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ORIGINAL RESEARCH PERIOPERATIVE MEDICINE

The association of atherosclerosis with cortisol and alpha-enolase levels and lipid profile

Ula Jaball Mohammed [1], Basim M. Ali [2]

Author affiliations:

1. Ula Jaball Mohammed, Chemistry Department, Facuty of Science, University of Kufa, Al Najaf, Iraq; E mail; ulaj.almamori@student.uokufa.edu.iq
2. Basim M. Ali, Chemistry Department, Facuty of Science, University Of Kufa, Al Najaf, Iraq; E-mail; basim.radhi@uokufa.edu.iq

Correspondence: Basim M. Ali; **E-mail;** basim.radhi@uokufa.edu.iq**; Mobile:** 07802361053

ABSTRACT

Background & objective: Atherosclerosis is a chronic disease characterized by the gradual buildup of plaque inside the arteries. It is the most common form of arteriosclerosis, which refers to the thickening and hardening of arterial walls. In atherosclerosis, some arteries have been narrowed by atherosclerotic plaque. We investigated the association of atherosclerosis with cortisol and alpha-enolase levels and lipid profile.

Methodology: This study focused on measuring alpha-enolase 1 (αENO1) in patients with atherosclerosis. sixty patients diagnosed with atherosclerosis (36 males and 24 females) participated in this study. Their ages ranged from (45 to 65 years). Samples were collected from the open-heart unit at Al-Sadr Teaching Hospital, Najaf Governorate, Iraq. Thirty healthy people (15 males, 15 females) were selected as a control group.

Results: The study showed that patients with atherosclerosis suffer from a clear increase in the concentration of alpha-enolase 1 (αENO1) and a clear increase in the concentration of cortisol, as well as an increase in the lipid profile (total cholesterol, triglycerides, low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL).

Conclusions: On the other hand, the study revealed a significant decrease in the amounts of high-density lipoprotein (HDL) in patients compared to the control group. Therefore, the findings of this investigation suggest that individuals suffering from atherosclerosis might.

Abbreviations: αENO1 - alpha enolase 1; HDL - high density lipoprotein; LDL - low density lipoprotein; (2-PG)-2-phospho-D-glycrate; NO - nitric oxide; TG - triglyceride; BMI - body mass index; PEP - phosphoenolpyruvate; ACTH - adrenocorticotropic hormone; ROS - reactive oxygen species.

Keywords: atherosclerosis, αENO1, cortisol, endothelial, macrophages, plasminogen, plasmin, reactive oxygen species.

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1. INTRODUCTION

Atherosclerosis is a chronic disease characterized by the gradual buildup of plaque inside the arteries. It is the most common form of arteriosclerosis, which refers to the thickening and hardening of arterial walls In atherosclerosis, there is an artery that has been narrowed by atherosclerotic plaque. Therefore, endothelium above the atherosclerotic plaque is abnormal, as it is dysfunctional, proinflammatory, and thrombotic, and recruits smooth muscle cells that came from the media layer and proliferating precursors that form part of the atherosclerotic plaque and scar, which plays a role in the process of atherosclerosis. Recent studies have found that the process of atherosclerosis is driven by macrophages, as studies have proven that this process is largely driven by innate immunity through the activation and recruitment of macrophages.[1].In small vessels, when there is a blockage due to plaque growth and it prevents blood flow, therefore, the coronary artery and small

vessels are blocked by a percentage (50 - 60)% of the blood vessel lumen due to plaque growth, do not get sufficient flow to distant blood vessels.). As for large vessels, it can occur sclerosis leads to abnormal function of endothelial cells, which leads to thrombosis). It can also lead to the production of plaques that are susceptible to fragmentation and disintegration, as in the aorta, where these plaques contain thrombi, platelets, fibrin, necrotic debris, and inflammatory debris, and thus this plaque breaks down easily in the lumen of this large blood vessel. Another complication associated with large blood vessels is the recruitment of macrophages as part of plaque growth, which leads to the production of proteases, which lead to the degradation of the extracellular matrix. Therefore, atherosclerosis is a very bad disease.[2]

