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Gender Differences in the Effects of Cadmium Exposure on Hematological Parameters in Wistar Rats

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

This study aims to investigate the gender dimorphism in cadmium exposure on hematological parameters in male and female Wistar rats. Twenty Wistar rats (120g-150g) were divided into four groups: male control, male cadmium-treated, female control, and female cadmium-treated. Cadmium chloride (50 mg/kg) was administered orally to the experimental groups for 45 days.

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Hematological parameters were analyzed using an auto hematological analyzer. Data were statistically evaluated using two-way ANOVA with significance set at $p < 0.05$. Cadmium exposure significantly increased white blood cell (WBC) counts in male rats compared to controls, with notable decrease in neutrophils and an increase in lymphocytes. Female rats showed significant increase in monocyte and basophil levels. Furthermore, red blood cell (RBC) parameters showed significant reductions in hemoglobin concentration, mean corpuscular volume (MCV), and mean corpuscular hemoglobin (MCH) in female cadmium-treated rats. No significant effects were observed on platelet count or distribution width in both male and female rats. The study concluded there are gender-specific hematological alterations due to cadmium exposure in Wistar rats. These findings underscore the need for gender-specific approach in the understanding and amelioration of cadmium toxicity.

Keywords: Gender dimorphism; cadmium exposure; hematological parameters.

1. INTRODUCTION

Cadmium (Cd) is a noxious heavy metal that has substantial environmental and occupational health ramifications [1]. Cadmium has been utilised in the manufacturing of nickel-cadmium batteries, as well as in the production of paint pigments, electroplating, and the creation of polyvinyl chloride plastic [2]. Moreover, cadmium is found in the majority of food items, and its concentration fluctuates significantly depending on dietary patterns [3]. Cadmium is present in the environment to a significant extent due to human activities, including the utilisation of fossil fuels, the combustion of metal ores, and the burning of waste materials [4]. Furthermore, the release of sewage sludge into agricultural soil can result in the transfer of cadmium compounds that have been absorbed by plants. This transfer can have a substantial impact on the food chain and lead to the accumulation of cadmium in different human organs. Additionally, cigarette smoke is another significant source of cadmium exposure. Analysis of blood samples from smokers revealed that their cadmium levels were 4-5 times greater than those of non-smokers [3].

Cadmium exposure, whether by breathing it in, swallowing it, or coming into touch with it on the skin, can cause a range of negative impacts on human health. Various studies have investigated the deleterious effects of cadmium exposure in human and animals. Reports of lung damage in workers exposed to Cd were documented as far back as the 1930s [5]. Furthermore, in the subsequent decades, there were documented instances of bone and renal toxicity resulting from exposure to cadmium [6]. Animal studies provide conclusive evidence that cadmium and its compounds can cause the development of both benign and malignant tumours at different locations in numerous species of experimental animals, regardless of the method of exposure [7,8,9,10].

Previous studies have also investigated the effects of cadmium exposure on haematological parameters. It was reported that cadmium intoxication led to decreased values of erythrocytes, hemoglobin and hematocrit in Wistar rats [11]. However, Bojarski et al. [12] reported cadmium exposure caused increased red blood cell counts, hemoglobin concentration, and hematocrit value in newly hatched Gallus gallus domesticus chicks. In an old study by Johansson-Sjöbeck & Larsson [13] significant reductions of hematocrit, hemoglobin, and red blood cell counts were observed in the cadmium-exposed fish. Furthermore, in humans, cadmium exposure may cause damage to hemopoietic system [14]. The effect may therefore depend age and type of animals used for the studies. Also, till date, the gender disparity in the effect of cadmium exposure on hematological parameters is yet to be well assessed. Therefore, this study aims to investigate the effects of cadmium exposure on hematological parameters in male and female Wistar rats.

2. METHODS

2.1 Animals

Twenty (20) Wistar rats weighing 120–150 g were used for this study. We obtained the animals from the Department of Anatomy at Ladoke Akintola University of Technology, Ogbomoso, Nigeria. Animals were acclimitised for two weeks before the commencement of the experiment.

2.2 Groupings

Five female animals were assigned to a female control group; another five female animals were

assigned as the female experimental animals; five male animals were assigned as the male control group, and the remaining five male animals were assigned as the male experimental animals. Throughout the study, we measured and recorded the rats' daily body weight changes using a digital weighing scale.

2.3 Exposure

The experimental rats received cadmium chloride (50 mg/kg) orally for 45 days, while the control rats received distilled water daily.

2.4 Biochemical Analysis

We sacrificed all rats with cervical dislocation. We immediately performed a cardiac puncture and collected and stored each rat's blood in an EDTA bottle for haematological analysis. Haematological parameters were analysed using a Mindray auto haematological analyzer (Shenzhen Mindray Bio-Medical Electronics, Co., Ltd., China).

2.5 Statistical Analysis

All results were presented as mean ± standard error of mean. For statistical analysis of the results, the two-way analysis of variance test was used. The statistical significance of the tests was represented as $p < 0.05$.

3. RESULTS

3.1 Effect of Gender on white Blood Cells Count Following Cadmium Exposure in Rats

Fig. 1 shows no significant difference between the white blood cell count between the female and male controls of the rats used in this study. However, cadmium exposure significantly increased white blood cell count in the male rats compared to the female and male control rats.

3.2 Effect of Cadmium Exposure on Neutrophil Count

Fig. 2 demonstrated the gender bias in neutrophil count following cadmium treatment. It was observed that there is no significant difference between the neutrophil count of the female and male control rats. In contrast, the male neutrophils were significantly suppressed following cadmium treatments compared to the male control and the cadmium-treated female rats.

3.3 Effect of Cadmium Exposure on Lymphocyte Count in Female and Male Rats

As shown in Fig. 3, cadmium exposure significantly increased lymphocyte levels in the male rats when compared to the female rats that were exposed to cadmium and their respective male and female controls.

