Polyvinyl chloride exposure induces Liver injury: A biochemical and histological evaluation

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ABSTRACT

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| **Objective**: Microplastics are ubiquitous in our environment, with evidence of its presence in various body tissues, however the extent of its toxicity at low dose from chronic administration and bioaccumulation in humans remains unknown. This study aims at evaluating the toxicological impact of sub-chronic administration of polyvinyl chloride on the liver.  **Methods**: 50 adults male wistar rats were orally administered 10 ml/kg of deionized water (control), and treatment groups received 0.1,0.2 and 0.3mg/kg of PVC daily for 42 days using an oro-gastric tube. Liver enzymes (AST, ALT, ALP), oxidative biomarkers (GSH, GPx, CAT, SOD and MDA) and the histoarchitecture were examined. Statistical analysis was performed using ANOVA with p value <.05  **Results:** There was a disproportionate elevation of liver enzymes with a dose dependent pattern, suggestive of hepatic damage, antioxidative stress biomarkers where decreased (GSH, GPx, CAT and SOD) with an increase in pro-oxidative biomarker (MDA) indicative of an overwhelmed liver oxidative stress defense mechanisms, additionally the histomorphology of the liver showed distorted with loss of radial symmetry, ballooning of hepatocytes and loss of parenchyma organization.  **Conclusion:** This finding provides empirical data that PVC induces dose dependent hepatotoxicity in wistar rats, with biochemical and histological evidence. This further demonstrates that sub-chronic exposure to PVC poses grave health risk to the liver of exposed population and the need for human translational studies and policy to safeguard exposed persons. |

*Keywords: Polyvinyl chloride (PVC), Microplastics, Sub-chronic toxicity, Oxidative stress, liver enzymes, bioaccumulation*

1. INTRODUCTION

The world invention of plastics changed the world in the last centuries (Pilapitiya *et al*., 2024). The first plastic was created in 1860, and the global plastic industry began in 1907. Industrialisation occurred in the 1920s, and plastic manufacturing increased in the 1940s. Plastic output rose from 2 million tonnes in 1950 to 368 million tonnes in 2019. Utilisation of plastic grew 180 times from 1950 to 2018. Global plastic manufacturing will exceed 400.3 million tonnes in 2022 (Bashir *et al*., 2021; Williams & Rangel-Buitrago, 2022; Li *et al*., 2023; Rafey & Siddiqui, 2023). Plastics are utilized by manufacturing industries for a wide variety of products, due to the desirable properties of light weight, resilience, durability, chemical inertness and cost-effectiveness, therefore serving as an effective substitute for traditional packaging materials such as glass and paper (Kumar *et al*., 2021; Chawla *et al*., 2022).

However, these plastics undergo degradation into minute particles known as microplastics (<5 mm) and nanoplastics (<1 μm) through environmental activities (Zhao *et al*., 2017; Zimmermann *et al*., 2021). They can be grouped as primary microplastics which are intentionally manufactured for industrial use, such as resin pellets used in textile fibres, toothpaste, plastic products, and cosmetic microbeads (Begum *et al*., 2020; Bashir *et al*., 2021; Lee *et al*., 2022) or secondary microplastics which are generated as products from environmental degradation such as hydrolysis, photodegradation, thermo-oxidative degradation, and biodegradation (Sharma & Chatterjee, 2017; Zarus *et al*., 2021; Ziani *et al*., 2023; Mathew *et al*., 2024).

Microplastic fragments are ubiquitous in our environment and pose a significant health and environmental risk (Chen *et al*., 2022; Lamichhane *et al*., 2023). Most plastic chemicals are not covalently bonded to polymer matrix, and can leach easily into food, drinks and other items for consumption (McCombie *et al*., 2016). Plastic chemicals can also leach into natural environments from littering, resulting in the exposure of wildlife, which in turn enters the food chain and through biomagnification get to man and finally induce toxicity (Capolupo *et al*., 2020; Cunningham *et al*., 2022). The abundance of the microplastics is largely due to the mismatch between the plastic waste generated and efficient waste management systems (McCombie *et al*., 2016; Imhof *et al*., 2016; Horton *et al*., 2017; Li *et al*., 2020; Zarus *et al*., 2021; Zimmermann *et al*., 2021; Ziani *et al*., 2023; Rajvanshi *et al*., 2024).