Alpha-enolase 1, also known as enolase 1 (ENO1), is an enzyme that plays a critical role in the glycolysis pathway. The process of glycolysis involves the metabolic conversion of glucose to pyruvate, leading to the production of energy in the form of ATP. αNO1 enzyme is responsible for facilitating the transformation of 2-phospho-D-glycerate (2-PG) into phosphoenolpyruvate (PEP) during the ninth stage of the glycolysis pathway. This reaction involves the removal of a water molecule from 2-PG, leading to the formation of PEP αENO1 is responsible for the reversible dehydration of 2-PG, and requires the presence of magnesium ions as a cofactor.[3] In addition to its involvement in the glycolytic pathway, αENO1 has been identified to possess alternative roles in various cellular populations. It serves as a receptor for plasminogen on the cellular membrane, enhancing the activation of plasminogen and aiding in cellular motility and infiltration, while also being associated with cellular signaling, transcriptional control, and cellular proliferation. In general, αENO1 is an important enzyme involved in glycolysis and has additional functions in various cellular processes, in cellular metabolism and in the pathogenesis of many disease. Many studies have investigated the relationship between αENO1 and heart disease.[4, 5] Many studies have investigated the relationship between αENO1 and heart disease, especially in the context of atherosclerosis. Research has shown that αENO1 is present in plaques that form inside arteries, suggesting its possible involvement in the development and progression of atherosclerosis. The enzyme may contribute to plaque formation by promoting the migration and proliferation of smooth muscle cells and by modulating inflammatory processes.[6] Moreover, studies have indicated that αENO1 may play a role in regulating endothelial function, and antibodies to αENO1 can inhibit the activity of αENO1 as a plasminogen receptor, which may cause several inflammatory diseases, including atherosclerosis.[4] This enzyme can also be considered a marker of oxidative stress, as it has been identified as a triggering factor in the response to ischemic hypoxia and reoxygenation of the heart exposed to ischemia. αENO1 improves contraction of weak heart muscles, so it is considered a marker for early diagnosis of acute myocardial infarction. Research has demonstrated that the plasminogen activation mechanism permits inflammatory cell infiltration and contributes to extracellular matrix remodeling following heart damage. It also plays a role in myocardial survival, since cardiomyocytes are terminally differentiated cells that cannot proliferate even if damaged. Recent studies suggest that failing heart cells die by apoptosis because plasmin triggers cell detachment and apoptosis of smooth muscle cells. Therefore, it has been speculated that αENO1 could function as a plasminogen receptor and regulate plasminogen activity in cardiac cells.[7]

The adrenal cortex of the human adrenal gland produces the steroid hormone cortisol, also known as hydrocortisone.[8] The tissue that produces this glucocorticoid in response to adrenocorticotropic hormone stimulation is called the zona fasciculate (ACTH). As a glucocorticoid, cortisol aids in the metabolism of proteins, lipids, and carbohydrates. Since cortisol plays a part in the body's natural reaction to stress, it is frequently referred to as the stress hormone. Cortisol has receptors on the majority of body cells, which enables it to carry out a variety of bodily tasks. Natural cortisol release helps to reestablish equilibrium following stressful situations. Cortisol is in charge of regulating metabolism and blood sugar levels in the body. It has anti-inflammatory properties and can accelerate the body's breakdown of lipids, proteins, and glycogen, lowering the amount of protein in the majority of cells.[9] Cortisol affects memory development, controls salt and water balance, and affects fetal growth.[10] Cortisol plays a physiological role by stimulating several processes, such as stimulating gluconeogenesis,[9] stimulating the synthesis of enzymes that are part of the gluconeogenesis pathway, the primary metabolic role of glucocorticoids, releasing amino acids from extrahepatic organs and preventing muscle and adipocytes from absorbing glucose, stimulating glycolysis, lipids in adipocytes and hydrolysis of triglycerides and consequent release of fatty acids provides the substrate for energy production via the beta-oxidation pathway in tissues such as muscle.[11] Chronically high cortisol can promote inflammation in the body. Inflammation is a major factor in the development of atherosclerosis because it leads to the accumulation of cholesterol and other substances in the walls of the arteries, leading to the formation of plaques and is involved in the regulation of blood pressure.[12] Persistently high levels of cortisol can lead to hypertension , which is a major risk factor for