3.4 Effect of Cadmium Exposure on Monocyte Count in Female and Male Rats

The results of the monocyte count as shown in Fig. 4 demonstrated that cadmium significantly increased monocyte levels in female rats, and an insignificant increase the male rats when compared to the respective controls.

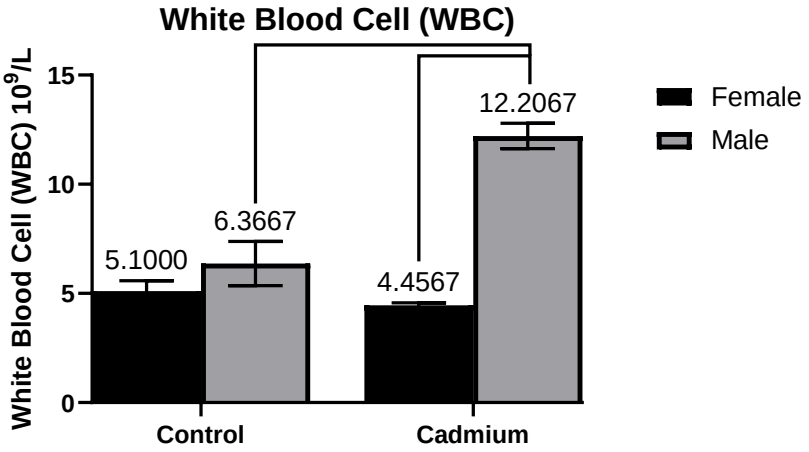

Fig. 1. Effect of gender on differential white blood cell count in cadmium-treated rats

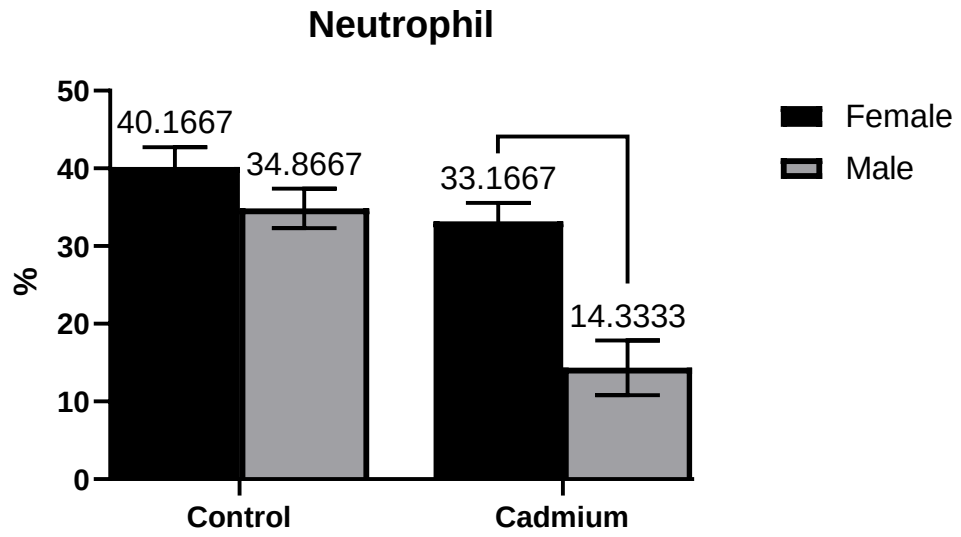

Fig. 2. Effect of cadmium exposure on neutrophil count

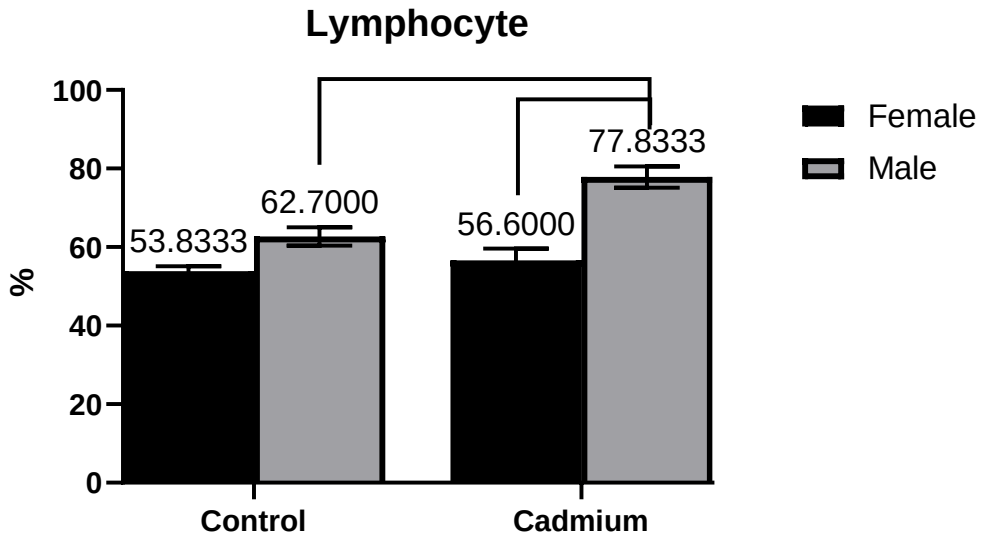

Fig. 3. Effect of cadmium exposure on lymphocyte count in female and male rats

A comparison of the female and male rats treated with cadmium showed a significant elevation in the level of monocytes in the female cadmium-treated rats when compared to the male cadmium-treated rats.

3.5 Effect of Cadmium Exposure on Eosinophil Level in Female and Male Rats

Results obtained for the eosinophil counts as shown in Fig. 5, cadmium treatment increased eosinophils levels in female rats when compared to the male treated rats. However, when compared to their respective controls the observed increment is insignificant.