Plastics are grouped into Polyethyelene (PE), Polypropylene (PP), Polystyrene (PS), Poly (ethylene terephthalate) (PET); and Poly vinyl chloride (PVC) (Andrade, 2011; Cunningham *et al*., 2022). Poly (vinyl chloride). Among these, PVC is the most widely used polymer due to its diverse array of short- and long-term use, low-cost, adaptability to manufacturers and users’ needs (Makris *et al*., 2020; Zhang *et al*., 2020; Lewandowski & Skórczewska, 2022; Amobonye *et al*., 2023; Chen *et al*., 2024; Xiu *et al*., 2024). Conversely, PVC production and use emits hydrogen chloride and dioxins, among other highly toxic and carcinogenic chemicals that have been demonstrated to induce multisystemic toxicity in rats, guinea pig and liver angiosarcoma in humans (Wagoner, 1983; Tickner *et al*., 2001; Isobe *et al*., 2017; Archana, *et al*., 2018; Banerjee *et al*., 2021; Amobonye *et al*., 2023).

The liver is the main metabolic hub for detoxification of xenobiotics (Zhao *et al*., 2023). Through the enterohepatic circulation xenobiotics like microplastic through a continuous process of reabsorption from the intestines into the liver, may accumulates in the liver hepatocytes (Wang *et al*., 2023; 2024). Consequently, eliciting oxidative stress, inflammation, and damage to the liver hepatocytes resulting in metabolic disturbance and liver failure (Muncke *et al*., 2020; Chiang *et al*., 2024). This failure results in increase levels of these particles in systemic circulation leading to neurotoxicity and other multisystemic (Li *et al*., 2022; Wang *et al*., 2022; Zhou *et al*., 2023).

Given the multisystemic consequences and growing concerns about the attendant health risk of PVC exposure, there still exist a need to evaluate the underexplored impact from long-term low dose PVC exposure on liver function. This study examines the effect of sub-chronic PVC exposure on wistar rats, liver enzymes, oxidative stress biomarkers and the histoarchitecture.

**2.0 MATERIALS AND METHODOLOGY**

**2.1 Experimental site**

This study was conducted at the Animal House of the Department of Pharmacology, Faculty of Basic Medical Sciences, Delta State University, Abraka.

**2.1.1 Experimental Animals**

Fifty (50) adults male Wistar rats weighing between 90–140 g were procured from the Animal House Unit, Faculty of Basic Medical Sciences, Delta State University, Abraka. The animals were acclimatized for two weeks under standard laboratory conditions: a 12-hour light/dark cycle, temperature range of 20–31°C, with unrestricted access to standard rat feed and water. Ethical approval was obtained from the Ethical Committee of the Faculty of Basic Medical Sciences, Delta State University, Abraka, Nigeria (approval no. RBC/FBMC/DELSU/25/921) and conducted in accordance with the Guideline for the Care and Use of Laboratory Animals (NIH Publication No. 85-23, revised 1985).

**2.1.2 Apparatus/Equipment**

The following equipment was used: plastic cages (42 × 30 × 27 cm), needles, syringes, oral cannula, wash bottles, hand gloves, Y-maze, open-field apparatus, tissue homogenizer, refrigerated centrifuge, digital weighing balance (JA 2003), VIS spectrophotometer (722N), thermostatic water bath (DK 420), incubator (Techmel and Techmel USA), refrigerator (Haier Thermocool), micropipettes (REMI) 100–1000 µl, mortar and pestle, cotton filters, plastic containers, test tubes, racks, floating bath, microtome, tissue processor, cassettes, microscope slides, measuring cylinders, staining racks, cover slips, dissecting kit, and laboratory coats.

**2.1.3 Chemicals/Reagents**

Analytical-grade reagents were used, including: Polyvinyl chloride (PVC), 5,5′-dithiobis (2-nitrobenzoic acid) (DTNB), trichloroacetic acid (TCA), thiobarbituric acid (TBA), Tris (hydroxymethyl)aminomethane (Tris buffer), acetic acid, sodium bicarbonate, sodium carbonate, disodium hydrogen phosphate monohydrate, sodium dihydrogen phosphate monohydrate, potassium dichromate, potassium chloride, and sodium hydroxide—all sourced from reputable suppliers such as Aldrich, BDH, and Sigma-Aldrich.

