Edelweiss Applied Science and Technology
ISSN: 2576-8484
Vol. 9, No. 2, 773-781
2025
Publisher: Learning Gate
DOI: 10.55214/25768484.v9i2.4593

Effect of striped catfish (Pangasianodon hypophthalmus) for cartilage thickness and chondrocyte count in mice (Mus musculus)

Izaak Zoelkarnain Akbar[1], Ika Kustiyah Oktaviyanti[2], Sukma Ihsan Rasyid[3*], Agung Ary Wibowo[4], Husna Dharma Putera[5], Tjahyo Kelono Utomo[6], Kenanga Marwan Sikumbang[7]
[1,5]Department of Orthopaedic and Traumatology, Faculty of Medicine, Lambung Mangkurat University; Indonesia; izaak.akbar@ulm.ac.id (I.Z.A.) hdputera@ulm.ac.id (H.D.P.)
[2]Department of Anatomical Pathology, Faculty of Medicine, Lambung Mangkurat University; Indonesia; ikoktaviyanti@ulm.ac.id (I.K.O.)
[3]Department of Surgery, Faculty of Medicine, Lambung Mangkurat University; Indonesia; Indonesia; sukmaihsanrasyid@gmail.com (S.I.R.)
[4,6]Department of Surgery, Digestive Division, Faculty of Medicine, Lambung Mangkurat University, Indonesia; agung.wibowo@ulm.ac.id (A.A.W.) tjahyo.utomo@ulm.ac.id (T.K.U.)
[7]Department of Anesthesiology and Intensive Care, Faculty of Medicine, Lambung Mangkurat University; Indonesia; kmsikumbang@ulm.ac.id (K.M.S.)

Abstract: Osteoarthritis (OA) is a leading cause of disability worldwide, characterized by progressive cartilage degeneration. Nutritional interventions, particularly omega-3 polyunsaturated fatty acids (PUFAs), have shown potential in slowing cartilage degradation. Striped catfish (Pangasianodon hypophthalmus) is a rich source of omega-3 PUFAs and essential amino acids, which may support cartilage health and regeneration. A post-test-only control group design was implemented using 50 male mice (Mus musculus), randomly assigned to either a control group (standard diet) or a treatment group (striped catfish-supplemented diet). The intervention lasted for eight weeks. Cartilage thickness and chondrocyte count were measured histologically using ImageJ software, and statistical significance was determined using independent t-tests and Mann-Whitney U tests. The treatment group exhibited significantly increased cartilage thickness ($p < 0.001$) and chondrocyte count ($p < 0.001$) compared to controls. These findings suggest that the nutrients in striped catfish enhance cartilage metabolism, reduce inflammation, and support extracellular matrix (ECM) integrity. Striped catfish supplementation demonstrates significant benefits for cartilage health, potentially aiding in OA management. Future research should explore optimal dosages and long-term effects to further validate these findings.

Keywords: *Articular Cartilage, Chondrocytes, Striped Catfish.*

1. Introduction

Specialized connective tissue called articular cartilage covers the ends of bones in joints called synovial joints. The principal functions are to reduce friction in joint movement and to distribute mechanical loads uniformly to the subchondral bone, facilitating smooth articulation and resistance to significant compressive forces. Articular cartilage is structurally comprised of type II collagen (12–14%), proteoglycans (7–9%), and chondrocytes, which account for merely 1–10% of the tissue's dry weight [1]. This composition is critical for its biomechanical properties, where type II collagen provides tensile strength, and proteoglycans, particularly aggrecan, confer compressive resistance by maintaining osmotic pressure [2].

Chondrocytes, the exclusive cellular element of articular cartilage, are tasked with synthesising, constructing, and preserving the extracellular matrix (ECM). For the reason that cartilage is avascular, chondrocytes depend exclusively on nutrition diffusion from synovial fluid for their metabolic functions.

History: Received: 30 November 2024; Revised: 27 January 2025; Accepted: 30 January 2025; Published: 5 February 2025
* Correspondence: sukmaihsanrasyid@gmail.com

The lack of blood vessels, combined with reduced cellularity, makes cartilage particularly vulnerable to degeneration and diminishes its ability to regenerate after damage or degeneration [3].

