



PERINATAL EXPOSURE TO BISPHENOL-A DISRUPTS LEPTIN SIGNALING AND INDUCES METABOLIC DYSFUNCTION IN PRE-ADOLESCENT WISTAR RATS.

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Abstract

*Bisphenol A (BPA) is a ubiquitous endocrine disruptor linked to metabolic syndrome. This study investigated the dose-dependent effects of perinatal BPA exposure on leptin levels and metabolic homeostasis in pre-adolescent Wistar rats. Pregnant rats received oral BPA at 0, 2.5, 25, or 2500 µg/kg from gestational day 0 to postnatal day (PND) 13. Pups were directly gavaged with the same doses from PND 14 to 28, then euthanized on PND 29. Serum leptin, insulin, glucose, GLP-1, lipids, and oxidative stress markers were analyzed. BPA exposure significantly reduced serum leptin levels in a dose-dependent manner ($p \leq 0.05$), correlating with increased body weight, particularly at 2500 µg/kg. A non-monotonic response was observed for insulin—decreasing at lower doses but increasing at 2500 µg/kg—while fasting glucose remained elevated across all BPA groups. Lipid profiles were disrupted: triglycerides increased at 2.5 and 2500 µg/kg, while LDL rose at the highest dose. **Conclusion:** Early-life BPA exposure, even at human-relevant doses, suppresses leptin and impairs glucose and lipid metabolism. These findings suggest that BPA-induced leptin suppression may be a primary driver of metabolic dysfunction, potentially predisposing individuals to obesity and metabolic disorders later in life.*

Keywords: Bisphenol A. Leptin. Endocrine disruptors. Metabolic syndrome. Oxidative stress.

Introduction

Bisphenol A (BPA) is a synthetic compound widely used in the production of polycarbonate plastics and epoxy resins, which are found in food containers, flame retardants, thermal papers, and various household items and equipment. (Badding et al., 2019; Dunder, 2021; Kodila et al., 2023). Human exposure to BPA primarily occurs through leaching from food packaging; however, additional

sources include occupational contact and environmental contamination of surface waters. (MacKay and Abizaid, 2018; Rotimi et al., 2021; Ucheana et al., 2024). Notably, BPA crosses the placenta in humans and experimental animals (Doerge et al., 2011; Nishikawa et al., 2010; Rasdi et al., 2023), raising concerns about its impact during critical developmental stages.

BPA is recognized as an endocrine-disrupting chemical with estrogenic and anti-androgenic activities. While its affinity for classical estrogen receptors (ER α/β) is significantly lower than 17 β -estradiol, BPA can still exert biological effects at nanomolar concentrations through non-genomic pathways, including G protein-coupled estrogen receptor (GPER)-mediated signalling, activation of MAPKs, and modulation of calcium oscillations (Nadal et al., 2018; Stanojević and Sollner Dolenc, 2025). BPA exposure in early life has been shown to alter gene expression, provoke epigenetic changes, and disturb glucose and lipid metabolism, even at doses comparable to measured human exposures (Doerge et al., 2011; Nadal et al., 2018).

Metabolic syndrome, marked by obesity, dyslipidemia, insulin resistance, and hyperglycemia, affects a growing number of individuals globally, with projections indicating an increase from 537 million cases in 2021 to 783 million by 2045 (Oyewole et al., 2023). Of particular concern is its rising prevalence among peri-adolescent populations in low-resource settings (Njan, et al., 2020; Vidal-Limon et al., 2022). Early life BPA exposure has been implicated in this trend; however, the mechanisms underlying it remain incompletely understood.

Leptin, an adipocyte-derived hormone, plays a central role in energy homeostasis by regulating appetite, insulin secretion, and lipid metabolism. (Choe et al., 2016; Dornbush and Aeddula, 2019, 2023; Martínez-Sánchez, 2020). Despite emerging data linking BPA exposure to altered leptin levels in adult rodents (Aja et al., 2023;

Mohsenzadeh et al., 2021), limited studies have examined its effects following perinatal exposure. Given the importance of leptin signalling in metabolic regulation and the non-monotonic dose-response patterns often reported with BPA, this study investigates the impact of perinatal BPA exposure on leptin levels and related metabolic parameters in pre-adolescent male Wistar rats.

MATERIALS AND METHOD

Drugs and reagents:

BPA was purchased from Sigma Aldrich (CAS No. 80-05-7), Munich, Germany. Other chemicals, all analytical grade, were obtained from the Central Research Laboratory in Ilorin, Nigeria. Enzyme-linked immunosorbent assay ELISA kits for Leptin (E-EL-R0582), rat insulin, and Glucagon-like peptide-1 (GLP-1) were products of Elabscience Biotechnology Inc., Houston, Texas, USA. Glutathione peroxidase (GPx) (BXC0261), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) (BXC0551) kits were products of Fortress Diagnostics, UK. Accu-Chek glucometer and associated test strips were products of Roche Diagnostics, USA.

