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Original Research Article

The Effect of Cadmium on Hematology, Oxidative Stress Liver and Kidney Function in Rats

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Abstract: This study aimed to know the effect of cadmium on hematology, oxidative stress liver and kidney function in rats. The study utilized a sample of thirty male Sprague Dawley Albino rats, aged 2-3 months, who were in good health. The rats had an average weight of 180 grams. These were divided into 2 groups (15 rats in each group). Group 1 (G1): involved the administration of a daily dose of 1 mg CdCl2/kg in a 0.9% NaCl solution via subcutaneous injection for a duration of two weeks. This approach was employed to ensure that the application of Cd^{2+} was carefully regulated and maintained at a consistent level. Group 2 (G2): consisted of rats that were administered equal amounts of sterile 0.9% sodium chloride solution via subcutaneous injections. Following a period of two weeks, the animals underwent anesthesia using pentobarbital (0.6 ml/kg). Subsequently, blood samples were obtained via heart puncture and divided into 2 parts first part were used for hematology by using hemolyser and second part for serum collection. This separated serum was then utilized for biochemical estimations, specifically for assessing liver and kidney function (AST, ALT, BUN, Creatinine) as well as total antioxidant. Following the sacrifice of the rats, the liver and kidney samples were subjected to fixation and subsequently embedded in paraffin blocks. Sections measuring 5 mm in thickness were then prepared from these blocks. These sections were stained using the (H&E) staining method. The current results showed that WBCs were decreased significantly in G1 as compared with another, while other parameters RBCs, PCV, Hb, MCV showed no significant differences between both groups. The present results showed a significant increase in AST and ALT in G1 as compared with control group, while the total antioxidant activity exhibit significant decrease in G1 as compared with control group. Histopathological investigations revealed evidence of hepatic and renal damage induced by exposure to cadmium. The hepatic damage observed following exposure to Cd was characterized by widespread degeneration and necrosis of hepatocytes, along with inflammation, cytoplasmic vacuolization, and the presence of various cellular debris within the central liver vein, as compared to the control group. The rats that were exposed to Cd intoxication exhibited cellular changes in the glomeruli, congestion in the cortex, and outer medulla. These changes included loss of the tubular brush border, interstitial edema, and necrosis of the epithelium, these observations were in contrast to the control group. In conclusion, our study has provided confirmation that Cadmium (Cd) exhibits interactions within environmental conditions. The present study demonstrates that the interaction observed in the liver is primarily synergistic, as evidenced by both histological and biochemical findings. Furthermore, an antagonistic relationship was observed between the two toxic metals in relation to kidney markers, specifically urea levels.

Keywords: Liver, Kidney, Cadmium, Hematology, Histology.

INTRODUCTION

Heavy metals pose a significant risk due to their propensity for bioaccumulation. Bioaccumulation refers to the progressive elevation of a chemical's concentration within a living organism over a period of time, relative to the chemical's concentration in the surrounding environment [1]. The accumulation of compounds in living organisms occurs when their uptake and storage rates exceed their rates of metabolism or excretion. The

toxicity of heavy metals can lead to impaired or diminished cognitive and central nervous system functioning, decreased levels of energy, and harm to the composition of blood, lungs, kidneys, liver, and other essential organs [2].

Prolonged exposure can lead to gradual physical, muscular, and neurological degeneration, resembling the symptoms of Alzheimer's disease, muscular dystrophy, Parkinson's disease, as well as multiple sclerosis. Allergies are a prevalent occurrence, and prolonged and repetitive exposure to certain metals or their compounds has the potential to induce carcinogenesis [3].

Environmental contamination by heavy metals has become a growing ecological and global public health concern [4]. Heavy metals play a crucial role in numerous biological processes, but their toxicity becomes evident at elevated concentrations. Extensive research has demonstrated that heavy metals can induce teratogenic effects during the embryonic stage, exhibiting dose-dependent relationships that result in congenital disorders, growth impairment, delayed cognitive development, morphological alterations, or other congenital disorders, without accompanying structural malformations [5].