3.6 Effect of Cadmium Exposure on Basophil Count in Female and Male Rats

Fig. 6 showed no significant difference in the basophil count in both the female and male control rats. However, the cadmium-exposed

female showed a significant increase in their level of basophils when compared to the control female, while the cadmium-treated male also showed an increase in their level of basophils, this is an insignificant increase when compared to the control male rats. A comparison of the effect of gender in cadmium-treated rats showed a significant elevation of the basophil count of the cadmium-treated female rats when compared to their male counterparts.

3.7 Effect of Cadmium Exposure on Red Blood Cell Count in Female and Male Rats

As observed in Fig. 7, there is no significant difference in the red blood cell count of the female and male control rats. Upon treatment with cadmium, the male showed an insignificant decrease in red blood cell count of the female rats when compared to their control, and an

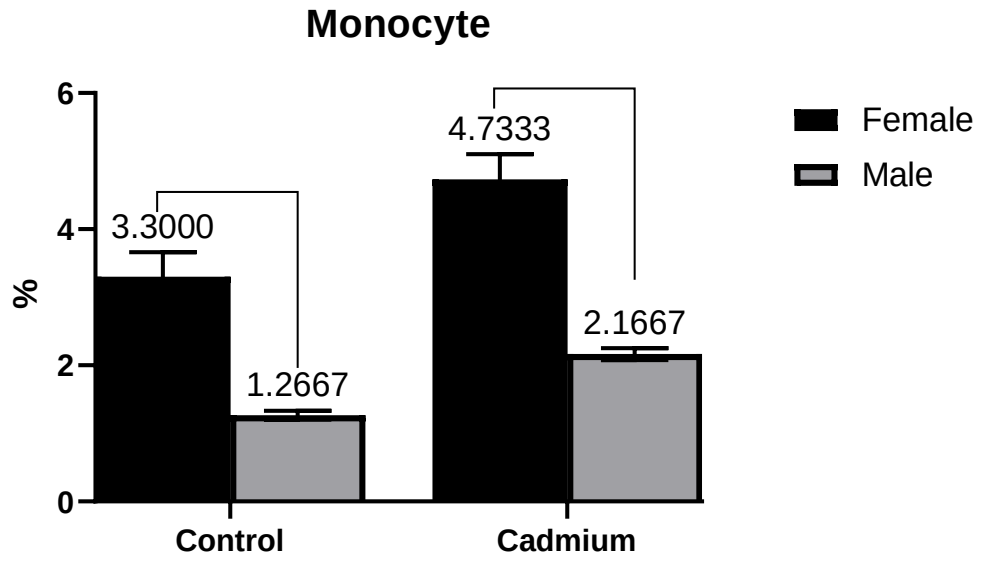

Fig. 4. Effect of cadmium exposure on monocyte count in female and male rats

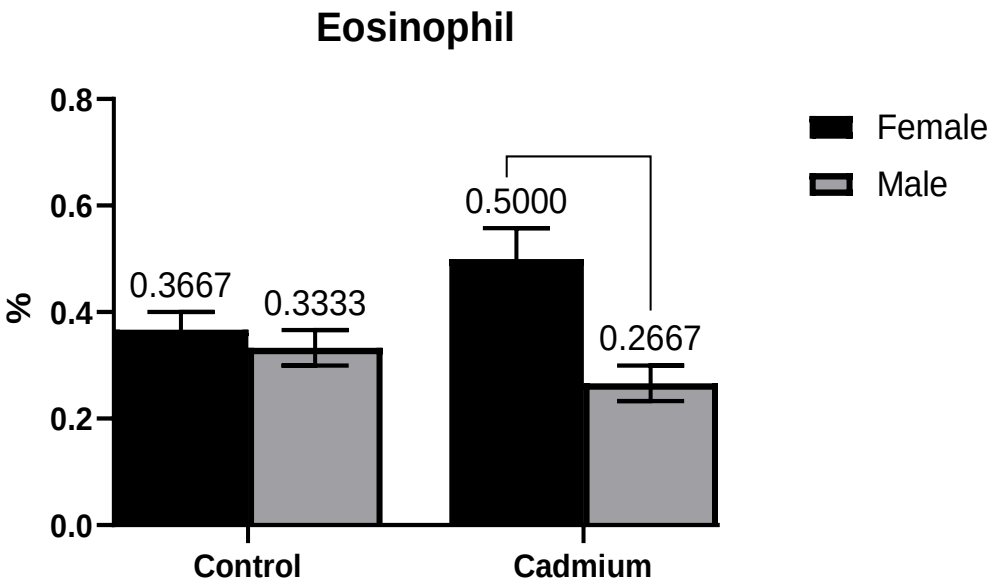

Fig. 5. Effect of cadmium exposure on eosinophil level in female and male rats

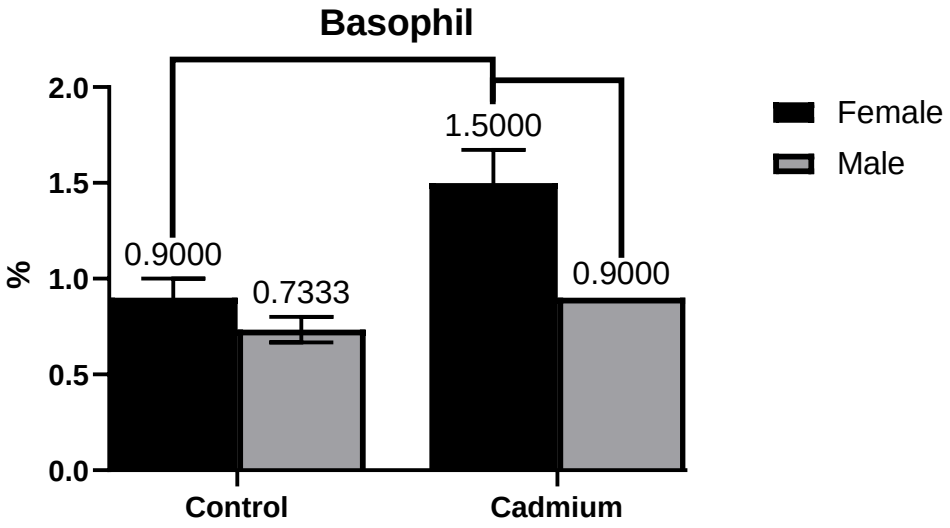

Fig. 6. Effect of cadmium exposure on basophil count in female and male rats

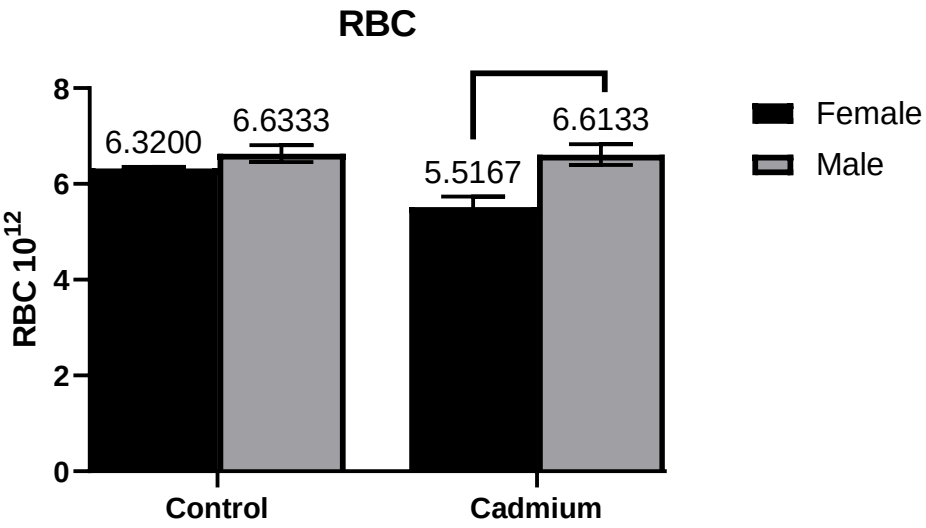

Fig. 7. Effect of cadmium exposure on red blood cell count in female and male rats

insignificant increase in the male treated with cadmium when compared to their control. Evaluation of the gender difference in the RBC count showed an elevated increase in RBC level in the male cadmium-treated group when compared to the female cadmium-treated rats.