Experimental animals, grouping, breeding, and treatment:

Adult female and male Wistar rats, 10 weeks old, weighing 175 ± 25 g, were procured from a private rodent farm in Ogbomosho, Oyo State, Nigeria. They were housed in polysulfone cages at an average daily temperature of $22 \text{ }^\circ\text{C} \pm 2 \text{ }^\circ\text{C}$ and a 12-hour light/dark cycle in the animal house of the Faculty of Basic Clinical Sciences, University of Ilorin,

Nigeria. Food and water were provided ad libitum, using glass containers. These housing and diet conditions were carefully designed to minimise unintended exposure to BPA.

Sexually mature male rats were introduced to adult female rats in the first stage of their oestrous cycle (the proestrus phase) for mating at a ratio of 1:2. Daily serial vaginal smears were obtained from the female rats to confirm mating, and the mating day was marked as gestational day 0 (GD 0). The pregnant females were isolated and nursed in separate cages under the same housing and feeding conditions as earlier described (Kadir et al., 2021a, 2021b; Marcondes and Bianchi, 2002). The dams were treated daily via the oral route in the following order:

Group I: (0.5 ml of vehicle [0.3% carboxymethylcellulose]),

Group II: 2.5 µg/kg/day of BPA,

Group III: 25 µg/kg/day of BPA and

Group IV: 2500 µg/kg/day of BPA (Demeneix et al., 2020a; Heindel et al., 2015).

Dosing was skipped on the day of birth, and this day was marked as postnatal day 0 (PND 0). However, dosing continued from PND 1 until PND 13 for the dams. Litters were culled to 5 healthy pups, comprising three males and two females, on PND 14, and these pups represented the test animals from the groups. The pups were further directly orally gavaged with BPA in doses like those of their respective dams between postnatal day (PND) 14 and PND 28.

Body Weight Measurement, Fasting Blood Glucose, and Animal Euthanasia:

The body weights of the pups were measured weekly from PND 7. On postnatal day 29 (PND 29), following an overnight fast, blood glucose was measured from blood obtained via a tail nick. Subsequently, the pups were anaesthetised with an intraperitoneal injection of pentobarbital sodium at a dose of 200 mg/kg body weight. The absence of reflexes confirmed deep anaesthesia. Blood was then collected through cardiac puncture, and death was verified by opening the thoracic cavity. All procedures were conducted in accordance with institutional and international guidelines for animal care and use approved by the Ethical Review Committee of the University of Ilorin (EERC/ASN/2024/2694). Blood samples obtained were centrifuged (LABCENT 5000) at 3000 rpm and 4°C for 10 min, and the serum was aliquoted into cryovials and stored at -80°C until needed for assay. The liver from each rat was excised, weighed, and then processed for biochemical analysis and histological examination.

Biochemical Assays:

Serum lipids were analysed using a chemistry autoanalyser, while other serum biochemical assays were performed with ELISA kits according to the manufacturer's instructions. According to the manufacturer's guidelines, ELISA kits were used to determine aspartate aminotransferase (AST) and alkaline phosphatase (ALP) levels in liver homogenates.

Liver Homogenate Preparation:

A 10% w/v liver homogenate was prepared in 0.05 M potassium phosphate buffer, pH 7.4, using an Elvehjem homogeniser (Dominique Deutscher, Issy-les-Moulineaux, France). The homogenate was centrifuged for 10 min at $3000 \times g$ at 4°C , and the supernatant was aliquoted and stored at -80°C until assayed.

Histological analysis:

The liver tissues were fixed in 10% neutral buffered formalin for 24 hours subsequently paraffin embedded. Sections were cut and processed for H&E staining as described by Njan et al., 2019.

Data Presentation and Analysis:

Data are presented in tables and line graphs as Mean \pm standard error of mean (sem). The results were analysed using GraphPad Instat software (Version 8) with one- or two-way Analysis of Variance (ANOVA)

followed by Dunnett's post-hoc test for comparisons of the means. The p-value for significance was set at $P < 0.05$.