Cadmium (Cd) is a prevalent industrial and environmental contaminant, primarily originating from various sources such as battery manufacturing, electroplating, pigment production, plastic manufacturing, fertiliser industries, and the combustion of cigarette smoke. Cadmium (Cd) poses a potential hazard to human health due to its bioaccumulation in plants and animals, which are subsequently consumed by humans [6].

The cited studies [7, 8], demonstrate the diverse mechanisms of toxicity exhibited by cadmium in specific species across various experimental settings. Previous studies have provided evidence that the presence of Cd induces the generation of free radicals, leading to the oxidative degradation of lipids, proteins, and DNA. This process has been found to initiate a range of pathological conditions in both humans and animals [8]. After being absorbed, cadmium (Cd) is promptly eliminated from the bloodstream and accumulates in different tissues. The long-term exposure to inorganic cadmium (Cd) leads to the buildup of this metal primarily in the liver and kidneys, as well as in various other tissues and organs. This accumulation causes numerous metabolic and histological alterations, membrane impairment, modified gene expression, and programmed cell death [9]. This study aimed to know the effect of cadmium on hematology, oxidative stress liver and kidney function in rats.

MATERIALS AND METHODS

The study utilized a sample of thirty male Sprague Dawley Albino rats, aged 2-3 months, who were in good health. The rats had an average weight of 180 grams. These were divided into 2 groups (15 rats in each group).

Group 1 (G1):

Involved the administration of a daily dose of 1 mg CdCl2/kg in a 0.9% NaCl solution via subcutaneous injection for a duration of two weeks. This approach was employed to ensure that the application of Cd^{2+} was carefully regulated and maintained at a consistent level.

Group 2 (G2):

Consisted of rats that were administered equal amounts of sterile 0.9% sodium chloride solution via subcutaneous injections.

Following a period of two weeks, the animals underwent anesthesia using pentobarbital (0.6 ml/kg). Subsequently, blood samples were obtained via heart puncture and divided into 2 parts first part were used for hematology by using hemolyser and second part left undisturbed for a duration of 30 minutes to allow for clotting. The serum was separated through centrifugation at a speed of 2500 revolutions per minute for a duration of 15 minutes. This separated serum was then utilized for biochemical estimations, specifically for assessing liver and kidney function (AST, ALT, Urea, Creatinine) as well as total antioxidant. Following the sacrifice of the rats through cervical dislocation, the abdominal region of the euthanized animals was promptly incised. Subsequently, the kidney and liver were carefully dissected and rinsed with Ringer Buffered Solution. Afterward, they were dried using filter paper and promptly transferred to the incubation medium.

Following the act of sacrifice, a representative sample of liver and renal tissue was promptly extracted for histopathological study.

Statistical analysis was done by using SPSS version 25.

RESULTS

The current results showed that WBCs were decreased significantly in G1 as compared with another, while other parameters RBCs, PCV, Hb, MCV showed no significant differences between both groups (Table 1).

Table 1: Hematological parameters in groups of the study

Parameters	G1	G2
Total WBCs (10^9/L)	3.49 ± 0.2b	3.82 ± 0.16a
RBCs (10^{12}/L)	5.53 ± 0.37a	6.84 ± 0.11a
PCV (L/L)	0.33 ± 0.02a	0.39 ± 0.04a
HB (g/L)	136±5.3a	148.5±8.2a
MCV (fl)	57± 2.4a	56.7± 3.1a
MCH (pg)	23.1 ± 2.1a	21.2 ± 2.6b

The present results showed a significant increase in AST and ALT in G1 as compared with control group, while the total antioxidant activity exhibit significant decrease in G1 as compared with control group (Table 2).

