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Article

Clinical Laboratory Prognostic Markers Evaluation for Onset Identification of Arrhythmia Complications in Diwaniyah City

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Abstract: Arrhythmia refers to an irregular heartbeat that may be too fast, too slow, or uneven. NGAL, a protein classified as an acute-phase reactant. Assess NGAL levels in serum of individuals with arrhythmia, this was the aim of our study, also to find associations with other markers. An action study including 120 participants, from Iraq, Diwaniyah city, 60 patients with arrhythmia, the results was compared with 60 healthy as control. Serum levels of NGAL and various metabolic markers including K^+, SOD, in addition to GPx, and D-dimer were measured in all subjects. Statistical analyses were performed to compare the two groups and evaluate correlations among the investigated parameters. The statistical evaluation revealed a significantly decline in serum SOD, K^+ , GPx levels in group of the arrhythmia as compared to the group of control. Serum levels of NGAL and D-dimer was a significantly increased in individuals with arrhythmia as compared to the control group. NGAL levels in this findings revealed a strong significant inverse correlations with K^+, SOD and GPx levels, while a strong significant direct correlation with D-dimer levels. The present study demonstrated that individuals with arrhythmia exhibited a significantly elevated serum NGAL levels as compared to the group of control. In the turn, NGAL had a significant strong inverse relationship with (SOD, K^+, GPx) and a significant strong direct relationship with D- dimer, these findings suggest that NGAL levels may serve a protective function during the early stages of cellular dysfunction associated with arrhythmia, contributing to stroke pathogenesis.

Keywords: Arrhythmia, NGAL, Oxidative Stress.

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1. Introduction

Arrhythmia refers to an irregular heartbeat that may be too fast, too slow, or uneven. Common causes of arrhythmia are heart diseases, high blood pressure, electrolyte imbalance, stress and anxiety, smoking and certain medications [1], [2], [3], [4].

Arrhythmia is recognized for its high toxicity to several vital organs, such as the brain , the liver as well as heart and blood vessels [5], [6]. Nevertheless, the exact pathways underlying arrhythmia's harmful effects remain largely unclear. Multiple investigations have indicated that its toxicity is partly driven by oxidative stress (OS) [7], [8]. Initially, enhancing the production of species of reactive - oxygen (ROS) and diminishing the function of defense system about antioxidant, particularly its key - glutathione (GSH), - enzymes of dismutase superoxide (SOD) - and catalase (CAT) by metabolites of arrhythmia, including its derivatives nitroxide and nitrosonium, have been identified as possessing greater toxicity [9], [10], [11], [12]. Furthermore, the accumulation of dopamine and its oxidized metabolites, especially dopamine quinone within brain promoting

elevated ROS generation because arrhythmia inhibits the reabsorption of dopamine and increase in dopamine concentrations [13], [14].

Lipocalin of Neutrophil – gelatinase - associated (NGAL), a lipocalin protein – superfamily; classified as an acute - phase reactant, is mainly secreted by neutrophils and monocyte-derived macrophages. Additionally, NGAL has emerged as a sensitive biomarker for oxidative stress-induced tissue injury in organs such as the kidneys, liver and other organs [15], [16]. In addition, the involvement of NGAL in oxidative stress defense and modulating microglial autophagy mechanisms was highlighted by recent research on NGAL's potential neuroprotective properties [17]. Recent studies have highlighted its wide range of biological functions, including roles in olfactory signaling and prostaglandin biosynthesis. Obesity and metabolic syndrome have also identified by increased NGAL concentrations [18]. However, to fully understand NGAL connection to diverse oxidative stress signaling pathways was more essential in-depth studies in human populations [19].