RESULTS

Effects of BPA on serum Leptin level in pre-adolescent Wistar rats:

Figure 1 illustrates the impact of Bisphenol A (BPA) exposure on serum leptin concentrations. Leptin levels were measured in animals treated with varying doses of BPA (2.5 $\mu\text{g}/\text{kg}$, 25 $\mu\text{g}/\text{kg}$, and 2500 $\mu\text{g}/\text{kg}$) and compared to a control group administered 3% carboxymethylcellulose (CMC). The data are presented as mean \pm SEM with five animals per group ($n=5$). Our findings indicate that BPA treatment significantly reduced serum leptin levels in a dose-dependent manner compared to the control group ($p \leq 0.05$). However, no significant differences were observed amongst the BPA treatment groups themselves.

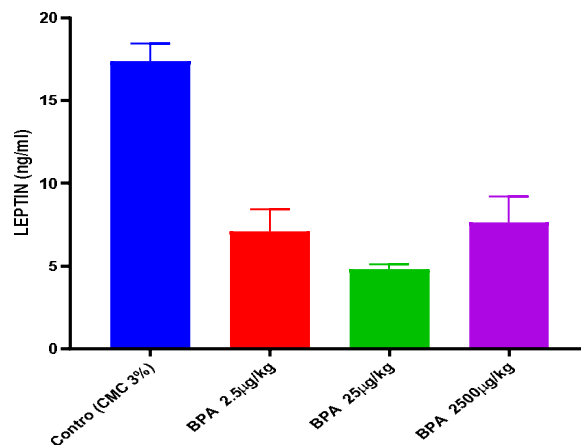


Fig 1: Effect of Bisphenol A (BPA) on serum leptin levels in experimental groups.

Leptin concentrations (ng/mL) were measured in animals treated with different doses of BPA: 2.5 $\mu\text{g}/\text{kg}$, 25 $\mu\text{g}/\text{kg}$, and 2500 $\mu\text{g}/\text{kg}$, compared to the control group receiving 3% carboxymethylcellulose (CMC; blue).

Data are presented as mean \pm SEM ($n=5$ per group). BPA treatment significantly reduced serum leptin levels in a dose-dependent manner compared to the control ($p \leq 0.05$).

Effects of BPA on critical metabolic parameters:

The data showed a complex dose-dependent effect of BPA on serum insulin levels; insulin levels were reduced in the 2.5 and 25 $\mu\text{g}/\text{kg}$ BPA groups but increased at the highest dose of 2500 $\mu\text{g}/\text{kg}$ (Fig. 2a). Regarding glucose levels, an increase was observed across all BPA treatment groups relative to the control. Notably,

the highest increase in glucose was observed in the 25 $\mu\text{g}/\text{kg}$ group (Fig 2b). In contrast, BPA significantly increased serum GLP-1 levels in all treatment groups compared to the control, with the most pronounced increase occurring at the 2.5 $\mu\text{g}/\text{kg}$ dose. GLP-1 levels at 25 $\mu\text{g}/\text{kg}$ and 2500 $\mu\text{g}/\text{kg}$ were similar (Fig 2b). Statistical significance was set at $p \leq 0.05$ for all observed differences.

