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Original Article

Aqueous Fruit Extract of *Telfairia occidentalis* Attenuates Nickel-Chloride-Induced Renal Oxidative Stress and Dysfunction in Wistar Rats

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Abstract

Introduction: Nickel chloride ($NiCl_2$) is an environmental toxicant that induces oxidative stress (OS) and renal dysfunction. Natural products with antioxidant properties, such as *Telfairia occidentalis*, may provide protective effects. Thus, this study aimed to investigate the nephroprotective potential of *T. occidentalis* aqueous fruit extract against $NiCl_2$-induced renal toxicity in adult Wistar rats.

Methods: Twenty-four adult female Wistar rats were randomly assigned to control, $NiCl_2$ (5 mg/kg, intraperitoneally), *T. occidentalis* + $NiCl_2$, and *T. occidentalis* only groups (n = 6 each). *T. occidentalis* aqueous fruit extract was orally administered by gavage at 200 mg/kg once daily. Then, body weight, kidney weight, renal function indices (urea and creatinine), serum electrolytes (sodium, potassium, and chloride), OS markers (superoxide dismutase [SOD], catalase [CAT], glutathione [GSH], malondialdehyde [MDA]), and kidney histology underwent assessment. Finally, data were analyzed using one-way analysis of variance followed by Tukey's honestly significant difference post hoc test.

Results: $NiCl_2$ exposure significantly reduced body weight and antioxidant enzyme activities (SOD, CAT, and GSH) while increasing MDA levels and renal biomarkers (urea, creatinine, sodium, and chloride) compared with controls ($P<0.05$). Moreover, histopathology revealed glomerular distortion, widened Bowman's space, tubular necrosis, and vascular congestion (blood vessels). Ultimately, the co-administration of *T. occidentalis* extract substantially improved antioxidant status, normalized renal biomarkers, and preserved renal histoarchitecture when compared to control animals.

Conclusion: The aqueous extract of *T. occidentalis* effectively mitigated $NiCl_2$-induced nephrotoxicity through antioxidant and cytoprotective mechanisms, suggesting that *T. occidentalis* may serve as a natural protective agent against heavy-metal-induced renal damage.

Keywords: Antioxidants, Heavy Metals, Nephrotoxicity, *Telfairia Occidentalis*, Nickel Chloride, Natural Products

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Introduction

Nickel (Ni) is widely utilized in industrial processes, increasing environmental and occupational exposure. Nickel chloride ($NiCl_2$), one of its most reactive forms, readily accumulates in the kidneys due to their high perfusion and filtration activity, making them a principal target of toxicity (1-3). Moreover, $NiCl_2$ exposure disrupts renal physiology by inducing oxidative stress (OS), impairing mitochondrial function, altering electrolytes, and activating inflammatory pathways, ultimately contributing to renal dysfunction (4, 5).

The kidney's susceptibility to metal-induced injury is attributed to its metabolic activity and lipid content. Experimental evidence indicates that $NiCl_2$ increases reactive oxygen species (ROS), suppresses antioxidant enzymes, including superoxide dismutase (SOD), catalase (CAT), and glutathione (GSH), and promotes lipid peroxidation, resulting in glomerular and tubular injury and altered renal biomarkers (6-8).

In response to the limitations of conventional therapies, attention has shifted to natural products with antioxidant potential. *Telfairia occidentalis*, a widely consumed West African vegetable, contains phytochemicals, such as flavonoids, phenolics and vitamins, which are known for cytoprotective and free-radical-scavenging effects (9–11). According to previous studies, extracts of the plant can

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enhance antioxidant defenses while reducing tissue damage caused by toxic agents (12, 13).

Given this background, the present study aims to evaluate whether aqueous *T. occidentalis* fruit extract can mitigate $NiCl_2$-induced nephrotoxicity in adult Wistar rats through biochemical, OS, and histopathological assessments.

Materials and Methods

Experimental Animals

Twenty-four adult female Wistar rats (185–200 g) were obtained from the Animal House of the University of Benin, Nigeria. The animals were housed in polypropylene cages under controlled environmental conditions (temperature: 22–25°C; relative humidity: 50–60%; 12-hour light/dark cycle). In addition, standard commercial rat pellets (Top Feeds Ltd., Nigeria) and water were provided **ad libitum**. A two-week acclimization period preceded the experiment.