atherosclerosis.[13] Cortisol has an impact on fat metabolism, which includes how fat is broken down and distributed. Triglycerides and low-density lipoprotein (LDL) cholesterol might rise as a result of increased fatty acid release into the bloodstream caused by elevated cortisol levels. High levels of LDL cholesterol lead to the progress of atherosclerosis.[14] Insulin resistance, a condition in which the body's cells become less receptive to the actions of insulin, can also result from prolonged cortisol exposure. Insulin resistance is associated with hypertension damages the walls of the arteries and makes them more susceptible to plaque formation. Metabolic disorders, such as dyslipidemia (abnormal lipid levels) and increased inflammation, which contributes to the development of atherosclerosis.[15] A vital component of keeping blood vessels healthy is the endothelium lining of the vessels. Endothelial dysfunction can result from high cortisol levels impairing endothelial function.[16] Reduced nitric oxide (NO) generation, which aids in blood vessel relaxation and normal function, is a characteristic of this disorder.[17] Because endothelial dysfunction increases inflammation and increases the susceptibility of artery walls to plaque formation, it plays a role in the development of atherosclerosis. [18] Cortisol has immunosuppressive effects, meaning it can suppress the immune response, while this can be helpful in acute cases, chronic elevation of cortisol can impair the immune system's ability to control inflammation.[19] Inflammation is a major driver of atherosclerosis, a dysregulated immune response can exacerbate inflammatory processes associated with plaque formation and progression.[20] Chronic stress and high cortisol levels have been linked to the accumulation of belly fat. Abdominal obesity is a known risk factor for atherosclerosis and cardiovascular disease.[21] Abdominal adipose tissue releases various substances, including inflammatory cytokines and adipokines, which contribute to systemic inflammation and insulin resistance, which increases atherosclerosis.[22] Sleep disturbances, such as insomnia or poor sleep quality, can disrupt the body's natural cortisol rhythm. Irregular cortisol patterns, including elevated evening or night time cortisol levels, have been associated with a higher risk of developing atherosclerosis and cardiovascular disease.[23] Adequate sleep and maintaining a regular sleep pattern are important for maintaining healthy cortisol levels and overall cardiovascular health.[24] Chronically high cortisol levels may be a factor in the body's oxidative stress. When the body's antioxidant defenses and the generation of reactive oxygen species (ROS) are out of balance, oxidative stress results. Oxidative stress is recognized to contribute to endothelial dysfunction, lipid oxidation, and inflammation in the development of atherosclerosis. Cortisol can increase the production of ROS and decrease the activity of antioxidants, thereby exacerbating oxidative stress and its detrimental effects on arterial health. It's worth noting that men and women differences may exist in the relationship between cortisol and atherosclerosis.[25]

2. METHODOLOGY

This is a case-control study which included sixty patients with atherosclerosis and thirty control are participated in this study. Their ages ranged between 45-65 years, all patients diagnosed with vascular diseases by ultrasound and diagnostic catheterization. Samples were taken in the morning when they were fasting, and it taken from the Al-Sadr Medical City's Open Heart Center is located in AL-Najaf Al-Ashraf, Iraq. Patients were evaluated through a complete medical history to explore the presence of other diseases related to vascular disease which may influence this study. healthy people were chosen to serve as the control group because their age ranges were similar to the patients'. All these people were not smokers and did not suffer from vascular diseases, kidney disease, inflammation and thyroid disease.

2.1. Blood sample collection

Five milliliters of venous blood samples were drawn using a disposable needle and plastic syringes from each patient and control subjects without a tourniquet, in the morning who had fasted for 10 hours. Samples were transferred into gel tubes to be separated by a centrifuge at 3000 rpm for 15 minutes.

2.2. Serum level of cytokine and hormone

αENO1and cortisol were measured by ELISA technique using ELISA kit from the ARS BIOCHEM company (China) for αENO1 and DRG company (Germany) for cortisol.

2.3. Serum level of lipid profile

Cholesterol, triglyceride, HDL and LDL were measured using the spectrophotometer technique by a special kit for each parameter from the Spinreact company (Spanish).