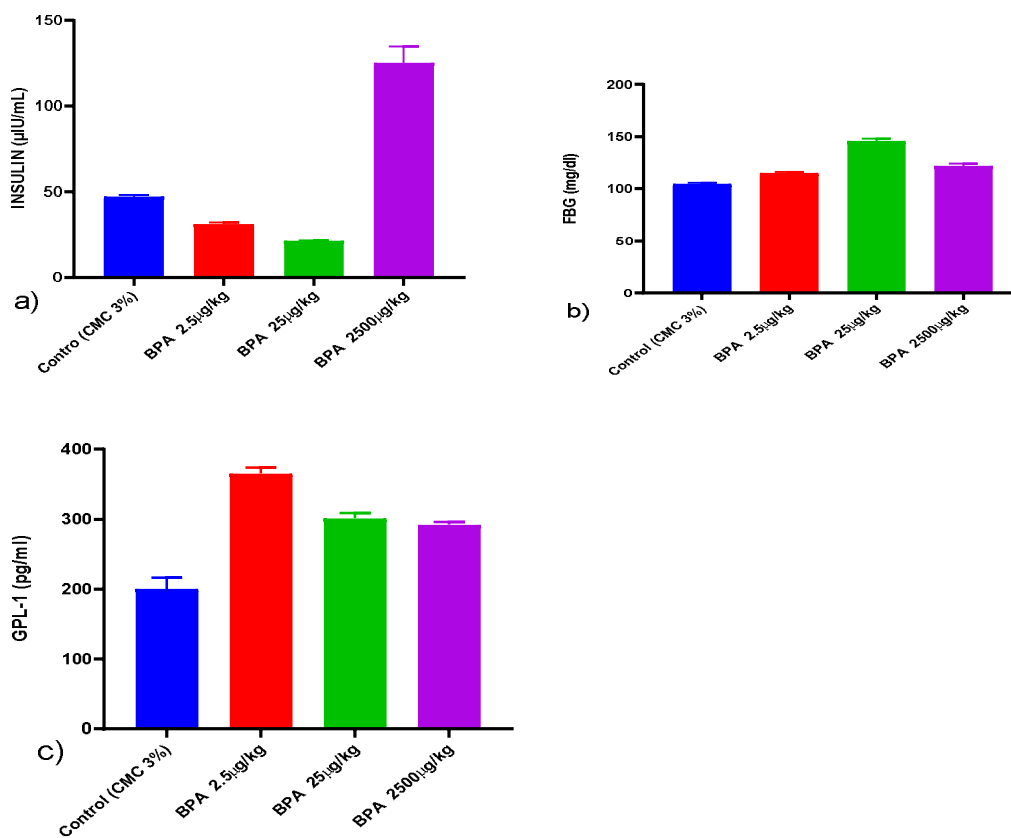


Fig. 2 Effect of Bisphenol A on experimental groups' key metabolic hormones and glucose levels.

Effect of Bisphenol A on experimental groups' key metabolic hormones and glucose levels (a) Serum insulin (IU/mL), (b) serum glucose (mg/dL), and (c) serum glucagon-like peptide-1 (GLP-1; ng/mL) concentrations were

measured in animals treated with BPA at doses of 2.5 $\mu\text{g}/\text{kg}$, 25 $\mu\text{g}/\text{kg}$, and 2500 $\mu\text{g}/\text{kg}$, compared to the control group receiving 3% carboxymethylcellulose (CMC). Data are presented as mean \pm SEM ($n = 5$ per

group). BPA treatment dose-dependently reduced serum insulin levels in the 2.5 and 25 $\mu\text{g}/\text{kg}$ groups, but levels increased at 2500 $\mu\text{g}/\text{kg}$. Glucose levels remained unchanged across all treatment groups. In contrast, BPA significantly increased serum GLP-1 levels in all treatment groups compared to control, with the highest increase observed at 2.5 $\mu\text{g}/\text{kg}$; levels at 25 and 2500 $\mu\text{g}/\text{kg}$ were similar. Statistical analysis was performed using one-way ANOVA followed by Dunnett's post hoc test; differences were considered significant at $p \leq 0.05$. Effect of Bisphenol A (BPA) on serum lipid profiles:

Lipid concentrations, measured in mg/dL , were assessed in animals treated

with BPA at doses of 2.5 $\mu\text{g}/\text{kg}$, 25 $\mu\text{g}/\text{kg}$, and 2500 $\mu\text{g}/\text{kg}$, as well as in a control group receiving 3% carboxymethylcellulose (CMC). Data are presented as mean \pm SEM, with five animals per group ($n=5$).

Our results indicate that BPA treatment significantly increased serum TG levels in the 2.5 $\mu\text{g}/\text{kg}$ and 2500 $\mu\text{g}/\text{kg}$ groups but not in the 25 $\mu\text{g}/\text{kg}$ group (Fig 3a). HDL levels significantly increased in response to the 2.5 $\mu\text{g}/\text{kg}$ doses but not at the 25 $\mu\text{g}/\text{kg}$ and 2500 $\mu\text{g}/\text{kg}$ doses (Fig 3b). Only the 2500 $\mu\text{g}/\text{kg}$ dose demonstrated a significant increase in LDL compared to the control group ($p \leq 0.05$) (Fig 3c).

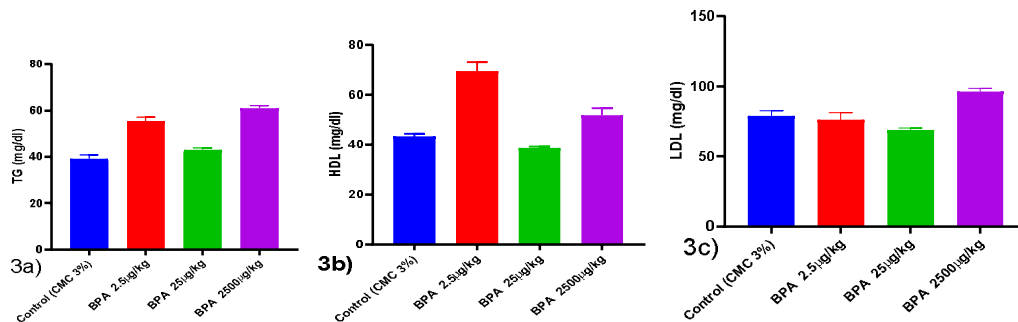


Fig. 3. Effect of Bisphenol A (BPA) on serum lipid profile.

