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Impact of Cadmium Intoxication on Health Status, Rumen and Blood Constituents in Egyptian Ossimi Sheep

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ABSTRACT

Toxic heavy metals particularly Cadmium (Cd) have a hazardous impact on animal health and productivity because of their ill-degradability and bio-accumulation for long periods. This study carried out on 52 Ossimi sheep belonging to Giza Governorate, including 12 sheep considered as control (kept in a private farm) and 40 sheep grazed on an area polluted with cadmium. Drinking water, animal blood and rumen fluid samples were collected from all sheep. Complete blood, rumen and serum constituents were analyzed. Iron, copper, zinc, oxidant and antioxidant markers were evaluated and Cd levels in water, rumen fluid and serum were investigated to show the impact of Cd on those parameters. Physical examination revealed significant disturbance in health status of Cd-exposed sheep. Rumen fluid examination showed significant increase in rumen pH, significant decrease in rumen ammonia-nitrogen, TVFAs, AST, ALT, GGT, Ca and Ph. Blood constituent revealed significant alteration as significant decrease in RBCs count, Hb, PCV, MCHC and TLC as well as impaired hepatic and renal function and significant decrease of antioxidant markers. These alterations associated with strong positive correlation between these altered parameters and cadmium level in drinking water, rumen fluid and blood samples which markedly increased more than permissible limits; these results should be put in consideration in interpretation of affected animals' status and during treatment and control of cadmium exposed sheep cases as well as consumption of such animals' meat and offal is not recommended.

Key words: Sheep, Cadmium, Blood, Rumen, Water, Antioxidants

INTRODUCTION

Environmental pollution is a major conundrum facing animal industry and of all living organisms at different trophic and systematic levels (Ferrante *et al*., 2017). In recent years, water contamination by toxic heavy metals such as cadmium (Cd) has accelerated dramatically due to natural and industrial sources (Masindi and Muedi, 2018) and subsequently, these metals reach to plants and animals and dramatically affect human health through food chain (Miedico *et al*., 2016). Toxic heavy metals particularly Cd have a hazardous impact on animal health and productivity because of their ill-degradability and bioaccumulation for long periods (Milam *et al*., 2017; Morsy *et al*., 2020b).

Grazing sheep, the most abundant ruminant livestock species is one of agriculture pillars in Egypt as it can convert low-quality roughages into meat and milk for human consumption in addition to producing wool and hides (Morsy *et al.*, 2020a). Water sources for grazing sheep are irrigation canals which contaminated with discharge of industrial, agricultural and municipal wastewaters which contain several types of hazards especially heavy metals such as lead, cadmium, nickel and mercury which are considered the most toxic for soil, plants and animals (Park and Shin, 2006).

Cadmium released into the environment via the smelting of other metals, the burning of fossil fuels, the incineration of waste materials, and the use of phosphate and sewage sludge fertilizers (Bampidis *et al.*, 2013). Entrance and absorption of Cd take place via skin, respiratory and alimentary routes (Godt *et al.*, 2006). Cd exposure has been speculated to affect numerous body systems especially hepatobiliary and renal system (Gunnarsson *et al.*, 2003) causing carcinogenicity, nephrotoxicity, osteoporosis, neurotoxicity, genotoxicity, teratogenicity and endocrine and reproductive effects (EFSA, 2009). Cd was found to be antagonist with micronutrients especially copper, zinc and iron (NRC, 2007) which are essential for all biochemical processes in the body, they are part of several enzymes, such as superoxide dismutase and glutathione peroxidase which are essential components of the antioxidant defense against oxidative stress by reactive oxygen species so protect tissues from damage (Evans and Halliwell, 2001).

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Oxidative stress is the consequence of an imbalance between oxidants and antioxidants in which oxidant activity exceeds the neutralizing capacity of antioxidants (Lykkesfeldt and Svendsen, 2007; Imran *et al*., 2020). Oxidative damage positively associated with cadmium level and occurs even at low levels of exposure to Cd. Cd stimulate the production of free radical's reactive oxygen species (ROS) which in turn cause RBCs damage and lipid peroxidation (Ercal *et al*., 2001; Wang *et al*., 2014). Antioxidant - enzymatic and non-enzymatic- deployed in face of elevated lipid peroxidation activity to scavenge ROS to protect body cells (Pietro Celi, 2011).