3.8 Effect of Cadmium Exposure on Hemoglobin Concentration in Female and Male Rats Treated With Cadmium

Fig. 8 demonstrates that there is no significant difference in the haemoglobin concentration levels of the female and male control rats. However, the cadmium-treated female rats exhibited a significant reduction in their haemoglobin concentration when compared to the control female rats, while the male cadmium-treated rats showed no difference in their haemoglobin concentration. However, a comparison between female and male cadmium-treated rats revealed that the female rats had a significant reduction in their hemoglobin concentration when compared to the male cadmium-treated rats.

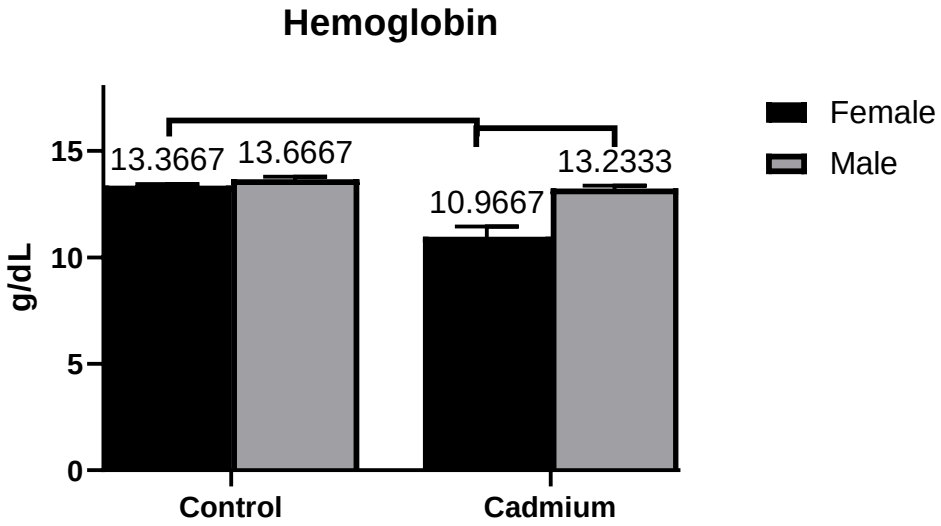

Fig. 8. Effect of cadmium exposure on hemoglobin concentration in female and male rats treated with cadmium

3.9 Effect of Cadmium Exposure on the Hematocrit Level in Female and Male Rats

Fig. 9, showed the female and male controls had no significant difference in their hematocrit levels. While treatment with cadmium reduced the hematocrit levels in both female and male rats. This is only significant in the female rats when compare to its control.

3.10 Effect of Cadmium Exposure on Mean Cell Volume (MCV) in Female and Male Rats

The mean cell volume of the controls as shown in Fig. 10, the female control had a significantly higher MCV in comparison to the male. Exposure to cadmium reduced the mean cell volume in both female and male cadmium-treated rats but significantly in the female only.

