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Original Research Article

AMELIORATIVE EFFECTS OF VITAMIN C ON THE SURGERY-INDUCED HEPATIC AND RENAL STRESS IN ALBINO RATS

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ABSTRACT

Surgical stress triggers systemic pathophysiological responses that can compromise the structural integrity and functional capacity of vital organs, particularly the liver and kidneys. Vitamin C is a potent antioxidant with established cytoprotective properties, yet its role in attenuating surgery-induced hepato-renal stress remains underexplored. This study evaluated the effects of vitamin C supplementation on surgical stress-induced histomorphological and functional alterations of the liver and kidneys. Sixteen male albino rats randomly assigned to two groups (n = 8) underwent dead space wound procedure to induce physiological stress. Both groups received routine post-operative care, while group 1 received vitamin C (200 mg/kg, IM) for five days post-surgery. Hepatic and renal tissues were harvested for histopathology. Serum biochemical indices of liver and kidney function, including albumin, globulin, fibrinogen, aminotransferases, bilirubin, urea, and creatinine, were assessed, and relevant functional ratios computed to evaluate systemic and organ-specific stress responses. Rats in the untreated group exhibited marked degenerative changes in hepatocytes and renal tubular epithelium, accompanied by significant alterations in functional biochemical ratios indicative of hepatic synthetic suppression, activated acute-phase response, and hepato-renal dysfunction. In contrast, vitamin C–treated rats showed preserved hepatic and renal histoarchitecture, with significantly improved albumin–globulin, fibrinogen-based, and aminotransferase ratios, as well as normalized urea and creatinine levels. Vitamin C supplementation effectively ameliorated surgical stress–induced hepatic and renal histomorphological damage and functional impairments in albino rats. Thus supporting the potential use of vitamin C as an adjunctive therapy in post-surgical management to mitigate systemic stress and preserve vital organ function.

Keywords: Histomorphology, Kidney, Liver, Surgical Stress, Vitamin C

INTRODUCTION

Surgical stress involves a complex interplay of neuroendocrine, metabolic, and immune alterations, affected by the magnitude, invasiveness, and duration of surgery (Ivascu *et al*., 2024). Disruption of tissue by manipulation and incisions can lead to localised trauma and inflammatory responses (Desborough, 2000). Central to the inflammatory process are reactive oxygen species (ROS) that play vital roles in signalling and mediation of inflammation (Stevens, 2018).

Surgical stress is an evolutionary adaptive mechanism for survival, directed towards homeostasis and involves mobilization of energy at the expense of tissue repair (Ivascu *et al*., 2024). Where not managed, surgical stress may lead to undesirable post-operative outcomes, including infection, poor wound healing, metabolic derangements, and even organ dysfunction (Carli, 2015).

A global postoperative complication rate of about 16.8% and an overall mortality rate of ≈2.8% (International Surgical Outcomes Study group, 2016), including an estimated 310 million surgery patients annually (Weiser *et al*., 2008), shows the importance of ameliorating post-surgical stress and improving patient's wellbeing. Antioxidants may offer a simple and accessible way of achieving such outcomes.

Vitamin C is a potent antioxidant and a cofactor to many enzymes. Vitamin C can neutralize reactive oxygen species (ROS) thereby preventing oxidative stress and cellular damage (See *et al*., 2024). It participates in the hydroxylation of collagen, the synthesis of carnitine and catecholamines, and the metabolism of tyrosine, folic acid, and tryptophan (Alberts *et al*., 2025) which are all vital to cellular

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metabolism, neurotransmission and physiologic stress management.

This study investigated the use of vitamin C to modulate the effects of surgical stress on the structural and functional integrity of liver and kidney tissues in albino rats.

MATERIALS AND METHODS

STUDY AREA

The study was conducted in the Department of Veterinary Surgery and Radiology, College of Veterinary Medicine, Michael Okpara University of Agriculture, Umudike.