The upregulation of expression for NGAL and secretion by glial cells in response to stimuli of oxidative stress was shown by recent studies [20]. In a mouse model of experimental autoimmune encephalomyelitis the increase in NGAL expression was observed in the secondary lymphoid organs and spinal cord following disease induction [21]. The expression of NGAL and its receptor were predominantly in neutrophils and dendritic cells, respectively in the spleen [22]. Notably, the mice that suffer from NGAL deficient exhibited significantly lower expression of oxidative stress mediators compared to wild-type counterparts and reduced inflammatory cell infiltration [23]. Collectively, As a key the progression of disease and oxidative stress factor involved in autoimmune inflammation was highlighted by these findings of NGAL. Additionally, the promotion of NGAL expression in both the spinal cord and peripheral immune tissues by administration of recombinant NGAL protein thereby contributing to pathogenesis [24].

The development of ischemic brain damage after a cerebrovascular attack contributes to brain blood vessels are highly vulnerable to oxidative stress [25]. Superoxide, it is a principal form of reactive oxygen species, along with its byproducts, has been demonstrated to induce vasodilation by activating potassium channels and modifying vascular responsiveness [26]. Despite their damaging potential, (ROS) also participate in essential physiological functions such as cellular signaling, immune system defense and initiation of cell proliferation. This review will primarily explore the suggested pathways through which oxidative stress induces neuronal cell death, concluding with a discussion on specific neuroprotective strategies aimed at mitigating oxidative damage and their relevance to stroke pathophysiology [27].

In serum of patients with arrhythmia, we will assess of NGAL levels, this was our aim of this study and to find associations with other indicators.

2. Materials and Methods

Experimental

Individuals and study design

From Al-Qadisiyah University / Science College, we were given ethical clearance for our study. Two groups contained 120 individuals, from Iraq, city of Diwaniyah, was the style of our study, 60 patients of arrhythmia (35 males and 25 females), their ages <35 – 75> years, compared with 60 healthy control, their ages <35 - 75> years, (35 males and 25 females). In Al-Diwaniyah at "Diwaniyah Teaching Hospital", Iraq, throughout the period from June 2025 to August 2025, patients were registered.

Exclusion criteria

Individuals that excluded from this study were suffering from metabolic syndrome, pregnant or breastfeeding women.

Collection of samples

The collection of blood samples from control in addition to patients at 8–12 hours fasting. The sample then clotted and centrifuged and finally were separated.

Biochemical evaluation

The serum (K+) levels assay kits from (China) by spectrophotometric. (NGAL) level assay kits from (China) by immunosorbent. (SOD) levels assay kits from (USA) by ELISA. (GPx) levels assay kits from (USA) by spectrophotometric. (D-dimer) levels assay kits from (Italy) by immunosorbent.

Bio-statistical analysis

SPSS software (version 24) and Microsoft Excel 2010 was the method to identification differences between groups.

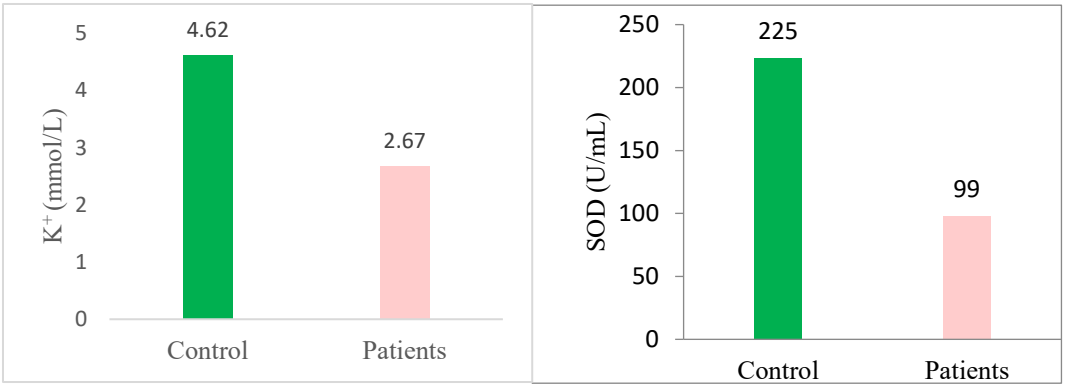
3. Results

As *compared* with *control, in Table 1, also Figure 1 (A, B, C, D, E), levels of D-dimer also NGAL showed an increased with significantly in *arrhythmia*, while K+, SOD and GPx levels were decreased also significantly - in arrhythmia; to compared by control.