**2.2.0 Experimental Design**

**2.2.1 PVC and Cyclohexanone Stock Preparation**

PVC stock was prepared by dissolving 0.01 g of PVC in 1 ml of cyclohexanone (modified from Finlayson & Cooke, 1951), followed by the addition of 9 ml of absolute ethanol and 190 ml of distilled water to make a final volume of 200 ml (adapted from Herrera *et al*., 2018).

**2.2.2 In vivo exposure**

The Fifty Adult Male Wistar rats, were grouped into 5 main groups: A-E containing 10 animals each. Group A (Negative control) Group B (Positive control), C, D and E served as treatment groups respectively. Group A (negative control) received food and deionized water only, while B (positive control received 0.1mg/kg of cyclohexanone), while treatment groups C, D and E received 0.1, 0.2, and 0.3mg/kg of PVC solution respectively. Treatment was orally administered daily for 45 days using oro-gastric tube, and terminated after 45 days, following which the animals were euthanized after behavioral evaluation.

**2.2.3 Dosage selection**

The doses of PVC utilized for this study were 0.1mg/kg, 0.2mg/kg and 0.3mg/kg, selected from previous studies (Deng *et al*., 2017) and duration of 45days for sub-chronic toxicity modelled based Said, *et al*., (2023) study.

**2.2.4 Protein estimation**

Total protein concentration was estimated using the biuret method. Briefly, 0.1 mL of sample was diluted with 0.9 mL distilled water and 3 mL of biuret reagent was added. The mixture was incubated at room temperature for 30 minutes and absorbance was measured at 540 nm. A bovine serum albumin standard (0.01–0.1 mg/mL) was used for calibration (Mahesha, 2012).

**2.2.5 Assessment of total bilirubin**

Total bilirubin level was determined by colorimetric method using assay kit (Randox, United Kingdom) according to the manufacturer’s protocol fol-lowing the method earlier described by Jendrassik and Grof, 1983. About 0.2 mL of sample was added to 3.0 mL of working solution (dilute hydrochloric acid; 0.7 mmol/L, pH 0.7: containing, 2.5 mmol of sodium nitrite, 10 mmol of sulfanilic acid, 1.0 mol of citric acid, 0.5 mol of caffeine, 3.0 mol of urea, and 0.5 g of surfactant) for the test and the sample blank, respectively. Thereafter, the mixture will be incubated at room temperature (25 o C) for 5 min and read at 578 nm vs the sample blank (George *et al*., 2011).

**2.2.6 Assessment of alanine aminotransferase**

The activity of alanine aminotransferase (ALT) in serum was quantified using spectrophotometry. Blood was obtained from each mouse via ocular puncture using a heparinised capillary tube, transferred into a lithium heparinised sample container, and centrifuged at 10,000 rpm for 15 minutes in a cool centrifuge. The serum was taken individually for each animal, and 0.1 mL of each sample was combined with 0.5 mL of a solution containing sodium phosphate buffer (100 mmol/L, pH 7.4), L-alanine (200 mmol/L), and α-oxoglutarate (2 mmol/L). The mixture was thereafter incubated for 30 minutes at 37˚C. Subsequently, 0.5 ml of 2,4-dinitrophenylhydrazine (2 mmol/L) was added to the reaction mixture and allowed to incubate for 20 minutes at 25˚C. Subsequently, 5.0 ml of sodium hydroxide (0.4 mol/L) was introduced, and the absorbance measured against the reagent blank after 5 minutes at 546 nm. The ALT units was denoted as U/L (George et al., 2011).