Cartilage degeneration is a defining feature of osteoarthritis (OA), the synovial membrane becomes inflamed, subchondral bone remodels, and articular cartilage deteriorates as a result of this chronic degenerative joint disorder. The World Health Organisation (WHO) reports that osteoarthritis (OA) impacts more than 240 million persons annually, rendering it the foremost cause of disability worldwide [4]. OA not only results in chronic pain and impaired mobility but also imposes significant economic burdens due to increased healthcare costs and reduced productivity.

Aging, oxidative stress, and chronic inflammation are primary contributors to cartilage degeneration in OA. Reactive oxygen species (ROS), predominantly generated by mitochondrial metabolism, damage cellular macromolecules such as DNA, proteins, and lipids, leading to impaired chondrocyte function and apoptosis [5]. Matrix metalloproteinases (MMPs) and aggrecanases (ADAMTS) are catabolic enzymes that ROS activate. These enzymes degrade cartilage by destroying components of the ECM. In addition, the degenerative processes are worsened by inflammatory cytokines such as TNF-α and interleukin-1 beta (IL-1β), which increase MMP expression and suppress ECM formation [6].

Considering these pathological pathways, treatment therapies for OA seek to preserve cartilage, diminish inflammation, and alleviate oxidative stress. Nutritional solutions have garnered more attention, especially those that use antioxidants and anti-inflammatory chemicals like omega-3 fatty acids. Omega-3 polyunsaturated fatty acids (PUFAs), including eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), are recognised for their ability to control inflammatory pathways, diminish the amount of ROS formation, and suppress catabolic enzymes including MMP-13 and ADAMTS-5 [7]. Also, omega-3 PUFAs help get rid of inflammation by creating special helpers called SPMs, which include resolvins and protectins and return tissues to a state of balance [8].

Widely eaten freshwater fish in Southeast Asia, the striped catfish (*Pangasianodon hypophthalmus*) is a wealth of essential nutrients, including protein, amino acids, essential minerals (calcium and phosphorus included), and omega-3 fatty acids (EPA and DHA among them) [9, 10]. These nutrients imply that by adjusting inflammatory reactions and improving ECM integrity, striped catfish may significantly benefit cartilage health. One notable finding is that omega-3 fatty acids obtained from striped catfish have lower concentrations of inflammatory mediators including IL-1β and prostaglandin E2 (PGE2). Important structural components of articular cartilage, type II collagen is synthesised from proteins and amino acids including glycine, proline, and lysine [11].

Many research have looked at how dietary omega-3 fatty acids might help to preserve cartilage integrity. For example, Harasymowicz, et al. [9] showed in animal models that a high-omega-3 diet lessened inflammation and cartilage degradation mostly via suppressing MMP expression and improving ECM synthesis [9]. Moreover, omega-3 supplements have been demonstrated to reduce NF-κB activation and increase production of resolving and other anti-inflammatory mediators, therefore shielding cartilage from greater damage [12]. Despite this growing body of evidence, most research has focused on isolated nutrients or supplements, with limited attention to whole-food sources such as striped catfish.

With a murine model, this study attempts to assess, using striped catfish supplementation, the effects on articular cartilage thickness and chondrocyte count. Mice were chosen for their physiological and biochemical similarities to humans, making them a reliable model for biomedical research. By investigating the combined anti-inflammatory, antioxidant, and metabolic effects of striped catfish nutrients, this study seeks to provide a comprehensive understanding of its potential in cartilage regeneration [12].

Furthermore, the findings from this research could lay the foundation for developing nutritional strategies to prevent and manage cartilage degeneration. As OA prevalence continues to rise and pharmacological options remain limited, exploring local, affordable, and sustainable dietary interventions such as striped catfish could offer a viable alternative. This study not only contributes to

Edelweiss Applied Science and Technology
ISSN: 2576-8484
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DOI: 10.55214/25768484.v9i2.4593

the scientific understanding of striped catfish's benefits for joint health but also supports public health initiatives promoting fish consumption as part of a balanced diet.

2. Methods

2.1. Study Design

The effect of striped catfish (*Pangasianodon hypopthalmus*) supplementation on the thickness of articular cartilage and chondrocyte count in mice was assessed using a post-test-only control group design. From October to December 2024 the study was carried out at the Anatomical Pathology Laboratory of Ulin Hospital, Banjarmasin, and the Biochemistry Laboratory of Lambung Mangkurat University.

