Study on the Effects of Combined Oral Contraceptives (Cop) on Some Red Cell Indices of Female Albino Wistar Rats

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Abstract
Oral contraceptives (OCs), commonly referred to as birth control pills, are pharmaceutical formulations designed to prevent pregnancy through the administration of synthetic hormones that regulate the female reproductive system Oral contraceptives are extensively used for fertility regulation and therapeutic indications; however, their systemic effects on haematological profiles remain a subject of concern. This study investigated the haematological impact of different doses of combined oral contraceptives in female albino Wistar rats. A total of 20 female rats, weighing 150 – 200 g were used for the study and the female rats were divided into 4 groups, each group containing 5 rats. At the end of the 21 and 28 days' experimental period, the animals were fasted overnight and anesthetized using diethyl ether. Blood sample was drawn via retro orbital plexus and cardiac puncture. Blood was collected into ethylenediamine tetra-acetic acid (EDTA), and the Packed Cell Volume (PCV), Haemoglobin Concentration (Hb), Red Blood Cell Count (RBC), Mean Cell Volume (MCV), Mean Cell Haemoglobin (MCH), Mean Cell Haemoglobin Concentration (MCHC), and Total White Cell Count (TWBC) were analysed using standard procedures. Data generated from this study were analyzed using Statistical Package for Social Sciences (SPSS) version 27.0, windows 10. The values were expressed as Mean ± Standard Deviation (SD). Differences among the groups were analysed using one-way Analysis of Variance (ANOVA), followed by post-hoc comparisons. Result revealed significant differences ($p< 0.05$) in combined oral contraceptive (COC) treatment groups at high, medium, and low doses in PCV, Hb, RBC, MCV, MCHC, TWBC, when compared with control group. In conclusion, this study demonstrated that higher doses of oral contraceptives exert significant, dose-dependent, and system-wide biological effects on haematological indices, with important implications for both clinical use and pharmacological safety. This study contributes to knowledge by providing a multi-system, dose-dependent effects of combined oral contraceptives on some haematological parameters. These findings highlight a strong foundation for future research and support the need for careful therapeutic monitoring of different oral contraceptive use.

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Keywords: Oral contraceptives, female reproductive system, systemic hormones, fertility regulation, haematological indices

Introduction

Contraception is defined as an intervention that reduces the chance of pregnancy after sexual intercourse (Stephanie & Alison, 2021) [19], primarily by preventing ovulation, fertilization and implantation. Approximately 88% of sexually active women not seeking pregnancy report using contraception at any given time (Kavanaugh & Pliskin, 2020) [10].

Data from the United Nations Population Fund (UNFPA) indicate that, as of 2022 in Nigeria, the contraceptive prevalence rate among women aged 15–49 using any method is 50%, with 46% using modern methods (United Nations, 2022) [22]. This suggests that while half of the reproductive-age women in Nigeria use some form of contraception, there is still significant room for improvement, particularly in the adoption of modern contraceptive methods.

Methods of contraception include oral contraceptives (OCs), implants, injectable, patches, vaginal rings, intrauterine devices (IUDs), condoms, male and female sterilization, lactational amenorrhea methods, withdrawal, and fertility awareness-based methods. These methods have different mechanisms of action and effectiveness in preventing unintended pregnancy (WHO, 2024) [23]. Oral contraception (OC) is the most widely used method of contraception due to its accessibility, reliability, and reversibility (Alshardan *et al*., 2020) [2].

Oral contraceptives (OCs), commonly referred to as birth control pills, are pharmaceutical formulations designed to prevent pregnancy through the administration of synthetic hormones that regulate the female reproductive system (Paton, 2022) [17]. They are steroid hormones that inhibit the release of gonadotropin-releasing hormone (GnRH) by the hypothalamus, thus inhibiting the release of the pituitary hormones that stimulate ovulation. Hormonal birth control pills are highly reliable, non- permanent means of contraception which are primarily used to avoid pregnancy when used correctly and consistently, and it is one of the greatest and most influential developments of the twentieth century.