**2.2.7 Assessment of aspartate aminotransferase**

The activity of aspartate aminotransferase (AST) in serum was quantified using spectrophotometry. Blood was obtained from each mouse via ocular puncture using a heparinised capillary tube into a lithium heparinised sample container and was spun at 10,000 rpm for 15 minutes in a cool centrifuge. Serum was collected individually for each animal, and 0.1 mL of each sample was combined with 0.5 mL of a solution containing sodium phosphate buffer (100 mmol/L, pH 7.4), L-aspartate (100 mmol/L), and α-oxoglutarate (2 mmol/L). The mixture was thereafter incubated for 30 minutes at 37˚C. Subsequently, 0.5 ml of 2,4-dinitrophenylhydrazine (2 mmol/L) was incorporated into the reaction mixture and allowed to stand for precisely 20 minutes at 25˚C. Subsequently, 5.0 ml of sodium hydroxide (0.4 mol/L) was introduced, and the absorbance measured against the reagent blank after 5 minutes at 546 nm. The units of AST will be denoted as U/L (George et al., 2011).

**2.2.8 Assessment of alkaline phosphatase**

The activity of alkaline phosphatase (ALP) in serum was measured spectrophotometrically. Blood was obtained from each mouse via ocular puncture using a heparinised capillary tube into a lithium heparinised sample container and subsequently spun at 10,000 rpm for 15 minutes in a cool centrifuge. Serum was taken individually from each animal, and 0.05 mL of each sample was combined with 0.5 mL of a solution containing diethanolamine buffer (1 mol/L, pH 9.8) and Magnesium Chloride (0.5 mmol/L) in a test tube. Subsequently, 3 ml of p-nitrophenyl phosphate (10 mmol/L) was incorporated into the reaction mixture and maintained at 25˚C. Subsequently, absorbance was measured at 0, 1, 2, and 3 minutes, respectively, at 405 nm (Augustine 2019). The units of ALP were denoted as U/L (George et al., 2011).

**2.3.0 Determination of glutathione (GSH) concentration**

Aliquots of liver supernatant from individual mice in the relevant treatment groups was collected, and GSH concentration was assessed using the method established by Moron et al. (1979). An equal volume (0.4 ml) of liver homogenate will be combined with 0.4 ml of 20% TCA and thereafter spun in a chilled centrifuge at 10,000 rpm at 4°C for 20 minutes. To 0.25 ml of the supernatant, 2 ml of 0.6 mM DTNB was added, and the final volume adjusted to 3 ml with 0.2 M phosphate buffer at pH 8.0. The absorbance was subsequently measured at 412 nm against a blank reagent use a spectrophotometer. The quantities of GSH in liver tissues were quantified in micromoles per gramme of tissue μmol/g tissue (Igben et al., 2023).

**2.3.1 Estimation of malondialdehyde level**

The liver concentration of MDA, a biomarker indicative of lipid peroxidation, was assessed using the technique established by Adam-Vizi and Seregi (1982). An aliquot of 0.4 ml of the supernatant was combined with 1.6 ml of Tris–KCl buffer, followed by the addition of 0.5 ml of 30% TCA. Subsequently, 0.5 ml of 0.75% TBA was introduced and incubated in a water bath for 45 minutes at 80°C. The mixture was subsequently chilled in ice and centrifuged at 3000 rpm for 15 minutes. The transparent supernatant was obtained, and absorbance was assessed relative to a distilled water reference blank at 532 nm utilising a spectrophotometer. The MDA concentration was determined utilising a molar extinction coefficient of 1.56×10^5 M^-1 cm^-1, with results represented as micromoles of MDA per gramme of tissue (Yilgor & Demir, 2024).

**2.3.2 Determination of superoxide dismutase (SOD) activity**

SOD activity was assessed using the technique established by Misra and Fridovich (1972). In summary, 0.1 ml of liver supernatant was combined with 2.6 ml of 0.05 M carbonate buffer (pH 10.2) for equilibration in the spectrophotometer, and the reaction commenced with the addition of 0.3 ml of newly generated 0.3 mM adrenaline to the mixture, which was promptly mixed by inversion. The reference cuvette had 2.6 ml of buffer, 0.3 ml of adrenaline, and 0.1 ml of distilled water. The absorbance at 480 nm was recorded at 60-second intervals for a duration of 3 minutes. The activity of superoxide dismutase (SOD) was quantified in units of adrenaline used per minute per milligramme of protein (Igben et al., 2025).