Studies on heavy metals pollution especially Cd were applied under experimental conditions (Stoev *et al*., 2003), and investigation of its effect on farm animals especially grazing sheep under natural practical condition rarely conducted (El-Sharkawy *et al*., 2008). Therefore, this study aimed to investigate the effect of water pollution with Cd on health status, rumen function, hematological parameters and serum constituents including hepatic, renal function tests and oxidant-antioxidant status of grazing sheep as well as correlation between Cd level and all parameters.

MATERIALS AND METHODS

Ethical approval

The current study was approved by Veterinary Medicine Cairo University Institutional Animal Care and Use Committee, Faculty of Veterinary Medicine, Cairo University, Egypt (VET CU 16072020202).

Animals and clinical examination

In Giza Governorate, a total number of 52 Ossimi sheep aging between 3-5 years with average weight 35-45 Kg were divided into two groups: 12 sheep raised in non-polluted grazing area (control group) and 40 sheep raised on grazing in rural polluted areas (exposed group). History of flocks concerning water sources, nutrition and management were recorded before the animals being clinically examined. All animals were subjected for careful clinical investigation including general body condition, inspection of visible mucous membranes of eye and examination of the skin and wool coat. Examination extended for other vital signs of health including pulse, respiratory rates, body temperature and examination of ruminal motility.

Samples and laboratory investigations:

Blood samples were collected by puncture of jugular vein and divided into two portions. First portion collected on EDTA tubes for hematological examination including total erythrocytic count (RBCs), hemoglobin content (Hb), packed cell volume (PCV), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC) and total leucocytic count (TLC) using automated hematology analyzer and the second portion collected in plain tubes for serum separation. Separated serum used for estimation of total protein, albumin, Aspartate Aminotransferase (AST), Alanine aminotransferase (ALT), Gamma Glutamyl Transpeptidase (GGT), Blood Urea Nitrogen (BUN), Creatinine, calcium (Ca) and inorganic phosphorous using specific kits produced by SPECTRUM Co., Egypt, according to the method described by (Young and Friedman, 2001). Globulin, A/G ratio and BUN/Creatinine ratio were calculated. Rumen fluid samples were collected from each animal via stomach tube and suction pump; immediately examined for color, odor, consistency, pH and protozoal activity according to method described by (Alonso, 1979). Total volatile fatty acids (TVFAs) estimated by steam distillation method as described by (Eadie *et al*., 1967). Rumen NH3-N was determined calorimetrically using specific kits produced by SPECTRUM Co., Egypt according to the method described by (Chaney and Marbach, 1962). Activity of AST, ALT and GGT and levels of calcium and phosphorus were determined in clear supernatant after separation of rumen fluid according to (Young and Friedman, 2001) using specific kits produced by SPECTRUM Co., Egypt. Water samples (50 ml) of drinking water were collected (six water samples from polluted area and one from non-polluted area). The technique of water sampling was conducted according to the recommendation of American Public Health Association (APHA, 2012). Cd level was estimated in water, rumen fluid and blood samples by Flame Atomic Absorption Spectrometer (model SensAA, GBC, Australia) in Micro Analytical Center, Faculty of Science, Cairo University, Egypt. All glass tubes and plastic containers used in this study for mineral estimation were cleaned twice with diluted HNO_3, then rinsed with deionized distilled water twice and then air-dried before using.

Statistical analysis

Normality, mean values, standard errors (SE), Correlation coefficient and significance of correlation were calculated using (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). Independent samples T-test was applied to make comparison between the mean values of groups to check the significance. The results are represented as means±SE and $P\leq0.05$ or $P\leq0.01$ was considered significant.

