



Contents lists available at [Bio-Research](#)  
Journal of Biological Research and Biotechnology  
journal homepage: <https://www.bio-research.com.ng> and  
<https://www.ajol.info/index.php/br/about>



## Impact of Combined Highly Active Antiretroviral Drugs on Ovarian Histoarchitecture, Oxidative Stress Markers and Fertility Outcomes in Female Sprague-Dawley Rats

Temitope Nimota Lawal<sup>1</sup>, Airat Adeola Bakare<sup>1</sup>, Abdulkareem Temitayo Olayinka<sup>2</sup>,  
Aigbe Gregory Ohihoin<sup>3,4</sup>

<sup>1</sup>Department of Anatomy, Faculty of Basic Medical Sciences, College of Medicine, University of Lagos, Nigeria.

<sup>2</sup>Department of Anatomy, Faculty of Biomedical Sciences, College of Medicine Kampala International University, Western Campus, Uganda.

<sup>3</sup>Clinical Sciences Department, Nigerian Institute of Medical Research, Lagos, Nigeria.

<sup>4</sup>Department of Cell Biology and Neuroanatomy, Mellowes Center for Genomic Sciences and Precision Medicine, Medical College of Wisconsin, Wisconsin Sussex, USA

### Abstract

Highly Active Antiretroviral Therapy (HAART) has substantially changed positively the clinical direction of human immunodeficiency virus (HIV) infection. Nevertheless, accumulating evidence of its disruptive influence on endocrine homeostasis has raised significant concerns on female reproductive health. The increasing documentation of ovarian pathology among HAART-exposed individuals underscores the urgency of elucidating its mechanistic impact to inform evidence-based therapeutic strategies. The understanding of the potential effects on organ oxidative stress status and impact on ovarian microscopic profile is crucial for developing strategies to preserve reproductive health in HIV-positive women. The present investigation evaluated HAART-associated alterations in ovarian oxidative stress indices and tissue architecture in female Sprague-Dawley rats. Ten animals were allocated into two groups of five: a HAART-treated group (Group A) administered 1.88 mg of the drug combination dissolved in 0.1 ml of normal saline, and a control group (Group B) receiving equivalent volume of normal saline as placebo. Following 28 days of administration, ovarian tissues were subjected to histomorphological examination alongside biochemical quantification of oxidative stress markers. HAART administration resulted in statistically significant suppression of antioxidant enzyme activity of catalase (CAT), superoxide dismutase (SOD), glutathione peroxidase (GPX), and reduced glutathione (GSH), alongside a marked elevation in malondialdehyde (MDA), a principal lipid peroxidation biomarker. Histomorphological evaluation revealed aberrant follicular architecture characterized by cystic formations and vascular congestions. These findings collectively indicate that combined HAART exposure may precipitate oxidative stress-mediated deterioration of ovarian function. Elucidation of the precise molecular pathways underlying these effects remains warranted to facilitate the development of targeted mitigation strategies.

**Keywords:** HIV; HAART; Ovary; Oxidative stress; Fertility

Received: 8<sup>th</sup> February 2026 / Accepted: 11<sup>th</sup> April 2026 / **Published online:**30<sup>th</sup> April 2026

© The Author(s), under exclusive license to Bio-Research-Journal-of-Biological-Research-and-Biotechnology (JBRB), ISSN: 2705-3822; **print-ISSN:** 1596-7409 (Online); *Open Access This article is available at <https://bio-research.com.ng/index.php/home>*, 2026.

DOI: <https://dx.doi.org/10.4314/br.v24i1.15>

\*Corresponding author: Airat Adeola Bakare, email: [aabakare@unilag.edu.ng](mailto:aabakare@unilag.edu.ng)