Table 2: Biochemical analysis and total antioxidant activity in both groups

Groups	AST (U/L)	ALT (U/L)	BUN (mmol/L)	Creatinine(µmol/L)	Total antioxidant activity (µmol/ L)
G1	184.3±8.2a	48.4±1.9a	8.3±0.3b	44.3±1.2a	3.72±0.1b
G2	104±2.1b	32.8±4.7b	10.7±0.5a	41.9±2.3a	6.23±0.09a

Histopathological investigations revealed evidence of hepatic and renal damage induced by exposure to cadmium. The hepatic damage observed following exposure to Cd was characterized by widespread degeneration and necrosis of hepatocytes, along with inflammation, cytoplasmic vacuolization, and the presence of various cellular debris within the central liver vein (Figure 1), as compared to the control group (Figure 2).

The rats that were exposed to Cd intoxication exhibited cellular changes in the glomeruli, congestion in the cortex, and outer medulla. These changes included loss of the tubular brush border, interstitial edema, and necrosis of the epithelium, as depicted in Figure 3. These observations were in contrast to the control group, as shown in Figure 4.

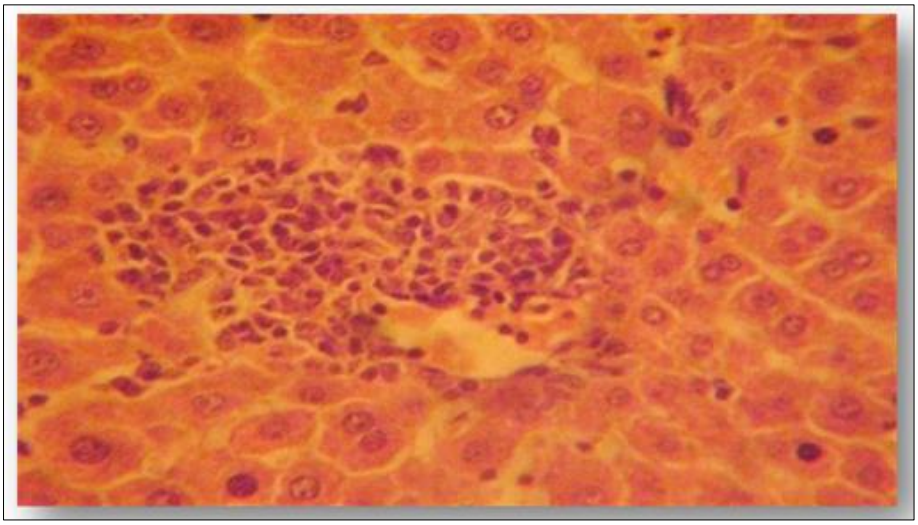

Figure 1: Histological section of liver of rat treated with $CdCl_2$ (50ppb) in drinking water (T1). Note: inflammatory cell infiltration mainly neutrophil and macrophage in liver parenchyma, and around the central vein, as well as in sinusoid (H and E, X40)