2.2. Sample Size and Grouping

Fifty male mice (*Mus musculus*), weighing 20-30 grammes at the age of 3 months were used in the investigation. To guarantee statistical reliability, the sample size was determined using Federer's formula, which took into account a 20% attrition rate. Two groups of mice were randomly assigned:

1. Control Group: Fed a standard diet of BR-2 feed (5 g/day).
2. Treatment Group: Fed a diet supplemented with striped catfish pellets (2.5 g steamed striped catfish + 2.5 g BR-2 feed/day).

2.3. Ethical Approval

The Lambung Mangkurat University Research Ethics Committee granted ethical clearance for the investigation (Approval Number: 200/KEPK-FKIK ULM/EC/X/2024). The study adhered to the Five Freedoms principles, which include freedom from hunger, discomfort, pain, disease, fear, and distress, and therefore rigorously adhered to animal welfare guidelines.

Supplement Preparation

Fresh striped catfish meat was purchased from local markets, cleaned, steamed for 10 minutes, and ground into a paste. The paste was oven-dried at 150°C for 5 minutes to create a powder, which was then mixed in a 1:1 ratio with BR-2 feed to form pellets. Pellets were prepared daily to ensure freshness and consistency in nutrient content. Mice were fed ad libitum, and fresh water was provided daily. Cage hygiene was maintained by cleaning and replacing bedding material regularly.

Experimental Procedures

Ketamine-xylazine anaesthesia (0.1 mL at a ratio of 0.1 mg/g ketamine and 0.01 mg/g xylazine) was employed to euthanise the rodents after 8 weeks of dietary intervention, in accordance with conventional humane protocols. Articular cartilage samples were obtained by meticulously dissecting the right hind extremities. Before histopathological investigation, the tissues were preserved for 24 hours in 10% neutral buffered formalin.

Hematoxylin and eosin was used to stain the samples to enable the visualisation of cartilage thickness and chondrocyte morphology under a light microscope, and histological sections were prepared using a microtome.

Outcome Measurements

1. Cartilage Thickness
   Sagittal sections of articular cartilage were analyzed under 200x magnification using calibrated Image J software. Cartilage thickness was measured in micrometers across 10 different fields of view for each sample. Calibration was performed using a stage micrometer to ensure accuracy in measurements.
2. Chondrocyte Count
   Chondrocytes, identified by their elliptical morphology and surrounding active extracellular matrix, were manually counted in the articular cartilage samples. Counts were performed using the Image J cell counter plugin, ensuring consistency in field selection and criteria for identification.

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2.4. Data Analysis

We used SPSS 25.0 to analyze the data. Using the Shapiro-Wilk test, we checked if the data was normal. The following was the method of conducting group comparisons:

- Independent T-test: Executed on data that is normally distributed.
- Mann-Whitney U **test**: Apply this method to data that does not follow a normal distribution.

The data were shown as the mean ± the standard deviation (SD), and a p-value < 0.05 was used to establish statistical significance.

2.5. Flow of Study Procedures

1. Random allocation of mice into control and treatment groups.
2. Daily preparation of striped catfish-supplemented pellets.
3. Administration of diets ad libitum for 8 weeks.
4. Humane euthanasia and dissection for sample collection.
5. Histopathological processing and evaluation of cartilage parameters.
6. Statistical analysis to compare group outcomes.

3. Results

There were a total of 50 mice used in the trial, with 25 serving as controls and 25 as treatments. During the trial, two mice from the control group perished, resulting in 23 control and 25 treatment samples available for analysis.

Table 1.
Characteristics of mice.

Variable	Control group (n=23)	Treatment group (n=25)	p-value
Age	3 months	3 months	-
Body length (Initial)	9.5 ± 0.4 cm	9.4 ± 0.7 cm	>0.05
Body length (Final)	9.6 ± 0.4 cm	9.5 ± 0.5 cm	>0.05
Body weight (Initial)	27.38 ± 3.35 g	27.18 ± 3.23 g	>0.05
Body weight (Final)	34.13 ± 3.32 g	35.6 ± 4.16 g	>0.05

The control and treatment groups did not exhibit any significant differences in body length and weight at any time point ($p > 0.05$), as indicated by the statistical analysis.

Table 2.
Cartilage thickness.

