J. Appl. Health Sci. Med., 5(1):19–24, 2025. DOI: 10.58614/jahsm513

Journal of Applied Health Sciences and Medicine

Journal homepage: https://www.jpub.org/journal-details.php?journal-id=39

Research Article

Lipid Profile Dysregulation in Postpartum and Non-Postpartum Female Wistar Rats Exposed to Pesticide Mixtures

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Article Info

Keywords: *Pesticide exposure, Lipid metabolism, Wistar rats, Postpartum adaptation, Biochemical toxicity.*

Received: *27.11.2024*
Accepted: *20.01.2025*
Published: *30.01.2025*

Abstract

This study investigated the effects of dichlorvos, dimethoate, and cypermethrin on lipid metabolism in non-postpartum and postpartum female Wistar rats. Sixty-four females were divided into eight groups (n=8/group) and exposed to pesticides for 28 days, followed by mating and postpartum assessments. Serum lipid profiles, including cholesterol (CHOL), high-density lipoprotein (HDL), low-density lipoprotein (LDL), and triglycerides (TRG), were analyzed. In non-postpartum rats Figure 1, cholesterol levels peaked at 250.3 ± 6.4 mg/dL in Group E (dichlorvos and dimethoate), significantly higher than the control (Group A, 110.2 ± 4.8 mg/dL, $p<0.05$). HDL was lowest in Group E (18.6 ± 1.2 mg/dL) compared to Group A (52.3 ± 3.1 mg/dL). LDL concentrations were also highest in Group E (155.8 ± 7.2 mg/dL) versus the control (40.5 ± 2.7 mg/dL). TRG levels were elevated in Group D (cypermethrin, 125.4 ± 5.9 mg/dL) compared to Group A (65.3 ± 3.6 mg/dL). In postpartum rats Figure 2, Group D (cypermethrin) showed the highest cholesterol (315.5 ± 7.8 mg/dL) and LDL (162.3 ± 6.4 mg/dL) levels, significantly exceeding control values of 195.3 ± 5.1 mg/dL and 55.4 ± 3.2 mg/dL, respectively. HDL was lowest in Group E (28.7 ± 1.9 mg/dL) compared to the control (60.5 ± 3.8 mg/dL). TRG levels were highest in Group D (135.7 ± 6.2 mg/dL) against Group A (70.4 ± 4.1 mg/dL). Postpartum rats exhibited relatively higher HDL levels than non-postpartum rats, suggesting adaptive mechanisms. These findings highlight the synergistic and adverse effects of pesticide mixtures on lipid profiles, emphasizing the need for regulatory measures and further research into protective interventions.

1. Introduction

The escalating use of pesticides in modern agriculture has generated significant concern about their potential impacts on health and the environment. Organophosphates such as dichlorvos and dimethoate, as well as pyrethroids like cypermethrin, are widely applied in pest control due to their high efficacy. However, their widespread usage has been associated with adverse effects on non-target organisms, including mammals, by inducing oxidative stress, metabolic dysregulation, and organ toxicity [1, 2]. These effects are particularly alarming given the increasing evidence of their cumulative and synergistic toxicological profiles, especially when pesticides are combined [3, 4].

Among the various biochemical pathways affected by pesticide exposure, lipid metabolism has emerged as a critical target. Lipids play essential roles in cellular function, including membrane structure, energy storage, and signaling processes. Disruption of lipid homeostasis is associated with several pathological conditions, such as oxidative damage, hepatic dysfunction, and cardiovascular diseases [5, 6]. Studies have shown that exposure to dichlorvos, dimethoate, and cypermethrin can elevate serum cholesterol and triglyceride levels, reduce protective

high-density lipoprotein (HDL), and increase low-density lipoprotein (LDL), thereby predisposing exposed organisms to atherogenesis and metabolic disorders [1, 7].