RESULTS AND DISCUSSION

Regarding history and clinical examination, the most obvious observations are depressed appetite, illthriftness, weakness, depression and rough wool. Disturbance in health status of these sheep in the form of emaciation, dullness, debility and other anemic changes especially pale mucous membranes could be attributed to the high level of heavy metals especially Cd. These findings agree with the findings of Bayoumi *et al*. (2013) and Oraby *et al*. (2015). Vital signs examination showed mild increase in respiratory rate which agreed with (Ali, 2005), moreover mild increase in pulse. In spite of non-significant mild increase in respiratory and pulse rate, physical examination revealed normal CH sound of lung and normal heart beats (70-90/min). This may be attributed to normocytic normochromic anemia which reflected by significant decrease in RBCs count, Hb and PCV recorded in such animals. In spite of previous obtained data including decrease of body condition scores, pale mucous membrane, slight increase of pulse and respiratory rate that were recorded in grazed sheep, some owners neglect or give no attention to that changes in clinical signs specially it appears only with pushing sheep to walk or to run with effort. Owners when notice these signs kept the sheep in

Table 1: Hematological findings in control and exposed sheep and correlation with blood Cd

	Control sheep	Exposed sheep	Blood Cd
RBCs ($\times10^6$)	11.27±0.27	9.82±0.06**	-0.599**
PCV (%)	28.83±0.90	25.20±0.28*	-0.443*
Hb (%)	9.74±0.29	8.18±0.06**	-0.569**
MCV(fl)	25.70±0.87	25.70±0.34	0.028
MCH (pg)	8.67±0.27	8.34±0.09	-0.118
MCHC (%)	33.79±0.17	32.61±0.42	-0.157
TLC ($\times10^3$)	7.25±0.17	5.66±0.10**	-0.634**

Values are expressed as mean±SE. *P≤0.05; **P≤0.01.

Table 2: Rumen pH, TVFA, ammonia N, Ca, Phos and some enzymes in control and exposed sheep and correlation with rumen Cd

	Control	Exposed	Rumen Cd
Rumen pH	6.62±0.06	7.08±0.02*	+0.697*
TVFA	56.60±0.36	41.86±0.85**	-0.763-**
Ammonia N	6.18±0.07	5.12±0.12**	-0.662**
AST (IU/L)	0.24±0.01	0.19±0.00*	-0.633**
ALT (IU/L)	0.49±0.01	0.41±0.00**	-0.686**
GGT (IU/L)	0.12±0.00	0.10±0.00**	-0.457**
Ca (mg/dl)	1.45±0.04	0.89±0.01**	-0.884**
Phos (mg/dl)	6.57±0.07	4.98±0.07**	-0.800**

Values are expressed as mean±SE. *P≤0.05; **P≤0.01.

Table 3: Serum Proteins, enzymes, BUN, Creatinine, Ca and Phos in control and Cd exposed sheep and correlation with blood Cd

	Control sheep	Exposed sheep	Blood Cd
Total Protein (g/dl)	7.02±0.11	5.86±0.07**	-0.570**
Albumen (g/dl)	3.40±0.06	2.71±0.04**	-0.675**
Globulin (g/dl)	4.31±0.09	3.15±0.08*	-0.205
A/G Ratio	0.63±0.01	0.89±0.03	-0.216
AST (IU/L)	68.92±1.39	97.70±1.77**	+0.682**
ALT(IU/L)	23.81±0.73	41.08±0.89**	+0.693**
GGT(IU/L)	37.48±2.09	72.08±1.27**	+0.763**
BUN (mg/dl)	20.38±0.31	35.27±0.44**	+0.805**
Creatinine(mg/dl)	0.68±0.03	1.03±0.02**	+0.590**
BUN / Creat. ratio	30.34±1.26	34.67±0.84	+0.395
Ca (mg/dl)	9.96±0.13	7.76±0.06**	-0.776**
Phos (mg/dl)	6.14±0.12	4.59±0.05**	-0.710**

Values are expressed as mean±SE. *P≤0.05; **P≤0.01.