Three types of oral contraceptive pills are broadly prescribed currently: combined oral contraceptives (COCs) containing estrogen and progesterone, progesterone-only contraceptives (POCs), and continuous or extended-use pills. The most commonly prescribed pill is the combined hormonal pill with oestrogen and progesterone (Cooper & Patel, 2026) [8].

Haematological profiles are measurable indices of blood that can be used to identify and monitor some pathological and physiological abnormalities (Tekle *et al*., 2022) [20]. These include parameters routinely given by complete blood count (CBC) that gives a clue about erythrocyte count (EC). Oral contraceptives (OCs) are one of the factors which may exert an influence on haematological laboratory test results and have critical importance (Tekle *et al*., 2022) [20].

Haematopoietic stem cells (HSCs) are specialized cells responsible for the lifelong replenishment of blood cells. HSCs possess immense competence to regenerate haematopoietic system when transplanted into an irradiated recipient present with bone marrow failure or leukemia. Estrogen clearly influences HSC proliferation and differentiation by modulation of different signaling pathways and production of cytokines. At the same time, it influences the cells comprising the HSC microenvironment and plays a significant role in immune cells development and maturation. Studies showed that estrogen administration can initiate the division and proliferation of Haematopoietic Stem Cells (HSCs) and thus explains the higher blood counts in women during the reproductive years. However, in some family planning clinics, women taking hormonal contraceptives face the problem of irregular vaginal bleeding, amenorrhea, and sometimes excessive bleeding which could lead to anaemia (Tekle *et al*., 2022) [20].

Long-term use of hormonal contraceptives can influence mean cell volume (MCV), mean cell haemoglobin (MCH), and red cell distribution width (RDW) causing macrocytic effect on the red blood cells (RBC) since it affects vitamin B12 and folate absorption. Studies showed that OCPs use could increase platelet count. Hormonal Contraceptive usage could also be associated with decreased percent packed cell volume (% PCV), WBC count, percent lymphocyte, and increased platelet count. White blood cells (WBC) are immune system cells that protect the body against external substances and infectious diseases (Tekle *et al*., 2022) [20].

Like any other medication, oral contraceptives (OCs) can have side effects some of which may not immediately be apparent. One of the potential areas of concern is the effect of OCs on blood physiology, immune system, liver, and the endometrial lining, particularly haematological parameters. Changes in these parameters can have significant health implications on blood and tissue physiology

Aim of the Study

This study was aimed at assessing the effect of Combine oral contraceptives (COCs) on the haematological, indices of female albino wistar rats.

Objective of the Study

Objective of the study was to:

Determine the packed cell volume (PCV), haemoglobin concentration (Hb), red blood cell (RBC) count, white blood cell (WBC) count and red cell indices (MCV, MCH, MCHC), of Female Rats treated with Combined Oral Contraceptives (COC) and compare with the Control.

Materials and Methods

Study Area

The study was conducted at the Animal House of the Faculty of Pharmacy, Madonna University Nigeria, Elele Campus, Rivers State. Rivers State is located in the south-south geopolitical zone (Niger Delta region) of Nigeria. It lies along the Bonny River, 41 miles (66 kilometer) upstream from Gulf of Guinea, latitude 5º6'N 6º 49'E / 5.1009 ºN 6.81411º E. Elele is a prominent town in Ikwerre local government of Rivers State, approximately 42 kilometers from Port Harcourt the capital city.

Study Population

The study population consisted of twenty (20) female albino wistar rats that were obtained from the Animal House of the Faculty of Pharmacy, Madonna University Nigeria, Elele Campus, Rivers State. The animals were housed in a well-ventilated room maintained under standard condition of light, feeding and temperature. The animals were allowed to acclimatize in the animal house for fourteen (14) days. Experimental animals in the study were treated in accordance with the National Protection Laws of Animal Welfare.

The rats were divided into four groups of five (5) animals each: Group one was the control group, while groups 2-4 were given combined oral contraceptive (COCs) high, medium and low doses respectively.