Additionally, all procedures complied with institutional animal-care regulations. Although no formal approval number was issued, oral ethical approval was granted by the University of Benin Ethics Committee. Furthermore, all procedures adhered to humane handling standards, including the minimization of stress and adherence to the 3Rs.

Plant Collection and Extract Preparation

Fresh mature fruits of *T. occidentalis* were purchased from a local farm market in Benin, Nigeria. Authentication was conducted at the Department of Plant Biology and Biotechnology, University of Benin, and a voucher specimen was deposited (Voucher No: UBH-T187).

Then, the fruit pulp was washed, sliced, and air-dried at ambient room temperature (27–30°C) until constant weight. Next, the dried samples were milled into fine powder using a mechanical grinder (Binatone BLG-595, China).

Exactly 500 g of the powdered fruit material was macerated in 2.5 L of distilled water for 72 hours with intermittent agitation on an orbital shaker (Stuart SSL1, UK). Afterward, the mixture was filtered through muslin cloth followed by Whatman No. 1 filter paper (Cat No. 1001-125, GE Healthcare Life Sciences). The filtrate was then concentrated using a rotary evaporator (Buchi Rotavapor R-300, Switzerland) at 40°C, and the resulting semi-solid extract was dried and stored at 4°C in airtight amber containers. Finally, working doses were freshly reconstituted in distilled water each day prior to administration.

Chemicals and Reagents

$NiCl_2$ hexahydrate (≥ 98% purity, Sigma-Aldrich, USA; Cat. No. 654507) was dissolved in normal saline and intraperitoneally administered at 5 mg/kg body weight (14).

All biochemical assay kits, including those for creatinine, urea, electrolyte, and OS parameters, were obtained from Randox Laboratories Ltd. (Crumlin, UK), comprising SOD (Cat. No. SD125), CAT (Cat. No. CA251), GSH (No. GT251), and MDA/TBARS (No. TBARS100) kits.

Experimental Design and Treatment Schedule

Rats were randomly divided into four groups (n = 6). Group A (control) received distilled water only orally. Groups B and C were given 5 mg/kg of $NiCl_2$ (intraperitoneally) and *T. occidentalis* aqueous fruit extract (200 mg/kg) + 5 mg/kg $NiCl_2$, respectively. Finally, group D received 200 mg/kg of *T. occidentalis* extract orally.

Treatment Duration

All treatments were administered once daily for 28 days. Furthermore, $NiCl_2$ was administered 30 minutes after extract administration in Group C, and body weight was recorded on a weekly basis.

Sample Collection

At the end of the 28-day treatment period, the rats were fasted overnight and anaesthetized using ketamine hydrochloride (80 mg/kg, intraperitoneally). Once deep anesthesia was confirmed, the blood sample was collected via cardiac puncture into plain and heparinized tubes (Greiner Bio-One, Austria). Then, the serum was obtained by centrifugation at 3,000 rpm for 10 minutes using a Hettich EBA 200 centrifuge (Germany). Next, kidneys were excised, rinsed in ice-cold saline, and weighed using a digital analytical balance (Mettler Toledo ME-T Series, USA); one kidney from each rat was stored at −20°C for OS assays, while the contralateral kidney was fixed in 10% neutral buffered formalin for histology.

Oxidative Stress Assays

Kidney tissue homogenates (10% w/v) were prepared in ice-cold phosphate buffer (0.1 M, pH: 7.4) using a Teflon homogeniser (IKA Ultra-Turrax T25, Germany). The samples were then centrifuged at 10,000 rpm for 15 minutes at 4°C. Subsequently, SOD activity, CAT activity, GSH levels, and lipid peroxidation (MDA) were determined using the Randox SD125, CA251, GT251, and TBARS100 kits, respectively.

Assays were performed according to the manufacturers' instructions (Randox Laboratories Ltd.; SOD kit SD125; CAT kit CA251; GPx kit GT251; TBARS100). Eventually, absorbance readings were taken using a UV-Visible spectrophotometer (Jenway 6305, UK).

Histopathological Examination

Fixed kidney tissues were processed using standard paraffin-embedding techniques with a Leica TP1020 tissue processor (Germany). Moreover, tissues were sectioned at 4–5 µm using a Leica RM2235 microtome and stained with haematoxylin and eosin (H&E). The slides were then examined using an Olympus CX43 light microscope (Japan) at 100x and 400x magnifications.