Furthermore, combined exposure to multiple pesticides often leads to more severe toxicological outcomes due to their synergistic interactions. [3] demonstrated that the co-administration of organophosphates and pyrethroids amplifies oxidative stress and lipid dysregulation beyond what is observed with individual pesticides. These findings align with evidence that combined exposures can interfere with lipid transport mechanisms, enzymatic activity, and hepatic lipid processing [8]. Such effects raise critical concerns about the cumulative impact of pesticides on lipid metabolism, especially in vulnerable populations.

Reproductive and physiological stages such as pregnancy, lactation, and postpartum introduce additional metabolic challenges that may exacerbate the effects of pesticide exposure. During pregnancy and lactation, there is a significant increase in energy demand and lipid mobilization to support fetal development and milk production [9]. These stages also involve hormonal changes, such as elevated estrogen levels, which may temporarily enhance antioxidant defenses and HDL production, potentially mitigating some toxic effects [1, 10]. However, despite these adaptations, the ability of female organisms to withstand pesticide-induced metabolic disruption remains poorly understood.

Emerging evidence suggests that pesticide exposure during critical biological stages not only impacts maternal health but may also have long-term and transgenerational effects on offspring. Studies have linked maternal pesticide exposure to disrupted lipid profiles in progeny, indicating a potential heritable component of metabolic dysregulation [4, 6]. These findings highlight the need for comprehensive research to understand how maternal and postpartum physiology interacts with pesticide toxicity and whether adaptive mechanisms can provide any degree of resilience.

This study seeks to fill critical knowledge gaps by assessing the biochemical impacts of dichlorvos, dimethoate, and cypermethrin on lipid metabolism in non-postpartum and postpartum female Wistar rats. By focusing on cholesterol, HDL, LDL, and triglycerides, this study provides a comprehensive evaluation of lipid dysregulation across different biological stages. It also investigates whether postpartum adaptations confer protection against pesticide-induced metabolic disturbances. The findings aim to enhance understanding of pesticide toxicity and support the development of interventions to mitigate associated health risks.

2. Materials and Methods

Reagents and solvents used in this study were of analytical grade, sourced from British Drug House, Poole, England. The research aimed to investigate the serum lipid profile impacts of a chemical mixture containing dichlorvos, dimethoate, and cypermethrin on female rats at key biological stages: exposure, mating, pregnancy, and lactation.

A total of 64 female and 16 male rats of uniform strain, age, and weight were procured for the study. The animals were acclimatized for one week to ensure optimal well-being and reduce stress-induced variability. The female rats were randomly assigned to eight groups (A–H), each comprising eight rats. The groups were exposed to graded doses of the chemical mixture, administered via a standardized route to ensure precise delivery. The exposure spanned 28 days, during which the rats' health and behavior were meticulously monitored. At the end of this phase, four rats per group (n=4) were randomly selected and sacrificed for haematological and histopathological evaluations, establishing baseline data on the exposure effects.

The remaining rats in each group were paired with two male rats per group to initiate mating. Behavioral observations confirmed successful copulation, following which the males were removed to minimize stress. The pregnant females were closely monitored for health and behavioral changes throughout gestation. After parturition, lactating dams were observed for maternal care behaviors, and the growth and health of their pups were recorded to evaluate potential transgenerational effects of the chemical exposure.

At the conclusion of the 10-day lactation period, the lactating dams were sacrificed, and comprehensive haematological and histopathological analyses were conducted. The data from both the exposure and lactation phases were subjected to rigorous statistical analysis to uncover dose-dependent trends, significant biological effects, and potential long-term impacts of the chemical mixture. This multifaceted approach provides valuable insights into the health risks associated with combined pesticide exposure during critical biological stages.

Animals

Adult virgin female albino Wistar rats, aged 2–3 months and weighing 190–200 g, were utilized for this study. The animals were sourced from the Animal House of the Federal University of Petroleum Resources, Effurun. Upon arrival, they were housed in groups of five per cage under controlled and hygienic conditions to ensure their well-being. Environmental parameters were meticulously maintained, including a room temperature of 25 ± 2°C, relative humidity of 50 ± 10%, and a 12-hour light/dark photoperiod.