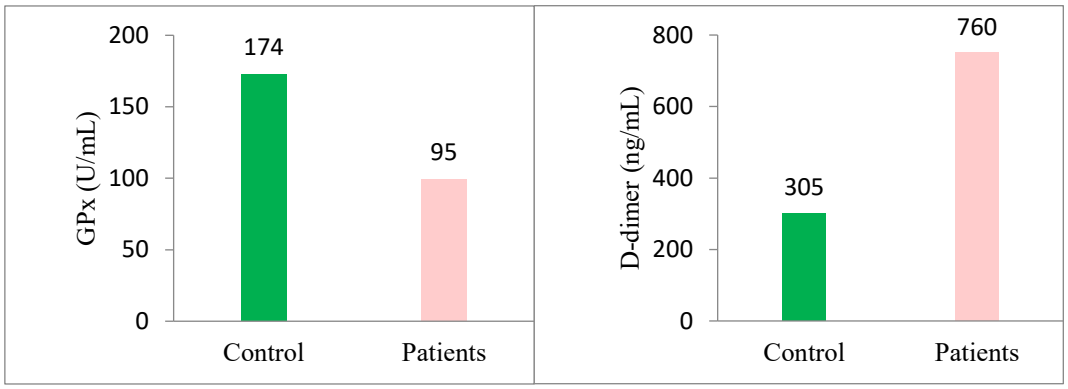
Table 1. Data for arrhythmia and control comparison

Parameters	Groups		P-value
	Control Mean ±SD (n=60)	Arrhythmia Mean ±SD (n=60)	
Age	55±2	55±2	0.21
Gender Males/Females	35(58.3%)/25(41.7%)	35(58.3%)/25(41.7%)	0.92
K^+ (mmol/L)	4.62±0.5	2.67±0.1	0.02
SOD (U/mL)	225±13	99±10	0. 04
GPx (U/mL)	174±9	95 ±7	0.02
D-dimer (ng/mL)	305±10	760±16	0.04
NGAL (ng/mL)	137±9	167±13	0.01

<Value P ≤ 0.05 Significance>, K^+: <Potassium>, SOD: <Superoxide Dismutase>, n: < Subjects Number* >, GPx: <Glutathione Peroxidase>, Mean ± SD; SD: < Standard Deviation>, NGAL: <The Neutrophil -Gelatinase-Associated Lipocalin>.



A **B**



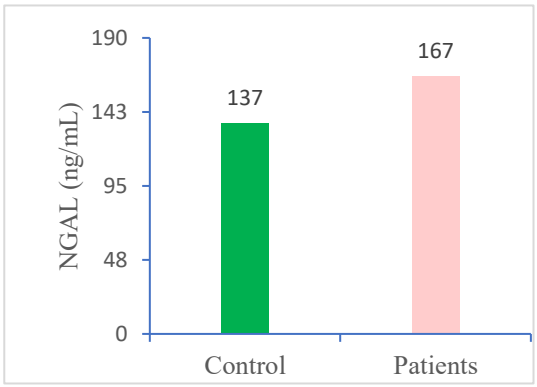
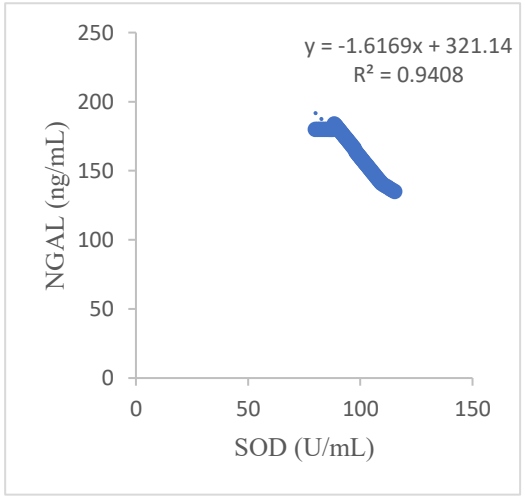


