria. *Bulletin of Environmental Contamination and Toxicology*, 88(3): 422 – 427. doi: 10.1007/s00128-011-0509-3
- Inoue KI. 2011. Heavy Metal Toxicity: *Journal of Clinical Toxicology*, s3(7): doi: 10.4172/2161-0495.S3-007
- Izah SC, Chakrabarty N and Srivastav A. 2016. A Review on Heavy Metal Concentration in Potable Water Sources in Nigeria: Human Health Effects and Mitigating Measures. *Exposure and Health*. Springer Netherlands, 8(2): 285 – 304. doi: 10.1007/s12403-016-0195-9
- Jagun AT, Olopade J and Taiwo VO. 2013. Evaluation of heavy metal levels in sheep and goat exposed to lead toxicity in Bagega, Zamfara state, Nigeria. in *Proceedings of the XVI ISAH International Congress on Animal Hygiene*. July 3 - 7, 2013, Nangjin, China. XVI ISAH International Congress on Animal Hygiene, pp: 360–361
- Jain NC. 1986. *Schalm's Veterinary hematology*. Philadelphia: Lea and Febiger
- Jaishankar M, Tseten T, Anbalagan N, Mathew BB and Beeregowda KN. 2014. Toxicity, mechanism and health effects of some heavy metals. *Interdisciplinary Toxicology*. Slovak Toxicology Society, 7(2): 60–72. doi: 10.2478/intox-2014-0009
- Järup L. 2003. Hazards of heavy metal contamination. *British Medical Bulletin*, pp: 167 – 182. doi: 10.1093/bmb/ldg032
- Jorhem L, Slorach S, Sundström B and Ohlin B. 1991. Lead, cadmium, arsenic and mercury in meat, liver and kidney of Swedish pigs and cattle in 1984–88. *Food Additives and Contaminants*, 8(2): 201 – 211. doi: 10.1080/02652039109373970
- Jubril AJ, Fagbohun O and Adekola AA. 2017. Detection of DNA Fragmentation in Liver of Goats Exposed to Lead Poisoning in Bagega District of Zamfara State, Nigeria. *Nigerian Journal of Physiological Sciences: official publication of the Physiological Society of Nigeria*, 32: 7–12
- Jubril AJ, Omadevuaye TO and Adekola AA. 2017. In vivo micronucleus test as a biomarker of genotoxicity in free-range goats from suspected contaminated environment. *Journal of Advanced Veterinary and Animal Research*, 4(3): 281–287. doi: 10.5455/javar.2017.d225
- Kaji M. 2015. Itai-itai disease: Lessons for the way to environmental regeneration. in *Lessons from Fukushima: Japanese Case Studies on Science, Technology and Society*. Cham: Springer International Publishing, pp: 141–165. doi: 10.1007/978-3-319-15353-7_7
- Koedrith P, Kim HL, Weon JII and Seo YR. 2013. Toxicogenomic approaches for understanding molecular mechanisms of heavy metal mutagenicity and carcinogenicity. *International Journal of Hygiene and Environmental Health*, 216(5): 587 – 598. doi: 10.1016/j.ijheh.2013.02.010
- Koedrith P and Seo YR. 2011. Advances in carcinogenic metal toxicity and potential molecular markers. *International Journal of Molecular Sciences*. Multidisciplinary Digital Publishing Institute (MDPI), pp: 9576–9595. doi: 10.3390/ijms12129576
- Latimer KS, Mahaffey EA, Prasse KW and Duncan JR. 2011. *Duncan and Prasse's Veterinary Laboratory Medicine: Clinical Pathology*. 5th edn. Wiley-Blackwell
- Lehmann I, Sack U and Lehmann J. 2011. Metal ions affecting the immune system. *Metal ions in life sciences*, 8: 157 – 185. doi: 10.1039/978184973211600157
- Liu ZP. 2003. Lead poisoning combined with cadmium in sheep and horses in the vicinity of non-ferrous metal smelters. *Science of the Total Environment*, 309(1–3), pp: 117–126. doi: 10.1016/S0048-9697(03)00011-1
- Lubran MM. 1980. Lead toxicity and heme biosynthesis. *Annals of clinical and laboratory science*, 10(5): 402 – 413