Temitope et al., *Impact of HAART...*  
**ORIGINAL ARTICLE**

JBRB 24(1):412-420 **412**  
VOLUME 24| APRIL 2026

## INTRODUCTION

Human Immunodeficiency Virus (HIV), the causative agent of acquired immunodeficiency syndrome (AIDS), continues to constitute a formidable global public health burden, with cumulative mortality exceeding 25 million fatalities over the preceding three decades (UNAIDS, 2024). Global estimates from 2013 placed the total number of individuals living with HIV at approximately 35 million. Nigeria accounted for approximately 9% of this global burden (UNAIDS, 2019), corresponding to an estimated 1.9 million affected persons, among whom a prevalence rate of 1.4% was recorded within the reproductive age bracket of 15 to 49 years. This fact has placed Nigeria as the third highest country with HIV burden (Ukaegbu et al., 2022; Bassey & Miteu, 2023). On a global scale, women are more disproportionately affected due to socioeconomic factors such as poverty, lower level or attainment of education which has led to limited information on HIV prevalence, management, and treatment (Charles-Eromosele et al., 2022). More so, biological factors such as the larger surface area of the vagina mucosa lining makes women more susceptible to infection. Likewise, the tradition of gender inequality amidst some clans which has given men more power in relationships, makes it difficult for women to negotiate the use of condoms during sex or refuse sex (Public Health and Global Societies, 2024; UNAIDS, 2016). The introduction and widespread adoption of Highly Active Antiretroviral Therapy (HAART) has fundamentally transformed the prognosis of HIV/AIDS, conferring significant improvements in patient survival, quality of life, and long-term clinical outcomes, thereby contributing to a marked global decline in AIDS-attributable mortality. The use of HAART usually involves the combination of three different drugs: (Efavirenz, Lamivudine and Tenofovir Isopropyl Fumarate) (Eggleton & Nagali, 2020). However, the prolonged usage of these drugs has been implicated to cause some complications and side effects relating to the reproductive health of women. Recent studies have reported concerns regarding the potential adverse effects of HAART on fertility and hormonal balance in women, underscoring the need for comprehensive investigations into the impact of its endocrine dysregulation on gonadal functions. (Zhao et al., 2018). Endocrine dysregulation has become an emerging trend associated with the usage of HAART. Some researchers have proposed that HAART can potentially disrupt the hypothalamic- pituitary-ovarian (HPO) axis at different levels. HAART medications may have a direct toxic effect on ovarian tissues that can subsequently affect the quality of developing eggs potentially impacting their ability to be fertilized and/or developed into healthy embryos (Chris, 2023; Zaid & Greenman, 2019). Moreso, fluctuations in hormonal concentrations may modulate the balance between pro-oxidant free radical generation and antioxidant defense mechanisms (Olojede et al., 2022). Free radicals are unstable molecules with unpaired electrons,

known for their highly reactive activity in causing damage to biologically relevant molecules within the body cells. Whereas antioxidants are stable molecules that counteract the actions of the free radicals through its ability to neutralize and terminate the free radical chain reactions from causing damage to the body cells and organs (Sharma, 2014). The amount of antioxidants in the body, thus serve as measurable indicators of the body's response to a disrupted equilibrium between free radicals and antioxidant defenses within biological systems (Lobo et al., 2010). Hence, it is important to assess a female's vulnerability to oxidative stress and its potential impact on fertility. Ovarian histology plays an indispensable role in maintaining female reproductive homeostasis, underpinning the intricate mechanisms behind fertility and hormonal regulation. The structure and function of the ovary are closely tied to the reproductive success of females, influencing the production of eggs, the secretion of hormones, and the overall reproductive actions. Disruptions in ovarian function can have significant side effects on women's health, including decreased fertility, premature menopause, and increased risk of metabolic disorders (UCSF, 2024; Toprak et al., 2023). Hence, the understanding of histomorphological changes induced by HAART can be very instrumental or helpful in understanding how it affects fertility and consequently the possibilities of developing an intervention to curtail its effects (Toprak et al., 2023; El-Din et al., 2023).

This study was therefore designed to characterize the histomorphological consequences of combined HAART on ovarian oxidative stress and reproductive function in female Sprague-Dawley rats, employing an integrative approach combining histological and biochemical assessment. The data generated are expected to advance mechanistic understanding of HAART-mediated oxidative perturbations and their downstream effects on ovarian function, with direct implications for reproductive health preservation in HIV-infected women. Importantly, this inquiry augments the expanding scientific discourse surrounding reproductive outcomes in HIV-seropositive women undergoing antiretroviral treatment, with potential to inform clinical practice and therapeutic innovation.

## Materials and methods

### HAART sourcing and oral administration dose determination

The fixed-dose antiretroviral combination comprising Efavirenz, Tenofovir Isopropyl Fumarate, and Lamivudine was procured from the AIDS Clinic of Lagos University Teaching Hospital, Idi-Araba, Lagos State, Nigeria. The clinically recommended human dose was scaled proportionally to the body weight of each experimental animal, and the calculated dose was administered once daily over a 28-day period.

### Animals- Sprague Dawley Rats

Twenty adult female Sprague-Dawley rats with body weights ranging from 122 to 135 grams were procured from Ilogbo Eremi Oko-Afo Farm, Badagry, Lagos State. All experimental animals had body weights within the range of 122 to 135 grams at the commencement of the study. Animals were maintained in adequately ventilated cages within the animal care facility of the Department of Anatomy, Faculty of Basic Medical Sciences, University of Lagos, under a controlled 12-hour light/dark photoperiod cycle. All rats received standard rodent chow with unrestricted access to potable water and underwent a 14-day acclimatization period prior to experimental commencement.

### Experimental design

Animals were randomly assigned to two groups of five each: Group A (treatment) received 1.88 mg of the HAART combination dissolved in 0.1 ml of normal saline, while Group B (control) was administered an equivalent volume of normal saline to maintain experimental uniformity. Drug and vehicle delivery was performed via oropharyngeal cannula on a daily basis over 28 consecutive days.

### Experimental animals and ethical clearance

Institutional ethical clearance was obtained from the College of Medicine Ethical Committee, University of Lagos (Approval No. CMUL/60574613), and all procedures were conducted in strict compliance with internationally recognized principles governing the humane use of laboratory animals in biomedical research.

### Necropsy schedule

Upon completion of the 28-day treatment protocol, all animals were humanely euthanized by cervical dislocation as previously described (Clarkson et al., 2022). Bilateral ovariectomy was subsequently performed, and excised ovaries were individually weighed. The left ovary from each animal was processed for biochemical quantification of oxidative stress indices, while the right ovary was reserved for histomorphological evaluation.