**2.3.3 Estimation of catalase activity**

Catalase activity was determined according to the method previously described (Sinha, 1971). Aliquots of mouse brain supernatant (0.1 ml) will be added to 2 ml of sodium phosphate buffer (0.05 M; pH 7.4) and 0.9 ml of H2O2 (800 µmoles). The reaction mixture was mixed by a gentle swirling motion at room temperature and 1 ml of this mixture was added to 2 ml dichromate/acetic acid reagent. The absorbance was read using a spectrophotometer at a wavelength of 570 nm and change in absorbance at 60 s intervals. The catalase activity was expressed as μmol of H2O2 decomposed per minute per mg protein (Eduviere, *et al*., 2015).

**2.4.0**  **Animal sacrifice**

At the end of the 45-day exposure period, rats were weighed and sacrificed by cervical dislocation to avoid interference from anaesthetics, exploratory laparotomy was carried out and the liver tissue harvested.

**2.4.1 Sample collection**

The liver tissue in whole was carefully dissected, weighed, and fixed in 10% formal saline for histological analysis.

**2.4.2 Tissue processing**

The harvested liver tissues were processed manually through standard histological stages: fixation, dehydration, clearing, embedding, sectioning, mounting, staining, and photomicrography.

**2.4.3 Photomicrograph**

Prepared slides were viewed under a digital microscope (SCOPETEK DCM 500, 5.0 MP) connected to a computer. Photomicrographs were used to evaluate the histological and cytological effects on the liver, hippocampus and prefrontal cortex.

**2.4.4   Statistical analysis**

Statistical analysis was performed using GraphPad Prism® version 7.01 (GraphPad Software, Inc., La Jolla, CA, USA). Data were presented as mean ± standard error of mean (SEM). One- or two-way ANOVA followed by Bonferroni post hoc test was used to determine statistical significance. The p-value of = .05 was considered statistically significant.

3. results and discussion

**a**

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**c**

**b**

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**Fig 1- Effect of PVC on serum total protein, albumin levels, total bilirubin, unconjugated bilirubin levels and liver function enzyme levels (ALT, AST, and ALP) in Wister rats**

**4.5 Effect of PVC on Liver function test and Liver protein level in wistar rats (a) Bilirubin level (b) Liver protein level (c) Liver enzymes of male wistar rats. Bars represent the Mean ± SEM (n=5). \*P < 0.05, \*\*P < 0.01, \*\*\*P < 0.001 vs control using one-way ANOVA followed by Bonferroni’s post hoc test.**

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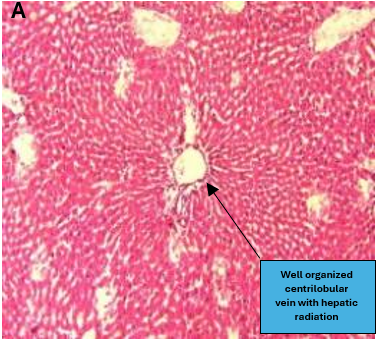


**e**

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**Fig. 2. Effect of PVC on liver oxidative biomarkers a. GSH (b) GPx (c) MDA (d) CAT (e) SOD Liver enzymes of male wistar rats.** Bars represent the Mean ± SEM (n=5). \*P < .05, \*\*P < 0.05, \*\*\*P < .001 vs control using one-way ANOVA followed by Bonferroni’s post hoc test.

**GSH-Glutathione, GPx-Glutathione Peroxidase, MDA-Malondialdehyde, CAT-Catalase, SOD-Super oxide Dismutase**

A close-up of a microscope

AI-generated content may be incorrect.

**e**

A close-up of a microscope slide

AI-generated content may be incorrect.A close-up of a red and white structure

AI-generated content may be incorrect.

A close-up of a red tissue

AI-generated content may be incorrect.