The rats were fed standard laboratory pelleted rodent feed and provided with clean drinking water ad libitum throughout the study. Cage bedding materials were regularly cleaned and replaced to uphold a high standard of hygiene. This controlled environment ensured optimal health and minimized external stressors, thereby supporting the reliability and consistency of the experimental outcomes. All procedures were conducted in strict compliance with ethical guidelines for the care and use of laboratory animals.

Dose Levels

The agrochemicals dichlorvos, dimethoate, and cypermethrin, procured from Hubei Sanonda Co. Ltd, China, were used in this study. These chemicals were purchased from a licensed agrochemical retailer and diluted with clean water following domestic usage guidelines. Dose combinations were prepared in specific ratios for each experimental group. Groups B, C, and D received individual chemicals diluted at a 1:1 ratio. Groups E, F, and G were exposed to binary mixtures of the chemicals prepared at a ratio of 1:0.5:0.5, while Group H received a ternary mixture prepared in a 1:0.33:0.33:0.33 ratio. Fresh solutions were prepared daily and used throughout the 28-day exposure period.

To simulate real-life scenarios of domestic pesticide use, the prepared solutions were sprayed into a poorly ventilated compartment housing the animal cages. A control group (Group A) was exposed to water sprayed under identical conditions. This exposure method mimicked the confined spaces where animals might encounter pesticide residues.

Daily monitoring of the animals ensured humane care in line with the *Guide for the Care and Use of Laboratory Animals* by the National Academy of Sciences and the National Institute of Health. These ethical practices upheld the welfare of the laboratory animals and ensured

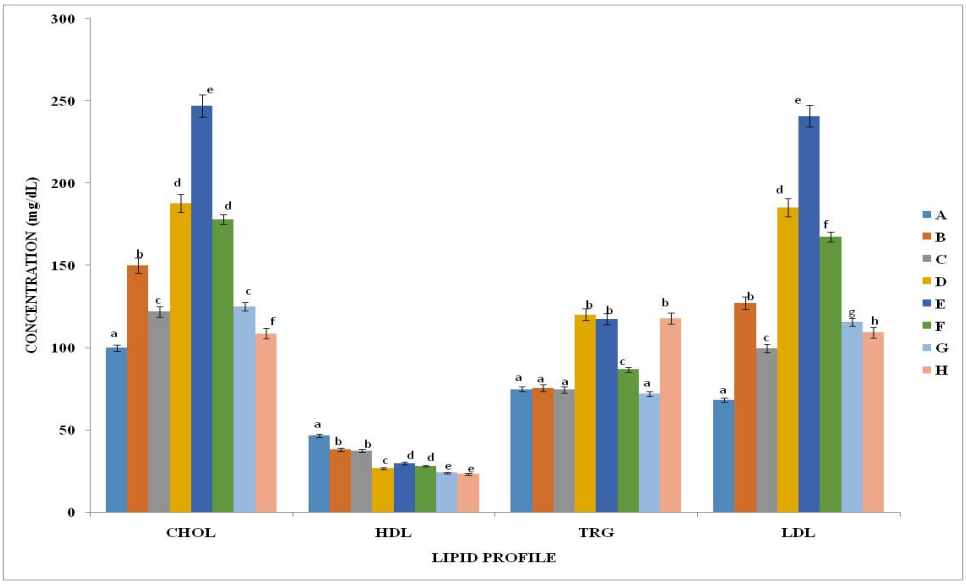

Figure 1: Serum lipid profile of female wistar albino rats exposed to mixture of dichlorvos, dimethoate and cypermethrin. Calculated values are means of four determinations ± SEM. Bars bearing different alphabets are significantly different ($p<0.05$)

reliable data on the biochemical and toxicological effects of the chemical exposure.