- Magwedere K, Shimwino J, Hemberger Y, Hoffman LC, Midzi EM and Dziva F. 2013. Lead and Cadmium Levels in Liver, Kidney and Muscle of Harvested Wild Springbok (*Antidorcus marsupialis*) Under Extensive Management in Southern and Southeastern Namibia. *South African Journal of Wildlife Research*, 43(1): 52 – 60. doi: 10.3957/056.043.0110
- Mañay N, Cousillas A and Heller T. 2011. Blood Lead Level (BLL, B-Pb) in Human and Animal Populations: B-Pb as a Biological Marker to Environmental Lead Exposure. in *Cellular Effects of Heavy Metals*. Dordrecht: Springer Netherlands, pp: 315 – 330. doi: 10.1007/978-94-007-0428-2_15
- Medecins Sans Frontieres. 2012. Lead Poisoning Crisis in Zamfara State northern Nigeria. (June 2010), pp: 1 – 4. doi: <http://www.msf.org/sites/msf.org/files/old-cms/fms/article-documents/MSF-Nigeria-Lead.pdf>
- Meltzer HM, Dahl H, Brantsæter AL, Birgisdottir BE, Knutsen HK, Bernhoft A, Oftedal B, Lande US, Alexander J, Haugen M and Ydersbond TA. 2013. Consumption of lead-shot cervid meat and blood lead concentrations in a group of adult Norwegians. *Environmental Research*, 127: 29 – 39. doi: 10.1016/j.envres.2013.08.007
- Mensah E, Kyei-Baffour N, Ofori E and Obeng G. 2009. Influence of human activities and land use on heavy metal concentrations in irrigated vegetables in Ghana and their health implications. in *Appropriate Technologies for Environmental Protection in the Developing World: Selected Papers from ERTEP 2007*, July 17-19 2007, Ghana, Africa. Dordrecht: Springer Netherlands, pp: 9–14. doi: 10.1007/978-1-4020-9139-1_2
- Miranda M, López Alonso M, Castillo Joaquín Hernández C, Luis Benedito J, Miranda M, Alonso M, Castillo C and Hernández Benedito JJ. 2001. Cadmium levels in liver, kidney and meat in calves from Asturias (North Spain). *European Food Research and Technology*, 212: 426 – 430
- Nagajyoti PC, Lee KD and Sreekanth TVM. 2010. Heavy metals, occurrence and toxicity for plants: A review. *Environmental Chemistry Letters*, pp: 199 – 216. doi: 10.1007/s10311-010-0297-8
- Needleman H. 2004. Lead Poisoning. *Annual Review of Medicine*, 55(1): 209–222. doi: 10.1146/annurev.med.55.091902.103653
- Nordberg G, Fowler BA and Nordberg M. 2014. *Handbook on the toxicology of metals*. 4th edn. Academic Press
- Okada IA, Sakuma AM, Maio FD, Dovidauskas S and Zenebon, O. 1997. Evaluation of lead and cadmium levels in milk in environmental contamination in the Vale do Paraíba Region, southeastern Brazil. *Revista de saude publica*, 31(2): 140 – 3
- Omonona O, Jubril A, Akinnibi O and Adekola A. 2016. Cadmium Bio-Accumulation and the Associated Biomarkers in Edible Frog Species (*Hoplobatrachus Occipitalis*) in Ibadan, Oyo State, Nigeria. *World's Veterinary Journal*, 6(October), pp: 70–79
- Van der Oost R, Beyer J and Vermeulen NPE. 2003. Fish bioaccumulation and biomarkers in environmental risk assessment: A review. *Environmental Toxicology and Pharmacology*, 13(2): 57–149. doi: 10.1016/S1382-6689(02)00126-6
- Orisakwe OE, Oladipo OO, Ajaezi GC and Udowelle NA. 2017. Horizontal and Vertical Distribution of Heavy Metals in Farm Produce and Livestock around Lead-Contaminated Goldmine in Dareta and Abare, Zamfara State, Northern Nigeria. *Journal of Environmental and Public Health*. Hindawi, 2017, pp: 1–12. doi: 10.1155/2017/3506949
- Otitoju O, Otitoju GTO, Iyeghe LU and Onwurah INE. 2014. Quantification of Heavy Metals in Some Locally Produced Rice (*Oryza Sativa*) from the Northern Region of Nigeria. *Journal of Environment and Earth Science*, 4(4): 67 – 71