Ethical Approval

Ethical approval was obtained from Madonna University Nigeria Research Ethics Committee (MUN-REC).

Selection Criteria

Inclusion Criteria

Apparently healthy female albino rats in the proestrous phase of the estrous cycle in rodents

Exclusion Criteria

Male albino rats.

Rats with any signs of illness, malnutrition, or pre-existing conditions

Female rats not in the proestrous phase of the estrous cycle in rodents

Composition/ Preparation of experimental doses

Combined oral contraceptives (COCs) Levofem containing twenty-one (21) tablets of ethinylestradiol; 0.03 mg, levonorgestrel; 0.15 mg and Ferrous Fumarate; 75mg, were purchased from certified pharmacies in Port Harcourt and used for the treated groups

Each tablet of COCs, was crushed into a fine powder and dissolved in 10 mL of distilled water to prepare a stock solution and the drug was given daily in different doses through oral gavage tube.

Lethal Dose (LD50**)**

LD50 was not determined in this study because of the following reasons:

1. Oral contraceptives used for this study is already clinically in use
2. LD50 is usually calculated in preclinical studies or experiments whereby the test substance or extract is initially checked to know the dose at which 50% of the subjects will die. Any drug that is in use has passed through this stage.

Dosage calculation

The exact quantity of drug that was administered to the female rats was calculated as follows:

For combined oral contraceptive (COC), using Levofem containing Levonorgestrel 0.15 mg and Ethinylestradiol 0.03 mg as an instance

$0.15 + 0.03 \text{ mg} = 0.18 \text{ mg}$

Low Dose = 0.27 ml

Medium Dose = 0.5 ml

High Dose = 0.83 ml

Table 1

Groups	No. of Rats	Treatment
Group A Control	5	Feed + water throughout the experiment
Combined oral contraceptive (COC) Group B (High dose)	5	Feed + water throughout the experiment + (0.6mg/kg body weight)
Group C (medium dose)	5	Feed + water throughout the experiment + (0.3mg/kg body weight)
Group D (Low dose)	5	Feed + water throughout the experiment + (0.15mg/kg body weight)

Determination of Estrous Cycle Phases of Rats

Visual Assessment of the Estrous Cycle

In visual assessment of estrous phase, the rats were held in the non-dominant hand and laid in the restraint with the forepaws resting on a surface, the tail was lifted gently, then it was examined and the vulva evaluated. A digital image for documentation was taken. Hasty examination was avoided to prevent misinterpretations. In the proestrus phase, the vaginal opening appears full, swollen and moist. The tissues appear pink, with striations in both the dorsal and ventral lips of the vulva. In estrus, the vagina appears similar to that in the proestrus, but it is less pink, less swollen and less moist with more prominent striations.

Blood Sample Collection

At the end of the experimental period which lasted for 21 and 28 days, the animals were fasted overnight and anesthetized using diethyl ether. Blood samples were drawn via retro orbital plexus and cardiac punture. Blood was collected into ethylenediamine tetra-acetic acid (EDTA)

Retro-orbital Blood Collection Procedure

This was done using aseptic technique. The animal was held by the scruff of the neck, and the skin of the head was tightened with the thumb and middle finger. The tip of the capillary tube was placed at the medial canthus of the eye under the nictitating membrane or third eyelid. The capillary tube was rotated and the tube was pressed past the eyeball to enter the slightly resistant membrane of the sinus/plexus. As soon as the sinus/plexus was punctured, blood entered the collection tube by capillary action and the tube was retracted a bit to facilitate blood flow. The tube was angled downward to increase the blood flow. Finally, the tube was withdrawn and slight pressure with sterile gauze/cotton was used to ensure haemostasis. Care was taken not to scratch the corne

Determination of Some Full Blood Count (FBC) parameters

Total White Blood Cell Count

Method: Manual Method (Using Improved Neubauer Counting Chamber)

Principle

Whole blood is diluted 1 in 20 in an acid reagent which haemolyzes the red cells (not the nucleus of nucleated red cells), leaving the white cells to be counted. White cells are counted microscopically using an Improved Neubauer ruled counting chamber (haemocytometer) and the number of WBCs per litre of blood calculated.