Figure 1. Between arrhythmia and control comparison of A: K+, B: SOD, C: GPx, D: D-dimer and E: NGAL levels

As shown in Table 2, in addition to Figure 2 (A, B, C, D), analysis of linear regression for levels of NGAL in addition to other biochemical indicators in serum of arrhythmia individuals. The correlation was strong -inverse - with significant between NGAL and K+ , also SOD in addition to GPx levels, while NGAL correlated by a strong direct significant with D-dimer levels.

Table 2. Correlation between NGAL levels with other biomarkers in arrhythmia

Parameters	**NGAL (ng/mL)**	
Age	r	0.47
	P-value	0.95
K^+ (mmol/L)	r	-0.92
	P-value	0.02



SOD (U/mL)	r	-0.96
	P-value	0.04
GPx (U/mL)	r	-0.95
	P-value	0.01
D-dimer (ng/mL)	r	0.96
	P-value	0.03

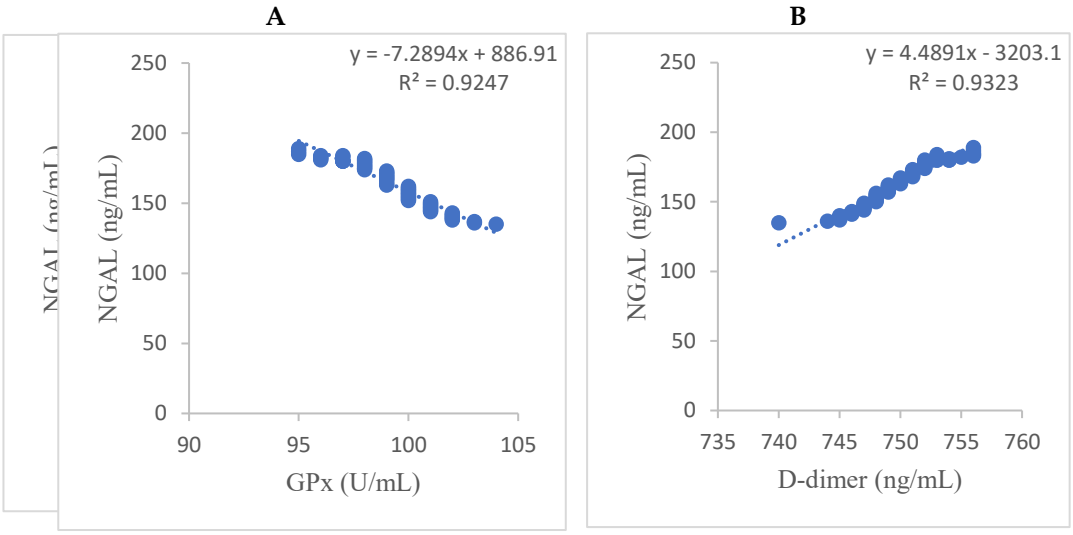


Figure 2. Correlation of NGAL levels with A: K+, B: SOD, C: GPx and D: D-dimer in arrhythmia

The analysis of operating characteristic receiver (ROC) curve in Table 3, Figure 3 for NGAL, a cut-off point of 77% for detecting arrhythmia patients. The *area* - *under* - the *curve* (AUC) was 0.948, a performance was high. NGAL sensitivity 77% and a specificity 100%.