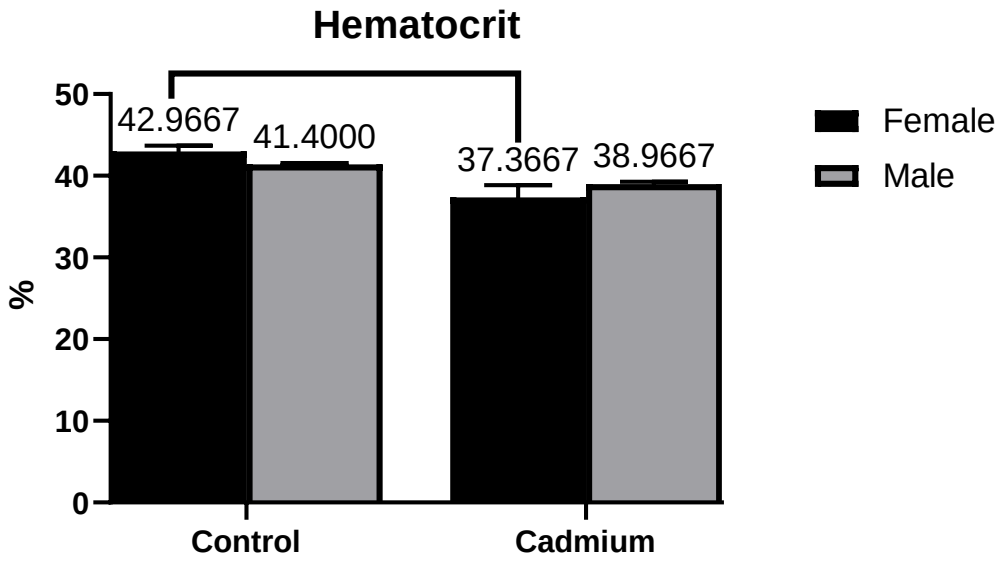

Fig. 9. Effect of cadmium exposure on the Hematocrit level in female and male rats

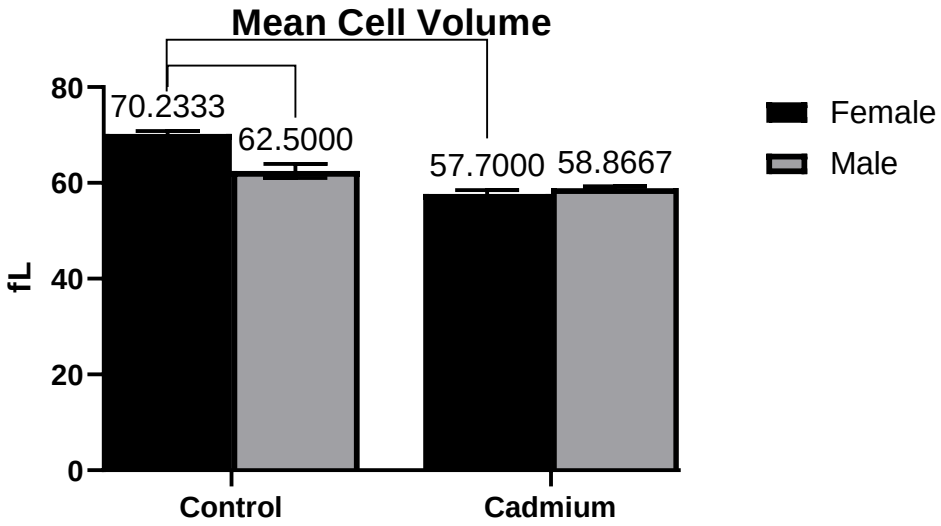

Fig. 10. Effect of cadmium exposure on mean cell volume (MCV) in female and male rats

3.11 Effect of Cadmium Treatment on Mean Corpuscular Hemoglobin Female and Male Cadmium-Treated Rats

The mean corpuscular haemoglobin is higher in the female than male controls, cadmium exposure significantly reduced the MCH levels in female cadmium-treated rats when compared to the female control. However, there is no significant difference between the female and male cadmium-treated rats MCH levels.

3.12 Effect of Cadmium Treatment on Mean Corpuscular Hemoglobin Concentration (MCHC) on Female and Male Rats

The results obtained for the MCHC showed no significant difference in both female and male controls, the male control, and cadmium-treated male rats (Fig. 12). However, there is a significant increase in MCHC levels in the cadmium-treated female when compared to their control female rats.

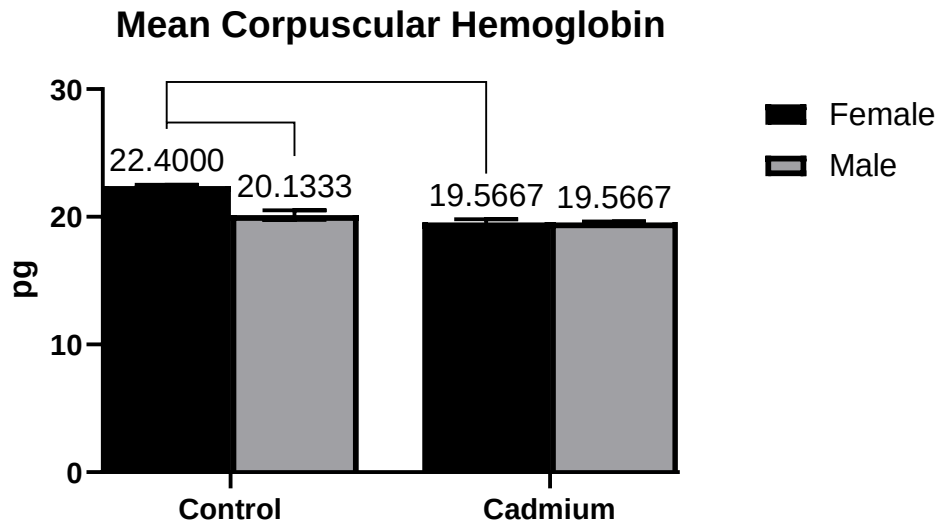

Fig. 11. Effect of cadmium treatment on mean corpuscular hemoglobin female and male cadmium-treated rats