Assay Procedure

0.38 mL of Turk's solution was measured and 0.02 mL of well mixed anticoagulated venous blood was added and mixed. The diluted blood sample was re-mixed. Using a Pasteur pipette, held at an angle of about 45, one of the grids of the chamber was filled with the sample, taking care not to overfill the area. The chamber was left undisturbed for 2 minutes to allow time for the white cells to settle and also to prevent drying of the fluid by placing it in a petri dish with dampened tissue and the lid was covered. The underside of the chamber was dried and placed on the microscope stage. The 10 × objective was used to focus with the condenser iris closed sufficiently to give good contrast, the rulings of the chamber and white cells were focused until they appear as small black dots. The cells in the four large corner squares of the chamber marked. The cells lying on the lines of two sides of each large square were also included in the count. The number of white cells per litre of blood was reported using the simple calculation: Divide the total number of cells counted by 2, then divide the number obtained by 10. The number obtained is the white cell count.

Packed Cell Volume (PCV)

Method: Microhaematocrit

Principle

The packed cell volume is that proportion of whole blood occupied by red cells, expressed as a ratio (litre/litre). Anticoagulated blood in a glass capillary of specified length, bore size, and wall-thickness is centrifuged in a microhaematocrit centrifuge at RCF 12 000–15 000g for 5 minutes to obtain constant packing of the red cells. A small amount of plasma remains trapped between the packed red cells. The PCV value was read from the scale of a microhaematocrit reader or calculated by dividing the height of the red cell column by the height of the total column of blood.

Assay Procedure

The plain capillary tube was three quarters filled with well mixed EDTA anticoagulated blood. The unfilled end was sealed using a sealant material. The filled capillary tube was carefully located in one of the numbered slots of the microhaematocrit rotor with the sealed end against the rim gasket (to prevent breakage). The number of the slot for each sample was recorded. The inner lid was carefully positioned to avoid dislodging the tubes. It was centrifuged for 5 minutes at 12000–15000g. Immediately after centrifuging, the PCV was read and results obtained was expressed in percentage or liter per liter.

Haemoglobin (Hb) Concentration Determination

Method: Cyanmethaemoglobin

Principle

Whole blood is diluted 1 in 201 in a modified Drabkin's solution which contains potassium ferricyanide and potassium cyanide. The red cells are haemolyzed and the haemoglobin is oxidized by the ferricyanide to methaemoglobin. This is converted by the cyanide to stable haemiglobincyanide (HiCN). Absorbance of the HiCN solution is read in a spectrophotometer at wavelength 540 nm or in a filter colorimeter using a yellow-green filter. The absorbance obtained is compared with that of a reference HiCN standard solution. Haemoglobin values are obtained from tables prepared from a calibration graph or if using a direct read-out haemoglobin meter, from the digital display.

Assay Procedure

20 µL or 0.02 mL of well-mixed venous blood was carefully measured and 4 mL Drabkin's diluting fluid was dispensed into a small test tube. The mixture was well- mixed, and the diluted blood was left at room temperature, protected from sunlight, for 4–5 minutes. The wavelength of the spectrophotometer was set at 540 nm. The spectrophotometer was blanked with Drabkin's fluid and the absorbance of the sample was read.

Red Blood Cell Count

Method: Formal Citrate Manual RBC (Using Improved Neubauer Counting Chamber)

Principle

Blood is diluted with an isotonic RBC diluting fluid containing formal citrate, which preserves and evenly distributes the red blood cells. A known volume of the diluted blood (1/200) (20ul blood and 4mL dilution) is loaded into the haemocytometer chamber, and the RBCs are counted microscopically in designated squares. The result is expressed in RBC/L of blood.

Assay Procedure

4mL of the diluting fluid was pipetted in a plastic tube and 0.02mL of well mixed blood was added to make dilution of 1/200. The tube was sealed tightly and the suspension was mixed for one minute. The cover slip was placed in position over the ruled area of chamber until rainbow rings appeared. The diluted blood was once again mixed thoroughly. The diluted sample was carefully introduced into the chamber by capillary action, overfilling or air bubbles was avoided.