Effect of Bisphenol A (BPA) on serum lipid profile, a) TG, b) LDL and c) HDL were measured in mg/dl in animals treated with different doses of BPA: 2.5 $\mu\text{g}/\text{kg}$, 25 $\mu\text{g}/\text{kg}$, and 2500 $\mu\text{g}/\text{kg}$, compared to the control group receiving 3% carboxymethylcellulose (CMC). Data are presented as mean \pm SEM ($n=5$ per group). BPA treatment significantly increased serum TG and HDL, but no significant changes were observed in LDL compared to the control ($p \leq 0.05$).

Effect of Bisphenol A (BPA) exposure on postnatal body weight gain in rat pups:

Figure 4 shows the body weights (g) of pups measured on postnatal days 7, 14, 21, and 28. The experimental groups included pups exposed to BPA at doses of 2.5 $\mu\text{g}/\text{kg}$, 25 $\mu\text{g}/\text{kg}$, and 2500 $\mu\text{g}/\text{kg}$, alongside a control group that received 3% carboxymethylcellulose (CMC). Data are presented as mean \pm SEM, with five pups in each group ($n =$

5/group). Our findings demonstrate that BPA exposure led to a dose-dependent increase in body weight, with the most significant weight gain observed in the

2500 µg/kg group by day 28. These differences were considered statistically significant at $p < 0.05$.

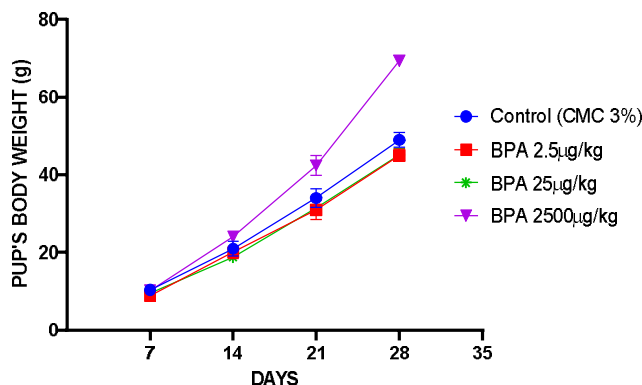


Fig. 4. Bisphenol A (BPA) affects postnatal body weight gain

Effects of BPA on the oxidative state in pre-adolescent Wistar rats:

Fig.5. presents the effects of Bisphenol A (BPA) on serum markers of oxidative stress. Specifically, we measured (a) serum malondialdehyde (MDA) concentrations (µM) and (b) serum glutathione peroxidase (GPX) activity (U/L). The data shows that BPA treatment significantly increased serum

MDA levels in the 2.5 µg/kg and 25 µg/kg groups but not in the 2500 µg/kg group. In contrast, only the 2500 µg/kg dose caused a significant decrease in GPX activity compared to the control group ($p \leq 0.05$). These findings indicate that BPA exposure can induce oxidative stress, as evidenced by alterations in MDA and GPX, with varied dose-dependent effects.

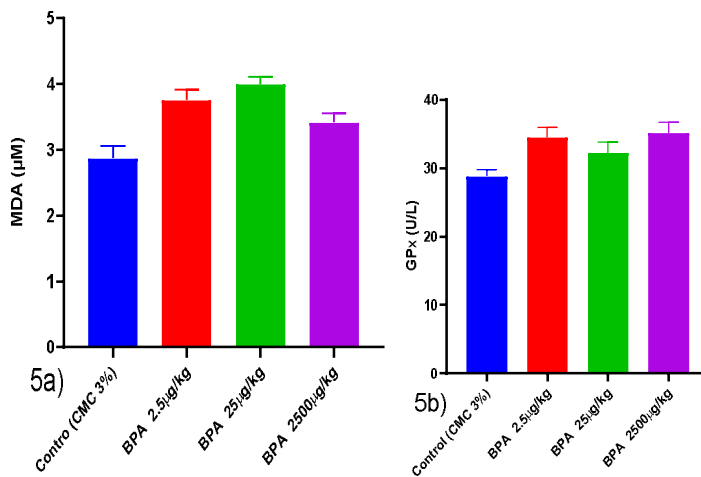


Fig 5: Effect of Bisphenol A (BPA) on serum oxidative stress markers in experimental groups.