EXPERIMENTAL ANIMALS

Sixteen (16) male albino rats (mean body weight; 261.94 ± 6.35 g) used for the study were acclimatized for one month, housed individually in stainless steel cages, fed rat feed (Chikun® Finisher, Crown Flour Mills, Nigeria) and provided water ad libitum throughout the course of the experiment. Ethical approval was obtained from the University Ethics Committee ((Approval Reference Number: MOUAU/CVM/REC/202537).

EXPERIMENTAL DESIGN

The rats were randomly assigned to two groups of 8 rats each. Group 1 rats were wounded and post-surgically treated with vitamin C at 200 mg/kg body weight, IM for 5 consecutive days (Mohammed *et al*., 2016) while Group 2 rats were wounded with no vitamin C treatment. Both groups received standard post-operative care with Procaine penicillin and Streptomycine (20 mg/kg body weight, IM) for 5 consecutive days post-surgery.

DEAD SPACE WOUND CREATION

The left groin region of each rat was routinely prepared for aseptic surgery. The rats were sedated with Diazepam (5 mg/kg body weight, IM) and anaesthetized with Ketamine hydrochloride (40 mg/kg body weight, IM). A nick was made on the prepared site and, like in dead space wound model, a sterilized polypropylene tube (2.5 cm length by 0.25 cm diameter) was implanted subcutaneously. The wound was sutured by placing two interrupted sutures with nylon suture material and the day of surgery was designated post-surgical day (PSD) 0.

DATA COLLECTION

BIOCHEMICAL ASSAYS

On PSD 10, blood samples were collected from each rat via cardiac exsanguination following inhalation anaesthesia in a gas chamber to assay for liver and kidney functionality using Randox® test kits (Randox Laboratories Ltd., UK) and TECO test kits (TECO Diagnostics®, U.S.A). Serum albumin levels were determined by the bromocresol green (BCG) dye-binding method (Doumas *et al*., 1971), and the serum globulin levels were calculated by subtracting the serum levels of albumin (Doumas *et al*., 1971) from the serum total protein (Tietz, 1995) levels. Plasma Fibrinogen levels were determined using the heat precipitation method (Stockham & Scott, 2008). Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT) activities (Reitman & Frankel, 1957) and serum alkaline phosphatase (ALP) activity (Kochmar & Moss, 1976) were determined. The serum bilirubin level were determined by the Jendrassik colorimetric method (Garber, 1981). Serum urea and creatinine levels were determined by the enzymatic colorimetric method (Tietz, 1983) and the Jaffe method (Henry, 1974) respectively.

To enhance sensitivity in detecting stress-induced hepatic alterations, biochemical parameters were evaluated using physiologically relevant ratios rather than absolute values alone.

HISTOPATHOLOGY

The rats were euthanized using inhalation anaesthesia in a gas chamber and samples of the liver and kidneys to be processed for histopathology were harvested and fixed in 10 % phosphate buffered formal saline for at least 48 h. They were dehydrated in alcohol, cleared in xylene for 1 h 30 minutes, and embedded in paraffin wax and sections (5 microns thick) were made and mounted on microscope slides (Drury & wellington, 1967). The slides were stained with hematoxylin, counterstained with eosin (H &E stains) and analysed under a light microscopy.

DATA ANALYSIS

Data obtained were analysed using IBM SPSS software® (Version 20) and Student's t-test was used to compare results. Significance was accepted at $p < 0.05$.

RESULTS

HISTOMORPHOLOGIC CHANGES IN THE LIVER AND KIDNEYS

Alterations in the histomorphology of the liver and the kidneys of rats post-surgically treated with vitamin C compared to the untreated control is presented in Figures I-III.

Figure 1 showed the liver architecture of the vitamin C treated rats remained preserved while in Figure II, the histoarchitecture of the untreated group 2 rats were disrupted by marked generalised degenerative changes in the hepatocytes.

In Figure III, the tubular epithelium of the vitamin C treated group of rats were relatively intact, compared to that of the untreated control, which were swollen with degenerative changes.

(p>0.05) vary from that of the untreated control. Similarly, the ALT: Bilirubin ratio of the vitamin C treated rats were not significantly (p>0.05) different from the control.