Table 4: Trace elements, oxidant and antioxidants levels in both control and Cd exposed sheep and correlation with blood Cd

	Control sheep	Exposed sheep	Blood Cd
Fe (PPM)	1.48±0.03	0.54±0.05**	-0.703**
Zn (PPM)	0.86±0.01	0.56±0.01**	-0.720**
Cu (PPM)	0.19±0.01	0.10±0.00**	-0.696**
MDA (nmol/ml)	0.46±0.01	0.86±0.01**	+0.720**
SOD (U/ml)	1.37±0.03	0.89±0.02**	-0.665**
CAT (U/l)	56.92±1.15	37.88±0.64**	-0.707**
GSH-PX (mu/ml)	1.06±0.05	0.37±0.01**	-0.753**
Vitamin A (µg/dl)	83.48±2.35	60.11±0.93**	-0.679**
Vitamin E (µmol/l)	24.92±0.85	15.44±0.31**	-0.786**
Vitamin C (mg/dl)	1.07±0.07	0.69±0.02**	-0.606**

Values are expressed as mean±SE. **P≤0.01. PPM: part per million: MDA: Malondialdehyde: SOD: super oxide dismutase: CAT: catalase: GSH-PX: glutathione peroxidase.

door and prevent them from grazing. Owners may be tried to treat these sheep while others get rid of them by selling or slaughtering. So, we could not obtain any sheep aged more than five years in this study.

Hematology showed significant decrease in RBCs count, Hb, PCV, MCHC and TLC, along with non-significant decrease in MCV and MCH in exposed group compared to control group, moreover, blood Cd concentrations recorded a significant negative correlation with RBCs count, Hb, PCV and TLC as showed in Table 1. These findings agreed with the findings of Bayoumi *et al.* (2013) and Oraby *et al.* (2015).

Examination of rumen fluid revealed that physical characters were whitish green to brownish color according to type of ration, watery to sticky in consistency according to drinking state accompanied with aromatic to offensive odor. Also protozoa were microscopically low in number and motility in grazed sheep compared to control ones, this may indicate that a lower supply of cadmium for long period had a significant negative influence on the production of protozoa in the rumen leading to decrease in rumen contraction and consequently decrease in feed intake. These findings agreed with Sviatko and Zelenak (2000) and Oraby *et al.* (2015). Chemical examination of rumen fluid revealed significant increase in pH associated with significant decrease in ammonia-nitrogen, TVFAs, AST, ALT, GGT, Ca and Phos in exposed group compared to control group. These data confirmed by a significant negative correlation between rumen Cd and ammonia-nitrogen, TVFAs, AST, ALT, GGT, Ca and Ph and a significant positive correlation with pH as shown in Table 2. Significant decrease in rumen ammonia nitrogen in grazed sheep compared to control group may be attributed to decrease in urease activity due to high level of cadmium leading to reducing the rate of ammonia nitrogen release from dietary urea and this urea accumulated in the rumen and not converted to ammonia (Faixova *et al.*, 2006; Oraby *et al.*, 2015). Significant decrease in rumen TVFAs in grazed sheep compared to control group may be attributed to high level of Cd which cause damage to rumen microbiota and decrease fermentation, this prove decrease in energy intake leading to poor body condition scores, emaciation and weakness (Faix *et al.*, 2005; Mousa, 2014). Significant increase in ruminal pH of grazed sheep compared to control group may be attributed to decrease of volatile fatty acids, drinking drainage water which mainly of more alkaline pH or accumulation of urea in rumen due to inhibition of urease activity as recorded by Faixova *et al.* (2006). These results indicate that long term exposure to pollutants in drainage areas can alter the ruminal parameters of sheep and these finding agreed with Sviatko and Zelenák (2000). Published papers on effect of cadmium on rumen functions under natural conditions are very scare but presence of correlation between cadmium level and rumen parameters may suggest these all changes occurred.

Serum biochemical estimation showed significant decrease in total protein, albumin, globulin, calcium and inorganic phosphorus along with significant increase in AST, ALT, GGT, BUN and creatinine in exposed group compared to control. Furthermore, blood Cd was significantly correlated in a negative mode with serum total protein, albumin, globulin, calcium and inorganic phosphorus and a significant positive correlation with AST, ALT, GGT, BUN and creatinine as showed in Table 3. These results agreed with findings published (Zaki and Mohamed, 2012; Oraby *et al.*, 2015).

Table 5: Cd level in drinking water, rumen fluid and blood of both control and Cd exposed sheep and its correlation with each other.