The counting chamber was left undisturbed for about 2-3 minutesto allow time for the red blood cells to settle and also to prevent drying of the fluid by placing it in a petri dish with dampened tissue and the lid was covered. The chamber was placed on stage of microscope and the RBC in Central Square

was counted. The central square is subdivided into 25 squares. Out of 25 squares, count four at each corner and one at center. Each of these five squares is subdivided into 16 small squares. Thus, RBCs are counted in 16 x 5 = 80 small squares.

Manual RBC Indices Calculation Formulas

Manual calculation of RBC indices (MCV, MCH, and MCHC) are calculated using haemoglobin (Hb), packed cell volume (PCV), and red blood cell (RBC) count to classify anaemia

$$MCV = \frac{\text{haematocrit}(\%)\text{x}10}{\text{RBC count}(\text{millions}/\text{mm}^3\text{blood})}\ (\text{Fl})$$

$$MCH = \frac{\text{Heeamoglobin in g}/1000\text{ml of blood}}{\text{RBC count (millions}/\text{ml)}}\ \text{Pg/cell}$$

$$MCHC = \frac{\text{Heeamoglobin (g}/100\text{ml)x }100}{\text{hematocrit}(\%)}\ \text{g/dl}$$

Statistical Analysis

Data generated from this study were analyzed using Statistical Package for Social Sciences (SPSS) version 27.0, windows 10. The values were expressed as Mean ± Standard Deviation (SD). Differences among the groups were analysed using one-way Analysis of Variance (ANOVA), followed by post-hoc comparisons. Level of significance was kept at 5%

Results

Table 1 is the Descriptive Statistic of study Population showing the baseline weight and final weight of the experimental animals after administration of high, medium and low doses of combined oral contraceptive

Table 2: Descriptive Statistic of study Population

Group	Dose	N	Baseline Weight (g)	Final Weight (g)
Control		5	165.00 ± 11.18	182.00 ± 7.14
COC	High	5	189.40 ± 2.97	212.00 ± 9.08
	Medium	5	147.60 ± 6.02	178.20 ± 11.23
	Low	5	144.00 ± 8.51	167.20 ± 9.09

Table 2 presents the comparison of haematological, parameters among the control group and female rats treated with Combined Oral Contraceptives (COC) at high, medium, and low doses. The values are expressed as Mean ± Standard Deviation (SD). Differences among the groups were analysed using one-way Analysis of Variance (ANOVA), followed by post-hoc comparisons, with the superscripts indicating statistically significant differences between groups. For Packed Cell Volume (PCV), the control group recorded 37.20 ± 1.30, while the high-dose group recorded 33.00 ± 3.39, the medium-dose group 38.00 ± 1.58, and the low-dose group 41.40 ± 1.82. ANOVA showed a significant difference among the groups (F = 12.55, p = 0.000). Post-hoc comparisons indicated that the high-dose group differed significantly from the control, medium-dose, and low-dose groups, while the low-dose group differed significantly from the control group. For Haemoglobin (Hb) concentration, the control group had a mean value of 13.10 ± 0.95, while the high-dose group recorded 11.32 ± 0.99, the medium-dose group 14.58 ± 1.27, and the low-dose group 13.62 ± 1.21. A statistically significant difference was observed (F = 7.58, p = 0.002). Post-hoc results showed that the high-dose group differed significantly from the medium- and low-dose groups, while the medium- and low-dose groups differed significantly from the high-dose group. For Red Blood Cell (RBC) count, the control group recorded 4.98 ± 0.63, while the high-dose group recorded 3.14 ± 0.15, the medium-dose group 6.34 ± 4.81, and the low-dose group 4.42 ± 0.46. The ANOVA result showed no statistically significant difference among the groups (F = 1.48, p = 0.258).