Variable	Control group (n=23)	Treatment group (n=25)	p-value
Cartilage thickness	0.011 ± 0.002 mm	0.017 ± 0.002 mm	<0.001*

The treatment group exhibited a substantial increase in cartilage thickness in comparison to the control group, as evidenced by microscopic analysis ($p < 0.001$). These findings are corroborated by representative histological images (Figure 1).

Table 3.
Chondrocyte count.

Variable	Control group (n=23)	Treatment group (n=25)	p-value
Chondrocyte count	72.35 ± 10.89	112.06 ± 7.76	<0.001*

The treatment group also exhibited substantially higher chondrocyte counts than the control group ($p < 0.001$), as evidenced by histological images (Figure 2).

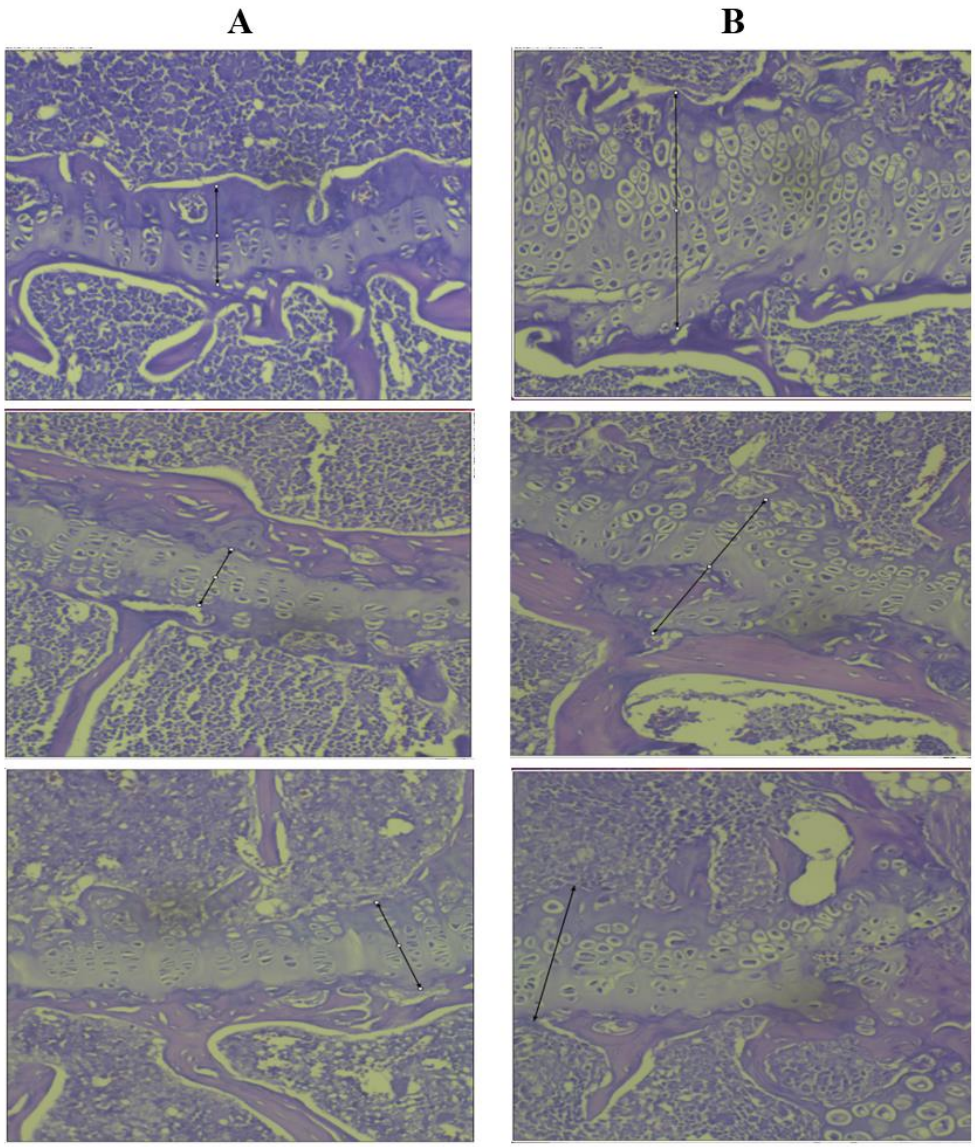

Figure 1.
Microscopic images of cartilago thickness (200x magnification). Arrows indicate the thickness.
(A) Control group: Mice administered a regular diet.
(B) Treatment group: Mice administered a regular diet augmented with striped catfish pellets.