Table 3. Analysis of (ROC) and (AUC) of NGAL in diagnosis arrhythmia

Variable	Group	Cut-off concentration %	Sensitivity %	Specificity %	AUC	Std. Error	95% CI of AUC	P-value
NGAL	Arrhythmia	77	77	100	0.948	0.018	0.912-0.984	0.001

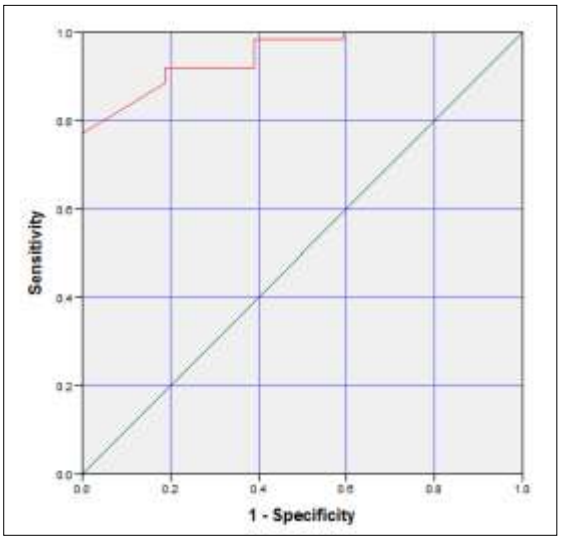


Figure 3. (ROC) analysis of NGAL in diagnosing arrhythmia

4. Discussion

An Increased with significantly in NGAL and D-dimer levels, these were the results of this study, alongside a significantly decreased in K+ , SOD and GPx, among individuals with arrhythmia as compared to the control group. The correlation was strong and inverse with significant between NGAL, K+ ,SOD as well as GPx, while a strong direct correlation with D-dimer in these patients. The explanation of our results that arrhythmia has been linked to significant disturbances in cellular equilibrium, most notably through the induction of oxidative stress caused by the excessive buildup for species of reactive oxygen (ROS). This oxidative stress arises multiple pathways. Arrhythmia neuronal stimulation and accelerates cellular metabolic activity, leading to elevated oxygen usage and the formation of incompletely reduced oxygen derivatives. It also impairs mitochondrial efficiency, triggers the activity of pro-oxidant enzymes like NADPH oxidase, and initiates pro-inflammatory signaling, all of which contribute to an abnormal and persistent rise in ROS within the central nervous system. Over time, the body,s innate antioxidant systems are depleted, weakening their ability to counterbalance the excessive ROS. The resulting antioxidant deficit compromises cellular defenses, leaving cells vulnerable to oxidative damage that affects proteins, membrane lipids and DNA. In response to this cellular stress, the expression of NGAL, is upregulated to stabilize damaged proteins and support cellular repair mechanisms. As oxidative damage progresses, vascular structures, particularly those in the brain, become increasingly susceptible to injury. The oxidative burden disrupts the endothelial layer of blood vessels, diminishes vascular elasticity, and amplifies local inflammation. These changes facilitate clot formation and increase the risk of vascular rupture, these vascular impairments greatly elevate the likelihood of both ischemic and hemorrhagic strokes among arrhythmia patients. Consequently, in arrhythmia patients, an early biomarker that indicating risk for stroke was NGAL levels.

Several investigations have explored the interaction between SOD and NGAL demonstrated that the expression of NGAL and SOD levels increased in retinal ganglion cells following the induction of elevated intraocular pressure in rats. Histological analysis further indicated that these proteins are essential for protecting the intestinal tissue after hatching and are likely involved in promoting the rapid maturation and functional development of the small intestine [28], [29]. Both SOD and NGAL expression levels were found to increase progressively with age, showing a positive correlation. Our findings are consistent with previous research aimed to examine the expression patterns of the SOD metalloenzyme and the NGAL chaperone during the developmental stages of ileal tissue in broiler chicks following hatching. That study suggesting that SOD may play a role in supporting the defense of antioxidant and immune systems of the ileum during the post-hatching period [30].