Tissue processing and H&E staining followed standard protocols (15), and photomicrographs were captured using an attached Olympus EP50 digital camera.

Statistical Analysis

Data were expressed as means ± standard error of mean (SEM). In addition, statistical analysis was performed

using IBM SPSS Statistics, version 25.0 (IBM Corporation, Armonk, NY, USA). Paired t-test was used to compare the initial vs. final weights. Additionally, one-way analysis of variance and Tukey's honestly significant difference test were employed for between-group and post-hoc multiple comparisons, respectively, and a P-value of < 0.05 was considered statistically significant.

Results

Body Weight Changes

All groups were monitored for changes in body weight over the experimental period. Rats in the control and *T. occidentalis* 200 mg/kg groups showed a significant increase in final body weight compared to their initial weights ($P < 0.05$), whereas the $NiCl_2$ 5 mg/kg group demonstrated no significant change ($P = 0.110$). Interestingly, the *T. occidentalis* + $NiCl_2$ group displayed a slight, non-significant decrease in weight ($P = 0.058$). Related data are summarized in Table 1.

Weight Change and Kidney Parameters

The weight change (ΔWeight), kidney weight, and reno-somatic index significantly varied among the groups ($P < 0.001$). $NiCl_2$ exposure alone caused a modest increase in kidney weight and ΔWeight compared to the control, whereas *T. occidentalis* + $NiCl_2$ substantially increased kidney weight but resulted in negative ΔWeight. Finally, *T. occidentalis* 200 mg/kg alone maintained normal ΔWeight and kidney parameters (Table 2).

Kidney Function and Electrolytes

Ni exposure remarkably increased serum urea, creatinine, and potassium and sodium ion levels, while chloride levels decreased compared to the control ($P < 0.05$). Based on the results, the co-administration of *T. occidentalis* could mitigate these alterations, with most values approaching those of the control group. Eventually, *T. occidentalis* alone maintained normal kidney function parameters (Table 3).

Oxidative Stress Parameters in Kidney

Exposure to $NiCl_2$ significantly reduced antioxidant enzyme activities (SOD, CAT, and GPx) while increasing MDA levels compared to the control ($P < 0.001$). Additionally, treatment with *T. occidentalis* either alone or in combination with $NiCl_2$ restored SOD and GPx activity close to or above the control values. CAT activity remained reduced in the TO+Ni group (Table 4).

Histopathology of the Kidney

Histology

Kidney histology was evaluated using H&E staining at 100x and 400x magnifications. Based on the results (Figures 1A and 2A), control kidneys exhibited normal renal architecture with intact glomeruli (G), Bowman's spaces (BS), proximal (PCT) and distal tubules, and minimal interstitial space (IS).

Discussion

The findings of the present study demonstrated that $NiCl_2$ induces significant renal toxicity characterized by impaired renal function, OS, electrolyte imbalance, and severe histopathological alterations, which aligns with prior reports, indicating that $NiCl_2$ promotes mitochondrial disruption, ROS generation, membrane lipid peroxidation and inflammatory pathways (1-6). The reductions observed in SOD, CAT, and GPx, alongside elevated MDA, confirm OS as a key mechanism of $NiCl_2$ nephrotoxicity (16). Antioxidant and lipid-peroxidation values are reported in Table 4. Elevated creatinine, urea, and sodium further reflect glomerular and tubular dysfunction, which is in line with the findings of earlier toxicological research (16).

$NiCl_2$ exposure produced modest weight loss and

Table 1. Body Weight Parameters (Initial, Final, and Δweight; Mean ± SEM)

Group	Initial (g)	Final (g)	ΔWeight	*P*-Value
Ctrl	190.5 ± 0.6	202.3 ± 0.9	11.8 ± 0.5	< 0.001*
Ni 5	186.3 ± 2.3	190.3 ± 2.7	4.0 ± 1.1*	0.110
TO+Ni	196.8 ± 3.8	187.5 ± 4.0	-9.3 ± 2.3†	0.058
TO 200	191.5 ± 1.9	201.5 ± 0.9	10.0 ± 1.8	0.005*