For Mean Cell Volume (MCV), the control group had 91.40 ± 4.22, while the high-dose group recorded 77.20 ± 3.83, the medium-dose group 84.60 ± 2.61, and the low-dose group 90.80 ± 6.76. A statistically significant difference was observed (F = 10.32, p = 0.001). Post-hoc comparisons indicated that the high-dose group differed significantly from the control and low-dose groups, while the low-dose group differed significantly from the high-dose group. For Mean Cell Haemoglobin (MCH), the control group recorded 27.66 ± 2.30, the high-dose group 27.00 ± 2.74, the medium-dose group 30.60 ± 1.14, and the low-dose group 31.20 ± 2.86. The ANOVA result indicated a statistically significant difference among the groups (F = 3.93, p = 0.028). For Mean Cell Haemoglobin Concentration (MCHC), the control group recorded 30.44 ± 1.54, while the high-dose group recorded 31.80 ± 2.95, the medium-dose group 33.80 ± 1.92, and the low-dose group 35.00 ± 2.00.

Table 3: Comparison of Haematological Parameters in Female Rats treated with Combined Oral Contraceptives (COC) and Control.

Parameter	Control A	High B	Medium C	Low D	F	P-value
PCV (%)	37.20 ± 1.30	33.00 ± 3.39^{acd}	38.00 ± 1.58^{b}	41.40 ± 1.82^{ab}	12.55	0.000
Hb (g/dl)	13.10 ± 0.95	11.32 ± 0.99^{cd}	14.58 ± 1.27^{b}	13.62 ± 1.21^{b}	7.58	0.002
RBC 1012/L	4.98 ± 0.63	3.14 ± 0.15	6.34 ± 4.81	4.42 ± 0.46	1.48	0.258
MCV (fl)	91.40 ± 4.22	77.20 ± 3.83^{ad}	84.60 ± 2.61	90.80 ± 6.76^{b}	10.32	0.001
MCH (pg)	27.66 ± 2.30	27.00 ± 2.74	30.60 ± 1.14	31.20 ± 2.86	3.93	0.028
MCHC (g/dl)	30.44 ± 1.54	31.80 ± 2.95	33.80 ± 1.92	35.00 ± 2.00^{a}	4.41	0.019
TWBC(109/L)	8.54 ± 1.98	13.84 ± 1.56^{ac}	8.56 ± 1.19^{bd}	12.24 ± 1.57^{ac}	14.00	0.000

Discussion

This study assessed the effects of different oral contraceptives (OCs) on some haematological parameters of female albino wistar rats. The key parameters evaluated in this study includes the following: PCV, Hb, RBC, MCV, MCH, MCHC and WBC counts. Oral Contraceptives contain synthetic forms of estrogen and progestin which influences blood cell production, coagulation pathways, and immune responses.

Table 4.1 presents the descriptive statistics of the study population. The present study showed that the control group recorded a significant increase in weight (165.00 ± 11.18 to 182.00 ± 7.14), which reflects normal growth and physiological maturation of female albino wistar rats over the study period. Increases in weight in laboratory rats are expected due to age-related anabolic processes and adequate nutrition (Turner *et al*., 2021). Combined oral contraceptive (COC)-treated groups exhibited greater weight gain, particularly in the high-dose group (189.40 ± 2.97 to 212.00 ± 9.08). This dose-dependent increase suggests a strong influence of oestrogen–progesterone combinations on body mass. Oestrogens and progesterone are known to modulate appetite regulation, lipid metabolism, and fluid retention, leading to increased body weight (Nappi *et al*., 2020) [16]. Oestrogen can enhance adipocyte differentiation and fat deposition, while progesterone may increase appetite (Mauvais-Jarvis, 2021) [15]. Also, COCs have been linked to insulin resistance and altered glucose homeostasis, which further promotes adiposity (Khan *et al*., 2023) [11].

Notable increases were observed in the final weight of female rats in the medium- and low-dose COC groups (178.20 ± 11.23 and 167.20 ± 9.09, respectively), supporting the dose-response relationship. Haematological profiles are measurable indices of blood that can be used to identify and monitor some pathological and physiological abnormalities. Oral contraceptives are one of the factors which may exert an influence on haematological laboratory test results and have a critical importance (Tekle *et al*., 2022) [20].