### Ovarian tissue processing for histological studies

The preparation of ovarian tissue for microscopic examination involved a multi-step process. The tissue was initially fixed, dehydrated, cleared, and infiltrated with wax using an automatic processor for roughly 17-19 hours. The tissue was further embedded in paraffin blocks to create a sturdy support for sectioning. Thin slices of approximately 4 micrometers thickness were meticulously cut from the paraffin blocks using a cryostat microtome. These sections were transferred to glass slides and dried on a hot plate. Finally, Hematoxylin and Eosin (H and E) staining techniques were applied to visualize various cell structures. The staining process involved removing the wax,

rehydrating the tissue, applying the stain itself, and refining the staining intensity for optimal examination under a microscope (Aziz & Zeman-Pocrnich., 2022).

### Determination of Ovarian Oxidative Stress Markers

#### Catalase (CAT)

Catalase (CAT) activity was determined spectrophotometrically at 620 nm, expressed as  $\mu$ moles of hydrogen peroxide ( $H_2O_2$ ) decomposed per minute per milligram of protein at 25°C. Each reaction mixture (total volume: 1.5 ml) comprised 1.0 ml of 0.01 M phosphate buffer (pH 7.0), 0.1 ml of tissue homogenate, and 0.4 ml of 2 M  $H_2O_2$  as substrate. Enzymatic activity was terminated by addition of 2.0 ml of dichromate-acetic acid reagent, prepared by combining 5% potassium dichromate with glacial acetic acid at a 1:3 volumetric ratio (Lukpata et al., 2022).

#### Superoxide dismutase

Superoxide dismutase (SOD) activity was quantified on the basis of the enzyme's capacity to inhibit the spontaneous auto-oxidation of epinephrine, monitored as an increase in optical absorbance at 480 nm. The assay mixture (3 ml) comprised 2.95 ml of 0.05 M sodium carbonate buffer (pH 10.2) and 0.02 ml of ovarian tissue homogenate; the reaction was initiated by the addition of epinephrine dissolved in 0.005 N HCl. The reference cuvette contained 2.95 ml buffer, 0.03 ml epinephrine, and 0.02 ml distilled water. Enzyme activity was derived from the rate of absorbance change at 480 nm over a 5-minute reaction interval (Ikumawoyi et al., 2016).

#### Glutathione peroxidase

Glutathione peroxidase (GPX) activity was determined using a commercially available ELISA kit. Ovarian tissue supernatants were obtained by centrifugation and stored at -80°C pending analysis. Enzymatic activity was quantified via a kinetic method employing t-butyl peroxide as substrate, expressed as  $\mu$ moles of oxidized NADPH per minute per milliliter of sample. Cumene hydroperoxide and glutathione served as substrates in a glutathione reductase (GR)-coupled reaction, whereby the oxidized glutathione (GSSG) generated following hydroperoxide reduction was recycled to its reduced form in the presence of NADPH, producing a proportional decrease in absorbance at 340 nm from which GPX activity was derived. Results were referenced against established normative values to characterize oxidative stress severity. Erythrocyte glutathione was quantified colorimetrically by reaction of sulfhydryl groups with 5,5'-dithiobis (2-nitrobenzoic acid) (DTNB), with absorbance read at 412 nm against a reagent blank; concentrations were determined by interpolation from a calibration curve. Total hemoglobin content was measured in g/dL by the cyanmethemoglobin method, and erythrocyte hemolysates were stored in microcentrifuge tubes at -20°C until analysis (Asif et al., 2023).

### Glutathione (GSH)

Tissue reduced glutathione (GSH) content was assessed as total non-protein sulfhydryls following the method of Sedlak and Lindsay (1968). Tissue homogenate was deproteinized with 10% trichloroacetic acid (TCA) and centrifuged to yield a protein-free supernatant. A 1.0 ml aliquot was combined with 0.5 ml of Ellman's reagent [19.8 mg of 5,5'-dithiobis (2-nitrobenzoic acid) (DTNB) per 100 ml of 0.1% sodium nitrate] and 3.0 ml of phosphate buffer (0.2 M, pH 8.0), and the resultant absorbance was recorded at 412 nm.

### Malondialdehyde

Lipid peroxidation was evaluated by quantification of malondialdehyde (MDA) using the thiobarbituric acid reactive substances (TBARS) assay. A 1.0 ml aliquot of tissue supernatant was combined with 2 ml of TCA-TBA-HCl reagent comprising 0.37% thiobarbituric acid, 0.24 N hydrochloric acid, and 15% trichloroacetic acid (1:1:1 v/v), and the mixture was heated at 100°C for 15 minutes before cooling to ambient temperature. Precipitates were removed by centrifugation at 3,000 rpm for 10 minutes, and the clarified supernatant was read spectrophotometrically at 532 nm against a reagent blank. MDA concentration was calculated using a molar extinction coefficient of  $1.56 \times 10^5 \text{ M}^{-1} \text{ cm}^{-1}$  for the MDA-TBA chromophoric complex (Nwabueze et al., 2020).