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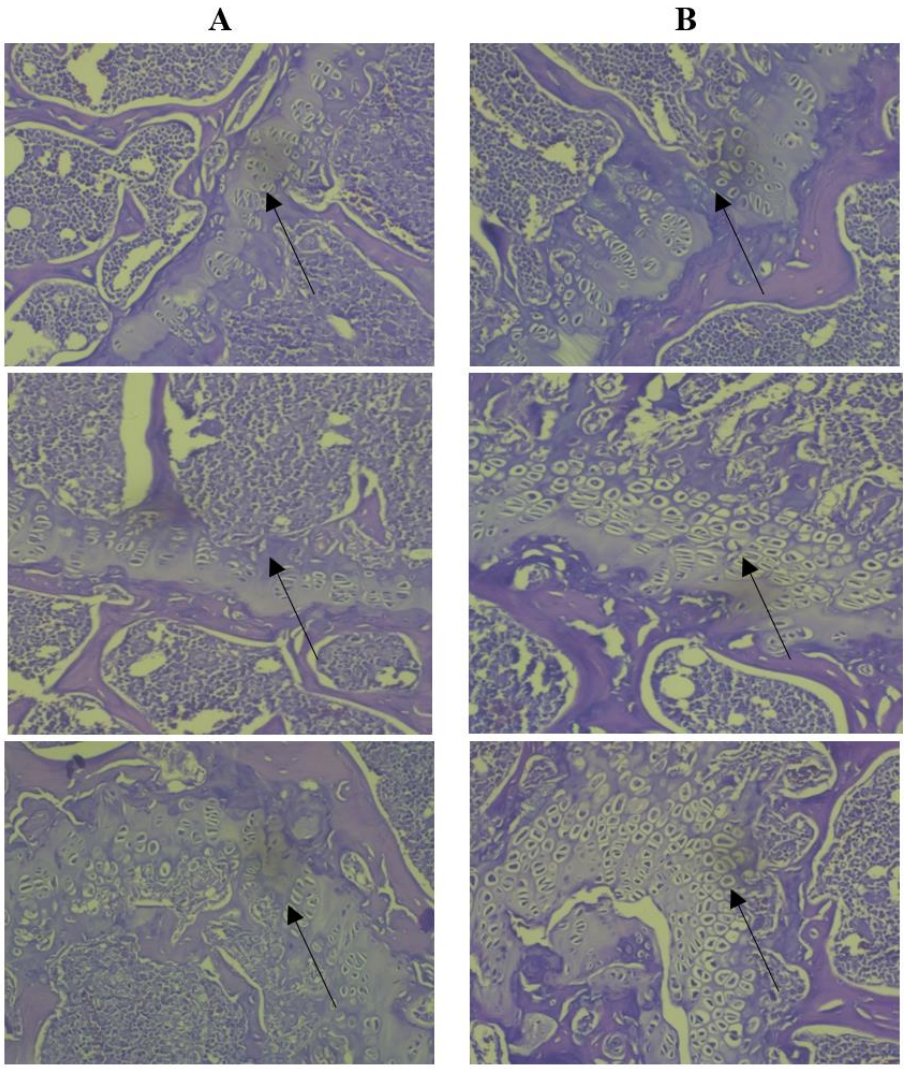

Figure 2:
Microscopic images of condrocyte count (200x magnification). Arrows indicate chondrocyte cells.
(A) Control group: Mice administered a regular diet.
(B) Treatment group: Mice administered a regular diet augmented with striped catfish pellets.

4. Discussions

The study demonstrates that supplementation with striped catfish (*Pangasianodon hypophthalmus*) markedly increases articular cartilage thickness and chondrocyte quantity in mice. No significant variations in body weight or length were found, suggesting that the intervention's effects are confined to cartilage metabolism rather than overall growth. These findings underscore the potential role of striped catfish as a dietary intervention for cartilage regeneration and repair.