These proteins play a strong role in cells protecting against oxidative damage by preserving protein integrity and supporting cellular recovery processes [31], [32]. NGAL which are vital components of the cellular defense system against oxidative stress has been shown to stimulate the production of NGAL.

Furthermore, the authors suggested that; the strengthening of the defense of antioxidant system and decreased accumulation of ROS were key factors contributing to reduced vulnerability to noise-induced damage. Notably, the study was the first to propose a novel mechanism involving the NGAL-SOD signaling pathway in mediating protective role [33], [34]. The protective effect was attributed to regulation of mitochondrial function and control for species of reactive oxygen (ROS) levels in rat SGNs.

Similar other findings, which reported in studies examining the impact of exercise intensity, this suggests that the induction of NGAL is closely linked to metabolic stress that resulting from the hight levels of species of reactive - oxygen (ROS), where NGAL expression was found to be significantly higher following high-intensity training compared to low or moderate-intensity exercise [35], [36].

A similar study conducted on rabbits reported findings consistent with ours, showing that an increase in NGAL expression because of oxidative, that was followed by a decline in the enzymes of antioxidant SOD and catalase [37]. The aiding in the repair of damaged cells, allowing them to restore normal function affected by NGAL exerts a protective anti-apoptotic. Therefore, The compensatory response to ischemic conditions and the heightened species of reactive oxygen (ROS) production that induced by submaximal physical exertion can be interpreted by the elevation in NGAL levels [38]. As a result of submaximal physical activity that showed the treadmill exercise significantly increased NGAL levels in rat muscle tissue, the current findings are consistent with this study that demonstrated elevated NGAL expression. A cellular defense mechanism, helping to protect against oxidative damage by stabilizing and repairing damaged proteins by upregulation of NGAL. The maintaining balance under ischemic conditions and mitigating the effects of increased free radical production it also contributes to NGAL [39]. Our findings align with previous research that reported an increase in NGAL expression following submaximal physical exercise, suggesting that stress of oxidative acts as a stimulater for the upregulation of NGAL in cells. The preserving cellular homeostasis by stabilizing protein structure and function under both normal and stress-induced conditions by a role of NGAL [40].

5. Conclusion

A significantly elevated levels of NGAL in individuals with arrhythmia as compared to the group of control was revealed in this study. In the turn, NGAL had a significant strong inverse relationship with (K^+, SOD, GPx) and a significant strong direct relationship with D- dimer, these findings suggest that the early indicating of stroke in arrhythmia patients was by NGAL levels. Further research was recommended to conduct longitudinal studies to monitor changes in NGAL expression across various phases of arrhythmia treatment such as withdrawal, recovery, and relapse to gain deeper insight into its dynamic role as a biomarker of oxidative stress and treatment responsiveness.

REFERENCES

[1] Cunha T, Rego C and Oliveira C, Oxidative Stress and Arrhythmia? An Update, *Mini Rev Org Chem*, 2013, 10: 321–334.

[2] Riezzo I, Fiore C and Carlo D, Arrhythmia: multiorgan toxicity and pathological consequences, *Curr Med Chem*, 2012, 19: 46-562.

[3] Norton C, Georgiopoulou V and Kalogeropoulos A, Epidemiology and cost of advanced arrhythmia, *Prog Cardiovasc Dis*, 2011 ; 54:78–85.

[4] Kousik S, Napier T and Carvey P, The effects of arrhythmia on blood brain barrier function and neuroinflammation, *Front Pharmacol*, 2012, 3: 121-147.

[5] Chu S, Lin H, Huang H and Chen Y. The hydrophobic pocket of 24p3 protein from mouse uterine luminal fluid: fatty acid and retinol binding activity and predicted structural similarity to lipocalins. *J Pept Res* 1998; 52(39): 15-22.

[6] Lipton J, Gyawali S and Borys E, Prenatal arrhythmia administration increases glutathione and alpha-tocopherol oxidation in fetal rat brain, *Dev Brain Res*, 2003, 147: 77–84.