### Fertility assessment

Male Sprague Dawley rats were placed with the females in the cage of the treatment and control groups in the ratio of 1:3 with the purpose of mating and after 24 hours were

removed thereafter. After 21 days, the method of cervical dislocation was employed to sacrifice the rats. The abdominopelvic region was cut open terminating the pregnancy, in order to assess the uterus. The litters were brought out if found and assessed for fertility based on the following parameters: number of litters, weight of each litter, gross fetal abnormalities, weight of placenta, head circumference, crown-rump length, length of umbilical cord, and tail length.

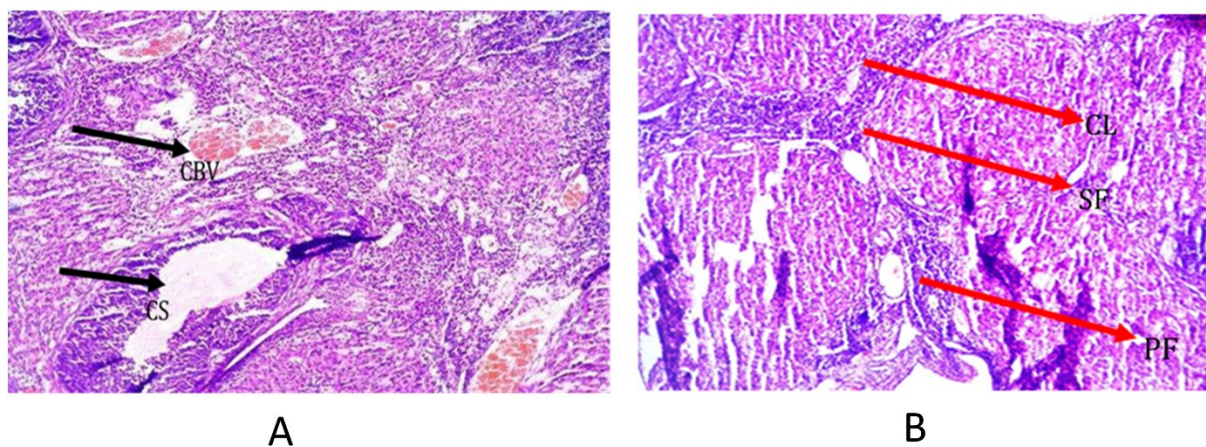
### Statistical analysis

All quantitative data were analyzed using GraphPad Prism software (version 8.0.1, GraphPad Software Inc., San Diego, CA, USA). Results are presented as mean  $\pm$  standard deviation (SD). Intergroup comparisons were performed using one-way analysis of variance (ANOVA), with Bonferroni's post-hoc test applied for pairwise multiple comparison testing.

## Results

### Effect of HAART on the histology of Ovaries

Histological examination of ovarian tissue from HAART-treated animals (Group A; Figure 1) revealed notable structural aberrations, including cystic formations within the cortical region and marked vascular congestion in the medullary compartment. In contrast, ovaries from control animals (Group B; Figure 2) exhibited well-preserved follicular architecture with clearly delineated cortical and medullary boundaries and no discernible histopathological changes.



**Figure 1: Treatment Group A:** Histological section of the ovary of animals treated with HAART showing congested blood vessels and cystic spaces. H&E STAIN X100. CBV- Congested Blood Vessels, CS- Cystic Space and **Control Group B:** Histological section of the ovary of the control group animals showing a well-defined follicle and corpora lutea at varying stages of development. Also, it indicates a well outlined ovarian cortex and medulla with no abnormalities seen. H&E STAIN X100. CL- Corpora Lutea, PF- Primary Follicle., SF- Secondary Follicle.

### Effects on oxidative stress markers

As illustrated in Figure 2, catalase activity (CAT) was significantly attenuated in HAART-exposed animals relative to control group counterparts ( $p < 0.01$ ), indicating substantial impairment of this primary enzymatic antioxidant defense following drug administration. Statistically significant reduction in superoxide dismutase activity in the treated group relative to control animals ( $p < 0.01$ ), reflecting a marked decline in enzymatic antioxidant capacity following HAART exposure. Also, reduced glutathione (GSH) levels in ovarian tissues of HAART-treated animals were significantly lower than those recorded in the control group ( $p < 0.01$ ),

indicative of pronounced depletion of non-enzymatic antioxidant reserves in response to drug treatment. A statistically significant reduction in glutathione peroxidase activity was observed in treated animals relative to control animals ( $p < 0.01$ ; Figure 2), further corroborating the suppressive effect of HAART on the ovarian enzymatic antioxidant system. Contrary to the antioxidant enzyme findings, MDA levels were significantly elevated in the HAART-treated group compared to control animals ( $p < 0.01$ ; Figure 2), signifying enhanced lipid peroxidation and heightened oxidative stress in ovarian tissue following HAART exposure.