The treatment groups were categorized as follows:

- Group A (Control): Exposed to sprayed water.
- Group B: Exposed to dichlorvos.
- Group C: Exposed to dimethoate.
- Group D: Exposed to cypermethrin.
- Group E: Exposed to a mixture of dichlorvos and dimethoate.
- Group F: Exposed to a mixture of dichlorvos and cypermethrin.
- Group G: Exposed to a mixture of dimethoate and cypermethrin.
- Group H: Exposed to a mixture of dichlorvos, dimethoate, and cypermethrin.

Mating and Fertility Assessment

On post-treatment day 29 (PTD 29), the remaining treated female rats (n = 4 per group) were paired with proven fertile adult male rats at a 2:1 female-to-male ratio to evaluate mating and fertility outcomes. Daily vaginal smears were collected from the cohabited females, and the presence of sperm in the smear was used as a definitive marker of successful copulation. The day sperm-positive vaginal smears were detected was recorded as gestational day zero (GD 0).

The time interval from cohabitation to the first observation of sperm-positive smears was meticulously documented to assess the potential impact of chemical treatments on mating efficiency and fertility. This approach provided critical data on the reproductive performance and potential disruptions caused by the agrochemical exposures.

Blood Sampling

At the end of the 28-day treatment period, blood samples were collected from the treated female rats under light chloroform anesthesia. Samples were drawn from the dorsal aorta of four females per group and transferred into non-heparinized tubes. The blood was allowed to clot at room temperature, then centrifuged at 3500 rpm for 15 minutes. The resulting supernatant (serum) was carefully separated and stored for lipid profile analysis, ensuring the integrity of the samples for accurate biochemical assessments.

Serum cholesterol concentration was measured using the method outlined by [11]. HDL cholesterol levels were determined through a combination of precipitation and enzymatic techniques, as described by [12]. LDL cholesterol was calculated indirectly using the Friedewald equation [13]. Triglyceride levels were analyzed using the enzymatic glycerol phosphate oxidase-peroxidase (GPO-POD) method, following the protocol of [14].

3. Results

The comparative analysis of lipid profiles in both non-postpartum Figure 1 and postpartum Figure 2 Wistar albino rats exposed to mixtures of Dichlorvos, Dimethoate, and Cypermethrin reveals significant changes in cholesterol, high-density lipoprotein (HDL), triglycerides, and low-density lipoprotein (LDL) levels.

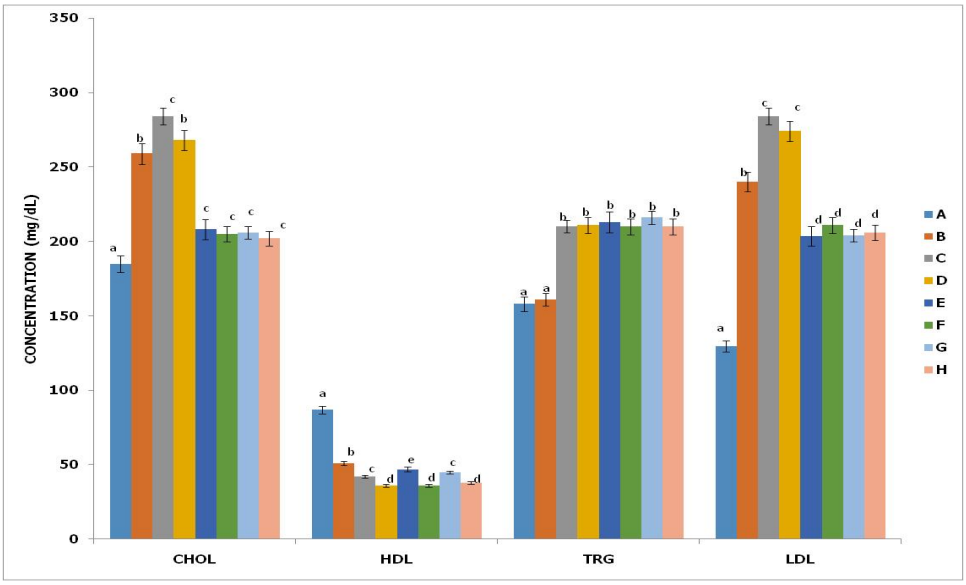

Figure 2: Serum lipid profile of postpartum female wistar albino rats exposed to mixture of dichlorvos, dimethoate and cypermethrin. Calculated values are means of four determinations ± SEM. Bars bearing different alphabets are significantly different ($p<0.05$)