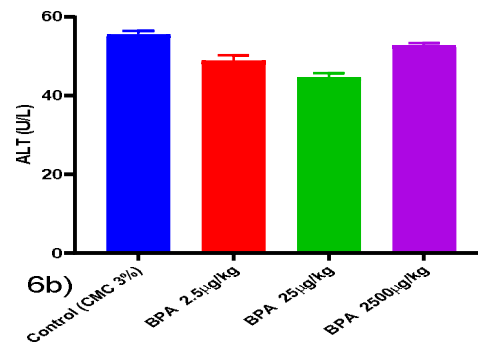
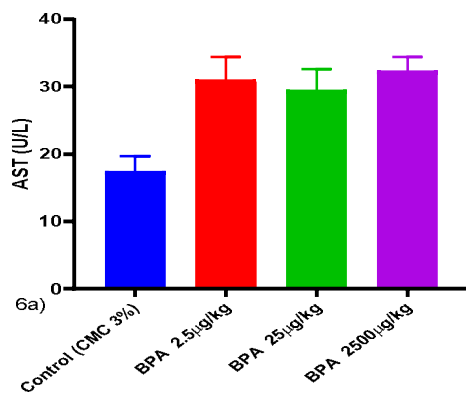
(a) Serum malondialdehyde (MDA) concentrations (μM) and (b) serum glutathione peroxidase (GPX) activity (U/L) were measured in animals treated with different doses of BPA: 2.5 $\mu\text{g}/\text{kg}$ (red), 25 $\mu\text{g}/\text{kg}$ (green), and 2500 $\mu\text{g}/\text{kg}$ (purple), compared to the control group receiving 3% carboxymethylcellulose (CMC; blue). Data are presented as mean \pm SEM ($n=5/\text{group}$). BPA treatment significantly reduced serum levels of both MDA and GPX in a dose-dependent manner compared to the control ($p \leq 0.05$).

Effect of Bisphenol A (BPA) on liver function markers in serum of experimental groups:

Fig. 6. illustrates the effects of Bisphenol A (BPA) on markers of liver function in serum. We assessed (a) aspartate aminotransferase (AST) concentrations (U/L), (b) alanine aminotransferase (ALT) concentrations (ng/mL), and (c) the AST/ALT ratio. These parameters were measured in

animals treated with BPA at 2.5 $\mu\text{g}/\text{kg}$, 25 $\mu\text{g}/\text{kg}$, and 2500 $\mu\text{g}/\text{kg}$ and compared to a control group administered 3% carboxymethylcellulose (CMC). Data are presented as mean \pm SEM, with five animals per group ($n = 5$).

The results show that BPA exposure significantly altered liver enzyme levels, with a notable increase in AST and the AST/ALT ratio across all BPA treatment groups compared to the control, suggesting potential hepatic stress or injury. Interestingly, no significant differences were observed among the 2.5, 25, and 2500 $\mu\text{g}/\text{kg}$ BPA doses for AST and AST/ALT ratio. Conversely, ALT levels significantly decreased in the 2.5 $\mu\text{g}/\text{kg}$ and 25 $\mu\text{g}/\text{kg}$ doses compared to the control, but this decrease was insignificant in the 2500 $\mu\text{g}/\text{kg}$ group. When comparing the three BPA groups, only the 25 $\mu\text{g}/\text{kg}$ and 2500 $\mu\text{g}/\text{kg}$ doses showed significant differences in ALT.



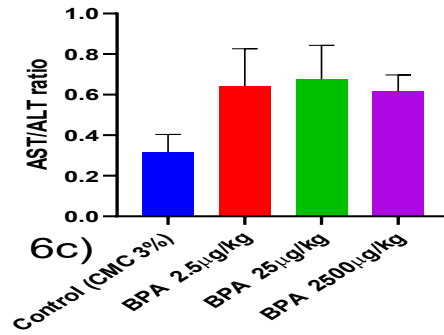


Fig 6: Effect of Bisphenol A (BPA) on liver function markers in serum of experimental groups.

(a) Aspartate aminotransferase (AST) concentrations (U/L), (b) alanine aminotransferase (ALT) concentrations (ng/mL), and were measured in animals treated with BPA at doses of 2.5 µg/kg (red), 25 µg/kg (green), and 2500 µg/kg (purple), compared to the control group receiving 3% carboxymethylcellulose (CMC; blue). (c) the AST/ALT ratio was also determined. Data are presented as mean ± SEM (n = 5 per group). BPA exposure significantly altered liver enzyme levels in a dose-dependent manner, with a notable increase in the AST/ALT ratio, indicating potential

hepatic stress or injury. Data was analysed using one-way ANOVA followed by Dunnett's post hoc test; differences were considered significant at $p < 0.05$.

Effect of BPA on Liver Histology in pre-adolescent Wistar Rats:

The Liver hepatocytes (black arrow) and stroma, consisting of connective tissue and the sinusoids (red arrow), were generally preserved. However, atrophy of the central veins was noted in the BPA-exposed group compared to the control (Figure 7).