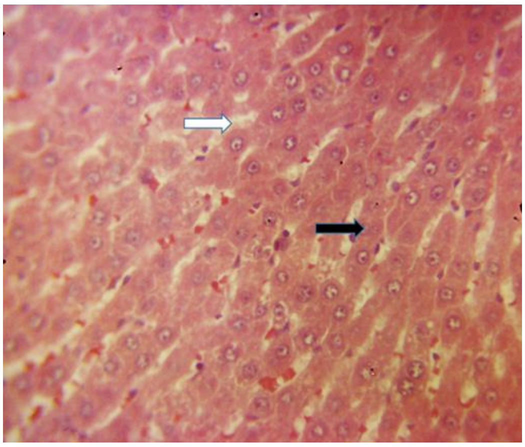


Figure I: Histoarchitecture of the liver of Vitamin C treated rats: Note the radiating plates of hepatocytes (black arrows) bordering the sinusoids (white arrows). (H & E: x400)

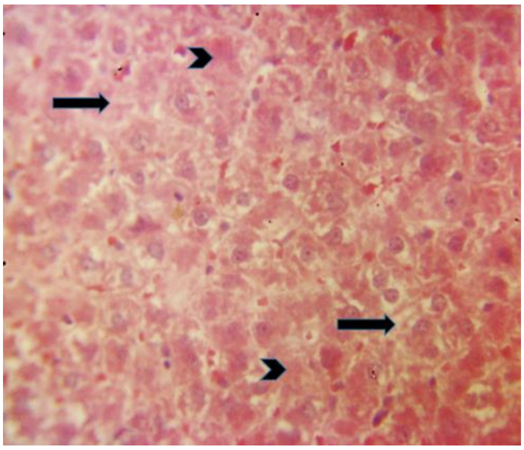


Figure II: Histoarchitecture of the liver of untreated rats: Note the disrupted architecture of the liver parenchyma, generalised hydropic degenerative changes (arrows) with areas of necrosis (arrow head). (H & E: x400)