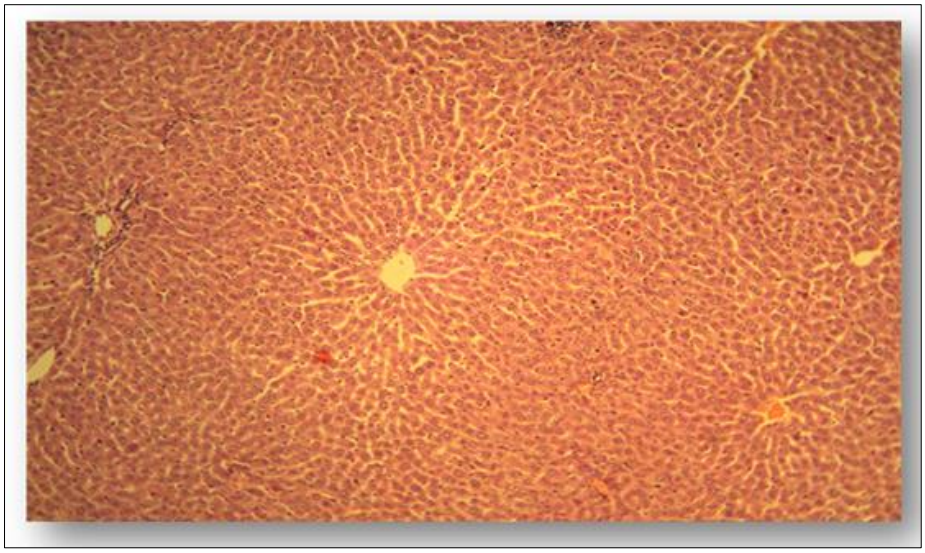

Figure 2: Histological section of normal liver of rat (H and E, X40)

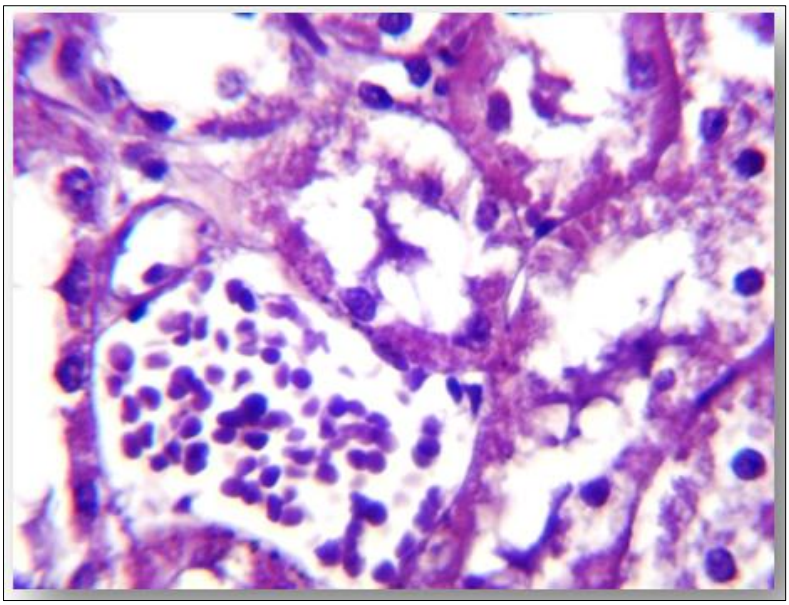

Figure 3: Histological section in the kidney of rats in G1 showed congestion of the blood vessels with inflammatory cells in their lumen, vacuolation and sloughing of epithelial lining cells of renal tubules (H &E stain; 40X)

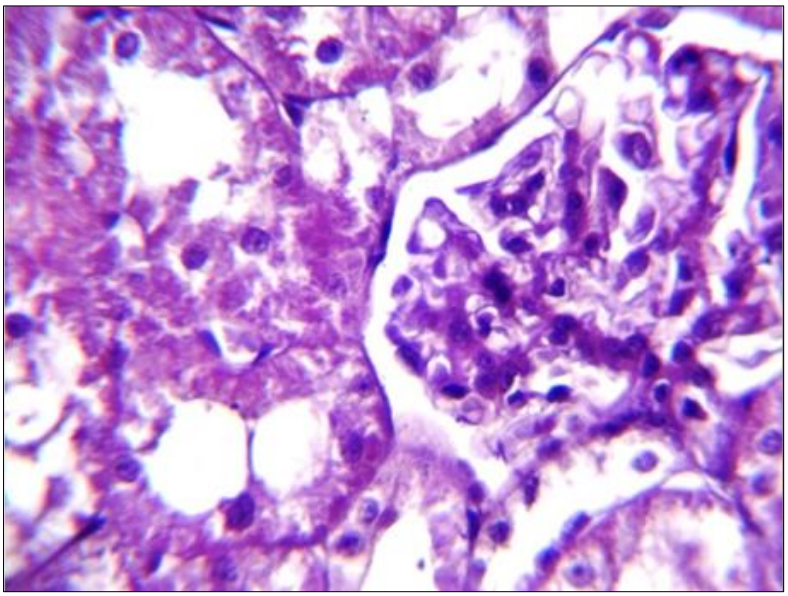

Figure 4: Histological section in the kidney of rats in G2 showed no clear lesion (H&E stain; 40X)