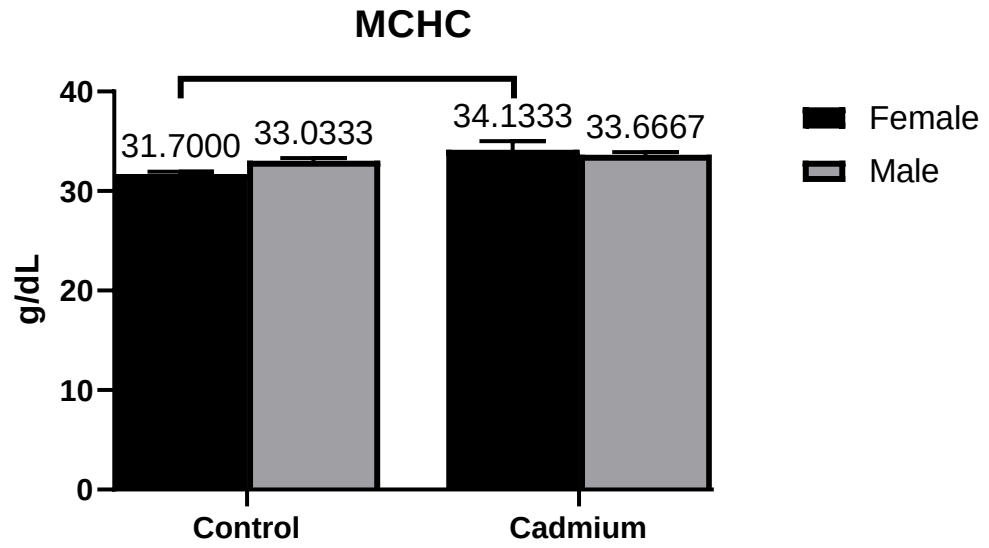

Fig. 12. Effect of cadmium treatment on mean corpuscular hemoglobin concentration (MCHC) on female and male rats

3.13 Effect of Cadmium Exposure on Red Blood Cell Distribution Width-CV in Female and Male Rats

The effect of cadmium exposure on RDW-CV was evaluated as shown in Fig. 13, the female control had a significantly higher RDW-CV than the male. Upon cadmium exposure, the female cadmium-treated rats had a significantly lower RDW-CV than the control group and the male cadmium-treated rats had a significantly higher RDW-CV than the control male rats. The effect of gender evaluated showed that the female cadmium-treated rats had a significantly lower RDW-CV than the male rats exposed to cadmium.

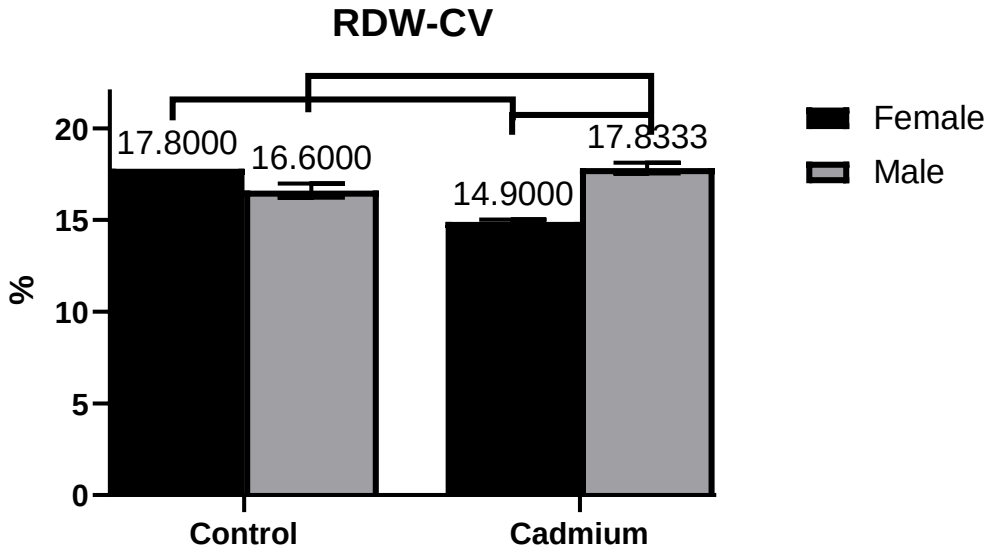

Fig. 13. Effect of cadmium exposure on red blood cell distribution width-CV in female and male rats

3.14 Effect of Cadmium Exposure on Female and Male Rats RDW-SD

The female control rats had a significantly higher RDW-SD than the male control rats (Fig. 14). In addition, the female cadmium-treated rats had a significantly lower RDW-SD than female male control rats and the male cadmium-treated rats also had a significantly lower RDW-SD than the male control rats. Assessment of the gender difference showed that the female rats exposed to cadmium demonstrated a significantly lower RDW-SD than the male cadmium-exposed rats.

3.15 Effect of Cadmium Exposure on Platelet Counts in Female and Male Rats Exposed to Cadmium

Fig. 15 shows that the female control had a significantly lower platelet count than the male control rats. However, upon cadmium exposure, there is an insignificant increase between the female and male cadmium-treated rats and their respective controls. Just as observed in the controls, the male rats treated with cadmium had a significantly higher platelet count than the female cadmium-treated rats.