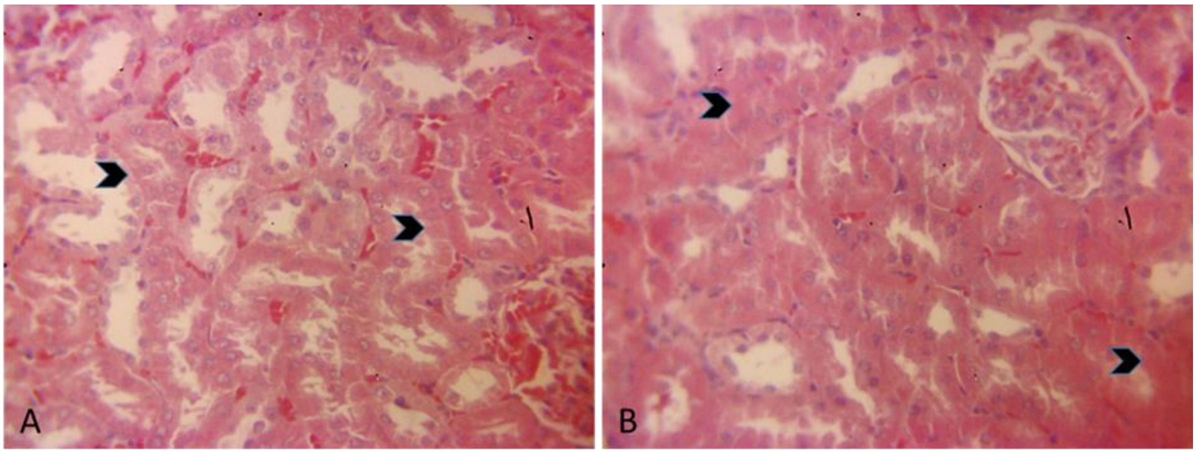


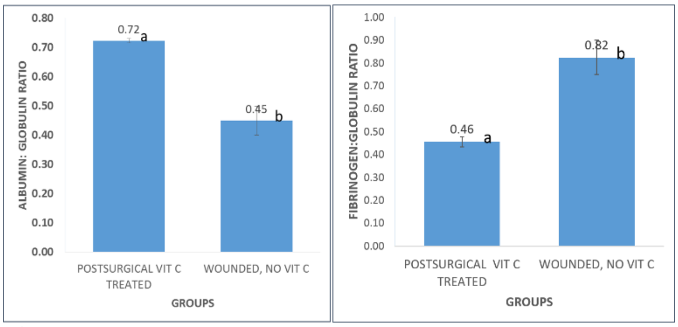
Figure III: Normal renal tubular epithelium (arrow heads) of Vitamin C treated rats (A); Degenerative renal tubular epithelium of untreated rats (B), giving the walls a thickened appearance. (H & E: x400)

HEPATIC FUNCTION AND INTEGRITY

The results of the Albumin: Globulin and Fibrinogen: Globulin ratios are presented in Fig. IV. The results showed the mean values of the Albumin: Globulin ratio of the Vitamin C-treated group 1 rats were significantly (P<0.05) higher than the untreated group 2 (Control). The Fibrinogen: Globulin values were also significantly (P<0.05) lower in the vitamin C treated group 1 compared to the control group 2. Figure V showed the results of the AST: ALT and Fibrinogen: Albumin ratios. The AST: ALT of the vitamin C treated group 1 rats were not significantly (p>0.05) different from those of the untreated group 2, while the Fibrinogen: Albumin of the vitamin C treated rats were significantly (P<0.05) lower compared to the untreated group 2. The results of the ALT: ALP and ALT: Bilirubin ratios as presented in Fig. VI showed the mean values of the ALT: ALP of the vitamin C treated group 1 did not significantly

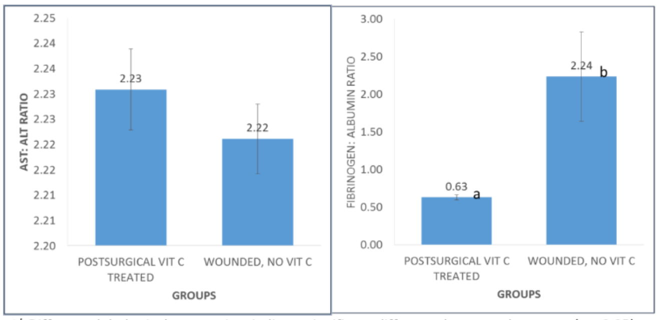
RENAL FUNCTION/CLEARANCE

There was a significantly (p<0.05) lower urea level in the vitamin C treated group 1 compared to the untreated control. The creatinine level was also lower in the control, though not significantly (p>0.05) (Fig. VII).



a,b Different alphabetical superscripts indicate significant difference between the means ($p < 0.05$)

Figure IV: Albumin-to-Globulin and Fibrinogen-to-Globulin ratios of rats post-surgically treated with Vitamin C compared to the untreated control.



a,b Different alphabetical superscripts indicate significant difference between the means ($p < 0.05$)

Figure V: AST-to-ALT and Fibrinogen-to-Albumin ratios of rats post-surgically treated with Vitamin C compared to the untreated control

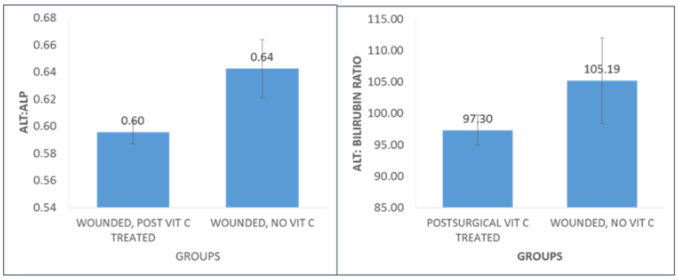
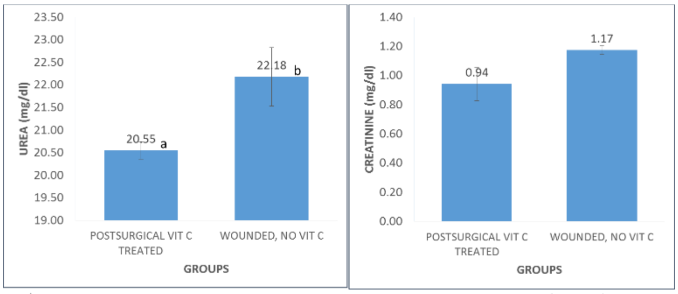