Note. SEM: Standard error of the mean; Ctrl: Control; Ni 5: $NiCl_2$ 5 mg/kg; TO+Ni: *Telfairia occidentalis* 200 mg/kg + $NiCl_2$; TO 200: *T. occidentalis* 200 mg/kg only. Values are shown as means ± SEM. *$P < 0.05$ vs. initial weight (paired t-test)

Table 2. Weight Change and Kidney Parameters

Parameter	Ctrl	Ni 5	TO+Ni	TO 200	*P*-Value
Kidney wt (g)	1.25 ± 0.05	1.17 ± 0.03	1.45 ± 0.02†	0.88 ± 0.05	< 0.001
Reno-somatic index (%)	0.63 ± 0.03	0.59 ± 0.02	0.77 ± 0.02†	0.43 ± 0.02	< 0.001

Note. ANVOA: Analysis of variance; SEM: Standard error of the mean; HSD: Honestly significant difference; ΔWeight: Weight change (final – initial, g); Kidney wt: Kidney weight (g); Reno-somatic index: Kidney weight/body weight × 100 (%); Ctrl: Control; Ni 5: $NiCl_2$ 5 mg/kg; TO+Ni: *Telfairia occidentalis* 200 mg/kg + $NiCl_2$; TO 200: *T. occidentalis* 200 mg/kg. Values are expressed as means ± SEM. *$P < 0.05$ vs. Ctrl; †$P < 0.05$ vs. Ni 5 (Tukey's HSD post-hoc after ANOVA)

Table 3. Kidney Function and Electrolytes

Parameter	Ctrl	Ni 5	TO+Ni	To 200	*P*-Value
Urea mg/dL	77.55 ± 0.45	179.63 ± 2.33*	92.01 ± 0.11†	90.08 ± 0.60	< 0.0001
Creat mg/dL	1.369 ± 0.0002	2.576 ± 0.060*	1.325 ± 0.034†	1.622 ± 0.084	< 0.0001
K^+ mmol/L	1.999 ± 0.006	3.575 ± 0.036*	2.106 ± 0.102†	1.852 ± 0.130	< 0.0001
Na^+ mmol/L	163.93 ± 3.44	243.08 ± 1.82*	158.48 ± 0.82†	137.72 ± 3.66	< 0.0001
Cl^- mmol/L	18.33 ± 0.30	12.47 ± 0.11*	15.86 ± 0.27†	17.85 ± 0.61	< 0.0001

Note. ANVOA: Analysis of variance; SEM: Standard error of the mean; HSD: Honestly significant difference; Creat: Creatinine (mg/dL); K^+: Potassium (mmol/L); Na^+: Sodium (mmol/L); Cl^-: Chloride (mmol/L); Ctrl: Control; Ni 5: $NiCl_2$ 5 mg/kg; TO+Ni: *Telfairia occidentalis* + $NiCl_2$; TO 200: *T. occidentalis* only. Values are provided as means ± SEM. *$P < 0.05$ vs. Ctrl; †$P < 0.05$ vs. Ni 5 (Tukey's HSD post-hoc after ANOVA)

Table 4. Oxidative Stress Parameters in the Kidney

Parameter	Ctrl	Ni 5	TO+Ni	TO 200	*P*-Value
SOD U/mg protein	0.746 ± 0.007	0.318 ± 0.015*	0.785 ± 0.015†	0.804 ± 0.006*	<0.001
CAT U/mg protein	0.698 ± 0.006	0.218 ± 0.037*	0.103 ± 0.001†	0.612 ± 0.019	<0.001
GPx U/mg protein	0.626 ± 0.010	0.207 ± 0.006*	0.508 ± 0.010‡	0.541 ± 0.026*	<0.001
MDA nmol/mg protein	0.292 ± 0.010	0.858 ± 0.029*	0.159 ± 0.006†	0.214 ± 0.034	<0.001

Note. ANOVA: Analysis of variance; HSD: Honestly significant difference; SEM: Standard error of the mean; SOD: Superoxide dismutase (U/mg protein); CAT: Catalase (U/mg protein); GPx: Glutathione (GSH) peroxidase (U/mg protein); MDA: Malondialdehyde (nmol/mg protein). Ctrl: Control; Ni 5: $NiCl_2$ 5 mg/kg; TO+Ni: *Telfairia occidentalis* + $NiCl_2$; TO 200: *T. occidentalis* only. Values are expressed as means ± SEM. *$P<0.05$ vs. Ctrl; †$P<0.05$ vs. Ni 5 (Tukey's HSD post-hoc after ANOVA)