Cholesterol (CHOL)

In non-postpartum rats, cholesterol concentrations are notably elevated in Group E (dichlorvos and dimethoate), showing a significant increase ($p < 0.05$) compared to all other groups. Additionally, Groups D (cypermethrin) and F (dichlorvos and cypermethrin) exhibit higher cholesterol levels than the control group (Group A), which has the lowest cholesterol concentration. For postpartum rats, Group D (cypermethrin) has the highest cholesterol levels ($p < 0.05$), followed by Groups C (dimethoate) and B (dichlorvos), both significantly higher than the control. In both non-postpartum and postpartum groups, cholesterol levels were significantly elevated in pesticide-exposed rats compared to controls, with the highest levels observed in Group E (non-postpartum) and Group D (postpartum).

High-Density Lipoprotein (HDL)

Non-postpartum rats in Group A (control) demonstrate significantly higher HDL levels ($p < 0.05$) than all pesticide-exposed groups. Groups E (dichlorvos and dimethoate) and H (dichlorvos, dimethoate, and cypermethrin) have the lowest HDL levels among all groups. In postpartum rats, Group A similarly shows the highest HDL levels, with significantly lower levels observed in Groups E and F (dichlorvos and cypermethrin). Across both rat groups, the control group consistently maintains significantly higher HDL levels, while groups exposed to multiple pesticides, especially Group E, have lower HDL levels, indicating reduced beneficial lipoproteins due to pesticide exposure.

Triglycerides (TRG)

In non-postpartum rats, triglyceride concentrations are significantly elevated in Groups D (cypermethrin) and E (dichlorvos and dimethoate), with Group A showing the lowest levels. For postpartum rats, Groups D and B (dichlorvos) have higher triglyceride levels compared to controls. Cypermethrin consistently leads to higher triglyceride levels across both non-postpartum and postpartum rats ($p < 0.05$), while the control group maintains significantly lower triglyceride concentrations in both rat groups.

Low-Density Lipoprotein (LDL)

Non-postpartum rats in Group E (dichlorvos and dimethoate) have significantly elevated LDL concentrations compared to all other groups ($p < 0.05$), with the control group showing the lowest LDL levels. In postpartum rats, Group D (cypermethrin) exhibits the highest LDL concentrations, while the control group maintains the lowest levels. Both non-postpartum and postpartum groups show significantly higher LDL in Groups E (non-postpartum) and D (postpartum) relative to controls, with Group A consistently presenting the lowest LDL values.

Overall Combined Insights

The combined lipid data indicate that both non-postpartum and postpartum rats experience marked lipid dysregulation after pesticide exposure. Cholesterol levels are significantly elevated in rats exposed to dichlorvos and dimethoate (Group E in non-postpartum) and cypermethrin (Group D in postpartum). The control group (Group A) consistently maintains higher HDL levels, while groups exposed to pesticide mixtures, especially Group E, exhibit significantly lower HDL levels. Cypermethrin exposure (Group D) is associated with elevated triglyceride levels across both groups, and the control group consistently shows lower triglyceride values. Additionally, LDL levels are significantly higher in Group E (non-postpartum) and Group D (postpartum), with the control group maintaining the lowest LDL levels across both groups.

These findings suggest that pesticide exposure, particularly involving cypermethrin and dichlorvos / dimethoate mixtures, leads to significant lipid dysregulation in both non-postpartum and postpartum rats. This dysregulation is characterized by increased levels of harmful lipids (cholesterol, LDL, triglycerides) and decreased beneficial HDL levels, indicating the detrimental impact of these pesticides on lipid

metabolism and overall health.