Figure VI: ALT-to-ALP and ALT-to-Bilirubin ratios of rats post-surgically treated with Vitamin C compared to the untreated control.



a,b Different alphabetical superscripts indicate significant difference between the means ($p < 0.05$)

Fig VII: Serum Urea and Creatinine levels of rats post-surgically treated with Vitamin C compared to the untreated control.

DISCUSSION

Surgical intervention represents a significant physiological stressor capable of disrupting cellular integrity and organ function (Ivascu *et al.*, 2024), particularly in metabolically active organs such as the liver and kidneys.

The degenerative changes observed in the hepatocytes and renal tubular epithelium of rats in the untreated control group, which were notably absent in the vitamin C-treated group, demonstrate the deleterious impact of post-surgical physiological and oxidative stress. Stress has been described as a state arising when animals are exposed to disease, trauma, or surgical procedures (Muir *et al.*, 2015). Vitamin C, a potent electron donor involved in numerous biochemical pathways, is well recognized for its antioxidant capacity and its role in limiting oxidative tissue damage under both physiological and pathological conditions (Padayatty *et al.*, 2003). As an antioxidant, vitamin C neutralizes reactive oxygen species (ROS) thereby preventing oxidative damage to cells and tissues (See *et al.*, 2024). The preservation of hepatic and renal histoarchitecture in the treated group therefore strongly suggests that vitamin C mitigated oxidative stress-mediated cellular injury. This observation aligns with reports identifying cellular degeneration as a primary pathophysiological response of the liver and kidneys to stress (Allameh *et al*., 2023).

These histomorphological disruptions were accompanied by functional derangements, reflecting compromised synthetic, metabolic, and excretory capacities of both organs in the untreated group. The significantly reduced Albumin-to-Globulin ratio, alongside the elevated Fibrinogen-to-Globulin ratio, indicates suppression of hepatic synthetic and metabolic function and suggests a shift toward a chronic physiological stress state. Additionally, the significantly increased Fibrinogen-to-Albumin ratio observed in the untreated rats is a recognized marker of systemic stress and an activated acute-phase response, which often precedes overt enzyme elevations during hepatic tissue injury (Muir *et al.*, 2015).

The concurrently elevated AST-to-ALT ratio in the untreated group provides further evidence of hepatic injury, reflecting ongoing mitochondrial dysfunction and oxidative damage, and is consistent with stress-induced metabolic overload (Paik *et al.*, 2013). The reduced ALT-to-Bilirubin ratio, although not statistically significant, suggests impaired bilirubin clearance and early hepatic excretory dysfunction, reinforcing the presence of subclinical hepatic compromise following surgical stress.

The hepatic dysfunction observed in the untreated control group likely contributed to secondary renal impairment through increased nitrogenous waste production and heightened inflammatory mediator release, as evidenced by elevated serum urea and creatinine levels. Physiological stress is systemic in nature and does not affect organs in isolation. The liver and kidneys are closely interconnected both metabolically and haemodynamically, and perturbations in one organ can exacerbate dysfunction in the other (Rad *et al*., 2024). The findings of this study therefore support the concept of a coordinated hepato-renal response to surgical stress.

CONCLUSION

The five-day administration of vitamin C as part of routine post-surgical management effectively protected treated albino rats from the development of hepato-renal surgical stress syndrome. This protective effect underscores the potential clinical relevance of vitamin C as an adjunctive therapeutic agent in mitigating surgery-related organ stress and preserving post-operative organ function.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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