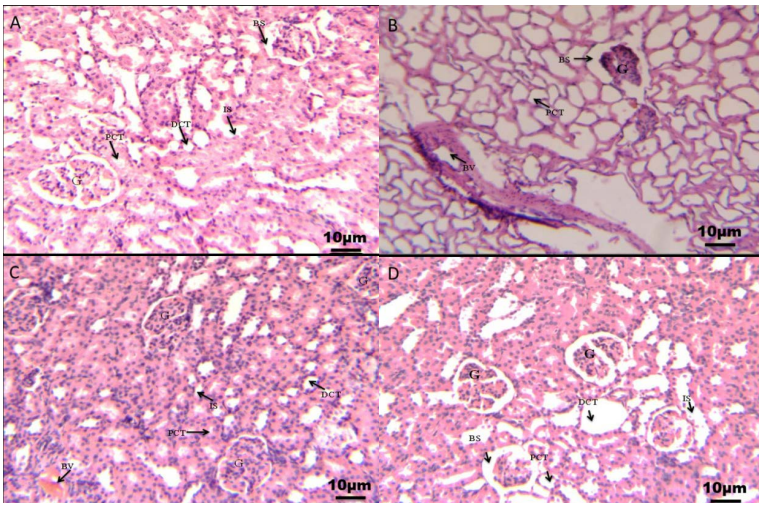


Figure 1. Photomicrographs of Kidney Sections (H&E Staining 100x) Showing: **(A)** Normal Renal Architecture With Intact G, BS, PCT, and Distal Convoluted Tubules, and Minimal IS, **(B)** $NiCl_2$-Treated Kidney With Distorted G, Widened BS, Tubular Necrosis, Cytoplasmic Vacuolation, Vascular Congestion (BV), and Expanded IS, **(C)** *Telfairia occidentalis* + $NiCl_2$-Treated Kidney Displaying Near-Normal Histoarchitecture With Restored G and Tubules, and **(D)** *Telfairia occidentalis*-Treated Kidney Depicting Preserved Renal Morphology Compared to Controls
Note. G: Glomeruli; BS: Bowman's spaces; PCT: Proximal convoluted tubules; IS: Interstitial space; BV: Blood vessels; H&E staining: Haematoxylin and eosin staining; $NiCl_2$: Nickel chloride. $NiCl_2$-treated kidneys showed distorted G, widened BS, tubular necrosis, cytoplasmic vacuolation, BV, and expanded IS (Figures 1B and 2B)