4. Discussion

The study demonstrated significant disruptions in lipid profiles among pesticide-exposed groups. Non-postpartum and postpartum rats exhibited elevated cholesterol, triglycerides, and low-density lipoprotein (LDL) levels, alongside reduced high-density lipoprotein (HDL) levels. These effects were most pronounced in groups exposed to Dichlorvos and Dimethoate mixtures (Group E) and Cypermethrin (Group D). Notably, postpartum rats maintained relatively higher HDL levels compared to non-postpartum females.

The dysregulation of lipid metabolism following pesticide exposure aligns with findings in other studies. Elevated cholesterol and LDL levels, as observed in the current study, are indicative of hepatic dysfunction and oxidative stress. [1] reported that Cypermethrin exposure significantly increased serum cholesterol and triglycerides in female rats, linking these changes to oxidative damage and altered lipid transport mechanisms [1].

Similarly, [7] observed hyperlipidemia and reduced HDL levels in rats treated with Dichlorvos, attributing these effects to the disruption of lipid regulatory pathways caused by pesticide-induced oxidative stress [7]. Elevated triglyceride levels, as seen in Cypermethrin-exposed groups, reflect a hepatic inability to process lipids efficiently, consistent with findings by [5] in pyrethroid-exposed rats [5].

The amplified effects of pesticide combinations, particularly involving Dichlorvos and Dimethoate, suggest synergistic interactions that exacerbate lipid dysregulation. [3] demonstrated that combined pesticide exposure significantly increased markers of oxidative stress and impaired lipid metabolism in rat models [3].

Postpartum rats displayed relatively higher HDL levels across groups, which may reflect adaptive physiological changes that enhance lipid clearance or antioxidant activity. This observation is consistent with reports of postpartum metabolic adaptations that confer transient protection against lipid dysregulation. Hormonal fluctuations, including increased estrogen levels, have been implicated in promoting higher HDL levels and counteracting oxidative damage [1].

Disruptions in lipid profiles, particularly elevated LDL and reduced HDL levels, are risk factors for atherosclerosis and cardiovascular diseases. The findings emphasize the potential long-term health risks associated with pesticide exposure. The elevated triglyceride levels further indicate a compromised lipid storage and transport system, potentially exacerbating hepatic stress and metabolic dysfunction.

The observed lipid dysregulation highlights the metabolic consequences of pesticide exposure, with combined treatments showing exacerbated effects. The resilience of postpartum rats warrants further investigation to uncover potential protective mechanisms. These findings underscore the need for regulatory measures to minimize human exposure to pesticide mixtures and suggest avenues for therapeutic interventions targeting lipid metabolism.

5. Conclusion

This study highlights the significant impact of pesticide exposure on lipid metabolism in both non-postpartum and postpartum female Wistar rats. The findings underscore that exposure to dichlorvos, dimethoate, and cypermethrin, individually or in combination, results in marked dysregulation of lipid profiles. These alterations are characterized by increased cholesterol, LDL, and triglyceride levels, alongside decreased HDL concentrations, which collectively heighten the risk of metabolic and cardiovascular complications.

Postpartum rats demonstrated relatively higher HDL levels compared to non-postpartum rats, suggesting a potential protective effect of postpartum physiological adaptations. Nevertheless, the observed lipid dysregulation emphasizes the detrimental influence of pesticide mixtures, particularly in synergistic combinations, which exacerbate metabolic disturbances.

These results underscore the urgent need for stringent regulatory measures to mitigate human and environmental exposure to these agrochemicals. Further research should explore the mechanisms underlying postpartum resilience and develop interventions to counteract pesticide-induced lipid dysregulation, ensuring better health outcomes for vulnerable populations.

Conflict of Interest Disclosure: The authors declare no conflict of interest regarding the publication of this study.

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