2.4. Statistical analysis

The data collected from the analysis of biochemical information was subjected to statistical calculations using statistical software (SPSS 26). The mean, standard deviation, and results of the F-distribution analysis were obtained. Any significant critical value or probability

Table 1: Comparative demographic data of the study population

Variables	Patients	Controls	P-value
Age	57.27 ± 7.0	59.93 ± 7.3	0.376
BMI (kg/m^2)	29.41 ± 3.5	30.04 ± 3.0	0.406

Data presented as Mean ± SD; P < 0.05 considered as significant

test below 0.05 (P < 0.05) was identified, in addition to the use of Microsoft Excel (2016) and SPSS 26(26).

3. RESULTS

3.1. Demographic characteristics

Table 1 shows the demographic characteristics of the study population. The mean age of patients with atherosclerosis was 57.26 ± 7.099, which was very close to that of controls (57.93 ± 7.35) with no significant difference. Also, the two groups were comparable BMI with no significant differences.

3.2. Hormonal and enzyme profile

Table 2 shows the levels of cortisol and ENO1 in areas affected by atherosclerosis compared to the control group. It also shows a significant increase in the levels of cortisol and ENO1 in the patient group compared to the control group.

3.3. Lipid profile and arterial stiffness index

Table 3 shows a significant increase (P = 0.001) in total cholesterol, LDL, and TG in patients compared with the control group. In addition, the results showed a significant decrease in HDL levels between the two groups.

3.3. Correlation between all variables in atherosclerosis patients

Spearman correlation test was used to explore the possible association of all parameters in patients and controls. Cortisol showed a significant positive relationship with all factors, and cortisol showed a significant negative relationship with HDL. On the other hand, there is a significant positive relationship between αENO and the lipid profile, except for HDL, which showed a negative significant relationship. There is also a significant positive relationship between the hormone cortisol and the enzyme αENO, as shown in (Table 4).

Table 2: Hormonal and cytokine profile in atherosclerosis patients and controls

Variables	Patients	Controls	P-value
Cortisol	113.82 ± 45.9	79.59 ± 32.77	0.001
αENO	4.84 ± 2.34	3.1365 ± 0.857	0.002

Data presented as Mean ± SD; P < 0.05 considered as significant

Table 3: Lipid profile in patients and controls

Variables	Patients	Controls	P-value
TG (mg/dL)	196.3 ± 81.4	133.26 ± 64.3	0.001
HDL (mg/dL)	31.23 ± 9.55	40.28 ± 8.76	0.001
CHO (mg/dL)	226.8829 ± 63.26	152.03 ± 37.04	0.001
LDL (mg/dL)	133.25 ± 37.0	89.89 ± 33.61	0.001
VLDL (mg/dL)	50.35 ± 19.0	33.993 ± 13.0	0.001
Index-I	8.595 ± 5.5	3.39 ± 1.23	0.000
Index-II	4.939 ± 2.9	2.3 ± 0.94	0.001
Index-III	6.99 ± 0.94	3.46 ± 1.06	0.001

Data presented as mean ± SD; P < 0.05 was considered as significant

3.4. Diagnostic value of Cortisol and αENO

Receiver operating characteristic (ROC) curve was used to evaluate the diagnostic value of cortisol and αENO in the context of discrimination between atherosclerosis patients and healthy group. The area under the curve (AUC) of cortisol was 0.769, 95% CI = 0.645-0.893, P = 0.001. The sensitivity and specificity of the test, at cut

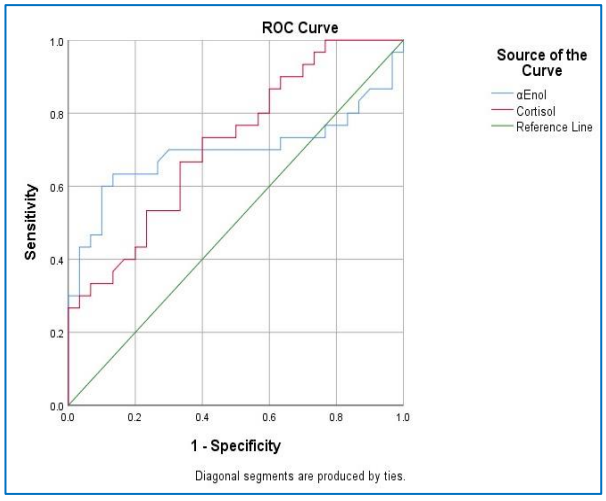

Figure 1: Receiver operating characteristic curve of cortisol and αENO in atherosclerosis patients.