Table 4.2 presents the results of the comparison of haematological parameters among the control group and female rats treated with combined oral contraceptives (COC) at high, medium, and low doses. The PCV, Hb, MCV, MCH, and MCHC, in rats treated with high dose combined oral contraceptives showed a significant decrease compared with the control group, medium and low dose groups. This decrease in erythrocyte indices suggest that hormonal contraceptives may influence erythropoiesis negatively. At physiological levels, oestrogen stimulates haematopoietic stem cells. At high doses, COCs may exert myelosuppressive effects, reducing erythropoiesis. This could also be as a result of increase oxidative stress, leading to damaged RBC membranes, increased haemolysis and reduced RBC lifespan (Barath *et al*., 2022) [4].

This is in line with the work of Barath *et al*., (2022) [4] which recorded decreased RBC count, haemoglobin and haematocrit caused by estradiol valerate demonstrating hormone-induced suppression of erythropoiesis. This is not in consonance with previous studies which observed increase in erythrocyte indices in oral contraceptive users compared to non-users (Tekle *et al*., 2022) [20].

It was also revealed that the WBC in rats treated with high dose and low dose combined oral contraceptives showed a significant increase from the control group, and the medium-dose group. White blood cells (WBC) are immune system cells that protect the body against external substances and infectious diseases. This changes in WBC may be driven by oestrogen –induced stimulation of haematopoietic stem cell proliferation (Tekle *et al*., 2022) [20].

This may also be caused by progesterone-induced leukocytosis (elevated WBC count). Leukocytosis, defined as an elevated white blood cell (WBC) count, can arise from physiological, infectious, neoplastic, or medication-related causes. Typically, a WBC count surpassing 11,000 cells/µL in adults (Mank *et al*., 2024) [14]. This is not in line with the work of Etura and Ogar. (2023) [9] who observed a reduction in the mean WBC count among oral contraceptive users compared to non-users.

Conclusion

This study broadly assessed the effects of combined oral contraceptives (COCs) on the haematological parameters of female albino wistar rats. The findings demonstrated that hormonal contraceptives exert multi-system, dose-dependent biological effects, with variations depending on formulation and dose. The present study observed that at higher doses, oral contraceptive administration is associated with increased body weight in female albino rats, mediated through combined effects on appetite regulation, lipid metabolism, and endocrine function.

It was also revealed that exposure to oral contraceptives resulted in significant alterations across haematological indices specifically in erythrocyte parameters (PCV, Hb, RBC, MCV, MCH, and MCHC). These changes were particularly pronounced at higher doses, indicating that exogenous sex steroids influence erythropoiesis and red cell morphology.

Recommendations

1. There should be careful dose selection and routine monitoring of haematological parameters in the use of hormonal contraceptives, especially formulations containing estrogen, due to their procoagulant and proliferative effects.
2. Long-term studies are needed to evaluate the chronic effects of hormonal exposure, particularly on liver architecture and function.

Contribution to Knowledge

1. This study contributes to knowledge by providing a comprehensive and comparative assessment of combined oral contraceptives on haematological in female albino Wistar rats. Unlike previous research, which studied this drug differently and noted wide range biological effects.
2. This study established clear dose-dependent relationships of oral contraceptive exposure by assessing

low, medium and high doses. Identifying threshold levels associated with physiological responses.

3. The study demonstrates that administration of oral contraceptives leads to significant alterations in haematological parameters. This provides experimental evidence of immune activation and potential anaemic tendencies, contributing to existing knowledge on contraceptive-induced haematological modulation.