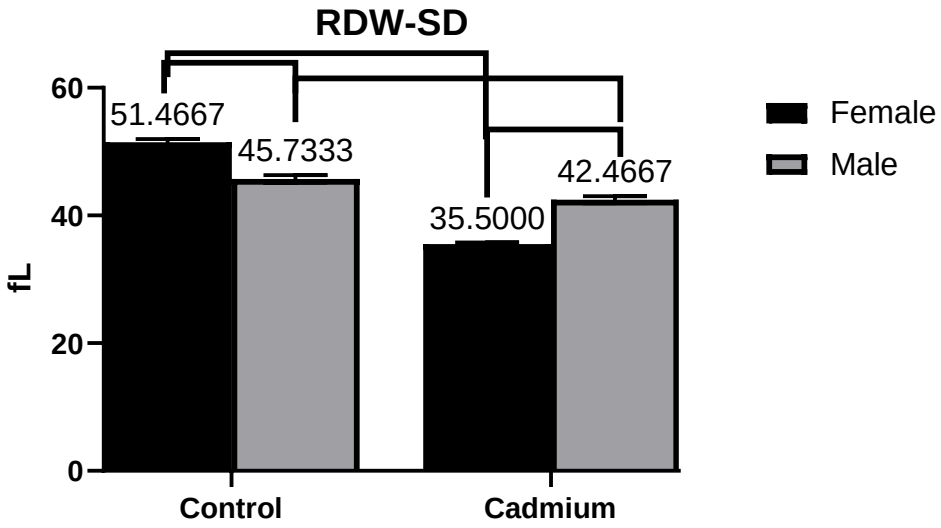

Fig. 14. Effect of cadmium exposure on female and male rats RDW-SD

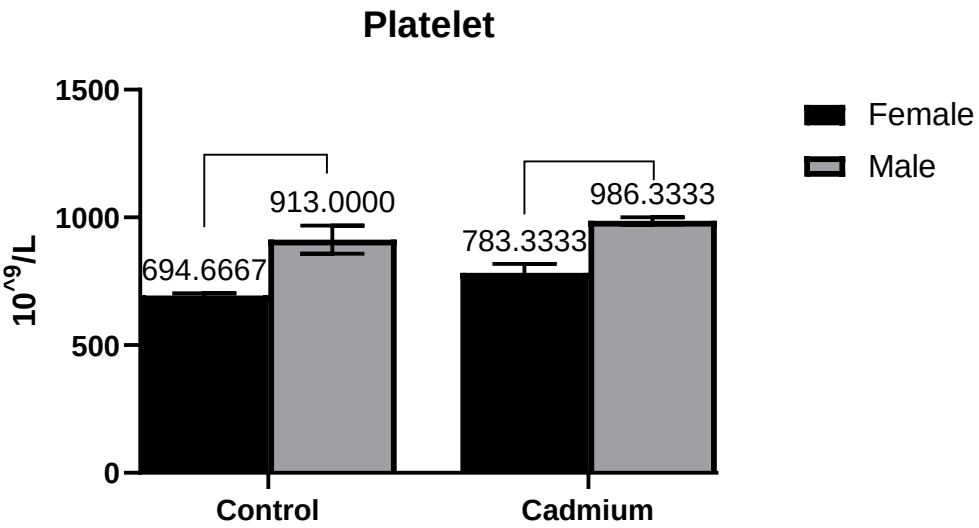

Fig. 15. Effect of cadmium exposure on platelet counts in female and male rats exposed to cadmium

3.16 Effect of Cadmium Exposure on Platelet Volume in Cadmium-exposed Female and Male Rats

As observed in Fig. 16, cadmium treatment had no significant effect on the mean platelet volume in male and female rats treated with cadmium on comparison between the male and female, and also with their respective controls.

3.17 Effect of Cadmium Exposure on Platelet Distribution Width in Female and Male Rats

As shown in Fig. 17, there is no significant difference between the platelet distribution width of the respective controls and cadmium-treated groups.

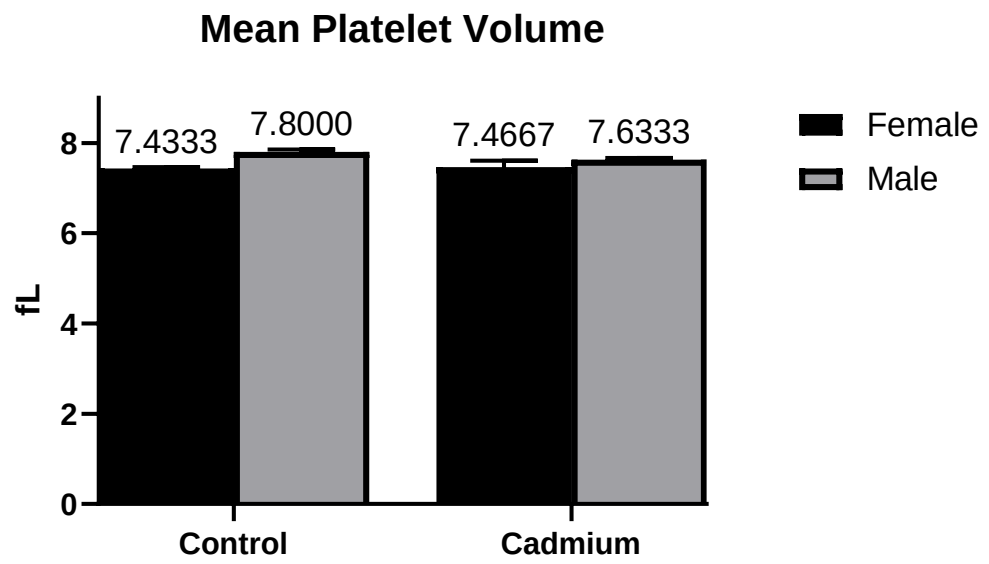

Fig. 16. Effect of cadmium exposure on platelet volume in cadmium-exposed female and male rats