[7] Kovacic P, Role of oxidative metabolites of arrhythmia in toxicity: Oxidative stress and electron transfer, *Med Hypotheses,* 2005, 64: 350–356.

[8] Kjeldsen L, Okamoto K and Arito M. Identification of neutrophil gelatinase-associated lipocalin as a novel matrix protein of specific granules in human neutrophils. *Blood* 1994; 33(21): 17-38.

[9] Yan Q, Yang Q and Mody N. The adipokine lipocalin 2 is regulated by obesity and promotes insulin resistance. *Diabetes* 2007; 56(25): 10-20.

[10] Hvidberg V, Jacobsen C, Strong R. The endocytic receptor megalin binds the iron transporting neutrophil-gelatinase- associated lipocalin with high affinity and mediates its cellular uptake. *FEBS Lett* 2005; 57(37): 13-33.

[11] Bao G, Clifton M and Hoette T. Iron traffics in circulation bound to a siderocalin (NGAL)-catechol complex. *Nat Chem Biol* 2010; 6(2): 23-37.

[12] Owen H, Roberts S, Ahmed S and Farquharson C. Dexamethasone- induced expression of the glucocorticoid response gene lipocalin 2 in chondrocytes. *Am J Physiol Endocrinol Metabol* 2008; 29(10): 14-30.

[13] Devireddy L, Hart D, Goetz D and Green M. A mammalian siderophore synthesized by an enzyme with a bacterial homolog involved in enterobactin production. *Cell* 2010; 14 (6): 17-37.

[14] Nairz M, Haschka D and Demetz E. Iron at the interface of immunity and infection. *Front Pharmacol* 2014; 5(3): 18-29.

[15] Go´mez R, Scotece M and Conde J. Nitric oxide boosts TLR-4 mediated lipocalin 2 expression in chondrocytes. *J Orthop Res* 2013; 31(10): 12-34.

[16] Srinivasan G, Aitken J and Zhang B. Lipocalin 2 deficiency dysregulates iron homeostasis and exacerbates endotoxin-induced sepsis. *J Immunol* 2012; 18(10): 11-40.

[17] Fernández M and Valpuesta J, NGAL chaperone: A master player in protein homeostasis, *F1000Research,* 2018, 7: 11-32.

[18] Yamamoto M, Kensler T and Motohashi H, The KEAP1-NRF2 System: A Thiol-Based Sensor-Effector Apparatus for Maintaining Redox Homeostasis, *Physiol. Rev,* 2018, 98: 1169–1203.

[19] Zhao H, Konishi A and Fujita Y. Lipocalin 2 bolsters innate and adaptive immune responses to blood-stage malaria infection by reinforcing host iron metabolism. *Cell Host Microbe* 2012; 12(7): 16-30.

[20] Korovila I, Hugo M, Castro J, Weber D, Höhn A, Grune T and Jung T, Proteostasis, oxidative stress and aging, *Redox Biol*, 2017, 13: 550–567.

[21] Choi S, Park K, Lee H, Expression of Cu/Zn SOD protein is suppressed in NGAL.1 knockout mice, *J Bio- chem Mol Biol*, 2005, 38: 111-114.

[22] Yang Y, Yin B and Lv L, Gastroprotective effect of aucubin against ethanol-induced gastric mucosal injury in mice, *Life Sci*, 2017, 15: 44-51.

[23] Allen X and Bayraktutan U, Oxidative stress and its role in the pathogenesis of ischaemic stroke, *Review Int J Stroke,* 2009, 6: 461-70.

[24] Nurwasis S, Suhendro G and Sudiana I, the role of SOD, Catalase, NGAL and TNF-α expression in apoptosis of retinal ganglion cells after intra ocular pressure increase on Rattus Norvegicus, *IJPHRD*, 2019, 10: 1174-1178.