DISCUSSIONS

The hematopoietic system is considered to be highly susceptible to toxicity evaluation. Following oral administration, cadmium (Cd) experience intestinal absorption and are subsequently transported through the bloodstream. Within the circulatory system, these substances have the ability to be transported through the utilisation of red blood cells and plasma proteins, particularly albumin [10, 11].

The administration of toxic metals resulted in a decrease in red blood cell count (RBC), haemoglobin (HGB) levels, and packed cell volume (PCV). The findings of our study align with those of previous researchers who utilised various animal models, exposure routes, and dosage regimens. These researchers also reported reductions in red blood cell count (RBC), haemoglobin (HGB), and hematocrit (HCT) levels [12, 13]. It is reasonable to hypothesise that the observed decrease in red blood cell count (RBC), haemoglobin (HGB), and hematocrit (HCT) levels may be attributed to intravascular hemolysis, given the elevated concentrations of these metals in the blood of the rats, as compared to the control group. The administration of acute treatments for the studied toxic metals did not result in any significant alterations in mean corpuscular volume (MCV) or mean corpuscular haemoglobin concentration (MCHC), which is consistent with findings reported by other researchers [12-14]. The current study showed a significant decrease in WBCs in G1 group, these were in agreement with many studies [15, 16]. Many studies reported that cadmium induced

liver toxicity which causes increase in the liver enzymes like AST and ALT, these were compatible with previous results [17, 18]. The experimental dosage regimes resulted in a significant decrease in the renal profile parameter, urea, when compared to untreated animals. Conversely, there was an observed increasing trend in creatinine levels. Alterations in the concentrations of urea and creatinine serve as indicators that the renal excretory function may be compromised, even subsequent to the administration of a solitary dose of toxic metals. Other studies have also reported similar findings regarding the alterations in urea and creatinine levels [13-16]. According to [18], it has been documented that Cd is a highly toxic metal that poses significant harm to individuals due to its ability to accumulate in tissues and induce metabolic, histological, and pathological alterations. The oxidative damage resulting from exposure to Cadmium (Cd) is attributed to its disruption of the delicate equilibrium between prooxidants and antioxidants within the tissues. Additionally, it was announced that the induction of oxidative stress damage by Cd occurs through the disruption of the cellular prooxidant-antioxidant balance. The current study observed hepatoportal blood vessel congestion, central vein congestion, portal tract edoema, and fatty changes in the liver of rats treated with mercury, suggesting the toxic impact of mercuric chloride. Previous studies have demonstrated that in cases of liver disease, certain cells within the liver undergo activation due to the release of factors by liver hepatocytes and Kupffer cells. These activated cells then undergo proliferation and exhibit characteristics similar to myofibroblasts, with or without the presence of lipid droplets [19]. Histopathological findings are consistent with the diagnosis of tubulo-interstitial nephritis. The progression of nephrotic syndrome, which predominantly affects the tubules but also the surrounding blood vessels and connective tissue, was found in cadmium-exposed rats. In addition, glomerular lesions arise secondarily, affecting the capillary loop and the epithelial cells [20].

CONCLUSION

Our study has provided confirmation that Cadmium (Cd) exhibits interactions within environmental conditions. The present study demonstrates that the interaction observed in the liver is primarily synergistic, as evidenced by both histological and biochemical findings. Furthermore, an antagonistic relationship was observed between the two toxic metals in relation to kidney markers, specifically urea levels.

Conflict of Interest: No conflict of interest is associated with this work

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