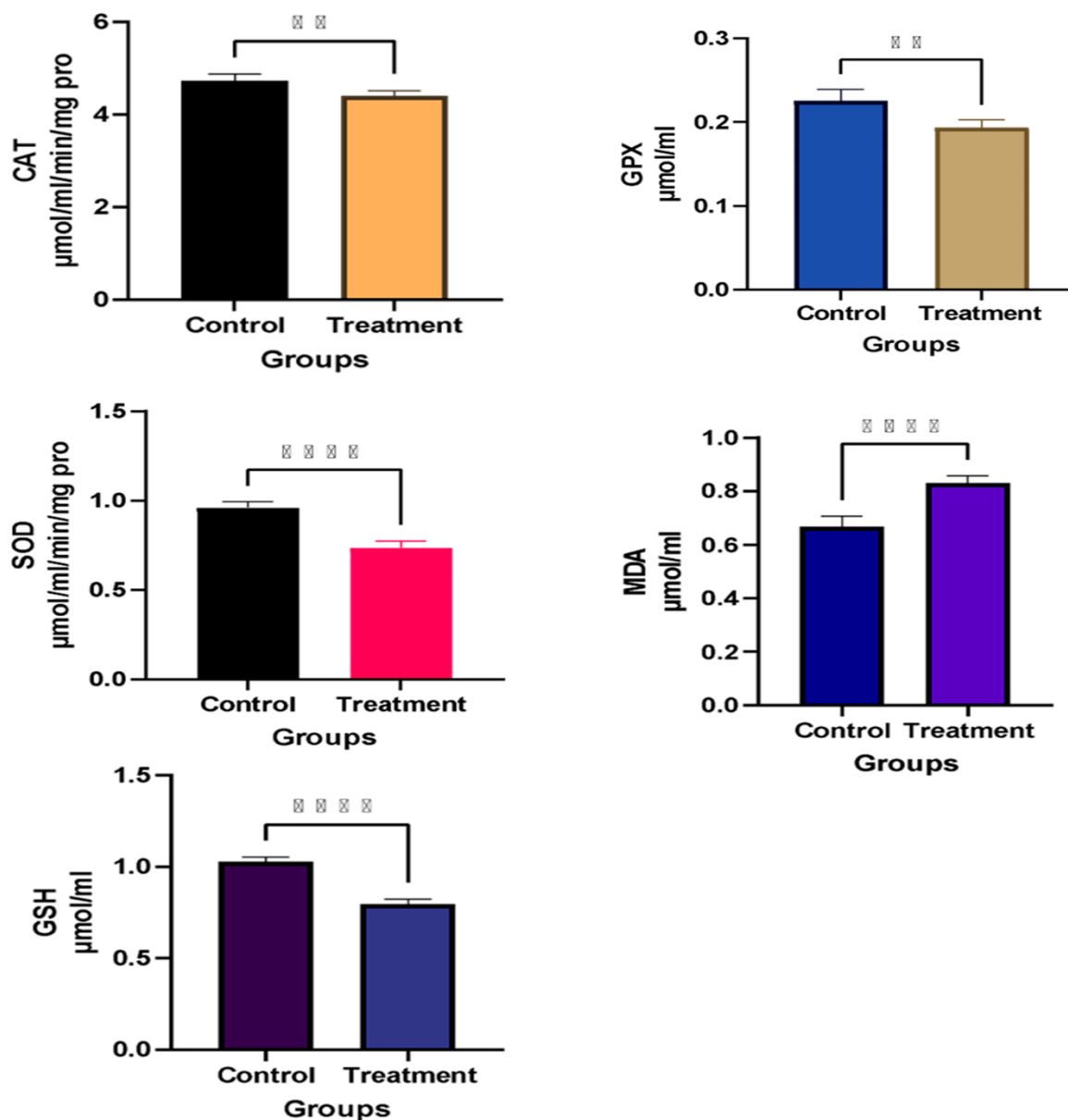
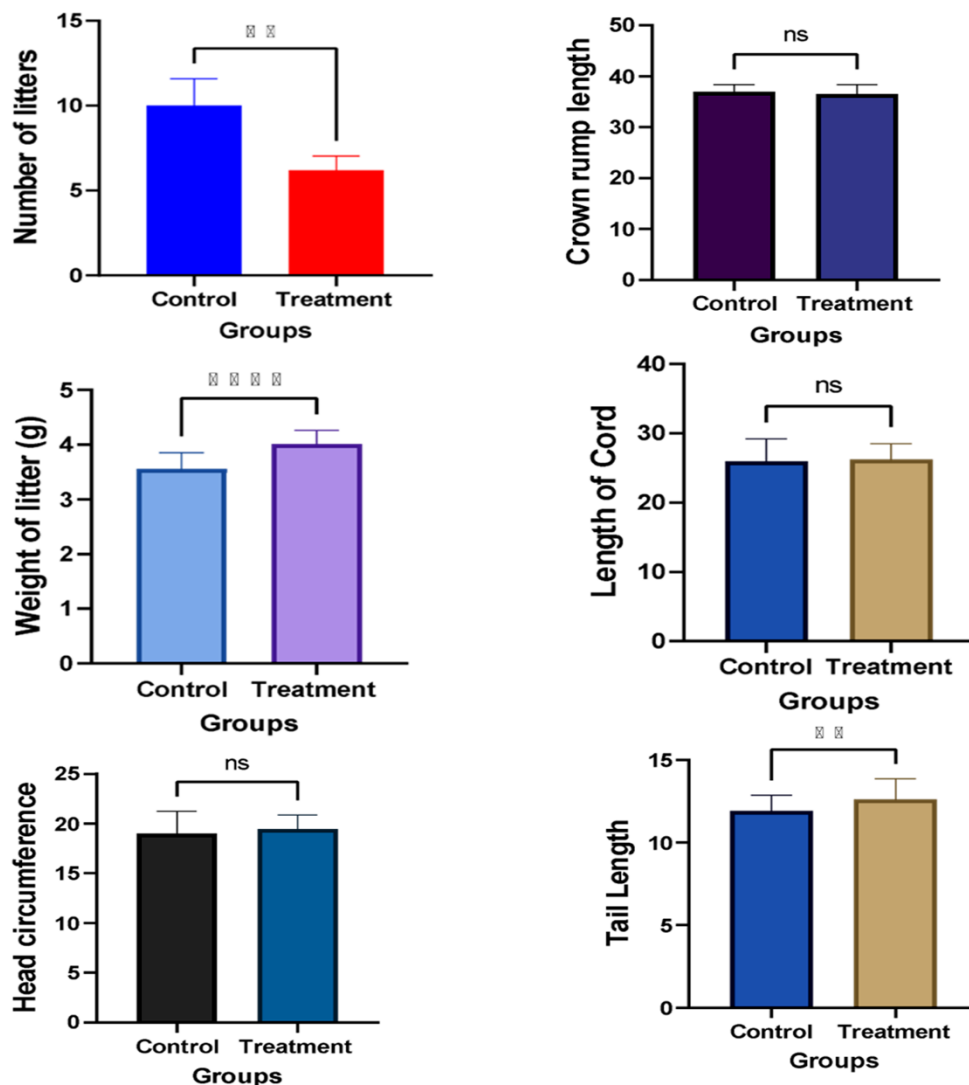