**Fig 3-** Photomicrographs of hematoxylin and eosin (H&E) stained liver sections, **(A)** there is preservation of the hepatic lobular architecture with clear central veins and radiating hepatic cords, sinusoidal spaces are intact, and hepatocytes display uniform morphology with no necrotic or signs of inflammation **(organized hepatic radial symmetry, with conserved central venule)** **(B)** the liver histoarchitecture appears normal, with well-organized hepatic cords radiating from the central vein. There is visible central nucleus in the hepatocytes with uniform well and distributed sinusoidal spaces. no visible signs of necrotic changes **(reactive hepatocytes, with increase basophilic nucleus, possible cell regeneration from repeated insults)** ( (**C**) there is mild disorganization of hepatic cords, and slight dilation of sinusoids, hepatocellular vacuolation and cytoplasmic granularity, as well as early ballooning degeneration in scattered hepatocytes, with minimal portal inflammation **(circle encircling disruption in radial symmetry of the hepatocytes)** **(D)** there is disorganization of lobular histoarchitecture with disruption of the radiating hepatic cords, there is observed inflammatory cell infiltration in periportal areas, along with early signs of vascular congestion. displays more pronounced changes, including increased cytoplasmic vacuolation and hepatocyte swelling, sinusoidal dilation, and mild inflammatory cell infiltration. Notably, focal necrosis is observed in some lobules **(blue arrow pointing at disorganization of the parenchyma architecture)** **(E)** there is significant hepatocellular degeneration, necrosis, and loss of lobular architecture. prominent vascular congestion, central vein dilation, and haemorrhagic foci are evident. Moderate portal inflammation accompanied by marked disruption of normal lobular architecture, widespread ballooning and necrotic hepatocytes, dense inflammatory cell infiltration, and sinusoidal congestion **(black circle shows loss of radial symmetry, and coalescent of the central venules)**. Furthermore, there is evidence of beginning fibrosis, areas with cell dropout, and possible regeneration nodules.

(A: Control, B: Cyclohexanone 2ml/kg, C: 0.1 PVC mg/kg, D: 0.2 PVC mg/kg, E. 0.3 PVC mg/kg)

**4.0 DISCUSSION**

Chronic exposure of human cells to microplastic results in increase generation of ROS, oxidative damage and inflammation (Mahmud, *et al*., 2020; Dong *et al*., 2020; Das, A., 2023; Lee, *et al*., 2024; Zou, *et al*., 2025). Data from studies have shown that PVC induces toxicity in in the liver and intestine of aquatic organisms and terrestrial mammals (Chen, *et al*., 2022; Chen, *et al*., 2022; Chen, *et al*., 22024; Lolescu *et al*., 2024; Romeo, *et al*., 2025).

Derangement in liver enzymes level of ALT (Alanine transaminases), AST (Aspartate transaminase) to ALP (Alkaline phosphatase), bilirubin and albumin, signifies liver damage rather than disturbance in liver's function. Hepatocellular damage is characterized by elevation in AST and ALT levels. While cholestatic diseases manifest as elevation in ALP and bilirubin levels. In mixed hepatic damage there is elevation of both ALP and AST/ALT levels (Lala, *et al*., 2023). These enzymes are non-specific, because they are also expressed in other organs (kidneys, pancreas, bones, and intestines). To improve reliability and specificity in our study, liver homogenate was used for enzyme assay analysis.

Findings from this study noted that there was significant increase in the liver enzyme levels (AST, ALT, ALP) in the 0.2mg/kg group and more in 0.3 mg/kg group, compared to 0.1group and control (negative and positive) p<.05, this corroborates the findings from the work of Kalas *et al*., (2021), which showed a similar alteration in enzyme levels. According to Rochling, (2001), ALT is a more specific enzyme marker that depicts hepatocellular damage when compared to AST or ALP, and our data showed significant elevation in ALT level, affirming that PVC induces hepatocellular damage in the liver.

Albumin is the commonest plasma protein and contributes about 80% of plasma colloidal osmotic pressure. It appears to have antioxidant, anti-inflammatory, ligand-binding, and transport properties in addition to regulating colloidal osmotic pressure. With hepatic dysfunction, advanced cirrhosis, liver albumin production decreases (Chen, *et al*., 2021; Jagdish *et al*., 2021; Sheinenzon *et al*., 2021; Cunningham and Porat-Shliom, 2021). In this study the results showed significant decrease in levels of total protein and serum albumin in the 0.2-0.3mg/kg treated groups (p<.05). These findings support already established data from meta-analysis studies confirming the benefits of albumin in reducing hyponatremia, post-PICD, GI bleeding, recurrence of ascites, renal failure, HE, and mortality in patients with liver cirrhosis after large-volume paracentesis, and consequent clinical implications of its reduction (Bernardi, et al., 2012; Carvalho & Machado, 2018; Shrestha *et al*., 2021; Zheng, *et al*., 2021).