Table 4: Spearman's correlation of variables in atherosclerosis patients

Variables		TG	HDL	CHO	LDL	VLDL	Index-I	Index-II	Index-III	CHORT	αENO
TG	Pearson Correlation	1	-.617**	.471**	.449*	.512	.0.141**	.647**	.729**	.549**	0.5
	Sig.		0	.009	..0.013	.0.004	.000	.000	.000	.002	..005
HDL	Pearson Correlation	-.617**	1	-.699**	-.65**	-.612	-.85**	-.853**	-.791**	-.773**	-.611
	Sig.	.000		.000	.000	.000	.000	.000	.000	.000	.000
CHO	Pearson Correlation	.526**	-.699**	1	.825**	.407	.827**	.578**	.792**	.536**	.638
	Sig	.003	.000		.000	.0.026	.000	.001	.000	.002	.000
LDL	Pearson Correlation	.449*	-.617**	.825**	1	.521	.666**	.744**	.533**	.45*	.651
	Sig.	.0.013	.000	.000		.001	.0000	.0000	.0020	.013	.000
VLDL	Pearson Correlation	.512	-.612	.407	.521	1	.566*	.59*	.489**	.412**	.688
	Sig.	.004	.000	.026	.001		.001	.001	.003	.024	.000
Index-I	Pearson Correlation	.141**	-.85**	.407**	.666**	.566*	1	.967**	.744**	.679**	.268
	Sig.	.0000	.0000	.0000	.0000	.001		.0000	.0000	.0000	.000
Index-II	Pearson Correlation	.647**	-.853**	.578**	.744**	.59*	.967**	1	.744**	.761**	.682
	Sig.	.000	.000	.000	.000	.001	.000		.000	.000	.000
Index-III	Pearson Correlation	.729**	-.791**	.792**	.533**	.533**	.744**	.744**	1	.701**	.51
	Sig.	.000	.000	.000	.002	.0.006	.000	.000		.000	.004
Cortisol	Pearson Correlation	.549**	-.773**	.536**	.45*	.412**	.679**	.744**	.701**	1	.49
	Sig.	.002	.000	.002	.0013	.024	.0000	.0000	0.000		.006
αENO	Pearson Correlation	.5	-.611	.638	.651	.688	.268	.682	.51	.49	1
	Sig.	.000	.000	.000	.000	0.000	.000	0.000	.004	.006	

** Correlation is significant at the 0.05 level*
*** Correlation is significant at the 0.01 level*

off value = 80.9, were 71% and 72.4%, respectively. While, the sensitivity and specificity of αENO was 70 and 63.3% respectively as shown in (Table 5, Figure 1).

4. DISCUSSION

Table 3 presents data demonstrating a statistically significant and distinct elevation in blood lipid profile concentration (P = 0.001) in patients diagnosed with atherosclerosis relative to the control cohort. This is because individuals with atherosclerosis have increased insulin resistance in their bodies, which causes an imbalance in the metabolism of lipids and carbs.[17] As a result, the construction of cholesterol and triglycerides increases in the liver and is transmitted to the blood, leading to an imbalance in fat metabolism, as well as atherosclerosis, is a condition of chronic inflammation of the walls of blood vessels, this inflammation leads to an increase in the process of fat oxidation and its transformation into more harmful forms such as oxidized cholesterol.[2] Oxidized cholesterol accumulates in the walls of blood vessels, which increases atherosclerosis. This process contributes to high LDL and low HDL.