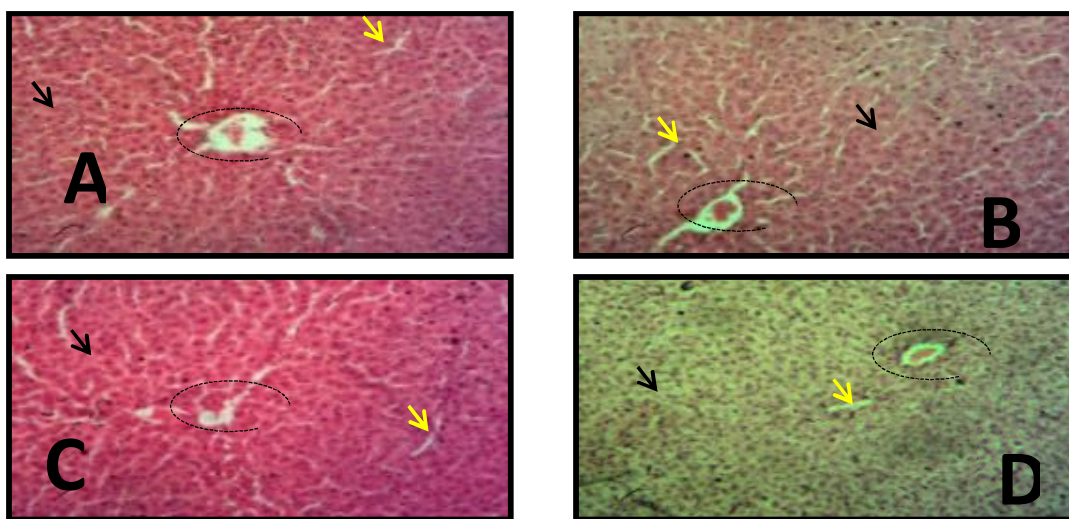


Fig. 7. Photomicrographs showing bisphenol A's effects on liver histology (9a - d). Haematoxylin and Eosin staining, Left column (i) x40; Right column (ii) x400. (Dotted

circle showing central vein (CV), yellow arrow: sinusoidal space (SP), black arrow: hepatocyte (H).

DISCUSSION

Intrauterine and early postnatal exposure to environmental toxicants have been shown to produce long-term adverse outcomes in animals. (Kochmanski et al., 2018; Ouazzani et al., 2021). This underscores the importance of investigating the effects of such exposures during critical developmental windows to anticipate or mitigate functional and structural deficits that may predispose to chronic diseases later in life. In this context, bisphenol A (BPA), a ubiquitous environmental toxicant and a component of food packaging materials (Demeneix et al., 2020b; Manzoor et al., 2022; Santoro et al., 2019), has garnered attention for its endocrine-disrupting potential, particularly at levels exceeding the tolerable daily intake (TDI) of 4 $\mu\text{g}/\text{kg}/\text{day}$ model (Demeneix et al., 2020b; Kodila et al., 2023; Prins et al., 2019). Despite this concern, the impact of early-life BPA exposure on leptin regulation and associated metabolic functions remains underexplored.

Our findings demonstrate a significant, dose-independent reduction in serum leptin concentrations across all BPA-treated groups, consistent with earlier reports of leptin suppression in the offspring of BPA-exposed dams. (Biddinger et al., 2020; Izquierdo et al., 2019). Leptin, an adipokine with key roles in appetite regulation, energy homeostasis, and lipid metabolism, is essential during early development. Its downregulation may disrupt hypothalamic appetite circuits and

metabolic signaling, potentially predisposing to increased food intake and weight gain. In our study, this reduction in leptin was accompanied by a dose-dependent increase in body weight, particularly in the 2500 $\mu\text{g}/\text{kg}$ group by PND 28, in agreement with previous findings on BPA-induced weight gain following perinatal exposure. (Angle et al., 2013; García-Arevalo et al., 2014; Heindel et al., 2017; Leslie et al., 2022; Santoro et al., 2019; Vom Saal et al., 2012).

Leptin deficiency has also been associated with increased insulin production, leading to hyperinsulinemia and insulin resistance - hallmarks of type 2 diabetes mellitus (Bally et al., 2017). Interestingly, our study observed a biphasic insulin response: decreased insulin levels at lower BPA doses (2.5 and 25 $\mu\text{g}/\text{kg}$) and a marked increase at the highest dose (2500 $\mu\text{g}/\text{kg}$). This non-monotonic response may reflect a progression from insulin suppression to compensatory hyperinsulinemia as the BPA dose increases, a pattern noted with other endocrine disruptors. (Naomi et al., 2022; Pérez-Bermejo et al., 2021; Wassenaar et al., 2017) .