References

1. Abbas S, Riaz A, Rehman MU, Khan H. Hematological parameters and their role in clinical diagnosis: a comprehensive review. J Hematol Clin Res. 2024;16(1):1-12.
2. Alshardan A, Bari M, AlSinan I, AlMuqhim M, AlRazeyg N. Knowledge and use of contraceptives among women in Al-Kharj City, Saudi Arabia. Int J Med Dev Ctries. 2020;4:902-909.
3. Arifin WN, Zahiruddin WM. Sample size calculation in animal studies using resource equation approach. Biochem Med (Zagreb). 2021;31(1):010502.
4. Barath B, Varga A, Attila A, Matrai, Deak-Pocsai K, Nemeth N, Deak AA. Estradiol valerate affects hematological and hemorheological parameters in rats. Metabolites. 2022;12(7):602.
5. Cagnacci A, Venier M, Xholli A. Effects of hormonal contraceptives on hematological parameters. Gynecol Endocrinol. 2022;38(3):189-195.
6. Centers for Disease Control and Prevention. United States medical eligibility criteria for contraceptive use, 2016 (US MEC) [Internet]. Atlanta (GA): CDC; 2024 [cited 2024 Dec]. Available from: https://www.cdc.gov/reproductivehealth/contraception/mmwr/mec/summary.html
7. Coffie S, Abaka-Yawson A, Quarshie SS, Elikplim EA. Effects of hormonal contraceptives on haematological parameters among women in the Cape Coast Metropolis, Ghana. Asian Hematol Res J. 2020;3(1):1-9.
8. Cooper DB, Patel P. Oral contraceptive pills. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430882/
9. Etura JE, Ogar AO. The rapid growth in the use of hormonal contraceptives gives grounds for assessing their influence on various biochemical parameters of the human system since its safety has become arguable and in doubt. Sokoto J Med Lab Sci. 2023;8(4).
10. Kavanaugh ML, Pliskin E. Use of contraception among reproductive-aged women in the United States. F S Rep. 2020;1(2):83-93.
11. Khan SM. Hormonal contraceptives and insulin resistance: emerging evidence. Endocr Rev. 2023;44(1):56-78.
12. Klamminger GG, Eltze E, Bitterlich A, Degirmenci Y, Hasenburg A, Wagner M, Nigdelis MP. Ki-67 as a prognostic marker in squamous cell carcinomas of the vulva: a systematic review. J Clin Med. 2025;14(6):2045.
13. Ko MJ, Lim CY. General considerations for sample size estimation in animal study. Korean J Anesthesiol. 2021;74(1):23-29.
14. Mank V, Azhar W, Brown K. Leukocytosis. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024. PMID: 32809717.
15. Mauvais-Jarvis F. Sex differences in metabolic regulation. Nat Rev Endocrinol. 2021;17:521-538.
16. Nappi RE. Hormonal contraception and metabolism. Best Pract Res Clin Endocrinol Metab. 2020;34(2):101379.
17. Paton DM. Estetrol and drospirenone: a novel oral contraceptive. Drugs Today (Barc). 2022;58(1):1-8.
18. Perry M. Menopausal symptoms and hormone replacement therapy. J Community Nurs. 2019;33:61-66.
19. Stephanie T, Alison E. Contraception selection, effectiveness, and adverse effects. JAMA. 2021;326(24):2507-2518.
20. Tekle E, Gelaw Y, Asrie F. Haematological profile changes among oral contraceptive users: a narrative review. J Blood Med. 2022;13:525-536.
21. Tekle E, Gelaw Y, Asrie F. Impact of oral contraceptives on APTT and platelet count. J Med Lab Sci. 2024;32(5):145-153.
22. United Nations Department of Economic and Social Affairs, Population Division. World family planning 2022: meeting the changing needs for family planning: contraceptive use by age and method [Internet]. New York: United Nations; 2022 [cited 2024 Dec]. Available from: https://www.un.org/development/desa/pd/sites/www.un.org.development.desa.pd/files/files/documents/2023/Feb/undesa_pd_2022_world-family-planning.pdf
23. World Health Organization. Family planning/contraception methods [Internet]. Geneva: World Health Organization; 2024 [cited 2024 Dec]. Available from: https://www.who.int/news-room/fact-sheets/detail/family-planning-contraception

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