The treatment group's increased thickness of articular cartilage implies that the nutrients in striped tilapia have a beneficial impact on cartilage metabolism. Choline and eicosapentaenoic acid are two of the most important omega-3 fatty acids. These fatty acids decrease inflammatory cytokines like TNF-α and interleukin-1β (IL-1β) as part of their anti-inflammatory processes. Enzymes including aggrecanases (ADAMTS) and matrix metalloproteinases (MMPs) degrade components of the

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extracellular matrix (ECM), mainly aggrecan and type II collagen. This inhibition reduces their activity, which is essential for the preservation of cartilage integrity. This anti-inflammatory effect is further enhanced by mediators such as resolvins and protectins, which originate from the fatty acids omega-3. These mediators promote tissue homeostasis by downregulating NF-κB signalling [6, 13, 14].

Besides their anti-inflammatory actions, omega-3 fatty acids demonstrate significant antioxidative capabilities. Reactive oxygen species (ROS), which accumulate in degenerative cartilage, can damage ECM components and induce chondrocyte apoptosis. DHA enhances the synthesis of glutathione, a primary antioxidant, which mitigates oxidative stress and preserves ECM integrity. Studies have demonstrated that DHA also inhibits p38 MAPK signaling, a pathway implicated in oxidative stress and chondrocyte apoptosis. Omega-3 fatty acids mitigate oxidative stress, hence preventing cartilage deterioration and fostering an environment favourable for cartilage repair [10, 15].

The protein and amino acid content in striped catfish further supports cartilage health by promoting ECM synthesis and chondrocyte proliferation. Essential amino acids like proline, lysine, and glycine are substrates for type II collagen synthesis, which is essential for cartilage structural integrity. Proline and lysine, in particular, facilitate collagen hydroxylation, ensuring the stability and functionality of the ECM. Moreover, arginine and glutamine provide metabolic substrates necessary for nucleotide synthesis and cellular energy production, supporting chondrocyte proliferation [16, 17].

The observed increase in chondrocyte count in the treatment group highlights the regenerative potential of striped catfish supplementation. Important to this procedure are the anti-apoptotic effects of omega-3 fatty acids. EPA and DHA regulate apoptotic signalling pathways by decreasing p38 MAPK and enhancing mitochondrial stability. Furthermore, these fatty acids improve chondrocyte longevity by reducing Bax expression and raising Bcl-2 expression, two proteins that promote cell death [18, 19].

While the findings are promising, several limitations must be acknowledged. For instance, the study did not measure biomarkers such as IL-1β, TNF-α, or malondialdehyde (MDA), which could provide a deeper understanding of the molecular mechanisms underlying the observed effects. Future studies should incorporate these biomarkers to elucidate the pathways by which striped catfish exerts its protective and regenerative effects on cartilage. Moreover, systemic factors such as blood lipid and glucose levels were not assessed, leaving open the possibility that these variables may have influenced the results.

Another critical area for further investigation is the optimal dosage of striped catfish supplementation. This study utilized a fixed dosage without exploring dose-response relationships. Higher or lower dosages may yield different outcomes, as suggested by studies showing that excessive omega-3 intake could have toxic effects on chondrocytes or exacerbate cartilage degeneration under certain conditions [20] Understanding the dosage threshold is essential to maximize therapeutic benefits while minimizing potential risks.

Despite these limitations, the study highlights the potential of striped catfish as a functional food for cartilage health. The synergistic actions of omega-3 fatty acids, proteins, and amino acids facilitate anti-inflammatory, antioxidative, and regeneration mechanisms, establishing a solid foundation for formulating nutritional strategies for degenerative cartilage disorders. These findings lay the groundwork for translational research aimed at developing dietary strategies to mitigate osteoarthritis and other cartilage-related disorders.

5. Conclusion

Striped catfish supplementation demonstrates significant benefits for articular cartilage health, as evidenced by increased cartilage thickness and chondrocyte count. Future studies should focus on elucidating molecular mechanisms, optimizing dosage, and exploring clinical applications to validate and extend these findings.

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DOI: 10.55214/25768484.v9i2.4593

Funding:
This research is self-funded

Institutional Review Board Statement:
Not applicable.

Competing Interests:
The authors assert that they own no conflicting interests.

Acknowledgments:
The authors acknowledge Lambung Mangkurat University and Ulin Hospital Banjarmasin for supporting this research.

Transparency:
The authors affirm that the text provides a truthful, precise, and transparent representation of the investigation; that no essential aspects of the study have been excluded; and that any deviations from the intended study have been explained. This research adhered to all ethical standards throughout the writing process.

Authors' Contributions:
All authors participated equally to the idea and design of the research. All authors have reviewed and consented to the published version of the study.

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