In the same table, the results indicated a significant and clear increase in the concentration of the hormone cortisol in the blood (P = 0.002) in patients with atherosclerosis compared to the control group. The reason for this increase is inflammation and deterioration of blood vessels in patients with atherosclerosis. Research has shown that patients with atherosclerosis often suffer from high levels of cortisol in the blood, and it is believed that this increase may result from the body's response to stress and psychological pressure accompanying the disease.[27] Also, the use of some treatments that work to activate the hypothalamic-

Table 5: Receiver operating characteristic analysis of cortisol and αENO as diagnostic markers for atherosclerosis

Item	Cut off	Sensitivity	Specificity	AUC	95% CI of AUC	P-value
Cortisol	86.7465	66.7	63.3	0.769	0.588-0.844	0.0.004
αENO	3.1815	70.	63.3	0.694	0.549-0.840	0. 010

pituitary-adrenal axis and thus increase cortisol concentration. [28]

The results in the same table showed that individuals with atherosclerosis had a significantly higher blood concentration of ENO1 (P = 0.001) than the control group. This is due to the fact that ENO1 is an enzyme that is essential to the oxidative and inflammatory processes that occur in the blood vessel walls of atherosclerosis patients. Additionally, this enzyme promotes the synthesis of inflammatory mediators including chemokines and cytokines, which draw and activate immune cells. Additionally, it encourages the generation of reactive oxygen species and free radicals, which harm blood vessel walls.[29]

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The same table shows that there is a significant relationship (P < 0.05) between ENO1 levels and lipid profile, which is positive as confirmed by many studies. Increased ENO1 activity has been associated with dysregulation of lipid metabolism, leading to lipid accumulation in the arteries. Overexpression of ENO1 can upregulate the expression of enzymes involved in lipogenesis (synthesis of fatty acids and triglycerides) in the liver, leading to cholesterol overproduction. Triglycerides, LDL and VLDL. ENO1 may also contribute to inflammatory processes within the arterial wall by acting as a pro-inflammatory mediator, leading to lipid accumulation in arterial walls. Increased ENO1 expression has been associated with the activation of inflammatory pathways and production of reactive oxygen species, which can exacerbate oxidative stress and endothelial dysfunction in patients with atherosclerosis.[31]

The same table shows that there is a positive and significant relationship (r = 0.49) between αENO1 and cortisol (P = 0.006), because cortisol affects the production of αENO1 by activating signaling pathways within the cell, and these pathways lead to increased gene transcription and RNA translation. To produce more αENO1 enzyme, as confirmed by some studies. Cortisol and αENO1 play an important role in inflammation and oxidation within blood vessels. An unhealthy lifestyle, such as the type of food, physical activity, and psychological state in patients with atherosclerosis, leads to a high concentration of cortisol and αENO1.[32]

With an AUC of 0.769 and 0.694, the ROC curve analysis was used to compare the atherosclerosis patient groups for the parameters αENO1 and cortisol specificity and sensitivity to that of the control group at the cut-off point 86.7465 and 3.1815 The corresponding values for,

αENO1 and cortisol were 63.3 and 63.3for specificity and 66.7 and 70 sensitivity respectively—Figure 1 of Table 3. For atherosclerosis patients, the significance for both parameters 0.004 and 0.010 are appear thought to be not reliable indicator that may be poor diagnosis. It proves that the standards are research-approved, given that there are not many interactions in the levels of the measured standards between patients and controls [33].

CONCLUSION

The findings of this investigation suggest that individuals suffering from atherosclerosis might exhibit resistance to cortisol, even when undergoing treatment.

Despite the ongoing treatment, the levels of αEnol, cholesterol, and low-density lipoprotein tend to remain elevated in these patients. Conversely, cortisol is deemed to be a more delicate indicator for detecting atherosclerosis.

7. Ethical considerations

All participants were fully informed about the conduct of the study and written informed consent obtained.