	Control sheep	Exposed sheep	Water Cd	Rumen Cd
Water Cd (PPM)	0.0026±0.0005	0.304±0.041**		
rumen Cd (PPM)	0.02±0.00	0.17±0.00**	0.956**	
blood Cd (PPM)	0.01±0.00	0.12±0.01**	0.877**	0.771**

** ($P \leq 0.01$).

The most acceptable explanation to such increase in enzymatic activities could be attributed to the destructive effects of Cd on liver and kidney tissues and consequently liberating their intra cellular enzymes into the blood stream (Stoev *et al*., 2003). This confirmed by the strong positive correlations between blood Cd with serum AST, ALT and GGT.

The decrement in serum calcium and inorganic phosphorous could be attributed to the toxic effect of ingested Cd on the mucosal epithelial cell of gastrointestinal tract causing decrease of intestinal absorption of both calcium and phosphorous (Abdel-Azeem and Hafez, 2006).

Trace element status of grazing sheep showed a significant reduction in serum iron, copper and zinc compared to control group and these results could be owed to the competition of Cd with those biometals together with the reduction in appetite observed in exposed animals as showed in Table 4. These results agreed with the published literatures (El- Sharkawy *et al*., 2008; Bayoumi *et al*., 2013). The decrease in zinc level may be attributed to hypoproteinemia where most of plasma zinc is protein bound and this supported by the negative correlation recorded between serum copper, iron and zinc with blood Cd. These results confirmed that study interaction of heavy metals with essential elements help to interpret the relation between heavy metals and the nutritional problems occur in the exposed animals. Thus, supplementation of copper, iron and zinc is essential in treatment and prevention of toxic effect of Cd.

Oxidant status of grazing sheep showed significant increase in serum Malondialdehyde (MDA) levels which in accordance with those previously mentioned by Kanter *et al*. (2009) and Bayoumi *et al*. (2013). Such elevation could be attributed to lipid peroxidation caused by Cd. The strong positive correlations between serum and MDA with blood Cd concentrations proved the fact that MDA is a marker for lipid peroxidation caused by Cd intoxication as recorded by Deger *et al*. (2009) and Crnogaj *et al*. (2010).

Antioxidant parameters showed significant decrease in SOD, CAT, GSH-Px, Vit.A, Vit.E and Vit.C in exposed group compared to control. And also blood Cd concentrations recorded a significant negative correlation with SOD, CAT, GSH-Px, Vit.A, Vit.E and Vit.C as showed in Table 4. The obtained results agreed with those recorded by Ercal *et al*. (2001), Ali (2005) and Bayoumi *et al*. (2013).

Cd level estimation showed significant increase of Cd in polluted water, rumen fluid and blood in exposed sheep compared with control group and a significant positive correlation between Cd level in water, rumen and serum as showed in Table 5.

Polluted water revealed significant increase in Cd concentrations which exceed the corresponding values in water collected from non-polluted water and exceed the recommended permissible limits recorded by WHO (2004). The obtained results were in accordance to those reported by Ali (2005), Bayoumi *et al*. (2013) and Oraby *et al*. (2015). The high concentrations of Cd in drainage water could be attributed mostly to the high level of pollution from continuous discharge of sewage, industrial and agriculture effluents. Agricultural wastes include a wide range of organic materials (often containing pesticides), animal wastes, sewage sludge, and phosphate fertilizer beside industrial wastes and its contents from heavy metals. This high-risk value indicated that many notices, awareness, laws, information and impressive attention should be taken to use this drainage water to plant irrigation or animal drinking rather than for human consumption.

Significant increase in ruminal cadmium level in grazed sheep compared to control group nearly agreed with the findings of Faix *et al*. (2005), who recorded high Cd level in rumen wall of grazed sheep and (Oraby *et al*., 2015). Mean values of blood Cd concentrations showed significant increase in exposed sheep compared to control group. Our results agreed with those recorded by Zaki and Mohamed (2012) and Bayoumi *et al*. (2013).

Conclusion

Exposure of sheep to cadmium pollutant has adverse effect on body condition scores, rumen functions, liver and kidney functions; reduction in antioxidants activity which enhances occurrence of infectious and non-infectious diseases. Significant alterations and correlations were detected in this study; these results should be put in consideration in interpretation of affected animals' status and during treatment and control of Cd exposed sheep cases.

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