Figure 2: Graph revealing the level of Antioxidants (CAT,SOD,GSH,GPx, and MDA) in treated group and control group. Level of significance ( $p < 0.01$ ).

### Fertility Assessment Result

Fertility assessment yielded statistically significant intergroup differences in litter number and individual litter weight ( $p < 0.01$ ). However, no significant differences were detected in the remaining fetal morphometric parameters evaluated, including head circumference, placental weight, crown-rump length, tail length, or the incidence of congenital malformations ( $p > 0.01$ ; Figure 3). a statistically significant reduction in litter number was documented in the

HAART-treated group (Group A) relative to the placebo-receiving control group (Group B) ( $p < 0.0001$ ), suggesting impaired reproductive output following HAART administration. Also, a statistically significant difference in individual litter weight between groups ( $p < 0.01$ ), with HAART-treated animals producing litters of greater mean body weight compared to control offspring, a finding that may reflect compensatory physiological adaptations.



**Figure 3:** Graph showing the number of litters, weight of the litters birthed by the rats, head circumference of the litters birthed, crown rump length of litters birthed, length of cords of the litters birthed, effect of HAART on the tail length of the litter birthed in the HAART treated group and the control group. Level of Significance: \*\*\*\* $p < 0.0001$

### Discussion

The present study comprehensively characterized the impact of HAART on ovarian oxidative stress biomarkers and the

associated histomorphological sequelae on ovarian structure and fertility parameters. HAART-exposed animals exhibited significant suppression of antioxidant enzyme activities,

specifically CAT, SOD, GPX, and GSH, alongside concurrent elevation of MDA, a well-established indicator of lipid peroxidation and oxidative burden, relative to untreated controls. Histomorphological assessment of the ovarian tissue obtained from treated animals disclosed the occurrence of cystic lesions and engorged blood vessels as prominent pathological features which have the potential of disrupting the process of folliculogenesis. Cystic spaces can interrupt the growth and development of ovarian follicles while congested blood vessels can hinder nutrient and oxygen delivery to the ovaries, potentially impacting events that will lead to the production of viable eggs. Existing study has previously suggested that HAART can disrupt follicular development and cause vascular dysfunction (Manokaran et al., 2022). Oxidative stress has furthermore been recognized as a pathogenic contributor to multiple female reproductive disorders, including polycystic ovarian syndrome (PCOS) and endometriosis. Prior investigations have demonstrated that excessive reactive oxygen species (ROS) accumulation in follicular fluid is associated with infertility, as oxidative injury disrupts critical reproductive processes encompassing folliculogenesis, ovulation, and fertilization (Mauchart et al., 2022; Menzel et al., 2021). ROS was also reported to induce inflammation and damage the endometrium leading to endometriosis. Additionally, oxidative stress has further been implicated in the pathogenesis of gestational complications, including preeclampsia and preterm parturition, suggesting that excessive ROS generation may impair placental functional integrity and precipitate adverse pregnancy outcomes. Reduced activities of CAT, SOD, GPX, and GSH alongside elevated MDA concentrations have been consistently reported across diverse reproductive pathologies, including PCOS and endometriosis (Manokaran et al., 2021; Mauchart et al., 2023). The follicular architectural disruptions identified in the present histological assessment are therefore attributable, at least in part, to the oxidative burden imposed on ovarian tissue by HAART exposure. Several investigators have advocated for the adjunctive use of antioxidant supplementation, particularly vitamins C and E, as a pharmacological strategy for attenuating oxidative stress-mediated reproductive dysfunction (Menzel et al., 2021). The observed reduction in litter number among HAART-treated animals is plausibly attributable to HAART-induced hormonal dysregulation that compromises oocyte maturation, developmental competence, and fertilization potential. However, the other fetal parameter have no statistically significant difference. Future research avenues could explore the specific mechanisms by which HAART regime affects litter size, potentially monitoring mating behaviour, accessing early pregnancy loss rates, or examining specific aspects of embryo development. (Dredjiza et al; 2022). Therefore, this may stand as a possible target of treatment of HAART and/or HIV induced dysregulation of the endocrine system leading to infertility.