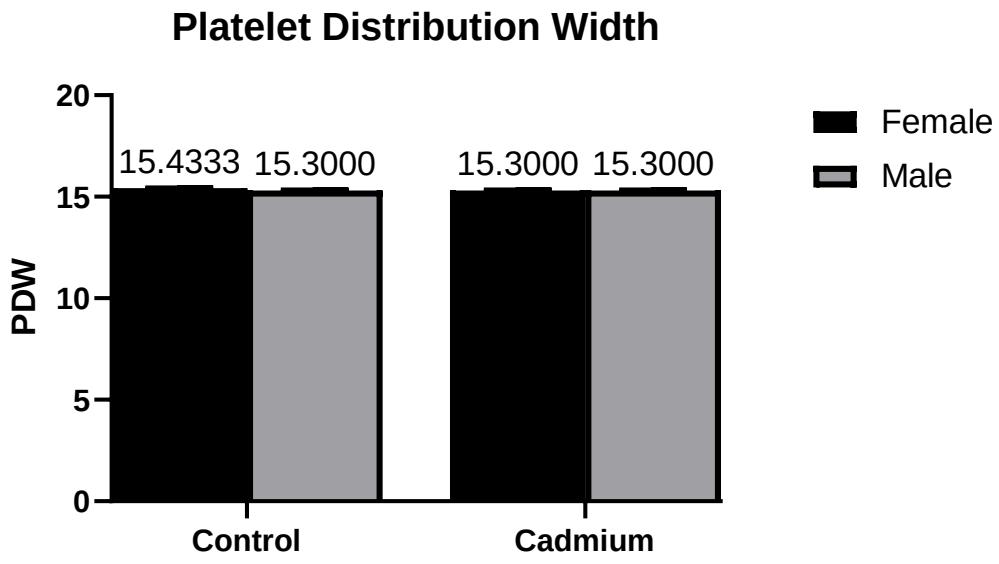

Fig. 17. Effect of cadmium exposure on Platelet distribution width in female and male rats

4. DISCUSSION

This study investigates the gender-specific haematological responses to cadmium exposure in Wistar rats, providing insights into how cadmium toxicity differentially affects male and female subjects. The findings reveal significant variations in white blood cell (WBC) counts, red blood cell (RBC) parameters, and platelet characteristics. In this study, cadmium exposure caused a significant increase in WBC count only in cadmium-exposed male rats compared to both male and female controls. On the differential WBC count, there are significant gender differences. In male rats, exposure to cadmium significantly suppresses neutrophils. However, it significantly increases lymphocyte levels in male rats compared to cadmium-treated female rats. In female Wistar rats, cadmium exposure significantly increases monocyte and basophil levels compared to cadmium-exposed male Wistar rats.

Cadmium exposure caused female rats to have a reduced RBC compared to their male counterparts. However, there was no significant difference between the RBC count in the female control and female exposed groups. In female cadmium-treated rats, there was a significant reduction in hemoglobin concentration compared to both female control and male cadmium-treated rats. In addition, there was a significant reduction in haemoglobin concentration in female cadmium-treated rats compared to only the female control. Cadmium-exposed female rats showed a significant reduction in MCV and MCH and a significant increase in MCHC in female rats compared to their controls. Cadmium-exposed female rats showed a significant decrease in RDW-CV compared to female control and cadmium-exposed male rats. Furthermore, there was a significant decrease in red blood cell distribution width in both genders exposed to cadmium. After exposure, females exhibit lower RDW-SD than males. In both genders, cadmium exposure had no significant effect on platelet count, platelet volume, or platelet distribution width.

Cadmium exposure significantly suppresses neutrophil counts in male rats. This suppression could imply a compromised innate immune response, potentially increasing susceptibility to infections [15]. According to Klein & Flanagan [16], adult females show a greater innate immune response than males. This could promote greater clearance of pathogens from the body. In this study, we observe an increase in lymphocyte levels in male rats exposed to cadmium, despite Klein & Flanagan's [16] argument that females have higher adaptive responses than males. This further shows a possible gender-specific adaptive immune response. Ayilara and Owoyele [17] earlier showed that immune response is specific to each gender. On the other hand, increased apoptosis may cause the insignificant increase in lymphocyte levels found in the female mice [18]. According to Wang et al. [19], cadmium exposure induces the differentiation of immune cells, especially influencing the proportion of different white blood cells. This may explain why there are gender-specific differences in the proportion of white blood cells found in this study. For example, this study found that in female rats, cadmium exposure leads to a significant rise in monocyte and basophil levels compared to males. The increased basophil and monocyte levels suggest an enhanced allergic response in females under cadmium stress [20].

This study showed resilience in both male and female rats in RBC counts following cadmium exposure. Nikoli et al. [11]'s findings suggest a decrease in RBC counts after cadmium exposure, but the discrepancy could potentially stem from strain or exposure concentration. Haemoglobin concentration was reduced in female exposed rats, indicating a more pronounced effect of cadmium on haemoglobin synthesis or stability in females. Cadmium's ability to prevent iron absorption could interfere with hemoglobin synthesis [21]. The significant decrease in MCV and MCH in cadmium-exposed female rats further demonstrates the effect of cadmium on RBC in females, further confirming iron-deficiency anaemia [22]. In this study, cadmium-exposed rats did not show increased RDW-CV and RDW-SD, indicating the absence of anisocytosis.

Cadmium exposure showed no impact on platelet parameters in both male and female rats. Zhao et al. [23] and Dong et al. [24] reported that cadmium-exposure caused a decrease in platelet counts. The route of administration, duration of exposure, and animal strains could cause the disparity. For example, Dong et al. [24] exposed the animals intraperitoneally, while Zhao et al. [23] exposed the rats via oral route for three months. A study using rabbits observed a significant increase in platelet counts after 85

days of exposure to cadmium. Additional research is therefore required.

5. CONCLUSION

The study showed significant gender-specific haematological alterations due to cadmium exposure in Wistar rats. Males exhibit increased WBC counts and lymphocyte levels but suppress neutrophils, while females show increased monocyte and basophil levels. RBC parameters also reflect gender differences, with females experiencing more pronounced reductions in hemoglobin concentration, MCV, MCH, and RBC counts. These findings highlight the need for gender-specific considerations in understanding and ameliorating cadmium toxicity and its impacts on haematological parameters.

The effect of cadmium exposure on platelets is currently inconclusive, so additional study is required. Future research should explore the underlying mechanisms responsible for the gender differences observed in this study.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

CONSENT

It is not applicable.

ETHICAL APPROVAL

Animal Ethic committee approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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