8. Acknowledgments

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9. Authors contribution

UJM: Wrote the manuscript

BMA: Conducted the study, Edited the manuscript

10. REFERENCES

1. Roy P, Orecchioni M, Ley K. How the immune system shapes atherosclerosis: roles of innate and adaptive immunity. Nature Reviews Immunology. 2022;22(4):251-65 https://doi.org/10.1038/s41577-021-00584-1.
2. Henein MY, Vancheri S, Longo G, Vancheri F. The role of inflammation in cardiovascular disease. Int. J. Mol. Sci. 2022, 23(21), 12906;.
3. González-Morena JM, Sánchez-Gómez FJ, Vida Y, Pérez-Inestrosa E, Salas M, Montañez MI, et al. Amoxicillin Haptenation of α-Enolase is Modulated by Active Site Occupancy and Acetylation. Frontiers in Pharmacology. 2022;12:80774210.1021/pr901109w.
4. Shi Y, Liu J, Zhang R, Zhang M, Cui H, Wang L, et al. Targeting endothelial ENO1 (Alpha-Enolase)-PI3K-Akt-mTOR axis alleviates hypoxic pulmonary hypertension. Hypertension. 2023;80(5):1035-47 https://doi.org/10.1161/HYPERTENSIONAHA.122.19857.
5. Chen S, Zou Y, Song C, Cao K, Cai K, Wu Y, et al. The role of glycolytic metabolic pathways in cardiovascular disease and potential therapeutic approaches. Basic Research in Cardiology. 2023;118(1):48 https://doi.org/10.1007/s00395-023-01018-w
6. Ma L, Zhao Y, Xiang P, Chen Q, Hassan M, Yu C. Single-Cell Transcriptomic Profiling Unveils Critical Metabolic Alterations and Signatures in Progression of Atherosclerosis. bioRxiv. 2024:2024.02. 06.579210 https://doi.org/10.1101/2024.02.06.579210.
7. Huang W-C, Chuang C-F, Huang Y-T, Chung I-C, Chen M-L, Chuang T-Y, et al. Monoclonal enolase-1 blocking antibody ameliorates pulmonary inflammation and fibrosis. Respiratory Research. 2023;24(1):280 https://doi.org/10.1186/s12931-023-02583-3.
8. Kamgang VW, Murkwe M, Wankeu-Nya M. 10.5772/intechopen.1003161. 2023 10.5772/intechopen.1003161.
9. Kamgang VW, Murkwe M, Wankeu-Nya M. Biological Effects of Cortisol. 202310.5772/intechopen.1003161.
10. de Kloet ER, Joëls M. The cortisol switch between vulnerability and resilience. Molecular Psychiatry. 2024;29(1):20-34 https://doi.org/10.1038/s41380-022-01934-8.
11. Prasad A. Molecular basis of pathogenesis of diabetes mellitus type 2-a new perspective. International Journal of Biochemistry Research & Review. 2018;21(2):1-13 https://doi.org/10.9734/IJBCRR/2018/40500.
12. Malekmohammad K, Bezsonov EE, Rafieian-Kopaei M. Role of lipid accumulation and inflammation in atherosclerosis: focus on molecular and cellular mechanisms. Frontiers in cardiovascular medicine. 2021;8:707529 https://doi.org/10.3389/fcvm.2021.707529.
13. Lu S-X, Wu T-W, Chou C-L, Cheng C-F, Wang L-Y. Combined effects of hypertension, hyperlipidemia, and diabetes mellitus on the presence and severity of carotid atherosclerosis in community-dwelling elders: a community-based study. Journal of the Chinese Medical Association. 2023;86(2):220-610.1097/JCMA.0000000000000839.
14. Libby P. The changing landscape of atherosclerosis. Nature. 2021;592(7855):524-33 https://doi.org/10.1038/s41586-021-03392-8.
15. Sinha S, Haque M. Insulin resistance is cheerfully hitched with hypertension. Life. 2022;12(4):564 https://doi.org/10.3390/life12040564.
16. Aresta C, Favero V, Morelli V, Giovanelli L, Parazzoli C, Falchetti A, et al. Cardiovascular complications of mild autonomous cortisol secretion. Best Practice & Research Clinical Endocrinology & Metabolism. 2021;35(2):101494 https://doi.org/10.1016/j.beem.2021.101494.
17. Kosmas CE, Bousvarou MD, Kostara CE, Papakonstantinou EJ, Salamou E, Guzman E. Insulin resistance and cardiovascular disease. Journal of International Medical

Research. 2023;51(3):03000605231164548 https://doi.org/10.1177/03000605231164548.