## Conclusion

The present investigation provides empirical evidence of the adverse impact of the studied HAART regimen on ovarian tissue, specifically demonstrating its capacity to induce follicular architectural disruption and significantly elevate the ovarian oxidative stress burden. Further investigation is needed on how HAART exerts endocrine dysfunction through the HPG axis. Where reproductive functions are propagated. More importantly, the understanding of an extensive mechanism on how oxidative stress affects ovarian function is needed for providing mitigating measures on the fertility indices exerted in HIV positive women on HAART. Additionally, dedicated investigations are further warranted to assess the therapeutic potential of antioxidant-based interventions in mitigating HAART/HIV-associated oxidative stress and ameliorating the associated reproductive impairments.

### Conflict of interest

The authors declare that there are no competing financial or personal interests that could have influenced the findings reported in this manuscript

### Acknowledgement

The authors gratefully acknowledge the Department of Anatomy, College of Medicine, University of Lagos, for providing the laboratory infrastructure utilized in executing this research.

### Author contributions

Conceptualization and Experimental Design: Airat A. Bakare and Temitope N. Lawal. The conduct of the research: Temitope N. Lawal and Airat A. Bakare. Analysis and interpretation of data: Airat A. Bakare, Temitope N. Lawal, Abdulkareem T. Olayinka and Aigbe Gregory Ohiohin. Manuscript writing: Airat A. Bakare, Temitope N., Abdulkareem Temitayo and Aigbe Gregory Ohiohin.

## References

- Asif A, Ishtiaq S, Kamran SH, Youssef FS, Lashkar MO, Ahmed SA & Ashour ML (2023) UHPLC–QTOF–MS Metabolic Profiling of *Marchantia polymorpha* and Evaluation of Its Hepatoprotective Activity Using Paracetamol-Induced Liver Injury in Mice. *Journal of Analytical Methods in Chemistry* 8(21), 19037–19046.
- Aziz and Zeman-Pocrnich: Aziz SJ & Zeman-Pocrnich CE (2022) Tissue processing. *Immunohistochemistry and Immunocytochemistry: Methods and Protocols*, 47–63.
- Bassey and Miteu: Bassey AE & Miteu GD (2023) A review of current trends in HIV epidemiology, surveillance, and control in Nigeria. *Annals of Medicine and Surgery* 85(5), 1790–1795.
- Charles-Eromosele TO, Kanma-Okafor OJ, Sekoni AO, Olopade BO, Olopade OB & Ekanem EE (2022) Gender disparities in the socio-economic burden of HIV/AIDS among patients receiving care in an