- Patra RC, Rautray AK and Swarup D. 2011. Oxidative Stress in Lead and Cadmium Toxicity and Its Amelioration. *Veterinary Medicine International*, 2011, pp: 1–9. doi: 10.4061/2011/457327
- Patra RC, Swarup D, Naresh R, Kumar P, Nandi D, Shekhar P, Roy S and Ali SL. 2007. Tail hair as an indicator of environmental exposure of cows to lead and cadmium in different industrial areas. *Ecotoxicology and Environmental Safety*, 66(1): 127–131. doi: 10.1016/j.ecoenv.2006.01.005
- Plumlee GS, Durant JT, Morman SA, Neri A, Wolf RE, Dooyema CA, Hageman PL, Lowers HA, Fernette GL, Meeker GP, Benzel WM, Driscoll RL, Berry CJ, Crock JG, Goldstein H L, Adams M, Bartrem CL, Tirima S, Behbod B, von Lindern, I and Brown MJ. 2013. Linking geological and health sciences to assess childhood lead poisoning from artisanal gold mining in Nigeria. *Environmental health perspectives*. National Institute of Environmental Health Science, 121(6): 744 – 50. doi: 10.1289/ehp.1206051
- Rabinowitz Pd, Wiley Jb, Odofin L, Wilcox M and Dein FJ. 2008. Animals as sentinels of chemical terrorism agents: An evidence-based review. *Clinical Toxicology*. Taylor & Francis, 46(2): 93–100. doi: 10.1080/15563650701664905
- Rao CT. 2016. Lead Residues in Milk and Blood of Cows at Selected Localities of Chittoor District of Andhra Pradesh, India. *J Vet Sci Technol*, 7(7). doi: 10.4172/2157-7579.1000353
- Reif JS. 2011. Animal sentinels for environmental and public health. *Public Health Reports*. SAGE Publications, 126(Suppl 1): 50–57. doi: 10.1177/00333549111260S108
- Reynolds L. 1986. Small ruminant production — the present situation and possible nutritional interventions for improvement. in *International Livestock Centre for Africa: ILCA Bulletin*. International Livestock Centre for Africa, p. 25: 13-16
- Santos DC, Souto FJ, Santos DR, Vitral CL and Gaspar AM. 2002. Seroepidemiological markers of enterically transmitted viral hepatitis A and E in individuals living in a community located in the North Area of Rio de Janeiro, RJ, Brazil. *Mem Inst Oswaldo Cruz*, 97. doi: 10.1590/S0074-02762002000500007
- Serpe FP, Russo R, Simone ADe, Florio S, Esposito M and Severino L. 2012. Levels of heavy metals in liver and kidney of dogs from urban environment. *Open Veterinary Journal*. Faculty of Veterinary Medicine, University of Tripoli, 2(1): 15 – 18
- Sharma B, Singh S and Siddiqi NJ. 2014. Biomedical implications of heavy metals induced imbalances in redox systems. *BioMed Research International*. Hindawi, p. 640754. doi: 10.1155/2014/640754
- Swaileh KM, Abdulkhaliq A, Hussein RM and Matani M. 2009. Distribution of toxic metals in organs of local cattle, sheep, goat and poultry from the west bank, palestinian authority. *Bulletin of Environmental Contamination and Toxicology*, 83(2): 265 – 268. doi: 10.1007/s00128-009-9704-x
- Swaileh KM, Hussein RM and Abu-Elhaj S. 2003. Assessment of heavy metal contamination in roadside surface soil and vegetation from the West Bank. *Archives of environmental contamination and toxicology*, pp: 23 – 30. doi: 10.1007/s00244-003-3045-2
- Tchounwou PB, Yedjou CG, Patlolla AK and Sutton DJ. 2012. Heavy metal toxicity and the environment. *EXS. NIH Public Access*, 101: 133 – 64. doi: 10.1007/978-3-7643-8340-4_6
- WHO 2000. *Cadmium in Air Quality Guidelines 2nd edn*. Copenhagen, Denmark: WHO Regional Office for Europe