Bilirubin is a by-product of hemoglobin catabolism, which is conjugated in the liver into soluble form for ease of excretion (Vitek *et al*., 2023). An elevation is serum bilirubin levels especially unconjugated fraction, indicates liver damage with consequent impair conjugation capability (Guerra Ruiz *et al*., 2021; Vítek & Tiribelli, 2021). In this study, the rats in the treated group all showed a significant increase (p<.05) in the level of total and indirect (unconjugated) bilirubin levels, this suggests severe impairment in the conjugating ability of the liver (Brites and Silva, 2021).

According to Hy’s law, concurrent elevations in AST/ALT and bilirubin strongly suggest drug or toxin related liver injury (Re *et al*., 2015; Barritt, *et al*., 2022), which supports our mechanistic hypothesis, that PVC microplastic induces direct liver injury through direct toxicity, oxidative stress, and hypoxia from vascular stasis or thrombosis.

Malondialdehyde (MDA) is a derivative from the peroxidation of polyunsaturated fatty acids. It serves as a biomarker used for measuring oxidative stress in biological models and its values are affected a range of diseases (Cordiano, *et al*., 2023). This study reported an increased MDA levels in 0.2-0.3mg/kg treated groups (p<.05), aligning with earlier evidence that PVC induces hepatotoxicity through ROS generation (Jawdhari et al., 2023).

Oxidative stress occurs due to disequilibrium between pro-oxidants (ROS), reactive nitrogen species (RNS) and antioxidants defense mechanisms. The release of free radicals damages subcellular and cellular biomolecules such as lipids, proteins, and DNA. The counter defense systems work to mitigate this impact through enzymatic antioxidants like superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx), as well as non-enzymatic antioxidants like glutathione (GSH) (Carmo *et al*., 2022; Tekin & Seven, 2022; Zarezadeh *et al*., 2022). Initially, these enzymes are upregulated, but chronic exposure results in their depletion. From our study, the levels of GSH, GPx, SOD, and CAT were significantly decreased (p<.05) in the treated groups 0.2 and 0.3mg/kg, especially in the 0.3 mg/kg group, this suggests a compromise in the antioxidant defences and increase vulnerability to oxidative damage

Histological sections of liver tissue revealed parenchymal distortion characterized by vascular stasis, nuclear enlargement, and disruption of hepatocyte radial symmetry. Hepatocytes appeared irregular in shape, with congestion of the central vein, there was also dilation and infiltrated by inflammatory cells and erythrocytes. These changes occurred in a dose-dependent manner in groups treated with 0.2 mg/kg and 0.3 mg/kg PVC, as compared to controls findings consistent with previous studies.

Taking together, the biochemical and histopathological finding from this study, it affirms the position that PVC at low dose and sub-chronic exposure, induces dose dependent hepatocellular injury with disturbance in metabolic, synthetic, biochemical, and enzymatic functions.

4.1. Limitation of study

While this study provides important data on the toxic impact of PVC on the liver, the methodology was limited by the use of male wistar rats, which does not take into consideration gender specific impact of reproductive hormones on metabolic outcome. Although biochemical assay was done, molecular analysis, such as gene profiling, inflammatory markers to determine the subcellular mechanism behind the cell death was not done which could give more insight on the mechanistic pathway of the induced toxicity. Additionally, other modulatory environmental and physiological variables like gut microbiota, diet et were not considered.

4.2 Conclusion

This study established that sub-chronic oral administration of low dose PVC to male wistar rats, resulted in dose-dependent hepatic tissue injury with distortion of physiological and anatomical structure through oxidative stress and inflammation. This finding highlights the attendant health and environment risks of PVC exposure and the need for stronger regulatory control from policy maker to help limit plastic exposure especially in occupational and industrial environments

Consent (WHEREVER applicable)

Not applicable

Disclaimer (Artificial intelligence)

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

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