[25] Samali A, Robertson J, Peterson E, Manero F, van L, Paul C, Cotgreave I, Arrigo A and Orrenius S, NGAL protects mitochondria of thermotolerant cells against apoptotic stimuli, *Cell Stress Chaperones*, 2001, 6: 49–58.

[26] Guoxia Z, Yongxiang W, Yang Q, Keyong T , Wenjuan M, Xinqin L, Yuanyuan C, Jinwen J, Jiasheng L, Lianjun L and Jianhua Q, NGAL-FoxO1-SOD Signaling Pathway Contributes to the Protective Effect of Sound Conditioning against Acute Acoustic Trauma in a Rat Model, *Neural Plasticity*, 2020, 4: 1-22.

[27] Tuğrul E, Şerife T, Ahmet C, Ali Ç, The Relationship Between Sod1 and NGAL Expression in Broiler Ileum Throughout Post-Hatching Development, *J Res Vet Med*, 2022: 41: 99-104.

[28] Ogawa K, Seta R, Shimizu T, Shinkai S and Calderwood S, Plasma adenosine triphosphate and NGAL concentrations after aerobic and eccentric exercise, *Exerc Immunol Rev*, 2011, 17: 136-149.

[29] Harahap N, Lelo A, Purba A, Sibuea A, Amelia R and Zulaini Z, The effect of red fleshed pitaya (Hylocereus polyrhizus) on NGAL and cortisol expression in strenuous exercise induced rats. *F1000Research*, 2019, 8:130-

136.

[30] Yamada P, Amorim F, Moseley P and Schneider S, NGAL response to exercise in humans, *Sports Med*, 2008, 38: 715-733.

[31] Khassaf M, Child R, McArdle A, Brodie D, Esanu C, Griffiths R and Jackson M, Time course of responses of human skeletal muscle to exercise-induced oxidative stress. *J App Physiol*, 2001, 90: 1031–1036.

[32] Liu Y, Gampert L and Nething K, Response and function of skeletal muscleNGAL, *Front Biosci*, 2006, 11: 25-30.

[33] Christians E, Liang Y and Benjamin I, NGAL and heat shock proteins: Critical partners in protection against acute cell injury, *Critical Care Medicine* 30, 1: 43-50.

[34] Starnes J, Choilawala A, Taylor R, Nelson M, Delp M, Myocardial NGAL expression in young and old rats after identical exercise programs, *The Journals of Gerontology*, 2005, 60: 963-969.

[35] Krause M, Heck T, Bittencourt A, Scomazzon S, Newsholme P and Curi R, The chaperone balance hypothesis: The importance of the extracellular to intracellular NGAL ratio to inflammation-driven type 2 diabetes, the effect of exercise, and the implications for clinical management, *Mediators Inflamm,* 2015, 5: 22-29

[36] Nugroho J, Darius C, Probohoesodo M and Ghea C, The Relationship of NGAL with Calcineurin, SOD and Catalase Post Infarction in Wistar Rats Model, *Journal of Cardiovascular Diseases & Diagnosis,* 2020, 8:1-4.

[37] Cheng L, Xing H and Mao X. Lipocalin-2 promotes m1 macrophages polarization in a mouse reperfusion injury model. *Scand. J. Immunol* 2015; 21(11): 18-39.

[38] Hemdahl A, Gabrielsen A, Zhu C and Eriksson P. Expression of neutrophil gelatinase-associated lipocalin in hepatitis. *Arterioscler. Thromb. Vasc. Biol* 2006; 26(13): 15-37.

[39] Snoeck L, Cornelussen R, Van F, Reneman R and Van d, NGAL and Cell Pathophysiology, *Physiological Rev*, 2001, 4: 14-61.

[40] TeBoekhorst B, Bovens S, HellingsW and vanderKraak P. Molecular MRI of kidney infraction targeting NGAL: A protein associated with unstable human plaque characteristics. *Cardiovasc. Res* 2011; 19(8): 18-45.