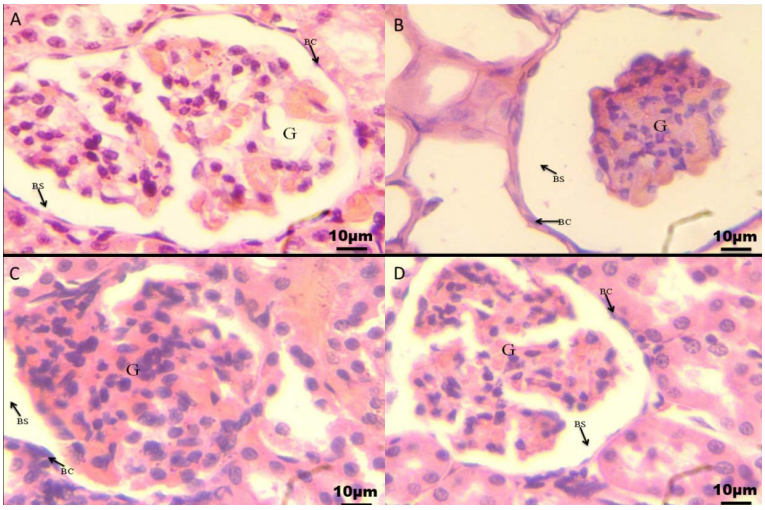


Figure 2. Photomicrographs of Kidney Sections (H&E Staining 400x) Illustrating: **(A)** Control With Normal Glomerulus, Open Capillary Loops, Clear Bowman's Space (BS), and Intact Bowman's Capsule (BC), **(B)** $NiCl_2$-Treated Kidney With Shrunken Glomerulus, Hypercellularity, Thickened BC, and Widened Bowman's Space, **(C)** *Telfairia occidentalis* + $NiCl_2$-Treated Kidney Showing Relatively Normal Glomerulus With Preserved BS, Capsule, and Minimal Tubular Degeneration, and **(D)** *Telfairia occidentalis*-Treated Kidney Depicting Normal Glomerulus, Open Capillary Loops, Clear Bowman's Space, and Intact Capsule
Note. *T. occidentalis*: *Telfairia occidentalis*; H&E staining: Haematoxylin and eosin staining; $NiCl_2$: Nickel chloride. Co-treatment with *T. occidentalis* resulted in near-normal histoarchitecture, with restored G and tubules and minimal tubular degeneration (Figures 1C and 2C). In addition, kidneys of the *T. occidentalis*-only group displayed morphology comparable to the control, confirming protective effects (Figures 1D and 2D)

increased kidney weight and reno-somatic index, consistent with systemic toxicity and renal inflammation. In addition, the electrolyte disturbances observed in this study (elevated Na^+ and K^+ and reduced Cl^-) likely reflect tubular dysfunction and impaired ion transport secondary to oxidative injury. These systemic and renal changes conform to previous reports regarding $NiCl_2$-induced metabolic disturbance, renal inflammation, and

tubular dysfunction (1, 5, 16). Moreover, the restoration of antioxidant enzymes (SOD and GPx) and reduction of MDA in extract-treated animals correlate with the observed near-normal histoarchitecture, suggesting that *T. occidentalis* mitigates oxidative membrane damage and preserves tubular reabsorptive function. Overall, our findings indicated that the extract's phytochemicals reduce ROS, limit inflammatory oedema, and help restore nephron ion-handling capacity, thereby explaining the improvements in serum urea and creatinine.

Treatment with *T. occidentalis* extract produced substantial renoprotection. The restoration of antioxidant enzymes indicated enhanced free-radical scavenging, which corroborates the plant's high phenolic and flavonoid content (9-12). Likewise, the improvement of creatinine, urea, and electrolytes reflected the functional recovery of nephrons. Histologically, *T. occidentalis* preserved glomerular architecture, mitigated tubular necrosis, and reduced blood vessels.

Furthermore, the combined biochemical and structural improvements revealed that the extract acts through multiple mechanisms, including ROS suppression, membrane stabilization and modulation of inflammatory pathways. The observed recovery of SOD and GPx activities alongside reduced MDA demonstrated a primary antioxidant mechanism; the persistent reduction in CAT activity in the TO+Ni group suggested partial enzyme-specific responses that merit further mechanistic study. In addition, the persistent reduction in CAT activity in the TO+Ni group indicated enzyme-specific recovery kinetics, warranting targeted time-course studies to determine whether CAT recovers later than SOD and GPx. Additionally, the normalization of electrolyte profiles further conformed improved tubular function, likely secondary to preserved epithelial integrity and reduced oxidative damage.

In summary, limitations of the present study included the use of a single extract dose, a single sex, and the absence of a formal dose-response assessment, limiting generalizability and precluding firm conclusions about the optimal therapeutic dose. For clarity, treatments were administered once daily for 28 days, and terminal sampling was performed under ketamine anaesthesia (80 mg/kg, intraperitoneally). Nonetheless, future studies should include both sexes, multiple extract doses, and additional markers of inflammation and apoptosis in order to delineate anti-inflammatory and anti-apoptotic contributions to renoprotection.

Conclusion

In general, the biochemical and histological data confirmed the therapeutic potential of *T. occidentalis* as an accessible natural product that attenuates $NiCl_2$-induced renal OS and dysfunction. Nonetheless, further pharmacological and mechanistic evaluation is warranted to characterize active constituents, dose-response relationships, and long-term safety.

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Authors' Contribution

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Competing Interests

The authors declare that they have no conflict of interests.

Ethical Approval

Permission for conducting this study was obtained from the College Ethics Committee of the College of Medical Sciences, University of Benin. Ethical approval was received on December 21st 2025 (approval No. CMS/REC/2025/869).

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