- HIV clinic in Lagos, Nigeria. *African Health Sciences* 22(4), 477–487.
- Chris R: Chris R (2023) Antiretroviral Therapy for HIV Infection. Available At: <https://emedicine.medscape.com/article/1533218-overview?form=fpf#A1>.
- Clarkson JM, Martin JE & McKeegan DE (2022) A review of methods used to kill laboratory rodents: issues and opportunities. *Laboratory Animals* 56(5), 419–436.
- Drejza MA, Rylewicz K, Majcherek E, Gross-Tyrkin K, Mizgier M, Plagens-Rotman K & Jarzabek-Bielecka G (2022) Markers of oxidative stress in obstetrics and gynaecology - A systematic literature review. *Antioxidants* 11(8), 1477.
- Eggleton JS & Nagalli S (2020) Highly active antiretroviral therapy (HAART). *European Review for Medical and Pharmacological Sciences* 24, 11982–1198.
- El-Din MA, Ghareeb AE, El-Garawani IM & El-Rahman HA (2023) Induction of apoptosis, oxidative stress, hormonal, and histological alterations in the reproductive system of thiamethoxam-exposed female rats. *Environmental Science and Pollution Research* 30(31), 77917–77930.
- Ikumawoyi VO, Awodele O, Rotimi K & Fashina AY (2016) Evaluation of the effects of the hydro-ethanolic root extract of *Zanthoxylum zanthoxyloides* on hematological parameters and oxidative stress in cyclophosphamide-treated rats. *African Journal of Traditional, Complementary and Alternative Medicines* 13(5), 153–159.
- Lobo V, Patil A, Phatak A & Chandra N (2010) Free radicals, antioxidants and functional foods: Impact on human health. *Pharmacognosy Reviews* 4(8), 118.
- Lukpata PU, Stella CG, Adugba AO & Oremosu AA (2022) Neuroprotective and anti-inflammatory effects of combined herbal therapy on amitriptyline-induced stroke in rats. *Unicross Journal of Science and Technology* 1(1), 126–147.
- Manokaran K, Bhat P, Nayak D, Baskaran R, Paramasivam P, Ahmed SF & Balaji VE (2022) Oxidative stress and female reproductive disorder: a review. *Asian Pacific Journal of Reproduction* 11(3), 107–116.
- Mauchart P, Vass RA, Nagy B, Sulyok E, Bodis J & Kovacs K (2023) Oxidative stress in assisted reproductive techniques, with a focus on an underestimated risk factor. *Current Issues in Molecular Biology* 45(2), 1272–1286.
- Menzel A, Samouda H, Dohet F, Loap S, Ellulu MS & Bohn T (2021) Common and novel markers for measuring inflammation and oxidative stress ex vivo in research and clinical practice—which to use regarding disease outcomes? *Antioxidants* 10(3), 414.
- Nwabueze JC, Sogbanmu TO & Ugwumba AA (2020) Physicochemical characteristics, animal species diversity, and oxidative stress responses in dominant fish from an impacted site on the Lagos Lagoon, Nigeria. *Ife Journal of Science* 22(2), 81–93.
- Olojede SO, Lawal SK, Faborode OS, Dare A, Aladeyelu OS, Moodley R & Azu OO (2022) Testicular ultrastructure and hormonal changes following administration of tenofovir disoproxil fumarate-loaded silver nanoparticle in type-2 diabetic rats. *Scientific Reports* 12(1), 9633.
- Public Health and Global Societies: Public Health and Global Societies (2024) Gender As A Determinant Of Health: Women's Health. Available At: <https://Publ110.Digital.Uic.Edu/Section-3-15-Gender-As-A-Determinant-Of-Health-Womens-Health/>.
- Sharma: Sharma B (2014) Oxidative stress in HIV patients receiving antiretroviral therapy. *Current HIV Research* 12(1), 13–21.
- Sedlak and Lindsay: Sedlak J & Lindsay RH (1968) Estimation of total, protein-bound, and nonprotein sulfhydryl groups in tissue with Ellman's reagent. *Analytical Biochemistry* 25, 192–205.
- The Well Project: The Well Project (2023) Hormones and HIV. Available: <https://www.thewellproject.org/hiv-information/hormones-and-hiv>.
- Toprak V, Akalın SA, Ocal E, Çavuş Y & Deveci E (2023) Biochemical and immunohistochemical examination of the effects of ephedrine in rat ovary tissue. *Acta Cirúrgica Brasileira* 38, 381523.
- UCSF Health: UCSF Health (2024) The Menstrual Cycle. Available At: <https://www.ucsfhealth.org/education/the-menstrual-cycle>.
- UNAIDS (2014) The Gap Report: Children and Pregnant Women Living With HIV.
- UNAIDS (2019) UNAIDS (2019) Children and Pregnant Women Living With HIV. Available at: [https://www.unaids.org/sites/default/files/media\\_asset/09\\_ChildrenandpregnantwomenlivingwithHIV](https://www.unaids.org/sites/default/files/media_asset/09_ChildrenandpregnantwomenlivingwithHIV).
- Ukaegbu E, Alibekova R, Ali S, Crape B & Issanov A (2022) Trends of HIV/AIDS knowledge and attitudes among Nigerian women between 2007 and 2017 using Multiple Indicator Cluster Survey data. *BMC Public Health* 22(1), 440.
- UNAIDS (2016): UNAIDS (2016) HIV Prevention among Adolescent Girls and Young Women. Available at: [https://www.unaids.org/sites/default/files/media\\_asset/un\\_aids\\_hiv\\_prevention\\_among\\_adolescent\\_girls\\_and\\_young\\_women](https://www.unaids.org/sites/default/files/media_asset/un_aids_hiv_prevention_among_adolescent_girls_and_young_women).
- Zhao Y, Wu Z, McGoogan JM, Shi CX, Li A, Dou Z, Ma Y, Qin Q, Brookmeyer R, Detels R & Montaner

JSG (2018) Immediate antiretroviral therapy decreases mortality among patients with high CD4 counts in China: a nationwide, retrospective cohort study. *Clinical Infectious Diseases* 66(5), 727–734. <https://doi.org/10.1093/cid/cix878>.

Zaid and Greenman: Zaid D & Greenman Y (2019) Human immunodeficiency virus infection and the endocrine system. *Endocrinology and Metabolism* 34(2), 95.

**Publisher's Note:** *Bio-Research remains neutral with regard to jurisdictional claims in published maps and institutional affiliations. Bio-Research or its licensor (e.g. a society or other partner) holds exclusive rights to this article under a publishing agreement with the author(s) or other rightsholder(s); author self-archiving of the accepted manuscript version of this article is solely governed by the terms of such publishing agreement and applicable law.*