18. Biswas I, Khan GA. Endothelial dysfunction in cardiovascular diseases. Basic Clin Underst Microcirc. 2020;10
19. Zefferino R, Di Gioia S, Conese M. Molecular links between endocrine, nervous and immune system during chronic stress. Brain and behavior. 2021;11(2):e01960 https://doi.org/10.1002/brb3.1960.
20. Song B, Bie Y, Feng H, Xie B, Liu M, Zhao F. Inflammatory factors driving atherosclerotic plaque progression new insights. Journal of Translational Internal Medicine. 2022;10(1):36-47 https://doi.org/10.2478/jtim-2022-0012.
21. Mohammadi H, Ohm J, Discacciati A, Sundstrom J, Hambraeus K, Jernberg T, et al. Abdominal obesity and the risk of recurrent atherosclerotic cardiovascular disease after myocardial infarction. European journal of preventive cardiology. 2020;27(18):1944-52 https://doi.org/10.1177/2047487319898019.
22. Kawai T, Autieri MV, Scalia R. Adipose tissue inflammation and metabolic dysfunction in obesity. American Journal of Physiology-Cell Physiology. 2021;320(3):C375-C91 https://doi.org/10.1152/ajpcell.00379.2020.
23. Mohd Azmi NAS, Juliana N, Azmani S, Mohd Effendy N, Abu IF, Mohd Fahmi Teng NI, et al. Cortisol on circadian rhythm and its effect on cardiovascular system. International journal of environmental research and public health. 2021;18(2):676 https://doi.org/10.3390/ijerph18020676.
24. Pulopulos MM, Hidalgo V, Puig-Perez S, Montoliu T, Salvador A. Relationship between cortisol changes during the night and subjective and objective sleep quality in healthy older people. International Journal of Environmental Research and Public Health. 2020;17(4):1264 https://doi.org/10.3390/ijerph17041264.
25. Juszczyk G, Mikulska J, Kasperek K, Pietrzak D, Mrozek W, Herbet M. Chronic stress and oxidative stress as common factors of the pathogenesis of depression and Alzheimer's disease: The role of antioxidants in prevention and treatment. Antioxidants. 2021;10(9):1439 https://doi.org/10.3390/antiox10091439.
26. Auda A, Furqan M. Evaluate some biochemical changes associated with chronic renal failure patients undergoing hemodialysis in al najaf al ashraf governorate. International Journal of Scientific and Research Publications. 2014;4(11)furqan.chmala@uokufa.edu.iq.
27. Sazonova MA, Sinyov VV, Ryzhkova AI, Sazonova MD, Kirichenko TV, Khotina VA, et al. Some molecular and cellular stress mechanisms associated with neurodegenerative diseases and atherosclerosis. International journal of molecular sciences. 2021;22(2):699 https://doi.org/10.3390/ijms22020699.
28. Leistner C, Menke A. Hypothalamic–pituitary–adrenal axis and stress. Handbook of clinical neurology. 2020;175:55-64 https://doi.org/10.1016/B978-0-444-64123-6.00004-7.
29. Shaker SA, Ali BM, Audah FM. Estimation the level of zonulin, antioxidant factors and some biochemical parameters in renal failure patients.
30. Bai M, Chen M, Zeng Q, Lu S, Li P, Ma Z, et al. Up-regulation of hepatic CD36 by increased corticosterone/cortisol levels via GR leads to lipid accumulation in liver and hypertriglyceridaemia during pregnancy. British journal of pharmacology. 2022;179(17):4440-56 https://doi.org/10.1111/bph.15863.
31. Kalafateli M, Aggeletopoulou I, Triantos C. Adrenal insufficiency in liver diseases-pathophysiology and underlying mechanisms. Reviews in Endocrine and Metabolic Disorders. 2024:1-14 https://doi.org/10.1007/s11154-024-09874-0.
32. Luo S-D, Tsai H-T, Hwang C-F, Chiu TJ, Li SH, Hsu Y-L, et al. Aberrant miR-874-3p/leptin/EGFR/c-Myc signaling contributes to nasopharyngeal carcinoma pathogenesis. Journal of Experimental & Clinical Cancer Research. 2022;41(1):215 https://doi.org/10.1186/s13046-022-02415-0.
33. Škvára V, Pevný T, Šmídl V. Is AUC the best measure for practical comparison of anomaly detectors? arXiv preprint arXiv:230504754. 2023 https://doi.org/10.48550/arXiv.2305.04754.