Consistent with this hormonal imbalance, all BPA-exposed pups exhibited elevated fasting blood glucose levels, with the most pronounced rise at 25 $\mu\text{g}/\text{kg}$. This suggests impaired glucose handling and aligns with prior reports on BPA-induced hyperglycemia. (Anderson et al., 2013; Angle et al., 2013; García-Arevalo et al., 2014). GLP-1, an

incretin hormone known to regulate insulin release and glucose homeostasis (Müller et al., 2019; Nicholson et al., 2018) was significantly elevated in all treated groups. This increase may represent an adaptive response to oxidative stress or hyperglycemia, as supported by studies indicating that GLP-1 upregulation precedes insulin secretion. (Gear and Belcher, 2017; Michałowska et al., 2021), and may itself induce hyperinsulinemia. (Kahles et al., 2022, 2014).

In terms of lipid metabolism, our results reveal dyslipidemia in BPA-treated animals. Triglycerides and LDL cholesterol were elevated at various doses, and a surprising increase in HDL cholesterol was observed at the lowest dose - contrary to previous findings (Moghaddam et al., 2015; Ozaydin et al., 2018). These mixed effects suggest a complex and possibly dose-specific influence of BPA on lipid regulatory pathways.

Oxidative stress appears to be a central mechanism linking BPA exposure to these metabolic disturbances. Elevated malondialdehyde (MDA) levels in treated animals, particularly at lower doses, indicate enhanced lipid peroxidation and cellular damage. (Marmugi et al., 2014; Moghaddam et al., 2015; Njan et al., 2020a, 2019). A significant decrease in glutathione peroxidase (GPx) activity was observed at the highest dose, implying potential exhaustion of antioxidant defences. These findings echo previous reports that BPA is a potent inducer of oxidative stress and a disruptor of redox balance. (Afolabi et al., 2021; Marmugi et al., 2014; Njan et al., 2020a, 2019; Ogunyemi et al., 2022).

Given the liver's critical role in regulating glucose and lipid metabolism, we assessed hepatic function and observed increased AST and AST/ALT ratios across BPA groups, consistent with hepatic injury. Although ALT levels decreased at lower doses, the overall profile suggests hepatocellular stress. This biochemical evidence was supported by histological findings of central vein atrophy in the livers of exposed pups, indicating structural disruption. These outcomes align with previous studies on BPA-induced hepatotoxicity and altered liver architecture. (Naomi et al., 2022; Njan et al., 2020a, 2019).

While our findings demonstrate clear evidence of metabolic disruption following perinatal BPA exposure, we acknowledge that extrapolation to human health must be approached with caution. Although the doses used in this study span environmentally relevant concentrations, interspecies differences in metabolism, development, and endocrine sensitivity may limit direct translation. Future studies involving longer-term follow-up, including both adolescent and adult stages, will be crucial in determining the persistence and long-term consequences of the observed early-life effects.

Furthermore, while the findings remain statistically significant for many parameters, replication with larger cohorts would provide more robust validation of these results and strengthen conclusions regarding dose-dependent effects.

This study provides evidence that perinatal exposure to BPA, even at environmentally relevant doses, disrupts leptin signaling and induces

early metabolic and hepatic dysfunction in Wistar rats. These disruptions include altered glucose and lipid metabolism, oxidative stress, and hepatic enzyme activity. The observed changes suggest a potential mechanistic link between early leptin suppression and subsequent metabolic dysregulation. While these findings contribute to our understanding of endocrine disruption during critical developmental windows, further studies are needed to establish these effects' long-term impact and relevance in human populations. Nonetheless, these results underscore the importance of minimizing BPA exposure during pregnancy and early life.

Declarations

Ethics approval and consent to participate

Ethical approval for this research was obtained from the University of Ilorin Animal Research Ethics Committee (Number: EERC/ASN/2024/2694), and the experiment was conducted in strict compliance with the committee's instructions, which conformed with internationally accepted guidelines and regulations for the care and use of

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Laboratory Animals in Biomedical Research.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests

Funding

The authors provided funding.

Authors' contributions

AA-O, AAN, and FMO conceptualised this work; YJS, TEO, FA, and SOO carried out the experiments; AA-O, AAN, and FMO supervised the work; YJS, AA-O, SOO, and AAN analysed the results and wrote the manuscript. All authors read the manuscript and approved it for submission.

Acknowledgements

The authors would like to acknowledge the staff of the Pharmacology and Therapeutics Department, University of Ilorin; the Central Research Laboratory, Ilorin; Bridge Biotech, Ilorin; and the Raw Materials Research and Development Council, Maitama, Abuja. Nigeria.

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